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The final version of an accepted article has to be printed, including tables, figures, and legends on CD, and presented as they are required to appear in the Annals. Three dimensional drawings of figures must be avoided.

Bcl-2 over-expression in urothelial tumors of the bladder. An immunohistochemical study

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ABSTRACT

Objectives: The aim was, to evaluate the frequency of Bcl-2 over-expression in urothelial tumors of the bladder in Mosul city, to correlate the over-expression with age and sex of the patients, and grade and stage of the tumors, and to compare the results with those of others.

Methods: A retrospective case-series study was performed on 50 urinary bladder urothelial tumors. The samples were collected from Al-Jamhuri Teaching Hospital in Mosul city, during a period of 8 months from November 2012 through June 2013.

Results: The patients' age was in the range of 23-91 years with a mean of 62.64 year, male:female ratio (9:1). Approximately half of them were in the seventh decade (42%). Bcl-2 immunoreactivity was observed in 42% of the cases, it was positive in 4/11 of papillary urothelial neoplasm of low malignant potential cases, 9/23 of low grade cases, and in 8/15 of high grade cases, and was negative in the one case of papilloma. It was observed in 2/2 of Tis stage, 4/14 of cases with Ta stage, 9/21 of T1 stage, and 6/11 of T2 stage. It was negative in the 2 cases of T4.

Statistically Bcl-2 over-expression was not significantly related to the age and sex of the patients, as well as the grade, and stage of the tumors. However, it was mainly found in the 6th decade of life (42.8%), in males (90.5%), in low grade (42.9%), and in stage T1 (42.9%).

Conclusion: Bcl2 over-expression was found in 42% of bladder urothelial tumors. Bcl2 over-expression mainly was observed in the 6th decade of life (42.8%), in males (90.5%), in low grade carcinoma (42.9%), and stage T1 (42.9%). Age and sex of the patients, and grade, and stage of the tumors had no significant correlation with Bcl2 over-expression.

Keywords: Urothelial tumors, Bcl-2 over-expression, immunohistochemistry.

فرط تعبيرBcl-2 في الأورام الظهارية للمثانة البولية، دراسة مناعية نسيجية

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الخلاصة

الأهداف: تم إجراء هذه الدراسة لتقييم حالة الظهور المناعي النسيجي الكيميائي لبروتين Bcl2 في أورام المثانة في مدينة الموصل والربط بينها وبين عمر وجنس المرضى، ودرجة التمايز ومرحلة الورم، ومقارنة هذه النتائج مع نتائج لدراسات أخرى.

الحالات والطرق:إن هذه الدراسة دراسة رجعية تم من خلالها جمع ٥٠ حالة من أورام المثانة الظهارية. تم جمع هذه الحالات من مستشفى الجمهوري التعليمي في مدينة الموصل خلال فترة ٨ أشهر إمتدت من شهر تشرين الثاني ٢٠١٢ إلى شهر حزيران ٢٠١٣.

النتائج: لقد تراوحت أعمار المرضى بين ٢٣ و ٩١ سنة بمتوسط قدره ٦٢,٦٤ سنة ، نسبة الذكورالى الإناث (١:٩). كان ما يقرب من نصفهم في العقد السابع (٤٢٪). ولوحظ فرط ظهور Bcl-2 في ٤٢ ٪ من الحالات. فإنه كان إيجابيا في ١١/٤ من ورم الظهارة البولية الحليمية للإمكانية الخبيثة المنخفضة، ٩/ ٢٣ من حالات سرطان المثانة الخُلَيمي من نوع درجة التمايزالمنخفضة، وفي ١٥/٨ من حالات لسرطان المثانة من نوع درجة التمايز العالية، وكان سلبيا في حالة واحدة من الورم الحليمي . لوحظ في

٢/٢من المرحلة Tis، في ١٤/٤ من المرحلة Ta، ٩/ ٢١ من المرحلة T1، في ١١/٦ من المرحلة T2، كان سلبيا في الحالتين من T4.

إحصائيا: فرط تعبير Bcl-2 ليس له صلة مع عمر وجنس المرضى، و مرحلة ودرجة تمايز الورم. فرط تعبير Bcl-2 وجد أساسا في العقد ٦ من الحياة (٤٢,٨ ٪)، في الذكور (٩٠,٥ ٪) ، في درجة التمايز المنخفضة (٤٢,٩%)، وفي المرحلة T1 (٤٢,٩%).

الاستنتاج: لقد لوحظ فرط تعبيرBcl-2 في ٤٢% من أورام المثانة الظهارية ولوحظ بالدرجة الاولى في العقد السادس من الحياة (٤٢,٨%)، في الذكور (٩٠,٥%)، في درجة التمايز المنخفضة (٤٢,٩%)، وفي المرحلة T1 (٤٢,٩%) . وقد لوحظ احصائيا عدم وجود ارتباط بين Bcl2 وعمر وجنس المرضى، ومرحلة ودرجة تمايز الورم.

INTRODUCTION

Urothelial bladder cancer is one of the most common cancer worldwide, with high incidence in industrialized countries. [1] It ranks fifth among the most common cancers in American men, approximately three quarters of all cases occur in men.[1] In Iraq, bladder carcinoma is recorded as the second most common carcinoma in males,[1] and the sixth most common in females. [1]

The neoplastic changes in the urothelium of bladder is a multistep phenomenon, the genetic events leading to urothelial transformation from normal to neoplastic, involve the activation of oncogenes, inactivation or loss of tumor suppressor genes, and/or alterations in the apoptotic gene products. [2] Loss of apoptotic response in tumor cells is thought to be one of the mechanisms involved in malignant progression and resistance to chemotherapy. [2]

Bcl-2, initially discovered in human B-cell lymphoma, is a proto-oncogene belongs to a family of related genes that regulates the apoptotic pathway, with Bcl-2 promoting a negative influence. [3] However; role of Bcl-2 protein gene expression in TCC is controversial. [3] Retrospective studies have demonstrated a correlation between Bcl-2 gene protein overexpression and poorer overall survival in patients with muscle-invasive disease treated with chemoradiotherapy.[3] Conversely, one of the largest retrospective series involving 119 patients with superficial or locally advanced disease has shown an unexpected association between Bcl-2 protein expression and favorable prognosis in muscle-invasive TCC of the bladder. [3]

The aim of the study was, to find out the frequency of Bcl-2 over-expression in urothelial tumors of the bladder, to correlate Bcl-2 over-expression with age and sex of the patients, and grade and stage of the tumors, and to compare the results with those of others.

PATIENTS AND METHODS

A retrospective study based on blocks collected from 50 cases of bladder urothelial tumor. Blocks were collected from Al-Jamhuri Teaching Hospital in Mosul city from November 2012 through June 2013.

Hematoxylene and eosin stained sections from formalin-fixed paraffin-embedded blocks were reevaluated concerning diagnosis, grading and staging of urothelial tumor according to the last WHO classification: [4]

- Urothelial papilloma.
- Papillary urothelial neoplasm of low malignant potential (PUNLMP).
- Papillary urothelial carcinoma, low grade.
- Papillary urothelial carcinoma, high grade.

Expression of Bcl2 protein by immunohistochemical staining was studied and compared in relation to patient's age, and sex, and grade and stage of the tumors. The biopsies were immunostained with Monoclonal Mouse Anti-Human Bcl-2 Oncoprotein Clone: 124, Isotype: IgG1Kappa. Dako Co.

Positive control slides were prepared from adenocarcinoma of colon known to be positive for Bcl2. While negative control slides were prepared from the same tissue block but incubated with tris buffered saline (TBS) instead of the primary antibody.

Immunohistochemical staining interpretation

Immunohistochemical reaction was scored as follows: negative if ≤10% of cells were stained and positive if >10% of cells were stained. Cytoplasmic staining intensity was scored using a scale of 0 to 3 (0: no staining, 1: weak, 2: moderate, 3:

intense).[5] The marker was placed in one of two categories, altered or not altered (normal). Bcl-2 immunoreactivity was considered altered when samples demonstrated positivity in >10% of tumor cells with an intensity of 2 or 3. [5] Cleaved caspase 3 index was calculated as number of positive cells ×100 per total number of cells in 10 random high-power fields (x400) in each tumor. This index was established by counting at least 2000 cells in fields a way from necrotic areas. [5] The sections were checked more than one time to exclude any error.

Statistical analysis: The relationship between Bcl2 over-expression and the some clinicopathologic variables was analyzed by the chi-square test. The results were considered statistically significant if the p-value was ≤ 0.05.

RESULTS

The patients' age was in the range of 23 to 91 years with a mean of 62.64 year. Most of them were in the seventh decade (42%). There were 45 males (90%) and 5 females (10%) with male: female ratio (9:1).

Histologically, there were 1 case of papilloma (2%), 11cases of PUNLMP (22%), 23 cases of low grade carcinoma (46%), and 15cases of high grade carcinoma (30%). Also there were 2 cases in stage Tis (4%), 14 cases in stage Ta (28%), 21 cases in stage T1 (42%), 11 cases in stage T2 (22%), and 2 cases in stage T4 (4%).

Bcl2 over-expression

Bcl2 immunoreactivity was observed in 21 cases (42%) of the total (**Figure1**).

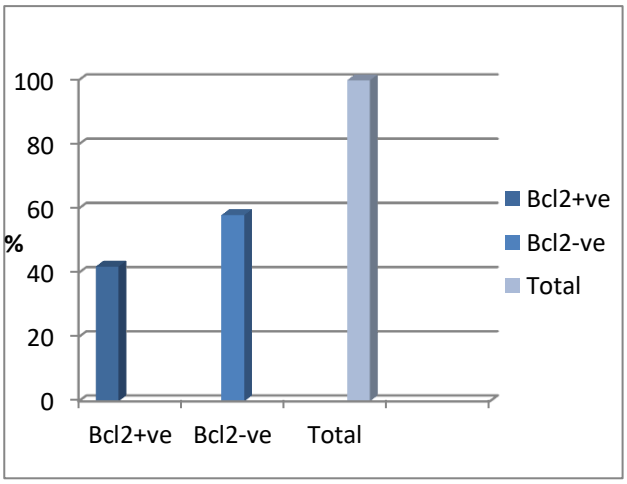


Figure 1. Bcl2 status in urothelial tumors.

In regarding to the Bcl2 over-expression and patient's age, there was no significant correlation with age with p-value of 0.488, (**Table 1**).

Concerning the patient's sex and Bcl-2 over-expression. There was no significant correlation with sex with p-value of 0.924, (**Table 2**).

Although no statistical significant correlation was identified between Bcl2 and the grade of the tumors, the higher percentage of positivity was seen in the low grade with p-value of 0.629, (**Table 3**), (**Figures 2 and 3**).

Bcl2 over-expression and stage of the tumors: no significant correlation to the stage of the tumors was found with p-value=0.202, (**Table 4**).

Table 1. Bcl2 over- expression and age of patient.

Age (year)	Total		Bcl2+ve		Bcl2-ve		p-value
	No.	%	No.	%	No.	%	
≤50	8	16.0	2	9.5	6	20.7	0.488
51-60	11	22.0	4	19.1	7	24.1	
61-70	21	42.0	9	42.8	12	41.4	
>70	10	20.0	6	28.6	4	13.8	
Total	**50**	**100.0**	**21**	**42.0**	**29**	**58.0**	

Table 2. Bcl2 over- expression and sex of patient.

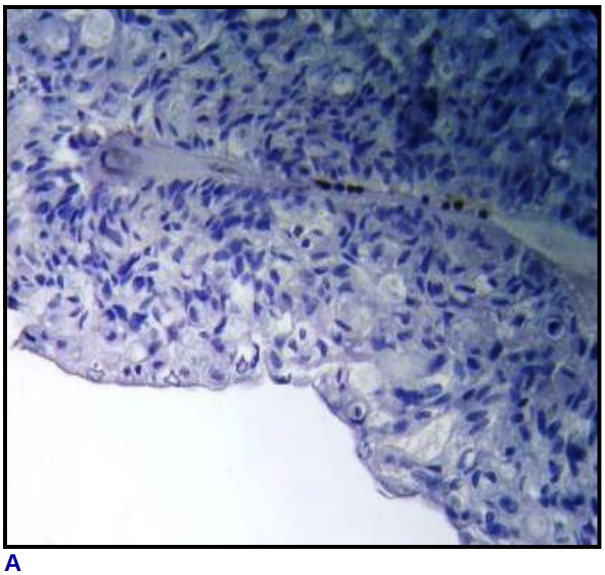
Sex	Total		Bcl2 +ve		Bcl2 -ve		p-value
	No.	%	No.	%	No.	%	
Male	45	90.0	19	90.5	26	89.7	0.924
Female	5	10.0	2	9.5	3	10.3	
Total	**50**	**100.0**	**21**	**42.0**	**29**	**58.0**	

Table 3. Bcl2 over-expression and grade.

Grade	Total		Bcl2 +ve		Bcl2 -ve		p-value
	No.	%	No.	%	No.	%	
Papilloma	1	2.0	0	0.0	1	3.5	0.629
PUNLMP	11	22.0	4	19.0	7	24.1	
Low grade	23	46.0	9	42.9	14	48.3	
High grade	15	30.0	8	38.1	7	24.1	
Total	**50**	**100.0**	**21**	**42**	**29**	**58**	

Table 4. Bcl2 over-expression and stage.

Stage	Total		Bcl2 +ve		Bcl2 -ve		p-value
	No.	%	No.	%	No.	%	
Tis	2	4.0	2	9.5	0	0	
Ta	14	28.0	4	19.0	10	34.5	
T1	21	42.0	9	42.9	12	41.4	
T2	11	22.0	6	28.6	5	17.2	0.202
T3	0	0.0	0	0.0	0	0.0	
T4	2	4.0	0	0.0	2	6.9	
Total	**50**	**100.0**	**21**	**42**	**29**	**58**	



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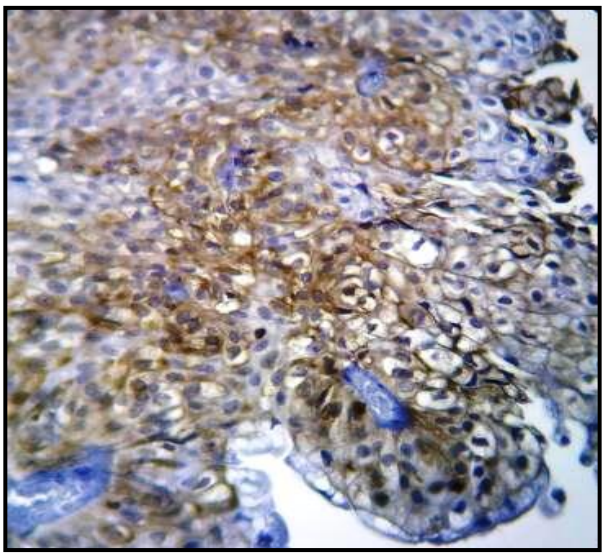
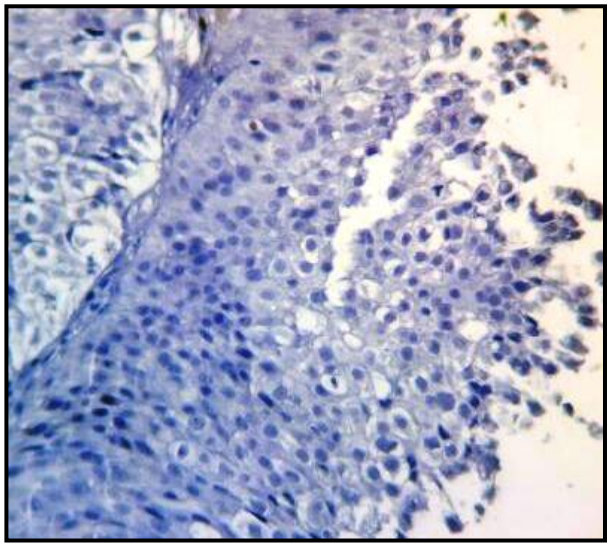


B

Figure 2. IHC, Low grade, (A) negative staining, (B) positive staining for Bcl2 protein (x 400).



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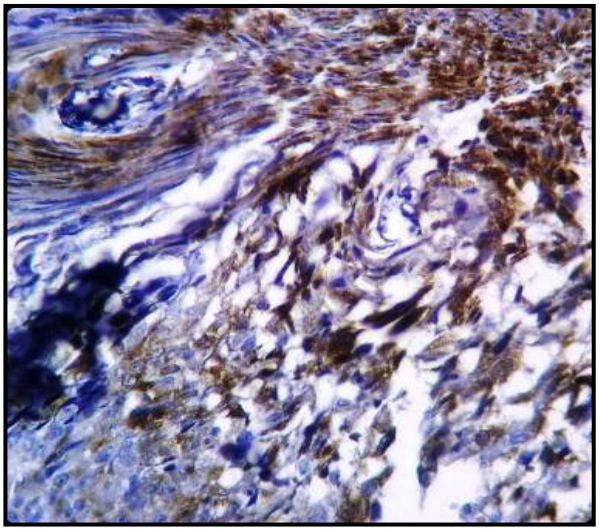

B

Figure 3. IHC, High grade, (A) negative staining, (B) positive staining for Bcl2 protein (x 400).

DISCUSSION

Urothelial cancer is a common cancers Worldwide (7th and 17th among males and females respectively).[6] and in western Countries (4th and 9th in males and females respectively). Bladder cancer is 2nd most frequent malignancy of the urinary tract after prostate cancer. [5,7] Transitional cell carcinoma of the bladder accounts for the 90%–95% of urothelial cancers. [6,8]

Oncogenes may contribute to transformation and progression of tumors by being either overexpressed or mutated to produce an

oncoprotein.[9] One of the more important mechanisms by which oncogenes are overexpressed in bladder cancer is through gene amplification. [9] Overexpression of Bcl-2 has been reported in a wide variety of cancers including those of prostate, colorectum, lung, kidney, and bladder.[10] Several studies have provided conclusive evidence that over-expressionof Bcl-2 causes resistance to both chemotherapy and radiotherapy and increases the proliferation of malignant cells. [10]

In the current study, 42% of cases with urothelial tumors showed Bcl2 over expression. Other similar studies have shown variable ratios ranging from 33.3% to 69%([11,12]) as shown in **Table 5**. The reasons for this variation are unknown. However; it might be attributed to; the properties of different antibodies, the scoring methods applied for Bcl2 immunoreactivity, the enzyme and microwave treatments of the tissue, and the tissue fixation procedure, but could be real, due to genetic, demographic or environmental factors.

Patients' age was in the range of 23 to 91 years with a mean of 62.64 year. In western countries, the median age is 65 years. [8] One age-related reason for an increased risk of cancer may be accumulation of somatic mutations in older people.[8] Bcl2 over-expression was mainly found in the 6th decade of life (42.8%). Statistically, there was no significant correlation between Bcl2 overexpression and age of the patients. This is consistent with the results of other studies [10,17]. Bcl2 immunoreativity was 90.5% for males and 9.5% for females.

This difference might be explained by the hormonal differences between men and women and social habits (tobacco smoking is more common in men). [1,18] In addition to the fact that androgen receptors have a major role in development of cancer,[1,18] which is much more active in men than in women. [1]

Statistically, there was no significant correlation between Bcl2 over-expression and sex of the patients. This is comparable to those of other studies. [10,17]

Bcl2 over-expression was mainly found in low grade tumors (42.9%). However, over-expression of Bcl2 in relation to grade was not significant statistically, this result is similar to that as noticed by others.[10,14,15,17,19] However, Abdulamir A *et al* [12] and Baspinar S *et al*,[13] reported significant correlation with high grades, this difference might be because, most of their tumors were in high grade.

These contradictory results might be due to the presence of inter- and intra-observational variations.[8]

The critical importance of tumor histological stage had been recognized in several studies.[8] Tumor growth in the presence of antiapoptotic effect of Bcl-2 is much slower than the one determined by proliferative factors.[13]

In this study Bcl2 over-expression was mainly found in T1 stage (42.9%). Statistically, the over-expression of Bcl2 in relation to stage was not significant confirming the observation by others.[9,14,15,17] On the contrary other studies had reported significant correlation with higher stages.[10,12,13,20]

Table 5. Frequency of Bcl2 over-expression in bladder urothelial tumors in different studies of the world.

Study	Year	Site	No. of cases	% of Bcl2+ve cases
Current study	2013	Mosul (Iraq)	50	42%
Baspinar S *et al* [13]	2013	Turkey	84	54%
Enache M *et al* [11]	2012	Romania	45	33.3%
WASAN *et al* [2]	2011	Baghdad (Iraq)	25	34%
Abdulamir A *et al* [12]	2009	Malaysia	82	69%
Maluf1FC *et al* [3]	2006	New York	59	37%
Matsumoto H *et al* [14]	2004	Japan	62	53%
Hani B *et al* [15]	2003	Egypt	49	61.2%
Asci R *et al* [16]	2001	UK	54	45.8%

CONCLUSION

1. Bcl2 over-expression was found in 42% of bladder urothelial tumors, and this result is within the range observed by others.
2. Bcl2 over-expression in descending order was observed: in low grade carcinoma (42.9%), in high grade carcinoma (38.1%), and in PUNLMP grade (19%).
3. As far as histological stage, Bcl2 over-expression was in descending order; 42.9% in T1 stage, 28.6% in T2 stage, 19% in Ta stage, and 9.5% in Tis stage.
4. Age and sex of the patients, and grade, and stage of the tumors had no significant correlation with Bcl2 over-expression.

REFERENCES

1. Alaa SJ. The assessment of proliferative activity in transitional cell carcinoma of the urinary bladder by using Ki67 overexpression and its effects on prognosis of the tumor in correlation to prognostic markers (staging and grading); (immuno-histochemical study). Kufa Med J 2011;14(2):121-6.
2. Wasan AB, Dina WA, and Amina YA. The Relationship Between Bcl-2, and P53 Protiens in transitional Cell Carcinoma of the Bladder. Iraq J Cancer Med Genet. 2011; 4(1):236-43.
3. Maluf FC, Cordon-Cardo C, Verbel DA, *et al*. Assessing interactions between mdm-2, p53, and bcl-2 as prognostic variables in muscle-invasive bladder cancer treated with neo-adjuvant chemotherapy followed by locoregional surgical treatment. Ann Oncol 2006; 17(11): 1677-86.
4. Eble JN, Sauter G, Epstein J, *et al*. Tumours of the urinary bladder. In: The World Health Organization Classification of Tumours. Pathology and Genetic of Tumours of the Urinary System and Male Genital Organs. 6th edition, Lyon, IARC Press, 2004:90-158.
5. Al-Samawi AS and Aulaqi SM. Urinary Bladder Cancer in Yemen. Oman Med J. 2013; 28(5): 337–40.
6. Velickovic L, Stojnev S, Petrovic A, *et al*. Pro- and Antiapoptotic Markers in Upper Tract Urothelial Carcinoma Associated with Balkan Endemic Nephropathy. Scientific World J 2011; 11:1699–711.
7. Maximilian B, James W. Catto b, *et al*. Epidemiology and Risk Factors of Urothelial Bladder Cancer. Eur Urology 2013; 63:15-32.
8. Tawfeeq KT and Salim HS. P53 over-expression in urothelial carcinoma of the bladder: An Immunohistochemical Study. Tikrit Med J 2012;18(2): 198-211.
9. Bevizova K, Jakubovsky J, Luha J, *et al*. Immunohistochemical analysis of urothelial bladder cancers. J Biol Sci 2013;13(2): 66-71.
10. Eissa S, Nabil M, Mohab S. Infectious diseases-Schistosomasis and Bladder Cancer. In:medicine, InTech, 2012:7.
11. Enache M, Simionescu C, Lascu LC. Ki67 and Bcl-2 immunoexpression in primitive urothelial bladder carcinoma. Rom J Morphol Embryol. 2012;53:521-5.
12. Abdulamir A, Rand R, Haider S, *et al*. Tumor markers of bladder cancer: the schistosomal bladder tumors versus non-schistosomal bladder tumors. J Exper Clin Cancer Res 2009; 28(1):27.
13. Baspinar S, Bircan S, Yavuz G, *et al*. Beclin 1 and bcl-2 expressions in bladder urothelial tumors and their association with clinicopathological parameters. J Pathol Res Pract. 2013;209:418-23.
14. Matsumoto H, Wada T, Fukunaga K, *et al*. Bax to Bcl-2 Ratio and Ki-67 Index are Useful Predictors of Neoadjuvant Chemoradiation Therapy in Bladder Cancer. Jpn J Clin Oncol 2004;34:124–30.
15. Hani B, Abd El-Hameed A, Nouh M, *et al*. The Prognostic Significance of p53, Bcl-2, Cytokeratin 20 and Ki-67 in Primary Superficial Papillary Transitional Bladder Carcinoma. J Egyp Nat Cancer Inst. 2003; 15(3): 183-91.
16. Asci R, Yildiz L, Sarikaya S, *et al*. p53 and bcl-2 Overexpression as Associated Risk Factors in Patients 40 Years Old or Less with Transitional Cell Carcinoma of the Bladder. Urol Int 2001;67:34–40.
17. Shiina H, Igawa M, Urakami S, *et al*. Immunohistochemical analysis of bcl-2 expression in transitional cell carcinoma of the bladder. J Clin Path.1996;49(5):395-9.
18. Touloupidis S, Fatles G, Kalaitzis C, *et al*. The significance of p53 and bcl-2 overexpression and other prognostic factors in transitional cell carcinoma of the bladder. Int Urol Nephr. 2006; 38: 231-6.
19. Hameed DA, Abdel Raheem AM, Mosad E, *et al*. Bcl-XL and Bcl-2 expression in bilharzial squamous cell carcinoma of the urinary bladder: which protein is prognostic ?. Urology 2008;72:374-8.
20. Vrabie CD, Petrescu A, Waller M. Molecular changes in superficial bladder cancer. Rom J Morphol Embryol. 2007;48(2):131-8.

Risk factors of acute otitis media among children in Mosul

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ABSTRACT

Context: Acute otitis media (AOM) is the most frequent diagnosis in the children visiting offices. The prolonged and recurrent episodes of AOM may lead to hearing impairment and delayed speech development, which will influence the child's performance at school.

Aim: The aim of this study is to identify the risk factors of acute otitis media in preschool children attending ENT clinics at Al-jamhory Teaching Hospital in Mosul.

Methods: To achieve this aim, a case control study design was adopted. The sample of the present study included 150 children (cases) who have been diagnosed by the responsible ENT specialist according to the otoscopic examination with another 150 children (controls) who were diagnosed not to have AOM. Period of data collection was from 1st of October 2011 to the 1st of April 2012.

Results: The present study showed that the highest frequency of acute otitis media occurred in the age group 1-2 years 39 patients (26%), and more frequent AOM attacks occurred in males. Clinical presentation among the cases were fever, otalgia, otorrhea, irritability, loss of appetite, vomiting, diminished hearing, and few patients presented with tinnitus and vertigo. The significant risk factors for AOM were day care attendance, bottle feeding for the 1st 6 months of life, supine bottle feeding, pacifier use in the second 6 months of life, parental tobacco smoking, preterm baby, and allergy. No association was found between craniofacial anomaly and occurrence of AOM in the present study.

Conclusion: Day care attendance, bottle feeding during the 1st 6 months of life, supine bottle feeding, pacifier use in the second 6 months of life, parental tobacco smoking, preterm baby, and allergy were found to be a significant risk factors for AOM among study population.

Recommendation: Additional studies on potential measures to prevent AOM through the reduction of risk factors are needed.

Keywords: Acute otitis media, risk factors, children, Mosul City.

عوامل الخطورة لإلتهاب الأذن الوسطى عند الأطفال في الموصل

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الخلاصة

المقدمة: إلتهاب الأذن الوسطى الحاد هو التشخيص الأكثر شيوعا في الأطفال المراجعين للعيادات الطبية. إطالة أمد وتكرر النوبات لإلتهاب الأذن الوسطى الحاد قد تؤدي إلى ضعف السمع وتأخر تطوير النطق، والتي سوف تؤثر على أداء الطفل في وقت لاحق في المدرسة، ونظرا للزيادة الأخيرة في عدد الأطفال الصغار المصابين بهذه الإلتهابات فقد توجب إجراء مراجعة للأعراض، والسببية المرضية، بالإضافة إلى العوامل الخطيرة ذات العلاقة.

الهدف: الهدف من هذه الدراسة هو التعرف على عوامل الخطورة لإلتهاب الأذن الوسطى الحاد في الأطفال قبل سن المدرسة الذين يراجعون عيادات الأنف والحنجرة في مستشفى الجمهوري التعليمي في الموصل.

طرق البحث: إعتمدت دراسة العينة والشاهد على ١٥٠ طفلا (حالة) شخصوا من قبل أخصائي الأنف والحنجرة وفقا للفحص بمنظار الأذن مع ١٥٠ طفلا (شاهد) شخصوا بعدم إصابتهم بإلتهاب الأذن الوسطى الحاد. إمتدت فترة جمع الحالات

والشواهد من الأول من أكتوبر ٢٠١١ حتى الأول من أبريل ٢٠١٢، ولقد أستخدمت إستمارة إستبيان خاصة وقد ملئت هذه الإستمارة عن طريق مقابلة أولياء الأمور لكل من الحالات والشواهد.

النتائج: أظهرت الدراسة أن أعلى معدل إصابة بإلتهاب الأذن الوسطى الحاد وقعت في الفئة العمرية ١-٢سنة (٢٦٪)، وفي الذكور أكثر بقليل من الإناث. الأعراض والعلامات لإلتهاب الإذن الوسطى الحاد بين الحالات كانت الحمى، ألم ألاذن، خروج القيح من الأذن، التهيج، فقدان الشهية، القيء، تضاؤل السمع، أما الطنين والدوار فقد ظهر في القليل من الحالات.

الاستنتاج: عوامل الخطورة الهامة لإلتهاب الأذن الوسطى الحاد كانت دور الحضانة، الرضاعة الصناعية بواسطة الزجاجة للستة أشهر الأولى من الحياة، رضاعة الزجاجة بوضع منبطح، إستخدام المصاصة في الستة أشهر الثانية من العمر، تدخين الوالدين، الطفل الخديج، والحساسية.

الكلمات المفتاحيه: إلتهاب الأذن الوسطى الحاد، عوامل الخطورة، الأطفال، مدينة الموصل.

INTRODUCTION

Otitis media is an irritation of the middle ear cleft, without reference to aetiology or pathogenesis. The clinical range may expand from a benign, self-limiting state to a expanded and sometimes complicated illness. Although in industrialised countries serious complications are rare, the burden of acute otitis media (AOM) is large, with impaired quality of life and high direct and indirect socio-economic costs. Otitis media primary described by Hippocrates in 450 BC, this illness continues to present one of the more troublesome health troubles of Infancy and childhood.[1]

Acute otitis media is one of the most widespread communicable diseases occurring during childhood. Prolonged and recurrent attacks of AOM may lead to hearing impairment and late speech development, which will influence the child's later performance at school. [2]

The yearly cost of AOM in the United States is an estimated $5 billion.[3]

AOM occurring most commonly between the ages of 3 months and 3 years.[1] By age of 7 years, 93% of children have had at least one incident of AOM and 75% have had repeated infections. AOM can occur at any age, 80-90% of cases occur in children younger than 6 years, and the highest incidence is between 6 months and 24 months of age in the United States.[4] Males are somewhat more affected than females; of unknown cause.[5]

Morbidity from this illness remains noteworthy, despite numerous use of systemic antibiotics to treat the sickness and its complications. Intratemporal and intracranial complications of OM are the 2 major types.[6] Risk factors of AOM are several including:[4]

1- Day Care attendance:

Contact to other children at home (siblings) or in a day-care surroundings increases the risk of otitis media, with the relative risk being proportionate to the quantity of kids in a setting.[7]

2- Type of Feeding:

In many studies, breast-feeding has been stated as reducing the risk of ear and pulmonary infections. A two-fold increase in hazard of first episodes of AOM was found in infants completely formula-fed as contrasting to those breast-fed for 6 months.[8]

3- Supine bottle feeding:

Lying position of the baby during feeding was associated with acute otitis media. Babies with otitis media were 38 times more likely to be fed in lying position than babies without otitis media.[9]

4- Use of Dummies (Pacifiers):

Studies from Finland have revealed that use of a pacifier is a hazard factor for otitis media.[10]

5- Passive Smoking and Environmental Pollution:

Meta-analyses confirm the increased incidence of otitis media associated with exposure to passive cigarette smoke.[11]

6- Premature birth:

Very low birth weight (<1500 g) or very preterm birth (<33 weeks of gestation) increases the risk of otitis media.[12]

7- Male gender:

A small but significantly higher incidence of AOM in males has been reported.[13]

8- Craniofacial anomaly:

Children with craniofacial defects or malformations are at risk for severe and recurrent AOM.[4]

9- Allergy:

Children with allergy were more probable to carry Hemophilns influenzae isolates than children with no allergies. Allergies in young children have also been defined as a risk factor for otitis media because upper respiratory mucosal swelling throughout an allergic episode may cause eustachian tube dysfunction.[14]

To prevent the beginning of AOM episodes and to decrease the occurrence of recurrent AOM, several environmental control measures are recommended. Prolonged breast feeding, restrictive pacifier use and eliminating exposure to tobacco smoke have been postulated as dropping the incidence of AOM.[15]

The aim of this study is to evaluate the main risk factors of acute otitis media in preschool children attending ENT clinic at Al-jamhory Teaching Hospital in Mosul.

PATIENTS AND METHODS

The present study was conducted in the ENT clinic at Al_ jamhory Teaching Hospital in Mosul city. The hospital is located in the right side of Tigris River and it delivers services to many areas in Mosul city.

Case control study design has been adopted in order to achieve the objectives of the present study.

Data were collected during six months period from 1st of Oct 2011 to the 1st of April 2012. The present study included 150 preschool child under the age of 6 years who attend the ENT clinic at Al jamhory Teaching Hospital and diagnosed to have AOM, and 150 control subjects in the same age group, in whom evaluation proved not to have AOM. A formal consent was obtained from parents before participation in the study. Moreover a convenient sample size was decided to be used in the study.

A questionnaire form was specially prepared in order to collect all the relevant information related to the study sample. The questionnaire form included information in regard to:

Age, gender, socioeconomic status, risk factors of acute otitis media which include day care attendance, bottle feeding during the first 6 months of life, supine bottle feeding, pacifier use in the second 6 months of life, passive tobacco smoke, craniofacial anomaly and allergy. Moreover the questionnaire contained detailed history of the disease regarding present complaint and duration and presenting symptoms. The main source of data was obtained directly from parents or relatives of the child (cases and controls) by the investigator through direct interview and filling the questionnaire form.

Clinical assessment of the cases and controls has been performed by the responsible ENT specialist. Otoscopic examination has been done for tympanic membrane for its color, translucency, light reflex, and position.

Data analysis was carried out by using Pentium four computer through the use of Microsoft Office Excel software programs.

Odds ratio was calculated by using the following equation:

$$OR = \frac{a \times d}{b \times c}$$

95% confidence interval (CI) has been calculated by using the following equation:

95% CI of the OR = $OR^{1 \pm 1.96 \sqrt{X^2}}$

Chi squared (x^2) test was used to find the statistical association.

P value < 0.05 used as a significance statistical association.

RESULTS

This study revealed that the highest frequency of AOM was found in the age group 1-2 years [39 patients (26%)] followed by age group 2-3 years [34 patients (22.7%)] and the lowest frequency of AOM was observed in the age group 4-5 years [12 patients (8%)].

The differences in the age groups 1-2 years and 2-3 years are statistically significant (p=0.003 and 0.005 respectively) as it shown in the **Table 1**.

Regarding the clinical presentation, the study showed that 99 patients (66%) out of 150 cases complained from otalgia; 58 patients (38.7%) complained from ear pulling; 28 patients (18.7%) and 123 patients (82%) complained from otorrhea and fever respectively. Moreover irritability, and vomiting were observed among 54%, and 16% respectively. On the other hand, vertigo was reported by only 4.7% of the patients. **Table 2**.

Table 3 illustrates the association between risk factors and the occurrence of AOM. It is clear from the table that (14%) of cases gave history of day care attendance in comparison to only (4.7%) among controls.

Table 1. Socio demographic characteristics and occurrence of AOM.

Age group (years)	Cases (No.=150)		Controls (No.=150)		OR	P*-value
	No.	%	No.	%		
0-<1	20	13.3	11	7.3	1.94	0.088
1-<2	39	26.0	19	12.7	2.42	0.003
2-<3	34	22.7	16	10.7	2.45	0.005
3-<4	19	12.7	33	22.0	0.53	0.033
4-<5	12	8.0	28	18.7	0.38	0.007
5-6	26	17.3	43	28.6	0.52	0.020
Gender						
Male	85	56.7	82	54.7	1.08	0.727
Female	65	43.3	68	45.3		
Residence						
Rural	52	34.7	38	25.3	1.56	0.078
Urban	98	65.3	112	74.7		

* x^2-test was used.

Table 2. Frequency distribution of cases according to their clinical presentation, Mosul, 2012.

Clinical presentation	No.	%
Fever	123	82.0
Otalgia	99	66.0
Irritability	81	54.0
Loss of appetite	77	51.3
Ear pulling	58	38.7
Otorrhea	28	18.7
Vomiting	24	16.0
Diminished hearing	17	11.3
Tinnitus	8	5.3
Vertigo	7	4.7

With a strong association between AOM and day care attendance (OR =3.33, 95%CI= 1.40-7.89) and the difference is statistically highly significant (P=0.005). History of bottle feeding in the 1st 6 months of life was reported in (17.3%) of the cases and (6.7%) of the controls, with a strong association between the occurrence of AOM and bottle feeding for the 1st 6 months of life (OR=2.93, 95%CI=1.37-6.23) and the difference is statistically highly significant (P=0.004). Moreover supine bottle feeding was reported by (21.3%) of the mothers of cases compared to only (7.3%) of the controls, also **Table 2** clarifies a highly significant association between supine bottle feeding and the occurrence of AOM (OR=3.42, 95%CI=1.67-7.00). and the difference is statistically highly significant (P=0.001).

Table 3 also shows that more than three quarters of mothers of cases gave a positive history of pacifier use in the second 6 months of life, on the other hand only 9 mothers (6%) gave positive history regarding pacifier use. There was a significant association between pacifier use in the second 6 months of life and the occurrence of AOM (OR=3.43, 95%CI=1.58-7.46) and the difference is statistically highly significant (P=0.001).

Regarding parental smoking, **Table 3** shows significant association with the occurrence of AOM (OR=2.46, 95%CI=1.54-3.92) and the difference is statistically highly significant (P=0.0001).

Table 3 shows association between baby maturity at birth and the development of AOM (OR=2.28, 95%CI=1, 26-4.12), the difference found to be statistically significant (P=0.006).

It is clear from **Table 3** that there is association between allergy and the occurrence of AOM (OR=2.29, 95%CI=1.30-4.02) and the difference is statistically significant (P=0.004).

Table 4 describes the parents education and occupations. It is clear from the table that (16.1%) and (8.1%) of the fathers and mothers of the cases had university education respectively compared to (25%) and (16.6%) among the control group respectively.

Moreover, the table shows that (6.7%) and (11.4%) of the mothers of cases and controls respectively were employed.

Table 3. Frequency distribution of study population according to risk factors for AOM, Mosul, 2012.

Risk factor	Cases No.=150		Controls No.=150		OR	95%CI of OR	P value *
	No.	%	No.	%			
Day care attendance	21	14.00	7	4.66	3.33	1.40-7.89	0.005
Bottle feeding	26	17.33	10	6.66	2.93	1.37-6.23	0.004
Supine bottle feeding	32	21.3	11	7.33	3.42	1.67-7.00	0.001
Pacifier use	27	18.00	9	6.00	3.43	1.58-7.46	0.001
Passive smoking	85	56.66	52	34.66	2.46	1.54-3.92	0.0001
Pre-term delivery	39	26.00	20	13.33	2.28	1.26-4.12	0.006
Craniofacial anomalies	5	3.33	1	0.66	5.13	0.78-33.47	0.099
Allergy	44	29.33	23	15.33	2.29	1.30-4.02	0.004

* x^2-test was use.

Table 4. Parents education and occupation of the study population.

Parents education		Cases (n=150)		Controls (n=150)		P*-value
		No.	%	No.	%	
Father	Primary	62	41.3	58	38.7	0.637
	Secondary	47	31.3	46	30.7	0.901
	University	24	16.1	38	25.3	0.046
	Others	17	11.3	8	5.3	0.060
Mother	Primary	92	61.3	79	52.7	0.130
	Secondary	26	17.3	28	18.7	0.764
	University	12	8.1	25	16.6	0.022
	Others	20	13.3	18	12.0	0.728
Occupation						
Father	Employer	35	23.3	45	30.0	0.728
	Retired	7	4.7	11	7.3	0.331
	Earner	108	72.0	94	62.7	0.085
Mother	Employer	10	6.7	17	11.4	0.158
	Retired	0	0.0	0	0.0	1.000
	Non Employer	18	12.0	23	15.3	0.401
	housewife	122	81.3	110	73.3	0.098

* x^2-test was used.

DISCUSSION

The present study used case control design in order to accomplish its objectives. The limitations of such design are selection bias, recall bias, and confounding. In this study, the maximum frequency of AOM was observed in the age group 1-2 years (26%), the lowest frequency was at the age group 4-5 years (8%). These values are close to the results obtained by other researchers, Alho O P *et al*, in their study of 2512 children in Finland 1991, found that children up to 24 months formed 50% of all attacks of AOM.[16]

Serhan N, in his study of 250 cases of AOM in Baghdad city 1997, found that the percentage of children up to 24 months formed (48, 4%).[17]

In the present study males formed (56.7%) of cases of AOM while females formed (43.3%).This result is comparable to other studies, Serhan N,found that male account for (51.6%) of the patients, while female account for (48.4%).[17]

Jack L *et al* in USA 1997, found that the males consistently had higher incidence of AOM attacks than females.[18]

Serhan N, found otalgia (or excessive crying, head rollings, irritability) was present in (89.2%) of patients, fever in (62.8%), discharge in (37.2%) and vomiting in (29.9%).[17]

In the present study fever was present in (82%) of children of AOM, Otalgia in (66%), irritability (54%), and vomiting in (16%). Symptoms

frequencies of the present study are comparable to some extend to the results of the above mentioned studies.

Alho O.P *et al*1991, found that the development of AOM higher in children attend daycare centers when compared with care in their homes.[16]

In the meta-analysis of Uhari *et al* in Finland 1996, the risk of AOM also increased with child care outside the home (daycare).[19,20]

The present study, found that there is a strong relationship between the occurrence of AOM and day care attendance (P=0.005), which is similar to what is found in the above mentioned studies.

The present study shows that there is strong association between the occurrence of AOM and bottle feeding for the 1st six months of life (P=0.004).

Jack L.*et al*, found in a study conducted in USA, 1997 a significant protective relationship between breast feeding only during the 1st year of life.[18]

Serhan N, found in (121) child below two years with AOM, (69.42%) were bottle fed, while (30.58%) were breast fed.[17]

A meta analysis conducted by Uhari *et al*, concluded that breast feeding in the first 3 months of life reduce the risk of AOM by (13%).[19]

The present study showed that the supine bottle feeding was significantly associated with the occurrence of AOM. (95%CI=1.67-7.00, P=0,001). This result was similar to that found by other studies.

Jose F *et al* (2006), found that one of the mechanisms involved in the association between bottle feeding and OM is "positional OM", according to which children bottle fed in an unsuitable position (lying down) are great risk for AOM, as shown in a cohort with (698) children followed up from birth to two years of age demonstrated that the supine bottle feeding position was associated with earlier onset of AOM.[21] This might be due to aspiration of milk during supine feeding.

The present study, demonstrates a significant association between occurrence of AOM and the use of pacifier in the 2nd 6 months of life. (95%CI=1.58-7.46, P=0.001).

Niemela *et al* in his study in Finland, demonstrated that those used pacifiers had a greater risk of presenting with four or more episodes of AOM than those who did not use them.[22,23]

Uhari *et al*, found that the use of a pacifier increase the risk for AOM by (24%).[19] Warren *et al* (2001) in his study in USA, demonstrated that pacifier sucking was significantly associated with AOM from the 6th to the 9th months and presented a strong trend towards statistical significant in the period from 9-12 months. [24] This is probably due to eustachian tube dysfunction associated with pacifier sucking.

The present study, parental tobacco smoking significantly associated with the occurrence of AOM. (95%CI=1.54-3.92, P=0.0001), this result found to be similar to many other studies which are conducted in Iraq and other countries. Serhan N, reported that children of smoking families had higher incidence of AOM (53.2%) compared to (46.8%) in those of non-smoking families.[17,25] Uhari *et al*, found that the parental smoking increased the risk of AOM. [19]

On the other hand Jose F.*et al* (2006), concluded that passive smoking does not increase the chance of non-recurrent AOM, with regard to recurrent AOM, passive smoking was classified as a probable risk factor.[21]

The present study, observed that there is significant association between pre maturity and the occurrence of AOM, this result found to be similar to the result of Becken *et al* (2001), in his study in USA, found that very preterm birth (< 33 weeks of gestation) and very low birth (< 1500g) increase risk of AOM.[26] This is probably due to altered immunity in this group.

A study conducted by Boston M *et al* (2003) in USA, demonstrated that the presence of craniofacial anomaly increased the chance of the child requiring multiple interventions for ventilation tube placement, so higher incidence of AOM occurred among children with un corrected cleft palate than in normal children , and when the cleft is corrected, AOM recurrence is reduced. [27]

Nevertheless the present study demonstrate no association between craniofacial anomaly and the occurrence of AOM, this result most probably attributed to small sample size and the little number of cases of craniofacial anomalies which are included in the study population.

The present study found there is significant association between allergy and the occurrence of

AOM (95%CI=1.30-4.02, P=0.004), this result found to be comparable with another study conducted by Bernstein JM (2002), New York, USA, found that atopic Eustachian tube obstruction may eventually lead to AOM by gradual accumulation of viruses and bacteria in ear effusion. [28,29]

In the other hand Jose F *et al* (2006), found that although there is epidemiologic, mechanical and therapeutic evidence showing that allergic rhinitis contributes to the pathogenesis of AOM it needs further study before more definitive conclusions can be drawn.[21]

CONCLUSIONS

From the results of the present study the following conclusions can be obtained:

The highest frequency of acute otitis media occurred in the age group 1-2 years. The significant risk factors for AOM were day care attendance, bottle feeding for the 1st 6 months of life, supine bottle feeding, pacifier use in the second 6 months of life, parental tobacco smoking, preterm baby, and allergy.

RECOMMENDATIONS

1. Supplementary studies on probable measures to prevent AOM through the reduction of risk factors are needed.
2. The main health care priorities in distant communities be supposed to: carry strategies that decrease the transmission of bacterial infections to infants and toddlers, support sensible vaccination, counsel on effective communication strategies for hearing impaired offspring, provide recurrent and precise assessment of middle ear disease in the first 18 months of life.

REFERENCES

1. John M Graham, Glenis K Scadding. Pediatric ENT 2nd ed. ISBN:978-3-540-3308-7. Springer Berlin Heidelberg New York;2007 :31-76.
2. Teele DW, Klein JO, Chase C, Menyuk P, Rosner BA, the Greater Boston Otitis Media Study Group. Otitis media in infancy and intellectual ability, school achievement, speech, and language at age 7 years. J Infect Dis 1990; 162:685-94.
3. Charles C, James S, Robert H Rakel: Text book of Family Medicine. 7th ed. New York: Saunders; 2011:626-79.
4. Robert E Rakel. Essential family medicine: fundamentals & case study. 3rd ed. Philadelphia, Pennsylvania: Elsevier; 2007.p.234-67
5. Marianne M Green, Jennifer A Bierman, JAMES j. Foody, Russell G. Robertson, Gary J. Martin. Prymary care mentor. Philadelphia, PA 19103, United States of America; 2009.
6. American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. Pediatrics 2004; 113(5):1451-65.
7. Bennett KE, Haggard MP Accumulation of factors influencing children's middle ear disease: risk factor modeling on a large population cohort. J Epidemiol Community Health 1998; 52: 786–793.
8. Duffy LC, Faden H, Wasielewski R, *et al.* Exclusive breastfeeding protects against bacterial colonization and day care exposure to otitis media. Pediatrics 1997; 100:E7.
9. Mumtaz Y, Habib F, Jahangeer A, Habib A. Determinations of Acute Otitis Media in infant. JDUHS 2009; 3(1):10-15.
10. Niemelä M, Pihakari O, Pokka T, Uhari M. Pacifier as a risk factor for acute otitis media: a randomized, controlled trial of parental counseling. Pediatrics 2000; 106: 483-488.
11. Jacoby P, Coates H, Arumugaswamy A, *et al.* The effect of passive smoking on the risk of otitis media in Aboriginal and non-Aboriginal children in the Kalgoorlie-Boulder region of Western Australia. Med J Aust 2008; 188: 599-603.
12. Engel J, Anteunis L, Volovics A, *et al.* Prevalence rates of otitis media with effusion from 0 to 2 years of age: healthy-born versus high-risk-born infants. Int J Pediatr Otorhinolaryngol 1999; 47: 243-251.
13. Zakzouk S M, Hajjaj M F. Epidemiology of Chronic suppurative otitis media among Saudi children a comparative study of 2 decades. Int J Paediatr Otorhinolarygol 2002;62:215-8.
14. Scottish Intercollegiate Guidelines Network. Diagnosis and management of childhood otitis media in primary care. SIGN guideline No. 66. February 2003.
15. Williams RL, Chalmers TC, Stange KC, Chalmers FT, Bowlin SJ Use of antibiotics in preventing recurrent otitis media and in treating otitis media with effusion: a meta-analytic attempt to resolve the brouhaha. JAMA 1993; 270:1344–1351.
16. Alho OP, Koivu M, Sorri M, Rantakallio P. The occurrence of acute otitis media in infants. Int J Pediatr Otorhinolaryngol.1991; 21(1):7-14.
17. Nasir Hindi Serhan. Acute otitis media in infant and children. Al_Nahrain University, Medical Collag; 1997; 4:34-35.
18. Jack L Paradise, Howard E Rockette, D. Kathleen Colborn, Beverly S. Bernard, Clyde G. Smith, Marcia Kurs-Lasky and Janine E. Janosky. Otitis Media in 2253 Pittsburgh-Area Infants: Prevalence and Risk Factors During the First Two Years of Life. Pediatrics J 1997; 99:318.
19. Uhari M, Mantysaari K, Niemela M. A meta-analytic review of the risk factors for acute otitis media. Clin Infect Dis. 1996; 22: 1079–1083.
20. Mottonen M, Uhari M. Absences for sickness among children in day care. Acta Paediatr 1992; 81: 929-32.

21. José Faibes Lubianca Neto, Lucas Hemb, Daniela Brunelli e Silva. Systematic literature review of modifiable risk factors for recurrent acute otitis media in childhood J Pediatr (Rio J) 2006; 82(2):87-96.
22. Niemela M, Uhari M, Hannuksela A. Pacifiers and dental structure as risk factors for otitis media. Int J Pediatr Otorhinolaryngol. 1994; 29:121-7.
23. Larsson E. Dummy- and finger-sucking habits in 4-year-olds. Swed Dent J 1975; 68: 219-24.
24. Warren JJ, Levy SM, Kirchner HL, Nowak AJ, Bergus GR. Pacifier use and the occurrence of otitis media in the first yearof life. Pediatr Dent 2001;23:103-7.
25. Ilicali OC, Keles N, Deer K, Asum OF, Guldiken Y. Evaluation of the effect of passive smoking on otitis media in children by an objective method: urinary cotinine analysis. Laryngoscope 2001; 11:163-7.
26. Becken ET, Daly KA, Lindgren BR, Meland MH, Giebink GS. Low cord blood pneumococcal antibody concentrations predict more episodes of otitis media. Arch Otolaryngol Head Neck Surg 2001; 127:517–522.
27. Boston M, McCook J, Burke B, Derkay C. Incidence of and risk factors for additional tympanostomy tube insertion in children. Arch Otolaryngol Head Neck Surg 2003; 129:293-6.
28. Bernstein JM. Immunologic aspects of otitis media. Curr Allergy Asthma Rep 2002; 2 (4): 309–15.
29. Kraemer JK, Richardson MA, Weis NS, Furukawa CT, Shapiro GG, Pierson WE. Risk factors for persistent middle-ear effusions. JAMA 1983; 249:1022-5.

Risk factors for development of transient tachypnea of newborns

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ABSTRACT

Background: Transient tachypnea of the newborn (TTN) is a frequently encountered form of neonatal respiratory distress. The underlying mechanism involves residual lung fluid that is delayed in clearance. TTN primarily occurs soon after birth and can last from 24 to 72 hours. Risk factors for TTN include elective cesarean section, male sex, late prematurity, low birth weight, macrosomia, polycythemia, maternal asthma and maternal diabetes. Treatment is often supportive with observation and potential oxygen supplementation.

Objective: To identify the risk factors associated with development of transient tachypnea of newborns who were delivered either normally or through cesarean section, at 36 weeks or beyound and to compare the results with those of others.

Patients and methods: This is a case -control study of 200 newborns suffering from respiratory distress during a period from the 1st of September 2011 to the 1st of September 2013 in the neonatal intensive care unit at AL-Kansaa Teaching hospital in Mosul. The perinatal history of newborns was analyzed. TTN was diagnosed on clinical basis and by exclusion of other diseases affecting the respiratory system including sepsis. The study included 200 healthy newborns as control.

Results: Multivariate analysis identified that the development of TTN was significantly associated with elective cesarean section 56% (p-value=0.001), male sex 66.5% (p- value=0.001), late prematurity 21% (p-value=0.009), maternal diabetes 8% (P-value=0.014), maternal asthma 10.5% (p-value=0.01), birth asphyxia (low APGAR score) 9.5% (p-value=0.005), low birth weight 16.5% (p-value=0.003), prolonged labor or using (forceps or vacuum) 22% (p-value=0.037) and in vitro fertilization 2.5% (p-value =0.024).

Conclusion: Transient tachypnea of newborns is strongly related to elective cesarean section, male sex, late prematurity, maternal diabetes, maternal asthma, birth asphyxia, low birth weight (1500-2500g), prolonged labor or using forceps or vacuum and in vitro fertilization.

Keywords: Transient tachypnea of newborn, elective cesarean section, low gestational weight, in vitro fertilization.

عوامل الخطورة لنشوء حالات تسارع التنفس المؤقت للأطفال الحديثي الولادة

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الخلاصة

الخلفية: تعتبر حالات تسارع التنفس المؤقت للأطفال الحديثي الولادة من الحالات الشائعة كجزء من حالات عسر التنفس للأطفال الحديثي الولادة. الآلية التحتية لعِلم الأمراض تَتضمّن تأخر إزالة سائل الرئة المتبقي، مبدئيا حالات تسارع التنفس المؤقت للأطفال الحديثي الولادة تحدث مباشرة بعد الولادة وممكن أن تستغرق من أربعة وعشرون إلى إثنان وسبعون ساعة. عوامل الخطورة لحالات تسارع التنفس المؤقت للأطفال الحديثي الولادة تشمل كلا من العمليات القيصرية الإختيارية والذكور، وحالات الربو القصبي للأمهات، حالات الإختناق الولادي، الخديج ذو الحجم الكبير، والولادات ذات الأوزان القليلة، حالات داء السكري للأمهات وحالات الولادات المتعسرة وأخيرا الإخصاب الصناعي. علاج هذه الحالات لايحتاج سوى المتابعة ومراقبة الطفل مع الحاجة لإستعمال الأوكسيجين في بعض الأحيان.

الهدف: إن هدف هذه الدراسة هو تشخيص عوامل الخطورة لحالة تسارع التنفس المؤقتة لدى الأطفال المولودين حديثا سواء عن طريق الولادة الطبيعية أو الولادة القيصرية ومقارنة نتائج البحث مع نتائج البحوث الأخرى.

المرضى وطريقة البحث: هذه الدراسة هي دراسة العينة والشاهد عليها وقد تم إجراءها في وحدة الخدج في مستشفى الخنساء التعليمي للأطفال في الموصل وللفترة إبتدءا من الأول من شهر أيلول ٢٠١١ وحتى الأول من أيلول ٢٠١٣, حيث تم إختيار عينة من ٢٠٠ طفل حديث الولادة من كلا الجنسين أعمارهم ستة وثلاثون أسبوع فأكثر أدخلوا إلى وحدة الخدج لإصابتهم بعسر التنفس، وكان تشخيص متلازمة تسارع التنفس المؤقت معتمدا على الأعراض السريرية للمريض ومختبريا وبإستخدام التصوير الشعاعي، وتم إستبعاد إصابة المريض بالأمراض التنفسية الأخرى وحالات تسمم الدم الخمجي وتم أخذ عينة أخرى مكونة من ٢٠٠ طفل حديث الولادة أصحاء ولا يعانون من أي شي من أجل المقارنة.

النتائج: بعد أن تم إجراء الدراسة على تلك العينة من المرضى ومقارنتها بالأطفال الأصحاء وإستبيان المعلومات وتحليلها تبين بأن حدوث حالات تسارع التنفس المؤقت كان أشد إرتباطا بالعمليات القيصرية الإختيارية ٥٦%، والذكور٦٦,٥% من دون الإناث، كذلك كان له إرتباطا معنويا بالولادة المبكرة (٣٦ أسبوع) ٢١% وحالات داء السكري والربو القصبي لدى الأمهات (٨% و ١٠,٥ % وبالتتابع) وكذلك حالات الإختناق الولادي ٩,٥% والولادات ذات الأوزان القليلة (١٥٠٠-٢٥٠٠غم) وحالات الولادات المتعسرة ٢٢% وأخيرا الإخصاب الصناعي ٢,٥%.

الإستنتاجات: إن حالات تسارع التنفس المؤقت كان لها إرتباطا معنويا بالعمليات القيصرية الإختيارية والذكور والولادات المبكرة وداء السكري وحالات الربو لدى الأمهات كذلك حالات الإختناق الولادي والولادات المتعسرة وأخيرا الإخصاب الصناعي.

الكلمات المفتاحيه: تسارع التنفس المؤقت للأطفال حديثي الولادة، العمليات القيصرية الإختيارية، الولادات ذات الأوزان القليلة، الإخصاب الصناعي.

INTRODUCTION

Transient tachypnea of the newborn (TTN), first described by Avery in 1966, represents the most common cause of respiratory distress, and occurs in approximately 6/ 1000 births.[1,2]

The incidence of neonatal respiratory distress in the newborn is approximately 7%.[1] In utero, fluid is produced by the neonatal lung. Some of this fluid is swallowed by the neonate and excreted by the kidneys resulting in amniotic fluid. The fetal larynx periodically opens and closes, so most of the fluid is swallowed but some fluid enters the lungs to keep them expanded.[3]

Lung fluid production drops as epinephrine levels increase, which also accelerates fluid transport via sodium channels. Recent studies have demonstrated that certain genetic abnormalities in catecholamine receptors can predispose a newborn to TTN.[4]

Malignant TTN has been reported in infants born by elective cesarean section who initially present with signs and symptoms of TTN that may last more than 72 hours. These infants demonstrate refractory hypoxia due to pulmonary hypertension and may require extracorporeal membrane oxygenation (ECMO).[5]

Transient tachypnea of the newborn represents the most frequent cause of neonatal respiratory distress among all newborns, constituting over 40% of cases.[6]

Newborns with TTN usually present with tachypnea intercostal or subcostal retractions, grunting, nasal flaring and poor feeding. Cyanosis is not common but could be present in severe cases. Symptoms can last from few hours to over 2 or 3 days. Although hypoxemia is not typical, it can be present.[7]

Chest x-ray (CXR) can show hyperaeration, parenchymal infiltrates, and intralobar fluid accumulation. CXR findings, however, are often shared by other causes of respiratory distress and rarely fit classical description. TTN diagnosis is usually based on the clinical assessment.[7] Copetti and Cattarossi demonstrated that differences in ultrasonographic findings between the upper and lower lung fields could potentially be diagnostic of TTN and can differentiate it from other causes of respiratory distress. Although tested in a small study using a high-resolution linear probe, the authors achieved a sensitivity and specificity rate of 100%. These findings suggest the need for larger, blinded, prospective studies.[7]

Risk factors for the development of TTN[7-9] include: elective cesarean section delivery without preceding labor (especially with gestational age < 38 weeks),maternal diabetes , maternal asthma, male sex ,multiple gestations, macrosomia (birth weight>4 Kg) and precipitous delivery. Less common risk factors for TTN [10,11] include: delayed clamping of umbilical cord (optimal time 45 seconds) which leads to increased placental transfusion and this causes left ventricular dysfunction, fluid overload of the mother, especially with oxytocin infusion, negative amniotic fluid phosphatidylglycerol, birth asphyxia, excessive maternal sedation and analgesia, exposure to B-mimetic agents, prolonged labor and polycythemia.

Aims of the study

1. To identify the risk factors associated with development of transient tachypnea of newborns.
2. To compare the results with others.

PATIENTS AND METHODS

This is a case-control study, it was conducted over two years period, from the 1st of Sep. 2011 to the 1st of Sep. 2013 in the neonatal intensive care unit at AL-Kansaa Teaching hospital in Mosul.

The perinatal history of two hundred newborns were reviewed regarding risk factors of TTN. They were delivered either by cesarean section or normally at 36 ≥ weeks of gestation, all of them were suffering from respiratory distress that lasted >6 hours after delivery. Cases with suspicion of TTN were validated through the absence of other morbidities affecting respiration, particularly perinatal infection, persistent pulmonary hypertension and meconium aspiration syndrome. Complete perinatal and post natal history was taken to rule out other causes of respiratory distress. They were investigated by complete blood count, sepsis screen and chest x-ray. All sepsis screen results including (blood culture, c-reactive protein and complete blood count) were negative.

The diagnosis of TTN was based on exclusion and observation of clinical features based on clinical features of tachypnea, chest retractions, expiratory grunting and occasionally cyanosis that is relieved by minimal oxygen supplementation (<40%).The chest examination revealed generally clear vesicular breath sound without rales or rhonchi and the chest radiograph showed prominent pulmonary vascular markings, fluid in the intralobar fissures, overaeration, flat diaphragms and rarely small pleural effusions.

The study also included two hundred healthy newborns as a control group, who were delivered either by cesarean section or normally. The perinatal and post natal history of these newborn were also reviewed for the presence of risk factors of TTN.

The studied risk factors for development of TTN were: elective cesarean section, male sex, gestational age 36 ≥ weeks, maternal diabetes, maternal asthma, birth asphyxia (low APGAR score), prolonged labor or by using forceps or vacuum, history of in vitro fertilization, macrosomia, fluid overload of the mothers specially with oxytocin infusion, breech delivery, exposure to B-mimetic agent, precipitous delivery and multiple gestations.

Statistics were calculated by mean of chi-square test for categorical variables. Odd ratios and 95% confidence intervals (CIs) were also calculated. Statistical analysis was performed and P-value of <0.05 was considered as a significant.

RESULTS

Table 1 showed that the risk factors; male sex, late prematurity, maternal diabetes, maternal asthma, birth asphyxia (low APGAR score < 7 at 1 minute), low birth weight (1500-2500 g), prolonged labor or by using forceps or vacuum and in vitro fertilization, were significant causes of TTN (P-values were 0.001, 0.009, 0.014, 0.01, 0.005, 0.003, 0.037, 0.024 respectively). While macrosomia, precipitated delivery, multiple gestations, exposure to B- mimetic drugs, maternal PET, maternal thyrotoxicosis, birth weight and fluid overload with oxytocin infusion failed to reach a significant level.

Table 2 showed the mode of delivery among the 2 groups. The number of patients who developed TTN was higher in those who were delivered by Cesarean section than normally with significant association (P=0.001). Among those patients who were delivered by cesarean section, a higher number of patients with TTN were seen in those delivered by elective cesarean section compared to emergency cesarean section.

Table 1. Distribution of risk factors among patients with TTN and control group.

Risk factors		TTN (n=200)		Control (n=200)		OR	95%CI	p-value
		No.	%	No.	%			
Sex	Male	133	66.5	96	48	2.578	1.720-3.865	0.001(s)
	Female	67	33.5	104	52			
Gestational age	< 36 wks	42	21	22	11	0.986	0.772-1.226	0.009(s)
	≥ 36 wks	158	79	178	94	0.465	0.267-0.809	
Maternal diabetic		16	8	5	2.5	3.391	1.262-9.089	0.014(s)
Maternal asthma		21	10.5	8	9	2.816	1.240-6.384	0.01(s)
Macrosomia >4kg		8	4	7	3.5	1.149	9.424-3.110	1.000
Precipitous delivery		4	2	2	1	2.02	0.427-9.533	0.411
Multiple gestation		2	0	17	8.5	0.109	0.028-0.430	0.001
Birth asphyxia. (APGAR score <7 at 1 minute)		19	9.5	5	2.5	4.094	1.549-10.790	0.005(s)
Birth wt.	Low birth wt	33	16.5	14	7	2.625	1.369-5.028	0.003
	Normal birth wt	167	83.5	186	93			
Prolonged labor or by using (forceps or vacuum)		44	22	28	16.5	1.682	1.001-2.828	0.037
Breech delivery		8	4	2	2	4.125	0.976-17.358	0.055
Exposure to B-mimetic agent		2	1	0	0	Inf	o.521-inf	0.499
Maternal PET		1	0.5	0	0	Inf	0.260-inf	1.00
Maternal thyrotoxicosis		1	0.5	0	0	Inf	0.260-inf	1.00
Fluid overload+oxytocin infusion		2	0.2	1	0	Inf	1.322-inf	0.124
In vitro fertilization		5	2.5	0	0	Inf	1.322-inf	0.024(s)

Table 2. Mode of delivery among the patients with TTN and control group.

Mode of delivery		Patients with TTN N=200		Control group N=200		OR	95%CI	P value
		No.	%	No.	%			
Cesarean section	Elective	112	56	58	29	6.817	4.399-10.563	0.001(s)
	emergency	37	18.5	29	14.5			
Normal vaginal delivery		51	25.5	113	56.5			
Total		200	100	200	100			

DISCUSSION

The present study showed that TTN was more common in males (66.5%) than females (38.5%), which was comparable with Kasap B *et al* (2008),[6] Asenjo M (2007),[12] and AL-jurjari Z (2012),[13] and Erol Tutdibi *et al* (2009).[14]

The TTN was more common in those newborns with gestational age of ≥ 36 weeks (late premature, 21%), which was comparable with Kasap B *et al* (2008)[6] and Erol Tutdibi *et al* (2009)[14] who found a significant association between TTN and late prematurity.

There was a significant association between low birth weight (1500-2500) and TTN (P=0.003), as also found by Liem JJ (2007),[15] and Tutdibi Erol (2010).[14] Both found a significant relationship between TTN and low birth weight.

No significant association was found between the most frequently encountered birth weight (2500-3000 grams) and TTN, and this may be due to small sample in this study.

A significant association was found between elective cesarean section delivery and TTN. This was similar to those found by Levine EM. (2001),[9] AL-jurjari Z (2012),[13] Liem JJ (2007),[15] and Erol Tutdibi *et al* (2009),[14] who found an increase of TTN by 2-3 folds in the neonates delivered by elective cesarean section than those delivered normally (P=0.001). Infants delivered through elective cesarean section often are deprived of the labor-related physiological stress response pattern at birth and consequently experience failure of postnatal respiratory transition.

A significant association between TTN and diabetic mothers was found, this was similar to that found by Dani C (1999),[8] AL-jurjari Z (2012),[13] and Nazarzaki (2008).[16] Also a significant association was found between TTN and asthmatic mothers, which is the same in AL-jurjari Z (2012),[13] Liem, JJ (2007),[15] and Subramanian KNS *et al* (2006),[17] studies.

Birth asphyxia (low APGAR score<7 at 1 minute) was also found to be significantly associated with TTN, which is similar to Michael S (1991),[18] results.

Prolonged labor or by using forceps or vacuum also had a significant correlation with TTN, in which it may cause dysfunctional catecholamine regulation, mild pulmonary capillary leak and myocardial dysfunction, which was similar to Erol Tutdibi *et al* (2009)[14] findings.

A significant correlation was found between TTN and in vitro fertilization, which is comparable to Takayata *et al* (2008)[19] findings.

CONCLUSION

Transient tachypnea of newborns is significantly correlated with elective cesarean section, late prematurity, male sex, maternal asthma, maternal diabetes, birth asphyxia prolonged labor and in vitro fertilization.

RECOMMENDATIONS

1. Good antenatal care is crucial in detecting early problems during pregnancy that may have relation to increase incidence of TTN.
2. Good obstetric care during delivery has an important role in prevention of perinatal asphyxia which by itself may lead to increase incidence of TTN.

REFERENCES

1. Kumar A and Bhat BV. Epidemiology of respiratory distress of newborns. Indian J. Pediatr 1966; 63(1): 93–98.
2. Avery ME, Gatewood OB, Brumley G. Transient tachypnea of newborn possible delayed resorption of fluid at birth. Am. J. Dis. Child. 1966; 111(4): 380–385.
3. Blackburn ST: Maternal fetal and neonatal physiology: a clinical perspective (3rd Edition). Elsevier Health Sciences, MO, USA; 2007: 338.
4. Aslan E, Tutdibi E, Martens S, *et al.* Transient tachypnea of the newborn (TTN): a role for polymorphisms in the b-adrenergic receptor (ADRB) encoding genes? Acta Paediatr. 2008; 97(10): 1346–1350.
5. Waldemar A. carlo. Respiratory tract disorders in NB Behram, Richerd, Robert M *et al* Nelson Textbook of pediatrics.19th ed. Philadelphia, WB Saunders Co: 2011; 95.4:P579-99.
6. Kasap B, Duman N, Ozer E, *et al* Transient tachypnea of the newborn: predictive factor for prolonged tachypnea. Pediatr Int.2008; 50:81–84.
7. Copetti R, Cattarossi L. The 'double lung point. An ultrasound sign diagnostic of transient tachypnea of the newborn. Neonatol. 2007; 91: 203–209.
8. Dani C, Reali MF, Bertini G, *et al.* Risk factors for the development of respiratory distress syndrome and transient tachypnea in newborn infants. Eur Respir J. 1999; 14: 155-159.
9. Levine EM, Ghai V, Barton JJ, Strom CM. Mode of delivery and risk of respiratory diseases in newborns. Obstet Gynecol 2001; 97: 439–42.
10. Tutdibi E, Gries K, Bucheler N, *et al.* Impact of labor on outcome in transient tachypnea of the newborn. Pediatrics 2010; 125: 577- 583.
11. John P. Cloherty, Eric C Eichenwald, Anne R. Honsen. Manual of neonatal care.17th ed. Philadelphia, PA: Lippincott Williams & Wilkin; 2012; 24G: PP403-405.
12. Asenjo M. Transient tachypnea of the newborn. E medicine.1; 2007:943-987.
13. ALjurjari Z. Risk factors for Transient tachypnea of newborn. Dissertation submitted to the Iraqi Board for medical specialization in partial fulfillment for the degree of fellowship of the Iraqi Board for medical specialization in pediatrics. 2013.
14. Tutdibi, Erol; Gries, Katharina; Bücheler, Monika; Misselwitz, Bjorn; Schlosser, Rolf L; Gortner, Ludwig. Impact of labor on outcomes in transient tachypnea of the newborn: population based study. Pediatrics 2010; 125: 577-583.
15. Liem JJ, Huq SI, Ekuma, O, Becker AB, Kozyrskyi AL. Transient tachypnea of the newborn may be an early clinical manifestation of wheezing symptoms. J Pediatr 2007; 151:29.
16. Zeki N. Risk factors for Transient tachypnea of newborn. Dissertation submitted to the Iraqi Board for medical specialization in partial fulfillment for the degree of fellowship of the Iraqi Board for medical specialization in pediatrics.2008.
17. Subramanian KNS, Bahri M, Kicklighter DS. Transient tachypnea of the new born. E medicine 2006; 54:1-11.
18. Michael S, Robert S, Clement P. Hoffman, Brian S, Kathleen M, Alan B Forsythe. Increase transient tachypnea of newborn in infants of asthmatic mothers Am J Dis Child. 1991; 145(2):156-158.
19. Takayata A, Igarashi M, Nakajima M, Miyaki H, Shima Y, Zusuki S. Risk factors for transient tachypnea of newborn in infant delivered vaginally at 37 weeks or later. J Nippon Med Sch 2008; 75: 269-273.

Effects of Bee Propolis on Blood Pressure Record and Certain Biochemical Parameter in Healthy Volunteers

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ABSTRACT

Objectives: To evaluate the effect of encapsulated bee propolis supplementation 500 mg twice daily for 2 months on blood pressure record, fasting serum glucose, lipid profile and serum uric acid in otherwise healthy volunteers in comparison to controls.

Design: The study was conducted from October 2017 to April 2018, subjects included in the study was healthy non-obese from different areas in Mosul city, so as the control.

Subjects and methods: Forty apparently healthy subjects (Sixteen male and twenty–four female) were included in this study. Blood pressure (BP) were recorded, body weight and body mass index (BMI) were calculated, then a blood sample was taken with assay of fasting serum glucose (FSG), lipid profile {Total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL –C), while serum low density lipoprotein (LDL –C), very low density lipoprotein (VLDL-C) and atherogenic index (AI)} were calculated by using certain equations and serum uric acid (SUA), was measured for both the intervention and the control groups.

After 2 months of supplementation with encapsulated bee propolis 500 mg twice daily, the BP, body weight, BMI, LDL-C, VLDL-C and AI were calculated and FSG, TC, TG, HDL and SUA were measured for the intervention group. All data were presented as means± standard deviation (SD) of mean. Independed t – test of two mean was used. Dependent t – test of two mean was applied for the differences in the intervention group (before and after). Chi square test of independence was used for categorial variables. P–value≤0.05 was considered statistically significant.

Results: Initially, at the start of the study, there was insignificant difference between the interventions and the control groups with regard age, sex, weight, BMI, systolic and diastolic BP, serum TC, HDL- C, LDL –C, AI and SUA, with a significant differences in FSG, TG, and VLDL. By comparison before and after supplementation in the intervention groups, there was a significant decrease in the systolic and diastolic BP record, FSG, TC, TG, LDL –C, AI, SUA, with a significant increase in body weight and HDL –C.

Conclusion: Bee propolis supplementation at a dose of 500 mg twice daily for 2 months carries a beneficial effects on BP record, FSG, lipid profile, and SUA, which should be taken in preventive medicine, since hyperglycemia, hyperlipidemia and hyperureciemia, contributed to the development of atherosclerosis, cardiovascular and cerebrovascular diseases.

Keywords: Propolis, healthy volunteers, FBS, lipid profile, uric acid, blood pressure.

تأثيرات عكبر النحل على قياس ضغط الدم وبعض الفحوصات البايوكيمائيه عند المتطوعين الأصحاء

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الخلاصة

الأهداف: تقيم إعطاء كبسول عكبر النحل بجرعة ٥٠٠ ملغم مرتين يوميا لمدة شهرين على قياس ضغط الدم ومستوى الكلوكوز وصورة الشحوم والحامض البولي في مصل الدم عند متطوعين أصحاء غير بدناء وبالمقارنة مع مجموعة ضبط.

التصميم: تم إجراء الدراسة للفترة من شهر تشرين الأول ٢٠١٧ إلى نيسان ٢٠١٨ وتم تجميع عينة المتطوعين للدراسة وعينة الضبط من مناطق مختلفة لمدينة الموصل.

طرق العمل: إشترك في الدراسة ٤٠ شخصا ١٦ من الذكور و٢٤ من الإناث. تم قياس ضغط الدم، وزن الجسم وحساب دليل كتلة الجسم ثم سحب عينة الدم وقياس مستوى الكلوكوز، الحامض البولي، الكوليستيرول، الشحوم الثلاثية والشحوم عالية الكثافة في مصل الدم مع حساب معدل الشحوم واطئة الكثافة وذلك لأعضاء الدراسة ومجموعة الضبط. بعد مضي شهرين من إعطاء كبسول عكبر النحل تم قياس ضغط الدم وزن الجسم مع حساب دليل كتله الجسم وتم سحب عينة دم لأعضاء مجموعة الدراسة وإجراء نفس الفحوصات المذكورة أعلاه.

النتائج: في البداية كان هنالك اختلافا غير معنوي بين أعضاء مجموعة الدراسة وأعضاء مجموعة الضبط فيما يتعلق بالعمر والجنس، الوزن، معامل كتله الجسم، قياس ضغط الدم الانقباضي والانبساطي وفي مستوى الكوليستيرول، الشحوم عالية وواطئة الكثافة معامل التعصد ومستوى الحامض البولي مع وجود اختلاف معنوي في مستوى الكلوكوز، الشحوم الثلاثية والشحوم واطئة الكثافة جدا. بالمقارنة بين إفراد مجموعة الدراسة قبل وبعد استخدام عكبر النحل ظهر هنالك انخفاض معنوي في معدل ضغط الدم الانقباضي والانبساطي، مستوى الكلوكوز، الحامض البولي والكوليستيرول، الشحوم الثلاثية، الشحوم واطئة الكثافة والشحوم واطئة الكثافة جدا ومعامل التعصد في مصل الدم مع زيادة معنوية في الشحوم عالية الكثافة ووزن الجسم.

الخلاصة: إعطاء عكبر النحل بجرعة ٥٠٠ ملغم مرتين يوميا لمدة شهرين كان له تأثيرات مفيدة على قياس ضغط الدم مستوى الكلوكوز، صورة الشحوم ومستوى الحامض البولي في مصل الدم ممكن الاستفادة منه في تطبيقات الطب الوقائي خاصة إن إرتفاع سكر الدم وإرتفاع مستوى الشحوم والحامض البولي في الدم مرتبط بتطور حدوث تصلب الشرايين وامراض القلب والدماغ الوعائية.

كلمات المفتاح: عكبر النحل، متطوعين أصحاء، مستوى الكلوكوز في حالة الصيام، صورة الشحوم، الحامض البولي وضغط الدم.

INTRODUCTION

In modern primary care, doctors spend considerable time and effort, concentrating on preventive medicine practice.[1] Hyperglycemia, hyperlipidemia and hyperureciemia were considered as main risk factor for developing atherosclerosis and cardiovascular diseases.[2,3,4] Type II diabetes mellitus (DM) is associated with 4 folds increased risk of both coronary and cerebrovascular disease[2] and atherogenic dyslipidemia characterized by abnormal changes in plasma lipid profile as low HDL –C and increased TG[3] and only recently the pathophysiological links between elevated SUA concentration and the risk for atherosclerotic cardiovascular and cerebrovascular disease become clear.[4]

Currently word attention were directed to traditional medicine.[5] Propolis is a resinous material , containing a variety of substances and is used in cosmetics, food supplement and in medicine for centuries in various health problems as treatment and prevention. It exhibit abroad spectrum activities including antibacterial,[6] antifungal,[7] antiviral,[8] anti-inflammatory,[9] antioxidant,[10] immunostimulating[11] and cytostatic proprieties.[12]

In this study we evaluated the preventive effect of encapsulated bee propolis as daily supplement of 500 mg twice daily for 2 months on BP record, FSG, lipid profile, SUA in otherwise non-obese healthy volunteer in comparison to the controls.

SUBJECTS AND METHODS

Forty otherwise healthy non-obese volunteer (sixteen male and 24 female) were included in the study that was conducted from October 2017 to April 2018. Pregnant and lactating women, those with history of allergy, asthma and bleeding disorders were excluded.

Also included in the study 43, age, sex and body weight matched healthy subjects as a control group.

Initially, for both the members of intervention and control groups, BP were recorded, body weight measured, BMI was calculated using following equation:

BMI= Weight (Kg) /Height (m2)[13]

FSG, TC, TG and HDL-C were measured Using kits of Biolabo Company (France).

LDL –C was calculated using the following equation:[14]

TC – HDL – VLDL –C

VLDL level was calculated by the following equation:[14]

TG/5=VLDL

Atherogenic index calculated as:[15]

A.I = TC/HDL-C

Also a kit from Biolabo Company – France was used for measurement of SUA.[16,17]

After 2 months of bee propolis (Forever Company –USA) supplementation in a dose of 500 mg twice daily, BP were recorded, body weight, BMI, LDL-C, VLDL-C and A.I were calculated and serum TC, TG, HDL-C, FSG and SUA were measured.

RESULTS

As shown in **Table 1**, the comparison between the intervention and the control groups with regard to personal characteristics, demonstrated insignificant differences.

Before 2 months of bee propolis supplement, there was a significant higher TG. and VLDL –C concentrationsand lower FSG in the intervention group in comparison to control **Table 2**.

After 2 months of encapsulated bee propolis supplementation and by comparing the intervention and the control groups, there was a significant differences in systolic and diastolic blood pressure record , FSG , TC . LDL –C and A.I (**Table 3, Table 4**).

By comparison before and after supplementation of bee propolis in the intervention group, there was a significant reduction in systolic and diastolic blood pressure (% of improvement: 8.39), diastolic blood pressure (% of improvement: 12.42) with a significant increase in body weight (1.62 %) (**Table 5**).

Also there was a significant reduction in FSG (% of improvement 10.95), SUA (20.64%), TC (15.33%), LDL –C (26.27 %), VLDL –C (34.39%), TG (34.47%) and A.I (34.47%), with a significant increase in HDL-C (8.18%) as shown in (**Table 6**).

Table 1. Comparison between the intervention and control groups with regard personal characteristics.

Characteristics	Intervention group [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
Age (years)	29.9 ± 11.1	29.5 ± 10.5	0.872
Systolic blood pressure (mmHg)	116.8 ± 10.2	113.3 ± 9.4	0.109
Diastolic blood pressure (mmHg)	76.5 ± 5.8	73.6 ± 8.5	0.074
Weight (kg)	59.8 ± 10.5	60.7 ± 9.4	0.662
BMI (kg/m^2)	22.39 ± 2.06	22.35 ± 1.80	0.923
Gender	No. (%)	No. (%)	
Male	16 (40.00)	16 (37.21)	0.794**
Female	24 (60.00)	27 (62.79)	

* Independent T-test of two means was used.

** Chi-square test was used.

Table 2. Comparison between intervention and the control groups with regard to measured biochemical parameters before bee propolis supplementation.

Parameters	Intervention group [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
FSG (mg/dl)	84.9 ± 13.6	93.3 ± 14.8	0.009
SUA (mg/dl)	3.73 ± 1.36	3.34 ± 1.14	0.168
S. cholesterol (mg/dl)	161.8 ± 29.6	155.9 ± 29.5	0.366
HDL (mg/dl)	55.23 ± 8.28	57.16 ± 7.18	0.257
LDL (mg/dl)	90.2 ± 28.4	86.9 ± 26.9	0.592
VLDL (mg/dl)	16.43 ± 7.61	11.86 ± 6.34	0.004
TG (mg/dl)	82.1 ± 38.0	59.3 ± 31.7	0.004
A.I	2.98 ± 0.66	2.76 ± 0.58	0.106

* Independent T-test of two means was used

Table 3. Comparison between the intervention group after bee propolis supplementation and control groups regarding personal characteristic.

Parameters	Intervention group after 2M. [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
Systolic BP (mmHg)	107.0 ± 9.7	113.3 ± 9.4	0.004
Diastolic BP (mmHg)	67.0 ± 7.6	73.6 ± 8.5	0.000
Weight (kg)	60.7 ± 11.3	60.7 ± 9.4	0.999
BMI (kg/m^2)	22.68 ± 2.29	22.35 ± 1.80	0.467

* Independent T-test of two means was used.

Table 4. Comparison between the intervention group after bee propolis supplementation and control groups regarding measured biochemical parameters.

Parameters	Intervention group after 2M. [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
FSG (mg/dl)	75.6 ± 10.6	93.3 ± 14.8	0.000
SUA (mg/dl)	2.95 ± 1.10	3.34 ± 1.14	0.117
S. cholesterol (mg/dl)	137.0 ± 32.2	155.9 ± 29.5	0.006
HDL (mg/dl)	59.73 ± 10.24	57.16 ± 7.18	0.188
LDL (mg/dl)	66.5 ± 31.1	86.9 ± 26.9	0.002
VLDL (mg/dl)	10.78 ± 6.73	11.86 ± 6.34	0.453
TG (mg/dl)	53.9 ± 33.6	59.3 ± 31.7	0.452
A.I	2.34 ± 0.62	2.76 ± 0.58	0.002

* Independent T-test of two means was used.

Table 5. Comparison between the pre and post- supplementation of bee propolis in the intervention group regarding personal characteristics.

Parameters	Base line Mean ± SD	After 2 months Mean ± SD	Before – after	% improvement rate	P-value
Systolic BP (mmHg)	116.8 ± 10.2	107.0 ± 9.7	9.8 ± 1.31	8.39	0.000
Diastolic BP (mmHg)	76.5 ± 5.8	67.0 ± 7.6	9.50 ± 6.77	12.42	0.000
Weight (kg)	59.8 ± 10.5	60.7 ± 11.3	- 0.97 ± 2.04	1.62	0.005
BMI (kg/m^2)	22.39 ± 2.06	22.68 ± 2.29	- 0.29 ± 0.17	1.30	0.092

* Paired T-test of two means was used.

Table 6. Comparison between the pre and post- supplementation of bee propolis in the intervention group regarding measured biochemical parameters.

Parameters	Base line Mean ± SD	After 2 months Mean ± SD	Before – after	% improvement rate	P-value*
FSG (mg/dl)	84.9 ± 13.6	75.6 ± 10.6	9.3 ± 13.0	10.95	0.000
SUA (mg/dl)	3.73 ± 1.36	2.95 ± 1.10	0.77 ± 0.82	20.64	0.000
S. cholesterol (mg/dl)	161.8 ± 29.6	137.0 ± 32.2	24.8 ± 28.1	15.33	0.000
HDL (mg/dl)	55.23 ± 8.28	59.73 ± 10.24	- 4.50 ± 7.91	8.15	0.001
LDL (mg/dl)	90.2 ± 28.4	66.5 ± 31.1	23.7 ± 28.3	26.27	0.000
VLDL (mg/dl)	16.43 ± 7.61	10.78 ± 6.73	5.65 ± 5.59	34.39	0.000
TG (mg/dl)	82.1 ± 38.0	53.9 ± 33.6	28.3 ± 27.92	34.47	0.000
A.I	2.98 ± 0.66	2.34 ± 0.62	0.64 ± 0.65	21.48	0.000

* Paired T-test of two means was used.

DISCUSSION

Propolis is a safe natural resinous product, made by bees from material extracted from plants, flowers and bees wax. It is regarded as a folk medicine possessing a broad spectrum of biological activities including hypoglycemic activity.[18]

This study revealed a significant weight gain in the intervension group after 2 months of bee propolis supplementation at a doses 500 mg twice daily. This is in agreement with study conducted by Denli *et al*, 2005[19], whom reported that the addition of propolis in the diet significantly increase the growth parameter of quail chicks such as body weight gain and feed consumption and improvement feed efficacy compared with controls and they suggested that it could be due to antimicrobial activity of the propolis extract that resulted in improvement of intestinal hygiene that lead to improved digestion and absorption, beside that it has been suggested that bee propolis contain protein, amino acids, vitamins, and flavonoids, for this resinous it has been used by some people as a nutritional supplement. [20]

Also on line with our results, the study conducted by albushabaa (2014)[21] , she reported that propolis extract has antihyperglycemic effect and significantly improved the body weight of diabetic rabbits. Yucel *et al*, (2012)[2], studied the effect of propolis administration on assessement of growth and neonatal diarrhea in calves, they found an improved live weight gain and growth this attributing to the the activity of propolis against many bacterial pathogens, thus preventing calves diarrhea.

Concerning the effect of propolis on blood pressure record, although all of our subject in the study were normotensive, propolis supplement causes a significant reduction in the mean systolic and diastolic blood pressure in comparison to pre-propolis supplementation period and the controls. This is similar to the results of Gogebaken *et al*., 2012[23], whom concluded that propolis decrease tyrosine hydroxylase ,which is the rate limiting enzyme in the biosynthesis of catecholamine in nitric oxide inhibited hypertensive rats.

Talas *et al*, 2013[24] also reported that propolis might be used to protect against the hypertensive effect of nitro L–arginine methyl ester by increasing the generation of vascular nitric oxide.

Concerning the effect of propolis on biochemical parameters under study, this study reported a significant beneficial effects on FSG, lipid profile indices and SUA. This is in agreement with Li *et al*, 2011[25] whom reported that encapsulated propolis can suppress the heightening of FBS in type II diabetic rats, 8 weeks after starting therapy and concluded that encapsulated propolis can improve the insulin sensitivity in type II diabetic rats.

Fuliang *et al*, (2005)[26] also reported that propolis lower FSG and lipids leading to deceased out puts of lipid peroxidation and scavenge the free radicals in rats with diabetes mellitus. Bankova (2005)[27], attributed the hypoglycemic effect of propolis to its flavonoids content. Again our findings were in accordance with study conducted by Zaahkouk *et al*, (2016)[28] reporting a significant lower FSG level and increase in plasma insulin level in streptozotocin induced diabetic rats. Lastly and in a human study conducted by Zhao *et al* (2016)[29] reported that a Brazilian propolis significantly improved FSG level and plasma insulin in human subjects with type II DM.

In contrast to our study finding, Bulalo *et al*, (2009)[30] reported that propolis had no effects on plasma glycemic control and lipid metabolism in diabetic rat model fed on propolis for 28 days, also in contrast to our findings the study conducted by fukuda *et al*, (2015)[31] they concluded that 8 weeks supplementation of Brazillian propolis did not have beneficial effect on serum FSG, although it prevented the action of hyperureciemia and dysfunction of renal glomerular filtrating function that commonly developed in patient suffering from DM.

With regard to lipid profile, Albokhadaim (2015)[32], reported that dietary supplementation of propolis induces a beneficial hypolipidemic effect as hypocholesterlomic and hypotriglyceridemic effect in the sera of rat fed on high cholesterol diet. The effect on serum cholesterol could be attributed to inhibition of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG –COA) reductase, the rate –limiting enzyme that mediates the first step in cholesterol biosynthesis ,while the effect on TG might be attributed to lipase stimulation.

Also in line with our findings, the study conducted by EL-Sayed *et al*, (2009).[33] They conducted that propolis extract offers promising

antidabetic and hypolipidemic effects that might be mainly attributed to its potent antioxidant property.

With regard to effect on SUA, our study reported a significant reduction in SUA after 2 month supplementation of bee propolis, this is in line with the study conducted by Omnia *et al*, (2014) [34], and concluded that propolis act as a protective agent against thioacetamide–induced hyperammonemia in rats and that bee propolis and bee pollen significantly reduces SUA.

In a recent research work Amin *et al*, (2017)[35], studied the reno protective and antioxidant effect of silymarine and propolis on diclofenac sodium induced renal toxicity in rats and concluded that propolis with pollen provide a natural protection against renal toxicity induced by diclofenac sodium and both resulted in a significant decrease in urea, creatinine and SUA level as compared to the group receiving diclofenac only.

In conclusion: Encapsulated propolis supplement for 2 months at dose of 500 mg twice daily in otherwise healthy volunteer, resulted in a beneficial effect on blood pressure record, FSG, lipid profile and serum uric acid which might through a light on the protective effect of propolis against atherosclerosis and cardiovascular diseases in a primary care preventive medicine practice.

REFERENCES

1. Sniplesky D, Careker K, Sundsted K, Burton MC. Primary care physicians practicing preventive medicine in out patient setting. International Journal Preventive Medicine 2016 ; 7 : 5.

2. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ *et al*. Diabetes control and complication trial/epidemiology of diabetes interventions and complication (DCCT / EDIC) study research group. intensive diabetes treatment and cardiovasculare diseases in patient with type I diabetes New England Journal of Medicine. 2005; 353 (25) : 2643 -53.

3. Nelson RH. Hyperlipidemia as arisk factor for cardiovascular disease. Primary Care. 2013 march; 40 (1) : 195- 211 .

4. Krishnan E, Pandya BJ, Chung L, dabbous O. Hyperurecemia and the risk for subclinical coronary atherosclosis. data from a prospective observational cohort study. Arthritis Research and Therapy 2011.13 :R 66 .

5. Cordell GA, C olvard MD. Natural product and tradional medicine : turning on a paradigm. Journal National product. 2012 ; 75 (3) : pp 514 – 525 .

6. Urgur A, Arslan T. An in vitr study on antimicrobial activity of propolis from mugla province of turkey. Journal of Medicinal Food 2004; 7(1) :90 – 4.

7. Ota C, U nterkir cher C, Fantinato V, Shimizu MT. Antifungal activity of propolis on different species of candida. Mycoses 2011;44 (9-10) : 375 – 378.

8. Amaros M, S imoes CMO, Grre L, saurvager F, Cormier M . Comparison of the antiherpes simplex virus activities of propolis and 3 mthyl –butyl – 2- enyl caffeate. Journal National Product 1994; 57: 644- 647 .

9. Miyataka H, Nishiki M, Matsumoto H, Fujimoto T, Matsuka M, Satoh T. Evaluation of propolis. Evaluation of brazilian and chinese propolis by enzymatic and physico-chemical methods. Biological and Pharmaceutical Bulletine 1997 ; 20: 496-56.

10. Nagai T, Inouse R, Inouse H, Suzuki N. Preparation and antioxidant properties of water extract of propolis. Food Chemistry 2003 .80: 29-33.

11. Dimov V, Ivanovska N, Manolova, Bankova V, Nikolov N, Popov S. Immunomodulatory action of propolis. influncing on anti-infectious protection and macrophage function. Apidology 1991 ;22 : 155-162.

12. Banskota AH, Tezuka Y, Midorikawa K, Matsushige K, kadota S. Two novel cytotoxic benzofuran derivative from Brazilian propolis. Journal National product 2000; 63 (9) : 1277- 1279.

13. Blak barn H, Jacobs D. Commentary origins and evaluation of body mass idex (BMI) continuing saga. Interntional Journal of Epidemioloy 2014 ;43(3) :665 - 669 .

14. Friedewald W T, Levy R I, Fredrickson D S."Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge,"Clinical Chemistry, 1972. 18. (6). 499–502.

15. Castelli W.P, Abbott R.D, McNamara PM. Summary estimated of cholesterol used to predict coronary heart disease . Circulation ,67(4):730-734(1983).

16. Burtis C.A, Ashwood E.R, Saunders W.B, Tietz N.W Text book of clinical chemistry, 3rd Edition. (1999). pp. 1245-1250.

17. Fossati P, Prencipe L, and Berti G. Use of 3.5-dichloro-2- Hydroxybenzene sulfonic acid / 4 Amino phenazone chromogenic system in direct enzymatic assays of uric acid in serum and urine. Clinical Chemistry.: 26(227-231) 1980.

18. Abo-Salem OM, El-del RH, Harison G.E.I EL – Halawany N, Ghoraim MM. Expermintal diabetic nephropathy can be prevented by propolis effect on metabolic disturbances and renal oxidative parameter. Pakistan Journal of Pharmaceutical Sciences 2009 ; 22 (2) : pp 205 – 201 .

19. Denli M, Cankaya S, Silici1 S, Okan F, Uluocak A N. Effect of Dietary Addition of Turkish Propolis on the Growth Performance, Carcass Characteristics and Serum Variables of Quail (Coturnix coturnix japonica). Ascian–Australasian Journal of Animal Sciences. 2005;18,(6) : 848-854.

20. Lee SW, Kim HJ, Hwangbo S. Studies on the chemical characteristic of Korean propolis. Korean Journal Society for Food Science of Animal Resources 2001 ;21 :383-388.

21. Albushabaa SHH. Effect of propolis on blood glycemic control and lipid metabolism in diadetic rabbits. International Journal of Sciences and Engineering Research 2014 .5(12) :800-807.

22. Yucel B, Onenc A, Kaya A, Altan O. Effect of propolis on growth performance and neonatal diarrhea of calves. Symbiosis Journal of Veterinary Sciences 2015; 1(1):1-5.
23. Gogebakan A, Talas ZS, Ozdemir I and Sahna E Role of propolis on tyrosine hydroxylase activity and blood pressure in nitric oxide synthase-inhibited hypertensive rats. Clinical and Experimental Hypertension, 2012. 34(6): 424- 428.
24. Talas ZS, Gogebakan A, Onen I. Effect of propolis on blood biochemical and heamaological parameter in nitric oxide synthase inhibited rats by nitro –L – arginine methyl ester . Pakistan Journal of Pharmaceutical Sciences. 2013; 26(5): pp 915-919.
25. Li Y, Chen M, Xuan H, Hu F. Effects of encapsulated propolis on blood glycemic control, lipid metabolism and insulin resistance in type 2 diabetes mellitus rats. Evidence–Base Complementary and Alternative Medicine 2011; 2012 :pp(1-8).
26. Fuliang HU, Hepburn HR, Xuan H,Chen M, Daya S, Radloff SE. Effects of propolis on blood glucose, blood lipid and free radicals in rats with Diabetes mellitus. Pharmacological Research, 2005.51, 147-52.
27. Bankova V .Chemical diversity of propolis and the problem of standardization. Journal of Ethnopharmacology 2005.100(1-2): 114-117.
28. Zaahkouk SAM, Ibrahim DF, Elarabi BE. Antioxidant and hypoglycemic studies on Egyptian propolis and foeniculum vulgare on alloxan induced diabetic rats. International Journal of Animal Biology 2016 ;2:pp1-10.
29. Zhao L, Pu L, Jingyu W, Jinghua L, Jianguan W, Zhonghao X, *et al*. Brazilian green propolis improves antioxidant function in patient with type 2 diabetes mellitus. International Journal of Environment and Public Health.2016;14:pp498-507.
30. Bufalo MC, Barreiro DP, Sartori DRS, Sforcin JM. Absences of propolis effect on plasma glycemic control and lipid metabolism in a diabetic rat model. Journal of Apiprodct and Apimedical Science 2009;1(2) ;pp 51-55.
31. Fukuda T, Fukui M, Tanaka M, Senmaru T, Iwase H, Yamazaki M, *et al*. Effect of brazilian green propolis in patient with type 2 diabetes: A double –blind randomized placebo-controlled study. Biochemical Report 2015;3:pp 355-360.
32. Albokhadam I. Influence of dietary supplementation of proplis on hematology, biochemistry and lipid profile of rats fed high cholesterol diet. Journal of Advance Veterinary Animal Research. 2015 ;2(1) :pp 56-63.
33. El-Sayed el–SM, Abo-Salem OM, Aly HA, Mansour AM. Potential anti diabetic and hypolipidemic effect of propolis extract in streptozotocin- induced diabetic rats. Pakistan Journal of Pharmaceutical Sciences 2009; 22(2) : pp 168-174.
34. Omnia MA, Nabila AM, Nada RR. Biochemical effect of propolis and bee pollen in experimentally – induced hyperammonemia in rats. Benha Veterinary Medical Journal 2014 ;27(1):pp 8-28.
35. Amin KA, Ahmed RR, Hozayen WG, Antar A. Renoprotective and antioxidant effect of silymarin and propolis on diclofenac sodium induced renal toxicity in rats. International Journal of Pure and Applied Biosciences 2017;5 (2):pp 31-42.

Early probing in congenital naso-lacrimal duct obstruction

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ABSTRACT

Aim: To evaluate the role of early probing in congenital naso-lacrimal duct obstruction (CNLDO).

Method: The medical records of patients who underwent nasolacrimal duct probing for CNLDO in ophthalmic theater of Al-Jamhori Teaching Hospital, between 1st January 2009 and 31st December 2010 were reviewed retrospectively. Nasolacrimal duct probing was performed on 76 eyes from 73 consecutive patients with CNLDO.

Results: Based on exclusion criteria, 76 eyes from 73 patients (30 males and 43 females), aged 6 to 84 months (mean, 15.67±13.58) were included. The success rate of the initial probing was 84.2% (64 of 76) for all patients, 92.15% (47 of 51) in the 6 to 12 month age group, 75% (12 of 16) in the 13 to 24 months age group, and 55.5% (5 of 9) among individuals older than 24 months.

Conclusion: The success rate of probing is very high in 6-12 months age group.

Keywords: Early probing, congenital obstruction, nasolacrimal duct.

التسليك المبكر للإنسداد الخلقي للقناة الدمعية الأنفية

عامر يحيى رجب
فرع الجراحة، كلية الطب، جامعة الموصل، الموصل، العراق

الخلاصة

الهدف: لتعميم عملية العلاج المبكر (بين ٦-١٢ شهر) بواسطة تسليك المجرى الدمعي الأولي للمرضى المصابين بإنسداد المجرى الدمعي الخلقي.

التصميم: دراسة تراجعية لـ (٧٦ عين) أجريت لهم عملية تسليك المجرى الدمعي الأولي.

المكان: عمليات العيون في المستشفى الجمهوري التعليمي بالموصل.

المشاركون: إعتمادا على معايير الإستثناء٧٣ مريضا و٧٦عين مصابة بإنسداد المجرى الدمعي الخلقي.

النتائج: معدل نجاح عملية تسليك المجرى الدمعي كان ٨٤,٢% لجميع المرضى ٩٢,١٥% في عمر ٦-١٢ شهر، ٧٥% بعمر ١٣-٢٤ شهرا، ٥٥,٥% لأكثر من ٢٥ شهرا.

الإستنتاج: يفضل إجراء عملية التسليك الدمعي للأطفال في سن مبكرة للحصول على أفضل النتائج.

الكلمات المفتاحيه: تسليك مبكر، الإنسداد الخلقي، القناة الأنفية الدمعية.

INTRODUCTION

Tear is secreted by lacrimal and accessory glands, circulate over the corneal and conjunctival surfaces, and is then pumped out to the punctum, from the punctum, tear flows through the canalicular system and emptie in the nasolacrimal sac. From there is travels through the nasolacrimal duct (NLD) and exists into the nasal cavity.[1]

The tear drainage was 25% by evaporation and the rest by excretion which is either passive by

gravity and capillarity or active by lacrimal pump through the action of lacrimal portion of orbicularis oculi muscle (Horner's muscle).[2]

The (NLD) lies in maxillary bone. Obstruction of the nasolacrimal drainage system is extremely common in the pediatric age group, occurring in as many as 20%-30% of newborns and spontaneous resolution occurs in 80%-90% of affected infant by one year of age.[3-6] In patients in whom the NLD fails to canalize the condition persists. The timing of probing for CNLDO has been a matter of controversy in recent years. When the condition persists beyond 6 months, early probing gives good results. An equally effective approach is conservative management until 9-12 months of age waiting spontaneous resolutions followed by probing for persistent obstruction.[7]

Traditional options include office probing with topical anesthesia at the age of 4 to 6 months or observation and medical management followed by probing under general anesthesia at approximately 12 months of age.[8]

It has been reported that delay in probing beyond 6 months is associated with lower rate of success and this worsens as the child gets older.[7-9]

Conversely, there are studies which indicate that primary probing continue to be an effective treatment well beyond 2 years of age and that the cure rate does not vary markedly with age.[7,10-13] There are thus no clear guidelines for management of CNLDO.

The aim of this study is to evaluate the result of early probing in children aged 6-12 months.

MATERIALS AND METHODS

The current study is a retrospective comparative case series of consecutive patients on whom the author performed nasolacrimal duct probing as the primary treatment method for CNLDO. The medical records of patients who underwent nasolacrimal duct probing at Al-Jamhori Teaching Hospital for CNLDO between 1st January 2009 and31st December 2010 were reviewed retrospectively.

In total, nasolacrimal duct probing was performed on 82 eyes of 78 consecutive patients with CNLDO (3 patients bilateral). After enrollment, six eyes from 5 patients were excluded, leaving 76 eyes of 73 patients. Exclusion criteria included epiblepharon (2 eyes from 1 patients), acute dacryocystitis (1 eye), canalicular obstruction (1 eye), and loss to follow-up (2 eyes). Patients with previous history of probing were also excluded, as were patients with dacryocistitis (diagnosed by visualizing pus after digital sac compression).

Patients with congenital craniofacial and lid abnormalities, punctal agenesis, a history of trauma, nasolacrimal surgery, previous probing or other nasolacrimal intervention, and postoperative follow-up <3 months were excluded from the study.

Inclusion criteria were; no prior nasolacrimal surgical procedure, history of epiphora and/or discharge since birth or shortly after birth in one or both eyes and at least one of the following clinical signs: epiphora, to eliminate any other ophthalmological problem which may cause epiphora such as congenital glaucoma, trichiasis, conjunctivitis, keratitis, and metabolic disorders.

Prior to probing, enrolled subjects received medical treatment by lacrimal sac massage and/or topical antibiotics till 6th month of age. Probing was done after failure of medical management.

The procedure of probing in all cases was performed in operating theater under general anesthesia by the author, probing was done via the lower punctum using standardized Bowman's probe.

In children younger than 36 months, an initial attempt was made using size 00 (0.90 mm diameter), while size 0 probe (1.00 mm diameter) was used in patients 37-48 months and sized (1.10 mm diameter) in patients older than 49 months after initial dilatation of lower punctum by fine punctual dilator.

The Bowman probe was inserted perpendicular to the lower eyelid margin reaching the ampulla. The probe was then rotated horizontally to the lower canicular and inserted toward the lacrimal sac at slightly upward angle, while lacrimal traction was applied to the eyelid, when a hard stop was felt, the probe was rotated 90 degree and advanced toward the NLD until a "popping" sensation is felt. The probe was then removed, and the patency of the lacrimal drainage system was confirmed by saline irrigation from lower punctum. Flow of saline in throat was confirmed by placing a pediatric size suction in throat or some time we do fluorescein dye disappearance test,[14] by adding fluorescein stain to the tear.

Each patient received optiflox drop four times daily for 2 weeks. Patients were seen in the clinic

at one week, one month, and 3 months after probing. Success of probing was the main outcome measure and was defined as a complete remission of watering, discharge and reflux of the lacrimal sac on pressure at one week of procedure.

Statistical analysis

Carried out by use of Chi-square analysis, the result considered significant if P-value was less than 0.05.

RESULTS

Seventy six eyes from 73 patients were evaluated (3 individuals with bilateral CNLDO): the range included 30 males and 43 females. At the time of initial probing, patients ranged in age from 6 to 84 months (mean 15.67±13.58SD).

The mean age of children in group 1 was 9.29 ± 2.38 SD, group 2 was 19.31 ± 4.37 SD & in group 3 was 45.33 ± 19.46 SD. The study period was from 1st Jan 2009 to 31 Dec 2010. The success rate of probing was shown in **Table 1**.

The success rate in group 1 was 92.2% (47 of 51), in group 2 was 75% (12 out of 16) and in group 3 55.5% (5 out of 9), the success rate was the whole sample was 84.2%. P value was 0.05. None of the patients had any surgery or anesthesia-related complication.

There were two types of obstruction encountered during probing, simple and complex. In simple obstruction the resistance could be easily by passed with the help of the Bowman's probe and post probing syringing revealed a patent lacrimal system.

In complex obstruction however, the resistance could not be by passed and post probing syringing was not patent in any of these patients.[15,16]

Chi-square (4.87) analysis, showed significant difference in the cure rate with increasing age (p=0.05).

Table 1. Success rate of primary probing for congenital naso-lacrimal duct obstruction in 76 eyes.

Age (month)	Success rate	Failure rate	P-value
6-12	92.2%(47/51)	7.8%(4/51)	0.05
13-24	75% (12/16)	25% (4/16)	0.05
>25	55.5% (5/9)	44.5%(4/9)	0.05
Total	84.2%(64/76)	15.8%(12/76)	significant

DISCUSSION

The lacrimal drainage system begins forming at approximately 6 weeks of gestational age as a depression termed the lacrimal groove.

A solid cord of ectoderm is eventually buried as the mesoderm develops and extends, from the eyelids to the nose. Canalization of cord begins at approximately 3.5 months of gestational age and is usually completed at or near the time of birth, with lower part of the system being the last to open.

Anomalies may occur anywhere along the course of system.[5] Atresia of the NLD or dacryostenosis is the most common cause of epiphora in pediatric population. The most common site of obstruction is at the mucosal entrance into the nose (Valve of Hasner) under the inferior turbinate.[3]

Although NLD probing is a standard therapeutic procedure in the management of CNLDO, some controversy exists regarding the optimal timing of probing. In this study, the success rates were 92.15% (47 of 51) for group 1 (6-12 months),75% (12 of 16) in group 2 (13-24 months) and 55.5% (5 of 9) for individuals in group 3 (>25months). In similar study, Katowitz and Welsh,[17] reported a probing success rates of 98.2% in subjects aged 0-6 months, 95.9% in subjects aged 7-12 months, 76.8% in subjects aged 13-18 months, and 54.1% in subjects aged 19-24 months. Likewise the success rates in a study from Mannor *et al* [18] were 92% for subjects aged 0-12 months, 84.4% for subjects aged 13-24 months, 65% for subjects aged 25-36 months, and 63.5% for subjects aged 37-60 months.

The data from Ahn *et al*,[19] the reported success rates with probing were 95.4% for subjects aged 3-5 months, 92.8% for subjects aged 6-8 months, 77.7% for subjects aged 9-11 months, 72.7% for subjects aged 12-14 months and 66.7% for 15≥ months subjects, so the success rate increased when the procedure was done at earlier age.

Many factors are believed to affect the success rate of NLD probing. Age, bilaterality, prior failed probing attempt, prior failed conservative treatment, dilated sac and non-membranous CNLDO have all led to significant impact on probing success rate ($p<0.05$).[13] Similarly, new evidence also suggests, that concurrent fistula can reduce the probing success rate.[20]

Advocates of early probing suggest that early correction avoids months of morbidity due to epiphora and chronic dacryocystitis. They also suggest that postponement of the procedure may result in decreased success rate with simple probing because of chronic inflammation and secondary fibrosis.[7, 9, 10]

Some reports have suggested that the success rate of the intervention drops substantially in older children.[9-11] More complicated and invasive procedures, such as silastic intubation or DCR, have been attempted in these individuals.[21] So an early initial probing is a better policy to be adopted in our patients.

CONCLUSION

Probing is highly successful in the early age group (6-12 months), and should be adopted as a first line of treatment.

REFERENCES

1. Young JDH, Mac Ewen CJ. Managing congenital lacrimal obstruction in general practice. BMJ 1997; 15:293-6.
2. Cassidy TC. Developmental anatomy of the nasolacrimal duct. Arch Ophthalmol 1952; 47:141-58.
3. Piest KL, Katowitz JA. Treatment of congenital nasolacrimal duct obstruction. Ophthalmology Clinics of North America 1991; 4: 201-9.
4. Robb RM. Congenital nasolacrimal duct Obstruction. Ophthalmology clinics of North America 2001; 14: 443-46.
5. Kerstein RC. Congenital lacrimal abnormalities In: Principles and Practice of Ophthalmic Plastic and Reconstructive Surgery. WB Saunders Company; 1996; 2: 731-747.
6. James DH, MacEwen CJ. Managing congenital nasolacrimal duct obstruction in general practice. British Medical Journal 1997; 315: 293-96.
7. Honavar S, Vasudha EP, Rao GN. Outcome of probing for congenital nasolacrimal duct obstruction in older Children. Am J Ophthalmol 2000; 130: 42- 48.
8. Mannor GE, Rose GE, Kwabena FA, Eric Ezra. Factors affecting the success rate of nasolacrimal duct probing for congenital nasolacrimal duct obstruction. Am J Ophthalmol 1999; 127: 616-17.
9. Katowitz JA, Welsh MG. Timing of initial probing & irrigation in congenital nasolacrimal duct obstruction.Ophthalmology 1987; 94: 698-705.
10. Stager D, Baker JD, Frey T, Weakley DR Jr, Birch EE. Office probing for congenital nasolacrimal duct obstruction. Ophthalmic Surg 1992; 23: 482-84.
11. Robb RM. Success rates of nasolacrimal duct probing at time intervals after 1 year of age. Ophthalmology 1998; 105: 1307-10.
12. Kushner BJ. Management of nasolacrimal duct obstruction in children between 18 months and 4 years old. J-AAPOS 1998; 2: 57-60.
13. Mansoury EJ, Calhoun JH, Nelson LB, Harley RD. Results of late probing for congenital nasolacrimal duct obstruction. Ophthalmology 1986; 93:1052-54.
14. Steindler P, Mantovani E, Incorvaia C, Parmeggiani F. Efficacy of probing for children with congenital nasolacrimal duct obstruction: a retrospective study using fluorescein dye disappearance test and lacrimal sac echography. Graefes Arch ClinExpOphthalmol. 2009; 247:837-846.
15. Limbu B, Akin M, Saiju R. Age-based comparision of successful probing in Nepalese children with nasolacrimal duct obstruction. Orbit. 2010; 29:16-20.
16. Choi WC, Kim KS, Park TK, Chung CS. Intranasal endoscopic diagnosis and treatment in congenital nasolacrimal duct obstruction. Ophthalmic Surg Lasers. 2002; 33:288-292.
17. Katowitz JA, Welsh MG. Timing of initial probing and irrigation in congenital nasolacrimal duct obstruction. Ophthalmology.1987; 94:698-705.
18. Mannor GE, Rose GE, Frimpong- Ansah K, Ezra E. Factors affecting the success of nasolacrimal duct probing for congenital nasolacrimal duct obstruction. Am J Ophthalmol.1999; 127:616-617.
19. Ahn DH, Lew H, Kim HY, Lee SY. The effect of probing for congenital nasolacrimal duct obstruction. J Korean Ophthalmol Soc.1998; 39:836-840.
20. Welham RA, Bergin DJ. Congenital lacrimal fistulas. Arch ophthalmol. 1985; 103:545-548.
21. Repka MX, Chandler DL, Beck RW, *et al.* Primary treatment of nasolacrimal duct obstruction with probing in children younger than 4 years. Ophthalmology. 2008; 115:577-584.

Assessment of health promoting behaviors in relation to physical activity in elderly

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ABSTRACT

Background: Health promotion refers to those behaviors in which a person is engaged in to prevent disease and maximize health, it is beneficial in older adult in reducing disability and improving quality of life.

Objective: To assess these behaviors in relation to health outcomes among old population for the last five years of their lives in Mosul city.

Methodology: After obtaining a formal consent from the participant, a random sample of 112 old persons were included in this case series study. They were collected from elderly home in Mosul and from two main health centers, data collected in a period from the first January to the end of March in 2011. Peers correlation was used to examine this relationship.

Result: The study founded that exercise is predictive for less Basic Activities of Daily Living limitation (washing, bathing, eating, dressing, getting in/out of bed), Balanced diet was also found to be predictive for fewer Limitation of Instrumental Activities of Daily Living (moving from room to room, walking out of door, shopping, doing own house work). Inverse relations were found between stress management and both BADL/IADL. It was also founded between subjectively related health with both exercise and healthy balanced diet.

Conclusion: The study concluded that old population in Mosul were poorly engaged in a real health promoting behaviors, mainly for exercise and balanced diet.

Recommendation: The study recommend that a special attention should be given for old population Through a health promoting centers to increase their years of healthy life.

Keywords: Balanced diet, exercise, health promotion, old population.

تقييم سلوكيات تعزيز الصحة وعلاقتها مع مخرجات الصحة لدى كبار السن

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الخلاصة

المحتوى: تعزيز الصحة هو السلوك الذي يقوم به الفرد ليمنع المرض ويرفع مستوى الصحة، وهو يقلل الوفيات والعوق ويحسن نوعية الحياة لدى المسنين.

هدف الدراسة: يهدف البحث الحالي الى تقييم سلوكيات تعزيز الصحة من خلال علاقتها مع مخرجات الصحة لدى كبار السن خلال الخمس سنوات الأخيرة من حياتهم في مدينة الموصل.

المنهجية: ضمت الدراسة الوصفية عينة عشوائية مكونة من ١١٢ مسن من دار المسنين في مدينة الموصل ومن مركزي القدس والحدباء للرعاية الصحية الأولية وذلك بعد إستحصال الموافقة من قبلهم، جمعت المعلومات للفترة من بداية كانون الأول إلى نهاية آذار من عام ٢٠١١، طبق إرتباط بيرز لدراسة هذه العلاقة.

النتائج: وجدت الدراسة أن التمارين الرياضية لها علاقة طردية مع فعاليات الحياة اليومية الأساسية (غسل اليدين، الإستحمام، تناول الطعام، تغيير الملابس، النهوض من الفراش) كما وجدت أن الغذاء المتوازن له علاقة طردية مع فعاليات الحياة التشغيلية (الحركة داخل المنزل، المشي، التسوق، أداء الأعمال الخاصة). كما شخّصت الدراسة علاقة عكسية بين علاج الشد النفسي وكل من فعاليات الحياة الأساسية والتشغيلية، كما وجدت بين التقييم الذاتي للصحة وكل من التمارين الرياضية والغذاء المتوازن.

الإستنتاج: تستنتج الدراسة أن سلوكيات تعزيز الصحة ضعيفة الى حد ما بين المسنين وإنها مقتصرة حول التمارين الرياضية والغذاء المتوازن.

التوصيات: توصي الدراسة بضرورة النهوض بسلوكيات تعزيز الصحة للمسنين من خلال مراكز متخصصة لهذا الغرض من أجل توفير حياة صحية لهم .

الكلمات المفتاحية: الغذاء المتوازن، النشاط البدني، تعزيز الصحة، كبار السن.

INTRODUCTION

Increasing numbers of senior people is clearly defined in both developed and developing countries. There is a quasi-agreement that old age is considered when person reachs 65 years or older.[1] In 2005 the number of old age in Iraq was 906000 divided into and three groups; 65-74 years old were (526000), 75-84 years old were (283000), 85 years and older (97000), all forming 4.5% of total population.[2]

Although aging is a complex and dynamic process with physiological, psychological and sociological components,[1] but a successful aging and maintain high level of wellness among old persons can be achieved, this act needs central concerns from gerontologist.[3] Usually elderly define health in term of ability to function independently and effectively regardless of the presence of disease.[3,4] Measures to prevent disability and enhance functional status can reduce current health care cost for the elderly by 38%. Another estimate that health promoting measures can prevent or postpone 80% of all health problems,[5] physical exercise improves to controls arthritis and limits it's disability effect.[3]

Health promotion refers to those behaviors in which one engages for the aim of preventing disease and enhance wellbeing, it is beneficial in older adult in reducing death and disability and improving quality of life, this is done by slowing down processes of decline and maintaining high level physical functioning.[6-8]

By 2030 the elderly population throughout the world is expected to increase to 973 million, and the number of old adult will be more than triple in developing countries which will account for 71% of the world elderly population.[5] As the world population ages, there will be a growing demand for health care services that improve the quality of life as well as longevity. This can be seen in the national health objectives for 2010 addressing the health needs of elderly. A major threat throughout these objectives is to reduce activity limitation that impair the quality of life for older persons.[5]

The objective of the study is to assess health promoting efforts of old population in relation to their physical activity.

METHODOLOGY

The study used a case series design, after obtaining a formal consent from the participants, data were collected from random sample of 112 old persons. Simple random technique was used. The eligibility criteria required that the participants be at 65 years or older and they live in Mosul city. The sample was collected from the residents of elderly home in Mosul city and from those visiting two main health care centers, AL Hadbba and AL Qudis family medicine centers seeking health care for their acute or chronic illnesses at right and left sides of the city, data was collected through a period of three months from beginning of January to the end of March 2011.

To achieve the study objectives a special tool was used that it is consisted from three parts; the first part reflects the socio demographic characteristics of the study sample includes age, sex, residence, number of family members, previous and present work, and educational level. The second part includes predictors of health promoting activities for the last five years of their lives in which the investigator asked each participant about certain activities like exercise, avoidance of smoking and alcohol, stress management, frequent medical check up and balanced healthy diet. The responses arranged in a rating scale consisted from three options (never, sometimes and always).The third part of the tool is reflecting the health outcomes variables which was concentrating on the physical functioning of the respondents and includes:

1. Number of chronic health problems or diseases.
2. Presence of disability.

3. Subjectively rated health.
4. Hospitalization.

For health problems, the chronic conditions subscale of Older American Resources Study was used.[9] Items include: arthritis, osteoporosis, orthopedic problems, heart problem, hypertension, cardiovascular problem, asthma, emphysema or chronic bronchitis, cancer or leukemia, stroke or diabetes, gastrointestinal or liver disorder and urinary tract problems.

Disability or limitation for both basic activities of daily living (ADL) and instrumental activities of daily living, both derived from OARS functional limitation subscale, value of zero for no difficulty and one for difficult basic activities of daily living include washing, bathing, dressing, and putting on shoes, toileting, getting in/out of bed and eating. Instrumental activities of daily living includes getting upstairs, short walk in between rooms, long walk outside home, work duties, home duties, shopping and food preparation.

Subjectively rated health was assessed by self report of health in response to questions considering health of old persons over the past five years as: very poor, poor, fair, good and excellent. For hospitalization, respondents were asked to recall the number of times they were hospitalized for the last five years: as no hospitalization, one or more times of hospitalizations.

Mean of scores and pears correlation was used for statistical analysis of the presented data.[10] Mean of scores for each item equal to summation of frequencies multiplied by its rating then divided by number of sample, value of 1.5 and more is significant.

RESULTS

Table 1 shows that (53.6%) of the study sample at 65-69 years of age, (58%) of them females, (90.2%) from urban residence, (55.4%) of them were married. In all, (32.1%) were illiterate,35 (31.3%) were educated to secondary and higher level, only (39.3%) gave history of employment.

The **Table 2** shows significant result in performing exercise and in taking balanced diet. There was a deficiency in other areas as: avoidance of smoking, stress management and regular medical check up.

Table 3 shows that exercise which is one of health promoting behaviors is significantly predictive for less limitation of Basic activities of daily living in a proportional relation (0.321), balanced diet is also significantly predictive for less limitation of Instrumental activities of daily living in a proportional relation (0.321). Inverse relation was found between stress management and both BADL and IAD (-0.525) and (-0.356), also between exercise and subjectively related health (-0.356), and between balanced diet and subjectively related health (-0.525).

Table 1. Distribution of the study sample according to socio demographic characteristics (No=112).

Age	No.	%
60-69 years	60	53.6
70-79 years	38	33.9
80 years older	14	12.5
Gender		
Males	47	42
Females	65	58
Residence		
Rural	11	9.8
Urban	101	90.2
Marital status		
Widow	40	35.7
Divorced	5	4.5
Single	5	4.5
Married	62	55.4
Educational level		
Illiterate	36	32.1
Read and write	13	11.6
Primary school	28	25.0
Secondary school	16	14.3
College & above	19	17.0
Occupation		
Housewife	24	21.4
Unskilled	24	21.4
Skilled	20	17.9
Employed	44	39.3

Table 2. Mean scores of health promoting activities for the last five years of life among the study sample.

	Health promoting activities	Mean of scores
1.	Avoidance of smoking	1.23
2.	Exercise	1.63*
3.	Stress management	1.17
4.	Regular medical check up	1.12
5.	Balanced diet	1.55*

*Mean of scores of ≥ 1.5 is significant.

Table 3. Pearson correlation between physical health outcomes and dependent variables of health promoting behaviors among the study sample (n=112).

Health Behaviors	Basic ADL	Instrumental ADL	Numbers Of health conditions	Subjective Related health	Hospital Admission
Avoidance of smoking	-0.028	-0.098	1	-0.047	-0.077
exercise	0.321*	1	-0.098	-0.356*	-0.016
Stress management	-0.525*	-0.356 *	0.047	1	0.124
Balanced healthy diet	1	0.321*	-0.028	-0.525*	-0.054
Frequent medical check up	-0.054	-0.016	-0.077	0.124	1

* Significant correlation at 0.01.

DISCUSSION

This research focuses on health promoting behaviors and their preventive impact on long term quality of life and physical health of old population, We hoped to contribute to more comprehensive understanding of the role of prevention and proactivity in attainment of successful aging. The study concluded that health promoting behaviors among old population were poorly performed when compared with curative one, it is only significant for exercise and for taking healthy balanced diet, this result might be attributed to poor definition of health promotion among them and they might not be familiar to such activities as the youngest group of population in which a new concepts of health promoting life style were adopted. A 17% of the study sample have higher education, this may explain the defect in conducting this behaviors. Other study found that certain reasons for not engaging in health promoting activities among old population were the advanced age, not being told to do by their health care providers and having no interest in pursuing abnormal findings, so health care provider should consider it as individual approach and help older adults make their own decision about participation in these activities.[11] The linkage between educational level and health promotion is of Interest, it is founded that education, income are linked to health outcomes,[12] this may explain the poor engagement of old person taken by this study in a health promoting activities because (32.1%) of the sample were illiterate, (11.6%) just read and write.

The main result in this study is that exercise is significantly predictive for Little Basic Activities of Daily Living limitation, this result go with result of Gardner *et al* in which exercise has been shown to result in fewer limitation in activities among old persons like washing and bathing, dressing, putting on shoes, eating getting in /out of bed.[13] Weight reduction is an important part in the prevention of osteoarthritis, along with moderate exercise.[14]

This study also shows that good balanced diet is predictive for improving Instrumental Activities of Daily Living as getting from room to room, going out of doors, walking up and down stairs, doing own house work, shopping, this is similar to the results of Amarantose *et al*, who reported a remarkable improvement of quality of life and physical functioning with good balanced diet for elderly.[15] No positive significant result is found in this study between smoking and the health outcomes, this may be attributed to the fact that 30% of study sample were smoker males for more than 20 years of their lives.

A considerable limitations were found in this study, a lot of difficulties arises in collecting such a sample of elderly with difficult communication, the residents of Mosul elderly home not exceeding 60, and many of them unfit for interview. In addition to difficulties in finding similar published studies in our locality to be a source for proper comparison of the findings.

CONCLUSION

The old population included in this study show poor enrollment in health promoting activities and programs, some activities like exercise, healthy diet related to less limitation of both Basic and Instrumental Activities of Daily Living.

RECOMMENDATION

Health promotion is a basic building block of health, so the community in need for continuous health promoting programs which should be developed through a special centers and through educational curricula in order to improve healthy behaviors, attention also should be given to older adult who should live a health promoting life style.

REFERENCES

1. Alford D, Futrell M. Wellness and Health Promotion of the Elderly, Journal of Gerontology Nursing. 2007; 40(5): pp 221-226.
2. Ministry of planning and development, center statistical and information technology, directorate for cemm and man power. 2005; p18.
3. Susan A .Significance of health promotion to older adults, Journal of Holistic Nursing, American Holistic Nurses Association. 1998; 16(3): pp356-357.
4. Kahana E, Kahana B. Contextualizing successful aging; Invitation to the life course; toward a new understanding of late life. Amityville (NY): Baywood Publishing, 2003; pp225-55.
5. Clark M. Community health nursing, care of old population, promoting healthy life style, 5th edition, USA, Saunders company. 2008; pp 873-874.
6. Mary A, Melanie McEwen. Community/Public Health Nursing. Health Promotion and Risk Reduction. 6th edition, Saunders, 2011; pp361-362.
7. Varrama M, Pieper R, Sixsmith A. Care related quality of life in old age. 4th edition, springer, 2008;pp; 32-36.
8. Chai W, Nigg C, Pagano L, Dishman R. Association of quality of life with physical activity, International Journal of Behavioral Nutrition and Physical Activity. 2010; 83(7): 83-84.
9. George L and Fillenbaum G. OARS Methodology. A decade of experience. J Am Geriatric Society. 1995; 33: 607-15.
10. Moore D, William I, Michael A. Basic practice of statistics, 6th edition, USA, W.H. Freeman & company. 2013; pp 8-11.
11. Gatterman MI. Chiropractic and Health Promotion and Wellness. Sudbury, Mass.: Jones & Bartlett, 2007; pp 88-89.
12. Akinpelu A, Alonge T, Adekanla B, Odole A. Prevalence and pattern of symptomatic osteoarthritis in old age in Nigeria. Journal of Allied Health Sciences and Practice. 2009; 7(3): pp 2-3.
13. Gardner M, Robertson M, Campbell A. Exercise in preventing falls and fall related injuries in older people: a Review of randomized control trials. British Journal of Sport Medicine.2005; 34(1): pp 7-17.
14. Jamison JR. Maintaining Health in Primary Care. Guidelines Wellness in the 21st Century. St. Louis: Churchill Livingstone, 2001; pp 10.
15. Amarantose E, Martinez A, Dwyer J. Nutrition and quality of life in older adults, Journal of Gerontology, 2001; 56(2): s54-56. J Nippon Med Sch 2008; 75: 269-273.

The adjuvant effect of allopurinol with valsartan on the treatment of essential hypertension

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ABSTRACT

Background: Hyperuricemia is thought to contribute to development of hypertension, an elevation of uric acid in hypertension could be a consequence of reduced renal function, or elevated renal vascular resistance.

Objective: This paper aims to evaluate the adjuvant effect of allopurinol on blood pressure in newly diagnosed essential hypertensive patients with hyperuricemia.

Design: Double-blind randomized controlled clinical trial.

Patients and methods: Sixty newly diagnosed essential hypertensive patients with hyperuricemia in private clinic were enrolled in the study. They were randomly divided into two equal groups, group 1 was put on valsartan and allopurinol therapy, and group 2 was given valsartan and placebo therapy. Both groups were followed for four weeks duration. Blood pressure and serum uric acid levels were measured in both groups, before and after therapy.

Results: The systolic and diastolic blood pressures showed a significant reduction in group 1 with a mean difference of -24.20 ± 2.00 mmHg, for systolic blood pressure and -16.93 ± 4.73 mmHg for diastolic blood pressure. The reduction in serum uric acid was -3.25 ± 0.18, while the patients group that received valsartan and placebo did not show the same improvement.

Conclusion: The administration of allopurinol had beneficial effect on blood pressure, and can be used as adjunctive therapy for patients with hypertension, particularly if they have coexistent hyperuricemia.

Keywords: Adjuvant effect, allopurinol, essential hypertension, valsartan.

التأثير المساند لعقار الالوبيورينول مع الفالسارتان في علاج إرتفاع ضغط الدم الشرياني

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الخلاصة

الخلفية: يساهم فرط حمض البول في الدم في إرتفاع ضغط الدم الشرياني، قد يكون نتيجة لإنخفاض وظائف الكلى، أو إرتفاع المقاومة الوعائية الكلوية.

الهدف: نحن نهدف لتقييم التأثير المساند للألوبيورينول على ضغط الدم الأساسي مع عقار الفالسارتان.

المرضى وطريقة العمل: إن المسجلين في هذه الدراسة ستون مريضا تم تشخيصهم حديثا بارتفاع ضغط الدم الأساسي مع إرتفاع حامض البول في الدم في عيادة خاصة، وقسمت العينة عشوائيا إلى مجموعتين متساويتين، المجموعة الأولى إعتمدت على عقار الفالسارتان مع عقار الألوبيورينول، والمجموعة الثانية على عقار الفالسارتان والعلاج الوهمي، وتم متابعة كلتا المجموعتين لمدة أربعة أسابيع. تم قياس ضغط الدم ومستوى حامض البول في المجموعتين قبل وبعد العلاج.

النتائج: أظهر ضغط الدم الإنقباضي والإنبساطي إنخفاضا كبيرا في المجموعة التي تلقت عقار الفالسارتان في تركيبة مع الوبيورينول مع فروق من -٢٤,٢٠ ± ٢,٠٠ (مم زئبق)، لضغط الدم الإنقباضي و-١٦,٩٣ ± ٤,٧٣ (ملم زئبقي) لضغط الدم الإنبساطي، وكان الإنخفاض في حمض البول في الدم -٣,٢٥ ± ٠,١٨، بينما كان التحسن أقل في مجموعة المرضى التي تلقت العلاج الوهمي مع الفالسارتان.

الإستنتاجات: بينت الدراسة الحالية أن لعقارالألوبيورينول تأثير مفيد على ضغط الدم، ويمكن إستخدامها كعلاج مساعد في المرضى الذين يعانون من إرتفاع ضغط الدم وزيادة حامض البول.

الكلمات المفتاحيه: التأثير المساند، الالوبيورنيول، فرط ضغط الدم الأساسي، فالسارتان.

INTRODUCTION

Essential hypertension affects 25% of the world's population and is a major cause of stroke, congestive heart failure, end-stage renal disease, and myocardial infarction.[1] Hypertension is a common disease, affecting 30% to 35% of adults, and is especially common in groups at high risk of cardiovascular disease.[2] Hypertension is commonly associated with hyperuricemia.[3] It has been noted that 20%-40% of patients with essential hypertension have hyperuricemia, and may represent an additional risk factor for the development of cardiovascular disease.[4]

Hyperuricemia is present in 25% of untreated hypertensive subjects, in 50% of subjects taking diuretics, and in 75% of subjects with malignant hypertension.[5] Elevation of uric acid in hypertension could be a consequence of reduced renal function, the use of diuretics, the presence of hyperinsulinemia and oxidative stress, or elevated renal vascular resistance, which are commonly present in this condition.[6] Urate level is routinely elevated in metabolic syndrome, because of high insulin levels, which decrease urate excretion, and it is unclear whether lowering urate levels will ameliorate any of the clinical features of this syndrome.[7]

Despite a large number of safe and effective antihypertensive agents and useful lifestyle modification measures, optimal blood pressure (BP) control is attained in less than 40% of patients receiving therapy.[1]

Interestingly, raising uric acid levels in rats resulted in increased BP and the development of microvascular disease.[8] The mechanism of hypertension uric acid–mediated reduction in endothelial nitric oxide levels,[9,10] and stimulation of renin expression. [11] Studies in humans have also correlated uric acid levels with both endothelial dysfunction[12,13] and elevated plasma renin activity.[14,15] Furthermore, several controlled clinical trials have reported that lowering uric acid with xanthine oxidase (XO) inhibitors improves endothelial function under a variety of conditions.[16,18]

Aim of the study: To evaluate the adjuvant effect of allopurinol with valsartan on blood pressure control in patients with essential hypertension.

SUBJECTS AND METHODS

The study had been approved from College of Medicine, university of Mosul. Administration and ethical approval was obtained from Nineveh Directorate of Health. Newly diagnosed cases of grade 2 hypertension defined as systolic BP ≥ 160 mmHg and diastolic Bp≥ 100mmHg, with serum uric acid level of ≥ 7 mg/dL,[19] with no evidence of target organ damage, had never been treated with antihypertensive medication for any indication were enrolled in this double-blind randomized control trial study during the period from June 2012 to July 2013. Patients with renal, cardiovascular and hepatic disease were excluded. Formal consent was obtained from all participants after discussing the purpose of the research with them and they were divided after gender stratification by simple random technique into two groups: each group consisted of 30 patients, group 1 received 80 mg valsartan daily (using Diovan manufactured by Novartis), and allopurinol 100 mg (using Zyloric manufactured by Glasgow, Smith, Klin) for 4 weeks, and group 2 received valsartan 100 mg and placebo for 4 weeks duration. Both allopurinol and placebo were arranged in the form of unmarked capsules. Blood pressure and serum uric acid were measured before starting therapy and at the end of 4 weeks in both groups. Fasting serum glucose, lipid profile, serum urea, serum creatinine were measured in all patients in addition to general urine examination, electrocardiography and echocardiography.

Measurement of blood pressure: It was vital that the blood pressure readings were as accurate as possible, measurements were made to the nearest 2mmHg, in the sitting position with the arm supported, after 5 minutes' rest; the cuff contained a bladder that encompasses at least two-thirds of the circumference of the arm.

Uric acid measurement was done, using standard kit manufactured by Randox Company following the instructions.

Independent t-test for two means was used in comparing between the two groups. Also paired t-test was used to analyze the difference of various parameters in each group. All values were expressed as mean ± standard deviation (SD).

RESULTS

Sixty patients were enrolled in this study, they were 44 males and 16 females as in **Table 1**.

Table 2 shows the patients characteristics of the studied groups before therapies. There were no differences between the groups regarding mean age and pretreatment systolic and diastolic blood pressure.

Table 3 shows the results of the comparison of the studied parameters of group 1 before and after therapy. There were a highly significant reduction in both systolic, diastolic BP, and uric acid (P = 0.001).

Table 4 demonstrates the results of the comparison of the studied parameters of group 2 before and after therapy. There were a highly significant reduction in both systolic and diastolic BP, and uric acid (P = 0.001).

Table 5 shows that the reduction in systolic and diastolic BP in group 1 was significantly superior to systolic and diastolic BP in group 2 with a mean differences of -24.20±2.00 systolic blood pressure and -16.93±4.73 for diastolic blood pressure in group 1 versus -20.33±2.33 for systolic BP, and -9.84±0.84 for diastolic BP in group 2.

Table 1. Sex distribution of the studied groups.

Groups	Group 1 (Hypertensive patient on Valsartan plus Allopurinol)		Group 2 (Hypertensive patient on Valsartan plus placebo)	
	No.	%	No.	%
Male	23	70%	21	65%
Female	7	30%	9	35%
Total	30	100%	30	100%

Table 2. Patient's characteristics of the studied groups.

Parameter	Group 1 Mean ± SD	Group 2 Mean ± SD	P-value *
Age (years)	51.47 ± 6.51	52.3 ± 0.6.8	0.631
Systolic BP (mmHg)	162.83 ± 6.25	167.3 ± 9.41	0.034
Diastolic BP (mmHg)	102.83 ± 10.06	102.67 ± 9.71	0.950
Uric acid (mg/dL)	7.43 ± 0.84	7.25 ± 0.68	0.365

*independent t-test for two means was used.

Table 3. The comparison of the studied parameters of the group 1 before and after the therapy.

Parameter	Before Mean ± SD	After Mean ± SD	Mean difference	P-value*
Systolic BP (mmHg)	162.83 ± 6.25	138.5±7.78	-24.20 ±2.00	0.001
Diastolic BP (mmHg)	102.83± 10.06	85.90±5.33	-16.93 ±4.73	0.001
Uric acid (mg/dL)	7.93 ± 0.84	4.70 ± 0.61	-3.25±0.18	0.001

*paired t-test for two means was used.

Table 4. The comparison of the studied parameters of group 2 before and after the therapy.

Parameter	Before Mean ± SD	After Mean ± SD	Mean difference	P-value*
Systolic BP (mmHg)	167.3±9.41	146.77±11.04	-20.33 ±2.33	0.001
Diastolic BP (mmHg)	102.67±9.71	90.83 ± 8.82	-11.84 ±0.84	0.001
Uric acid (mg/dL)	7.25 ± 0.68	6.52 ± 0.52	-0.73 ± 0.16	0.001

*paired t-test for two means was used.

Table 5. The comparison of the mean difference of the systolic and diastolic BP of group 1 versus group 2 after therapies.

Parameter	valsartan and allopurinol	valsartan and placebo	P- value *
Systolic BP (mmHg)	-24.20±2.00	- 20.33±2.33	0.001
Diastolic BP (mmHg)	-16.93±4.73	- 9.84±0.84	0.001

*paired t-test for two means was used.

DISCUSSION

Hypertension is associated with endothelial dysfunction. One major factor responsible for the impaired regulation of vascular tone is the increase in oxidative stress, leading to a premature breakdown of endothelium derived vasoactive nitric oxide.[20]

An important source for oxygen free radical production within the endothelium is the enzyme xanthine oxidoreductase. In its oxidase form this enzyme generates superoxide anion and hydrogen peroxide as byproducts. [21]

The present study was performed to evaluate the effect of allopurinol on a sample of hypertensive patients in Mosul population treated by valsartan. The study involved 60 patients were randomly allocated into two equal groups to rule out the effect of different variables as potential confounders.

The study clearly showed amarked improvment in the systolic and diastolic blood pressurs in the group who were taken valsartan (80 mg) and allopurinol (100 mg) daily for four weeks compaired to the group who were put on valsartan (80 mg) alone.

A study done by Feig *et al* in 2004,[2] in which adolescents with newly diagnosed essential hypertension were treated with allopurinol for one month, a reduction of serum uric acid level from a mean of 6.9 mg/dL to 3.3 mg/dL with 200 mg of allopurinol twice daily significantly reduced casual blood pressure measurements, and led to normalization of blood pressure in 4 of 5 subjects.

A study done by Feig *et al* in 2008,[6] using allopurinol 200 mg twice daily for 4 weeks resulted in amean change in systolic BP for group who were on allopurinol of −6.9 mm Hg (95% confidence interval [CI], −4.5 to −9.3 mmHg) vs −2.0 mm Hg (95% CI, 0.3 to−4.3 mm Hg; P=.009) for placebo, and the mean change in diastolic BP for allopurinol groupwas −5.1 mm Hg (95% CI, −2.5 to −7.8 mm Hg) vs −2.4 (95% CI, 0.2 to −4.1; P=.05) for placebo group, and allopurinol treatment resulted in normal BP in 20 of 30 participants, including 19 of the 22 (86%) whose uric acid levels were lowered to less than 5.0 mg/ dL. In contrast, only 1 of 30 participants became normotensive while receiving placebo during the study.

It has been shown that allopurinol treatment can improve forearm blood flow and endothelial dysfunction in patients with hypertension. [22] In the context of reperfusion injury, it is understood that xanhhine oxide derived oxygen free radicals are a major contributor to impaired flow and tissue damage and that allopurinol may exert protective effects against these reperfusion injuries.[23]

Theoretically, inhibiting xanthine oxide with reducing serum uric acid may improve endothelial function and vasodilator capacity. A potent way to prevent xanthine oxide-generated free radicals in the clinical setting is to use the orally allopurinol. There is evidence to suggest that allopurinol may prevent free radical–induced tissue damage; for example, allopurinol decreases reperfusion injury during coronary artery bypass graft surgery[24,25] and improves cardiorespiratory function in an animal transplantation model [26] and in humans.[27] Allopurinol may even speed up the repletion of high-energy phosphates during ischemia[28]. More recently, data have emerged to suggest that the acute intra-arterial infusion of oxypurinol, the active metabolite of allopurinol, may improve endothelial function in hypercholesterolemic humans.[29] It is possible that part of the beneficial effect exerted by allopurinol may be attributed to its antioxidant properties. Allopurinol, by blocking xanthine oxide, will reduce superoxide anion and uric acid production by this enzymatic pathway.[30]

In experimental animals intrarenal renin expression has been shown to be mediated by uric acid,a clue to the mechanism by which allopurinol lowe rBP, and this was the observation that systemic vascular resistance and plasma renin activity both decreased significantly with this drug.[9]

Toma *et al*,[31] reported that uric acid stimulates renin release via a macula densa dependent mechanism using an in vitro microperfused afferent arterioleglomerular preparation. Those studies showed that lowering uric acid may act at least in part, through reducing plasma renin activity.

In conclusion the study represent a potentially new therapeutic approach, that of control of a biochemical cause of hypertension, rather than nonspecifically lowering elevated BP. Although not representing a fully developed therapeutic strategythe study raises an alternative strategy that may prove to be more effective than currently available options.

REFERENCES

1. Sarafidis PA, Bakris GL. State of hypertension management in the United States: confluence of risk factors and the prevalence of resistant hypertension.J Clin Hypertens (Greenwich). 2008; 10(2):130-139.

2. Feig DI, Nakagawa T, Karumannchi SA *et al.* Hypothesis: Uric acid,nephron number, and the pathogenesis of essential hypertension. Kidney International, 2004; 66: 281–287.

3. Cannon PJ, Stason WB, Demartini FE, Sommers SC, Laragh JH. Hyperuricemia in primary and renal hypertension .N Eng. J Med. 1966; 275(9):457- 464.

4. Trachtman H, Valderrema E, Futterweit S. Nephrotoxicity of allopurinol is enhanced in experimental hypertension. Hypertension 1991; 17: 194- 202.

5. Johnson RJ, Segal MS, Srinivas T, *et al.* Essential hypertension, progressive renal disease, and uric acid: a pathogenetic link? J Am SocNephrol. 2005; 16(7):1909-1919.
6. Feig DI, Soletsky B, Johnson RJ. Effect of Allopurinol on blood pressure of adolescents with newly diagnosed essential hypertension. JAMA. 2008; 300:924-932.
7. Fields TR, Paget SA, Beary JF. Gout etiopathogenesis: Manual of Rheumatology and Outpatient Orthopedic Disorder 5th edition. Philadelphia. 2006; 328-335.
8. Mazzali M, Hughes J, Kim YG, *et al.* Elevated uric acid increases blood pressure in the rat by a novel crystal-independent mechanism. Hypertension. 2001; 38:1101-1106.
9. Sanchez-Lozada LG, Tapia E, Lopez-Molina R, *et al.* Effects of acute and chronic L-arginine treatment in experimental hyperuricemia. Am J Physiology. 2007; 292(4):1238-1244.
10. Johnson RJ, Kang D, Feig D, *et al.* Is there a patho-genetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension .2003; 41:1183-1190.
11. Mazzali M, Kanellis J, Han L, *et al.* Hyperuricemia induces a primary renal arteriolopathy in rats. blood pressure-independent mechanism. Am J Physiol Renal Physiol. 2002; 282(6): 991-997.
12. Erdogan D, Gullu H, Caliskan M, *et al.* Relationship of serum uric acid to measures of endothelial function and atherosclerosis in healthy adults. Int J Clin Pract. 2005; 59(11):1276-1282.
13. Zoccali C, Maio R, Mallamaci F, Sesti G, Perticone F. Uric acid and endothelial dysfunction in essential hypertension. J Am SocNephrol. 2006; 17(5):1466-1471.
14. Gruskin AB. The adolescent with essential hypertension. Am J Kidney Dis. 1985; 6(2):86-90.
15. 15. Saito I, Saruta T, Kondo K, *et al.* Serum uric acid and the rennin angiotensin system in hypertension.J Am Geriatr Soc. 1978;26(6):241-247.
16. Doehner W, Schoene N, Rauchhaus M, *et al.* Effects of xanthine oxidase inhibition with allopurinol on endothelial function and peripheral blood flow in hyperuricemic patients with chronic heart failure: results from 2 placebo-controlled studies. Circulation, 2002; 105(22):2619-2624.
17. Mercuro G, Vitale C, Cerquetani E, *et al.* Effect of hyperuricemia upon endothelial function in patients at increased cardiovascular risk. Am J Cardiol. 2004; 94(7):932-935.
18. Farquharson CA, Butler R, Hill A, Belch JJ, StruthersAD. Allopurinol improves endothelial dysfunction in chronic heart failure. Circulation, 2002; 106(2):221-226.
19. Crook MA. Clinical chemistry and metabolic medicine ,7thedition, Holder Arnold.UK.2006;pp 301-307.
20. Cockcroft JR, Chowienczyk PJ, Benjamin N, Ritter JM. Preserved endothelium dependent vasodilatation in patients with essential hypertension. N Eng. J Med. 1994; 330: 1036 –1040.
21. Doehner W, Schoene N, Rauchhaus M *et al*. Effects of xanthine oxidase Inhibition with allopurinol on endothelial function and peripheral blood flow in hyperuricemic patients with chronic heart failure : results from 2 placebo-controlled studies. Circulation 2002, 105:2619-2624.
22. Butler R, Morris AD, Belch JJF, *et al.* Allopurinol normalizes endothelial dysfunction in Type 2 diabetics with mild hypertension. Hypertension 2000, 35:746-751 .
23. Alper AB,Chen W,Yau L *et al*, Childhood uric acid predicts adult blood pressure. Hypertension. 2005; 45(1): 34-38.
24. Selby JV, Friedman GD, Quesenberry CP. Precursors of essential hypertension: pulmonary function, heart rate, uric acid, serum cholesterol, and other serum chemistries. Am J Epidemiol. 1990;131(6): 1017-1027.
25. Gimpel JA, Lahpor JR, Vandermolen AJ, Damen J, Hitchcock JF. Reduction of reperfusion injury of human myocardium by allopurinol: a clinical study. Free Radic Biol Med. 1995;19:251–255.
26. Qayumi AK, Godin DV, Jamieson WRE, Ko KM, Poostizadeh A. Correlation of red cell anti-oxidant status and heart-lung function in swine pre-treated with allopurinol. Transplantation. 1993;1:37– 43.
27. Coghlan JG, Flitter WD, Clutton SM, Panda R, Daly R, Wright G, Ilsley CD, Slater TF. Allopurinol pre-treatment improves postoperative recovery and reduces lipid-peroxidation in patients undergoing coronary artery bypass grafting. J Thorac Cardiovasc Surg. 1994;1:248 –256.
28. Pisarenko OI, Lakomkin VL, Studneva IM, Timochin AA, Kuzmin AL, Ruuge EK, Kapelko VI. Allopurinol-enhanced post ischaemic recovery in the isolated rat heart involves repletion of high energy phosphates. Biochem Med Metab Biol. 1994;51:16 –26.
29. Cardillo C, Kilcoyne CM, Cannon RO III, Quyyumi AA, Panza JA. Xanthine oxidase inhibition with oxypurinol improves endothelial function in hypercholesterolemic but not in hypertensive patients. Hypertension. 1997;30:57– 83.
30. Laura G, Sanchez-Lozada, Tabia E *et al.* Mild hyperuricemia induces glomerular hypertension in normal rats. Am J Physiol Renal Physiol 2002; 283 :1105–1110.
31. Toma I, Kang J, Meer E, Pet-Peterdi J. Uric acid triggers renin release via a macula dens dependent pathway. JAMA. 2008; 300:924–32.

Prospective randomized comparison of low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy

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ABSTRACT

Background: Postoperative shoulder tip pain occurs frequently following laparoscopic cholecystectomy. The origin of shoulder pain is partly understood, but it is commonly assumed that the cause is overstretching of the diaphragmatic muscle fibers due to high rate of insufflations. The aim of this study is to compare the frequency and intensity of shoulder tip pain between low pressure (7 mmHg) and standard-pressure (14 mmHg) pneumoperitoneum after laparoscopic cholecystectomy.

Setting: Aljumhori Teaching Hospital during the period from January 2011 to June 2012.

Design: A prospective randomized study.

Patients and methods: One hundred and forty consecutive patients undergoing elective laparoscopic cholecystectomy were randomized prospectively into two groups, either low pressure (group A) or standard pressure (group B) pneumoperitoneum, they were blinded to the research doctors who assessed the patients during the postoperative period by the visual analogue scale (VAS) of pain. Comparative analysis between the two groups included gender, mean age, operative time, complication rate and postoperative shoulder tip pain.

Results: The demographic data were nearly similar in the two groups. There were no significant intraoperative complications in both groups, likewise the mean operative time was nearly similar in either group. The mean frequency and intensity of postoperative shoulder tip pain assessed by visual analogue scale was less in group A than in group B.

Conclusion: No difference was found between low pressure and standard pressure pneumoperitoneum in the duration of operation and complication, but low pressure pneumoperitoneum tended to produce lower incidence and intensity of shoulder tip pain.

Keywords: Gall stones, laparoscopy, low pressure, standard pressure.

مقارنة مستقبلية عشوائية بين الضغط الواطئ والضغط القياسي للصفاق في عمليات إستئصال المرارة بالناظور

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الخلاصة

أهداف الدراسة: هو مقارنة شدة وتكرار الآم الكتف بين الضغط الواطئ (٧ ملم زئبق) والضغط المعياري (١٤ ملم زئبق) داخل الغشاء البروتيني بعد عمليات إستئصال المرارة بالمنظار.

المشاركون وطريقة إجراء البحث: دراسة مستقبلية عشوائية، أجريت في المستشفى الجمهوري على ١٤٠ مريضا ومريضة مصابين بحصى المرارة خلال الفترة من كانون الثاني ٢٠١١ الى حزيران ٢٠١٢، تم تقسيم المرضى إلى مجموعتين كل مجموعة تتكون من ٧٠ مريضا، المجموعة (آ) تم إجراء عملية إستئصال المرارة لهم بواسطة تنظير البطن تحت الضغط الواطئ (٧ ملم زئبق)، والمجموعة الثانية تم إستئصال المرارة بواسطة تنظير البطن تحت الضغط المعياري (١٤ ملم زئبق)، وتم قياس شدة الآم الكتف عن طريق أطباء لايعرفون عن أي مجموعة يعودون هؤلاء المرضى بواسطة المقياس البصري المماثل.

النتائج: لا يوجد أي زيادة في فترة إجراء العملية أو المضاعفات في المجموعة (أ) مقارنة بالمجموعة (ب) وهي متقاربة جدا بين المجموعتين. ولكن وجدنا أن معدل شدة الآم الكتف بعد العملية كان أقل في المجموعة (أ) مقارنة بالمجموعة (ب).
الإستنتاج: لايوجد فرق في فترة إجراء العملية والمضاعفات بين الضغط الواطئ والضغط المعياري في عمليات إستئصال المرارة بالمنظار، لكن في حالة الضغط الواطئ تكون شدة الآم الكتف أقل.
الكلمات المفتاحيه: حصيات المرارة، منظار البطن، الضغط الواطئ، الضغط المعياري.

INTRODUCTION

Within an exceptionally short time, laparoscopic cholecystectomy (LC) has widely replaced open cholecystectomy (OC) as the standard treatment for symptomatic cholelithiasis.[1] Since the introduction of (LC), pneumoperitoneum at 15 mmHg has been commonly used for all laparoscopic procedures. Despite its widespread use, this pressure is not without its problems and disadvantages.[2] Alternative surgical technique, low- pressure CO_2 maintained pneumoperitoneum, has been used in an attempt to reduce the impact on the cardiopulmonary function associated with the application of conventional pressure (14-15mmHg).[3,4,5] Serious and potentially lethal complications including DVT, MI, atelectasis and pneumonia, especially in elderly or high risk patients, have been attributed to the physiological effects of pneumoperitoneum at 14 mmHg.[2]

During laparoscopic cholecystectomy adequate working space is required in the abdomen for good exposure that contributes to satisfactory results and patients safety.[5] The most common method to create working space in the abdomen is carbon dioxide insufflation into the peritoneal cavity and then holding it at constant pressure.[5,6] Low pressure pneumoperitoneum (7mmHg) is enough to warrant a sufficient operative space without a need for conversion in a significant percentage of laparoscopic operations.[7]

Shoulder tip pain frequently occurs after (LC) making postoperative recovery less comfortable. The etiology of postoperative pain is extremely complex and a precise evaluation of the various causes is still difficult to achieve. In particular, shoulder-tip pain is presumed to be linked to CO_2 insufflation, and its intensity is often so strong that analgesics must be administered frequently. The reported incidence of shoulder-tip pain following (LC) varies between 30% and 50%.[6] It is well known that the visceral peritoneum is sensitive-free to pain on sharp cutting and puncture wounds, on the other hand, it is highly sensitive to distension, tearing and separation.[8] Visceral pain and shoulder pain account for most of the pain experienced after LC, whereas patients complain more of the parietal pain after laparotomy.[1]

An emerging trend has been the use of low pressure pneumoperitoneum instead of the standard pressure pneumoperitoneum in an attempt to lower the impact on the human physiology while providing adequate working space.[5,9,10]

This method appears to have little adverse effect on the cardiac and respiratory functions. Other possible advantages of low pressures during pneumoperitoneum appear to be lower incidence of shoulder tip pain in the post-operative period and better quality of life in the early postoperative period.[5,11,12]

Pain is a subjective sensation, and its measurement and analysis are difficult. Visual analogue scale (VAS) is usually presented as 100-mm horizontal line on which the patient pain intensity is represented by points between the extremes of 'no pain at all' and ' worst pain imaginable'. Its simplicity, reliability, and validity, as well as its ratio scale properties make (VAS) the optimal tool for describing pain severity and intensity.[1]

Aim of the study is to evaluate the influence of low pressure pneumoperitoneum on the feasibility, safety, and the postoperative shoulder tip pain pneumoperitoneum during laparoscopic cholecystectomy.

PATIENTS AND METHODS

One hundred forty patients with American Society of Anesthesiologists (ASA) grade 1 or 2 having symptomatic gall stones scheduled for elective laparoscopic cholecystectomy during the period from January 2011 to June 2012 were enrolled in this study. The patients were divided into two

groups (70 in each group) and were randomly allocated to one of the two groups. In group A which represent the odd numbers, low pressure pneumoperitoneum (7 mm Hg) was generated, and in group B which represent the even numbers, standard pressure pneumoperitoneum (14 mmHg) was created. Exclusion criteria included acute cholecystitis, choledocholethiasis, and previous abdominal surgery, in addition five patients who were changed from low to standard pressure pneumoperitoneum because of poor visualization of the surgical field were excluded from the study; four of them were obese females, and one was muscular male. All patients were admitted to the hospital the day before surgery, for investigations, anesthetic consultation, and had an informed consent.

All the surgical procedures were performed under standard general anesthesia, by surgeons experienced in LC. Pneumoperitoneum was created with CO_2 insufflation using the open (Hasson) method until abdominal pressure of either (7 mm Hg) low pressure group or (14 mmHg) standard pressure group was reached. In all patients, the routine 4 ports and the standard American technique was achieved. Residual carbon dioxide was evacuated at the end of the procedure, through the open valve trocars, and then removal of the trocars under vision. Duration of surgery, intraoperative complications, and bile spillage were recorded but no drain was left. All patients were prescribed postoperative analgesia with diclofenac 75 mg.

The degree of postoperative shoulder-tip pain was assessed by means of a visual analogue scale (VAS) at 3, 6, 12, and 24 h, postoperatively. The pain scale, with scores ranging from 0 (no pain) to 10 (unbearable pain), was recorded by a doctor who was blind to the group allocation of the patients, allowing patients to mark a point along the scale that represented their pain at that time. The patients were aware and informed that the scale is analyzing the presence and intensity of the shoulder pain alone, but not the postoperative abdominal pain. The postoperative shoulder pain was assessed in a double blinded manner; neither the patient nor the assessor were aware of the technique to which the patients has been randomized. Analgesic requirement and duration of hospital stay were recorded.

RESULTS

The age, gender, and the ASA grade were similar in both groups. There were no differences in the mean duration of surgery, length of hospital stay or intraoperative bile spillage **Table 1**.

The proportion of patients that complained of shoulder tip pain presenting during the first 24 hours after operation was lower in group A than in group B. In group A 12 (19%) out of 70 patients complained of shoulder tip pain in the postoperative period, while in group B 23 (33%) out of 70 patients complained of shoulder tip pain which was highly significant as in **Table 2**. Shoulder tip pain started after 3-6 hours and peaked in both groups after 12 hours, then gradual improvement was felt after that time.

The mean intensity of shoulder tip pain was significantly lower in group A than in group B. Pain score revealed that postoperative shoulder tip pain was significantly less intense at 12 and 24 hours postoperatively. The shoulder tip pain score was very low in group A at 24 h compared with group B, and the mean intensity of the shoulder tip pain exceeded a score of 3 at 24 hour in group B as in **Table 3**.

Table 1. Patients details (mean ±SD).

	Group A low pressure	Group B high pressure	*p* value
Mean age (years) ±SD	41.7± 12.3	39.5± 11.9	0.449
Female/Male	58/12	54/16	0.582
Operation time (min) ±SD	50.7± 12.7	47.4± 10.6	0.729
Postoperative hospital stay	1.23	1.12	0.322
Bile spillage	9	7	0.290
Analgesic (not required)	27	22	0.356

Table 2. No. of patients with postoperative shoulder tip pain.

Group	Group A	Group B	*p* value
Postoperative Shoulder pain	12 (19%)	23 (33%)	0.001

Table 3. postoperative shoulder tip pain (mean ±SD).

Time after surgery (h)	Group A (n= 70)	Group B (n=70)	*p* value
3	0.83±0.71	2.46±1.31	0.000
6	3.20±1.51	4.06±2.11	0.055
12	4.91±1.36	6.37±1.91	0.001
24	1.14±1.03	4.31±1.51	0.000

In both groups there were patients who did not require any analgesic medication 27 (38.5 %) in group A, and 22 (31.4 %) in group B, with no significant difference between the two groups. During the first 24 hours 6 patients in the low-pressure group and 10 patients in the high-pressure group required extra analgesic medication for severe pain, but also it was not significantly different between the two groups.

Apart from postoperative pain, there were no significant intraoperative or postoperative complications in either group. There was no correlation between duration of surgery and postoperative shoulder tip pain. There were no significant difference between the two groups in terms of time to return to oral food, and discharge.

DISCUSSION

Although pain occurring post laparoscopic surgery is less severe and of shorter duration than that after open surgery, it still causes considerable discomfort and increases stress response in some patients.[13] The maintenance of elevated intraabdominal pressure for the duration of the procedure is associated with numerous undesirable consequences including postoperative shoulder tip pain.[14] The etiology and pathogenesis of the shoulder tip pain is only partly understood, but it is commonly assumed that the cause is overstretching of the diaphragmatic muscle fibers owing to the high rate of insufflation, and the low insufflation rate significantly reduces shoulder pain.[6,13] Some authors claim that it may be caused by diaphragmatic irritation by a chemical material, as carbon dioxide may be transformed by combining with fluid in the peritoneal cavity into an irritative carbonic acid.[15] This opinion is supported by the observation that, patients experience less pain if nitrous oxide is used instead of carbon dioxide in laparoscopic cholecystectomy.[16]

This study demonstrated that the incidence of shoulder tip pain after low pressure pneumoperitoneum was significantly lower as compared to the standard pressure laparoscopic cholecystectomy, 23 (33%) patients had shoulder pain in group B, while only 12 (19%) in group A with a (*p* value 0.001). This result differs from the study done by Kanwer who found no significant difference between the two groups, but he found lower demand for analgesia in the low pressure group.[5] These results are slightly different from those of Mir Y *et al*[14] where only 10% of their low pressure group developed shoulder pain. On the other hand, studies conducted by Sandhu T,[13] Sarli[6] and Berczynski[11] showed that the incidence of shoulder tip pain in low pressure group is lower than shoulder tip pain in standard pressure group, but this results did not reach statistical significance.

In the present study the mean intensity of postoperative shoulder tip pain at 3, 6, 12, 24 h recorded on VAS was lower in patients who underwent laparoscopic cholecystectomy with low pressure pneumoperitoneum compared with standard pressure. The difference between low pressure and standard pressure was highly significant at 3, 12, and 24 hrs, but did not reach statistical significance at 6 h postoperatively, although the intensity of pain was lower in the low pressure group. These results are different from the results of Sarli L[6] and Yasir M,[14] also it is different from the study done by Mahmut K *et al*[1] where the mean intensity pain was lower in the low pressure group than the standard pressure group, but it was statistically not significant. Many centers have reported that LC performed with low pressure pneumoperitoneum resulted in a better quality of life postoperatively as compared to LC performed with standard pressure, this is attributed to lower incidence and intensity of postoperative pain in low pressure pneumoperitoneum group with fewer requirement of analgesics in the postoperative period.[5]

None of our patients needed conversion to open cholecystectomy with no major complication in both groups, and the bile leakage is comparable between the two groups. Likewise the operative time and the duration of hospital stay were comparable in the two groups. These results warrant the feasibility and the safety of low

pressure LC. The majority of the patients in group A could be operated on easily and safely with good visualization of the Calot's triangle, but when the operative field is not well visualized in low pressure LC, it can be increased to the standard pressure, as in five of our patients who were obese or muscular; and this may be attributed to the thick abdominal wall which requires more pressure to lift. In agreement with our study, Sarli[6] mentioned that he had no significant complications and no significant difference in the time of operation.

In this study the analgesic requirements for shoulder tip pain were less in low pressure laparoscopic cholecystectomy as compared to standard pressure laparoscopic cholecystectomy, but the difference between the two did not reach statistical significance, this result was comparable with that of Sandhu.[13]

In conclusion, no difference was found between low pressure and standard pressure pneumoperitoneum regarding duration of operation and complication, but low pressure pneumoperitoneum resulted in lower incidence and lesser intensity of shoulder tip pain, although it did not reach statistical significance at some recordings. However, low pressure may affect the visual field especially in obese or muscular patients, therefore it is not recommended in these patients.

REFERENCES

1. Mahmut K, Tamer E, Mesut T, *et al.* Randomized, prospective comparison of postoperative pain in low versus high pressure pneumoperitoneum. ANZ J Surg 2005; 75: 693-696.
2. Davides D, Birbas K, Vezakis A. Routine low pressure pneumoperitoneum during laparoscopic cholecystectomy. Surg Endosc 1999; 13: 887-889.
3. Yih-Huei U, chen –Yi Kuo, Kuo Chang Wen. Randomized trial of low pressure carbon dioxide elicited pneumoperitoneum versus abdominal wall lifting for laparoscopic cholecystectomy. J Chin Med Assoc 2007; 70(8): 324-330.
4. Bhandari D, Tidke S, Sharma V, *et al*. Hemodynamic changes associated with laparoscopic cholecystectomy: effect of oral clonidine premedication. Journal of pharmacy 2012; 2(4): 72-77.
5. kanwer DB, Kaman L *et al*. Comparative study of low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy- a randomized controlled trial. Gastroenterology 2009; 30(3): 171-174.
6. Sarli L, Costi R, *et al*. Prospective randomized trial of low pressure pneumoperitoneum for reduction of shoulder tip pain following laparoscopy. B J Surg 2000; 87: 1161-1165.
7. Duck-Kyoung Kim, IL- Young Cheong, Ga-Young Lee *et al*. Low pressure pneumoperitoneum does not reduce the incidence and severity of postoperative nausea and vomiting following gynecologic laparoscopy. Korean J Anesthesiol 2006; 50 (6): 36-42.
8. Hodzic E, Imamovic S, Hasukic S, *et al*. Postoperative pain in open vs. laparoscopic cholecystectomy with and without local application of anesthetic. Medicinski Glasnik 2011; 8 (2): 243-248.
9. Joris J, Cigarinil L, Legrand M, *et al*. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. Br J Anaesth 1992; 63: 341-5.
10. Baraka A, Jabbour S, Hammond R, *et al*. End tidal carbon dioxide tension during laparoscopic cholecystectomy. Anaesthesia 1994; 49: 403-6.
11. Barczynski M, Herman RM. Aprospective randomized trial on comparison of low pressure and standard pressure pneumoperitoneum for laparoscopic cholecystectomy. Surg Endosc 2003; 17:533-538.
12. Wallace DH, Serpell MG, Baxter JN, *et al*. Randomized trial of different insufflation pressures for laparoscopic cholecystectomy. Br J Surg 1997; 84: 455-8.
13. Sandhu T, Yamada S, Ariyakachon V, *et al*. low pressure pneumoperitoneum versus standard pneumoperitoneum in laparoscopic cholecystectomy, a prospective randomized clinical trial. Surg Endosc 2009; 23(5): 1044-1047.
14. Yasir M, Mehta KS, Banday VH, *et al*. Evaluation of postoperative shoulder tip pain in low pressure versus standard pressure pneumoperitoneum during laparoscopic cholecystectomy. The surgeon 2012; 10(2): 71-4.
15. Nyerges A. Pain mechanisms in laparoscopic surgery. Semin laparosc surg 1994; 1: 215-18.
16. Aitola P, Airo I, Kaukinen S, *et al*. comparison of N_2O and CO_2 pneumoperitoneums during laparoscopic cholecystectomy with special reference to postoperative pain. Surg Laparosc Endosc 1998; 8:140-4.

Objective Structured Clinical Examination for Undergraduate Surgery Finals in the College of Medicine, University of Mosul

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ABSTRACT

Background: The objective structured clinical examination is gaining popularity in most medical schools for its validity, reliability, and objectivity. It requires a lot of physical and financial resources and commitment.

Objective: To outline steps important to be considered when conducting objective structured clinical examination as an assessment skill for final undergraduate candidates in surgery with emphasis on the student's perception, satisfaction and acceptability.

Design: A purposive sample of 151 of 6th year undergraduate medical students attempted final objective structured clinical examination in Surgery.

Setting: Department of Surgery, College of Medicine, University of Mosul during the academic year 2011-2012.

Method: Purposive sample including 151 participants, who attempted objective structured clinical final examination in surgery for graduation. There were 65 males & 86 females. The examination was performed over 8 days. A well-organized ten objective structured clinical examination stations were chosen for assessment. The time allowed for each station was 6 minutes. An objective structured clinical examination organizing committee was established. The subjects for objective structured clinical examination stations were determined, a detailed plan of the students grouping and movement was established, and a notice for all students about objective structured clinical examination details was given. At completion of examination, students were given self-administered questionnaire and feedback to test their perception and satisfaction about the examination.

Results: Data of completed self-administered questionnaire were analyzed. Regarding station information, 78.8% of students reported that the task questions in the stations are appropriate to the length of station, 82.7% replied that the stations are practical and 72.1% answered that the information in stations are clear. Reply from 86.7% was that the task was clearly stated, 82.1% responded that patient`s complaint in the clinical stations is brief and given in basic language, while 74.1% replied that findings are "well understood" and clearly described. Analyzing the stations structure, 80.7% of students stated that the number of the stations was enough and 84.7% agreed that the location of stations was good.

Conclusion: Objective structured clinical examination for undergraduates' surgical finals is a practical assessment tool even if large numbers of students are involved. Data of this study showed that overall student's perception, satisfaction and acceptability of objective structured clinical examination were encouraging.

Keywords: Objective structured clinical examination, assessment, clinical, undergraduate, medical schools.

الإختبار السريري الهادف المنظم لطلاب المرحلة النهائية في الجراحة: تجربة فرع الجراحة في كلية طب الموصل

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الخلاصة

الخلفية: يحظى الإختبار السريري الهادف المنظم بشعبية متزايدة حيث تبين أن له مصداقية وموضوعية وإعتمادية عالية. يتطلب هذا النوع من الفحص الكثير من التجهيزات من ناحية المكان والدعم المادي.

الهدف: يسلط هذا البحث الضوء على الخطوات الهامة التي يجب الإنتباه إليها وأخذها بنظر الإعتبار عند إجراء هذا النوع من الفحص عند إجرائه للمرحلة السادسة النهائية مع التركيز على التغذية الراجعة منهم من حيث التقبل والرضا لهذا النوع من الإمتحانات.

التصميم: تم دراسة عينة تتألف من ١٥١ طالبا من المرحلة السادسة للدراسة الأولية خضعوا لإمتحان الإختبار السريري الهادف المنظم النهائي مادة الجراحة العامة.

المكان والزمان: تمت الدراسة في السنة الدراسية الأكاديمية ٢٠١١-٢٠١٢ في فرع الجراحة لكلية الطب–جامعة الموصل.

الطريقة: شمل البحث عينة من ١٥١ طالبا (٦٥ ذكر و٨٦ أنثى) في الصف السادس للدراسة الأولية لكلية الطب للسنة ٢٠١١-٢٠١٢ أجري لهم الإمتحان السريري النهائي بطريقة الإختبار السريري الهادف المنظم على مدى ٨ أيام وقد أختيرت ١٠محطات منظمة بشكل جيد للإمتحان. الزمن المسموح به لكل محطة كان ٦ دقائق. وقد شكلت لجنة خاصة لتنظيم الإمتحان مكونة من ٤ أعضاء، ثم عقد إجتماع للفرع وتم الإتفاق على مواضيع المحطات والسادة التدريسيين المسؤولين عنها. لكل محطة تم وضع أوراق خاصة للسادة الممتحنيين وللمرضى وللطلاب. وتم وضع خطة مفصلة لكيفية تحرك الطلبة بين المحطات وتجميعهم قبل وبعد إجراء الإمتحان. تم إعطاء التعليمات وشرحها للطلبة قبل الإمتحان. أعطي الطلبة ورقة التغذية الراجعة بعد الإمتحان لملئها.

النتائج: تم تحليل نتائج التغذية الراجعة لل(١٥١) طالبا الذين دخلوا الإمتحان، أجاب ٧٨,٨% من الطلبة بأن المشكلة والمهمة المحددة في المحطة مناسبة، فيما أجاب ٨٢,٧% من الطلبة بأن المحطات كانت تغطي الناحية العملية السريرية. كانت المحطات واضحة ومركزة عند ٧٢,١%من الطلبة، وأوضح ٨٤,٧% منهم أن التعليمات المعطاة في الإمتحان كانت وافية وأعطيت بشكل واضح. كانت شكوى المرضى مختصرة ومعطاة بلغة بسيطة عند ٨٢,١% من الطلبة بينما أجاب ٧٤,١% منهم أن المعطيات في المحطات كانت مشابهة للواقع ومشروحة بشكل وافي. أكد ٨٠,٧% من الطلبة أن عدد المحطات كان كافيا ووافق ٨٤,٧% منهم على جودة نوعية ومواقع المحطات.

الإستنتاج: الإختبار السريري الهادف المنظم الذي أجري لطلبة الصف السادس في مادة الجراحة النهائي أعطى نتائج مقبولة للأداء. نتائج هذه الدراسة أوضحت أن إجمالي قبول ورضا الطلبة بهذا الإمتحان كانت مشجعة بعد تحليل إستمارات التغذية الراجعة.

الكلمات المفتاحيه: الإختبار السريري الهادف المنظم، تقييم، سريري، طلبة كلية الطب.

INTRODUCTION

Objective structured clinical examination (OSCE) had been practiced in most medical schools, many residency programs and by the Licensure Boards in Canada since the mid 1970s.[1] In 1975 Harden *et al* [2]

Introduced OSCE in an effort to improve the evaluation of medical student's clinical performance. They claimed that when used correctly, the OSCE can be highly successful as an instrument to assess skills and competence in medicine. This type of evaluation as a means of assessing clinical competency by direct observation, is being used for both under- and post- graduate students as a 'gold standard' of health professional assessment.[3,4] It is increasingly replacing the traditional long-case, short-case and viva-based clinical finals where other important aspects of clinical expertise, such as physical examination skills, technical skills, problem-solving abilities, doctor-patient communication skills, decision-making abilities, and patient treatment skills are assessed objectively.[5,6] All candidates are presented with the same test at each station within a specified time period, it proved to be a reliable, valid, and reproducible test.[7] Many factors can influence reliability of OSCE namely the time and number of stations, the diversity of skills involved, training of the involved examiners and standardized patients, and checklists.[8]

The current study is an attempt to show in some detail of the experience of the Department of Surgery, College of Medicine, University of Mosul, in running OSCE for large group of undergraduate 6th year medical students for final examination in surgery in the academic year 2011-2012.

PARTICIPANTS AND METHOD

A purposive sample included 151 sixth year undergraduate medical students during the academic year 2011-2012. The examination was performed over 8 days. Each day 19 students were examined and 12 examiners supervised the examination. There were 9 comprehensive stations (with an additional rest station) at six minutes per

station. Each station dealt with specific medical skill, **Table 1.**

A detailed plan of the students grouping and movement was done **Table 2**.

Labels indicating station numbers, examination lines, waiting rooms and staff lounges were affixed. Students were provided with an assignment card detailing the group assignment. Student's mobile phones were switched off and taken away before the examination.

Students rotated through all stations and have to move to the next station at a signal bell. During the examination, students were observed and evaluated as they pass through the stations where they did the tasks assigned in each station.

Since the stations are generally independent, students can start at any station and complete the cycle. Thus, using 10 stations, 6 minutes each, 10 students can complete the examination within 60 minutes. As there were 19 students /day, the whole examination lasted on an average of 2 hours daily for 8 days. Time was considered as an important issue to run the examination. Three junior staffs were allocated to be responsible for timekeeping. In each active station which involves practical skill to be performed, there were 2 examiners while for each inactive station which involved data interpretation, there was 1 examiner. All examiners used checklists for the answers according to predetermined criteria. The checklists contain the standard questions / answers. The items in the checklist were used to assess the medical skill specific to the station in spot, such as: focused history, symptoms, signs, data interpretation, and management, plans.

A pre-examination introductory symposium on OSCE was established by the OSCE committee in the department addressing the guidelines for OSCE. The OSCE committee discussed through several meetings the following points:

- OSCE location and the room set up for stations.
- Examiners/staff, standardized patients (SPs),
- Catering, time and record keeping.
- Station information. **Fig1.**
- Instructions to candidates.
- Instructions to examiners.
- Examiner's marking guide and scoring sheet.

After completing the examination, students were given a self–administered questionnaire to test their perception and satisfaction of the examination.

RESULTS

Data of one hundred and fifty one students who attempted the OSCE and completed the questionnaire were analyzed. Replies from 82.7 % of students were that the stations were practical, and 72.1% answered that the information in station provides clear focus to student. Concerning candidate's instructions**,** 84.7% of students perceived that basic patient information for examination was clearly given and 86.7 % reported that task was clearly stated**.** Analyzing patients information in the clinical station, 82.1 % of students responded that patient complaint was brief and given in basic language, and 74.1 % replied that findings were "well understood" and clearly described. Regarding the stations structure, 80.7% of students stated that the number of stations was enough, and 84.7 % agreed that the types and locations of stations were good.

One important factor in designing OSCE stations is the duration of the station and whether it is sufficient to achieve the task or not, 78.8 % of the respondents stated that the duration of each station was adequate, those who felt that the time was insufficient were 21.2 %, **Table 3.**

As regard to the conduct of examination, there were no problems encountered while running the examination. It was only noted that the place of examination needs further extension. Staff and students expressed high satisfaction with this type of examination**.** Additional benefit was that all the students on the same day were exposed uniformly to the same staff and same assessment tools in the same environment.

Table 1. Objective structured clinical examination stations used to assess skills.

Station no.	Name of station
Station (1)	Slides interpretation (photos)
Station (2)	Physical examination on real patients
Station (3)	Investigation (data interpretation scenarios , radiology films)
Station (4)	Focused history taking
Station (5)	Instrument
Station (6)	Examination skills on a dummy
Station (7)	Orthopedics
Station (8)	Emergency and CPR
Station (9)	Urology
Station (10)	Rest

Table 2. Students grouping and movements

Group/time.	No	Movements line
8.30-9.00 Am	18	All students directed to secretariat room for ID check and assignment card. & label distribution
9.00-9.20 Am	18	All students attempted surgical slide station exam in one hall
9.20-10.20 Am	9	Students will come out from slide hall and will be allocated to the stations in unidirectional flow with continued supervision of the remaining 9 students in the surgical slide station hall
10.30-11.30 Am	9	Students will come out from surgical slide hall and will be allocated to the stations in unidirectional flow

Table 3. Summary of questionnaire results

TASK	GOOD (no.)	NEEDS FURTHER EVALUATION (no.)
Problem or question is-appropriate to time of station	131	20
The required skill or question is real to life OR PRACTICAL	125	26
Provide(s) clear focus to student	109	32
Basic patients information are clearly given	117	34
Task is clearly stated	131	20
Patient s complaint is brief and in basic language	124	27
Findings are "*well understood*" & clearly described	128	23
Number of stations /examination	122	29
Types of& location of stations/examination	132	19
Time /duration of stations	119	32

DISCUSSION

Clinical skills examinations, such as OSCEs, are daunting but are essential component of medical undergraduate education. [9] However controversy still exists. Bora *et al*,[5] stated that although OSCE style finals are fairer than the traditional style of clinical finals, they are not a perfect assessment of competence. Until an OSCE begins, candidate stress is high, students had to pull together vast amount of information from many resources.[4] This tedious and time consuming process can be avoided, if information about stations and conduct of OSCE structure were successfully given, a fact that was already attempted by the Department of Surgery through introductory symposia. The principles of running OSCE examinations do not differ regardless the number of students. Yet, the logistics of running such an examination for 150 or more students are extensive.[9, 10]

In his study, Davis[11] stated that a high degree of discipline and enthusiasm are required, and a big number of examiners and support staff are essential.

In the current study, despite many obstacles regarding the place of examination and the shortage of examination staff, OSCE examination was successfully established by our department. Capriccio, Englander[12] and Abdulla[13] reported that a very important factor in the success of the examination is meticulous and detailed written documentation of every aspect.[12,13] This was achieved by frequent meetings of the examination committee to ensure that all parts of the stations coordinate with all aspects of skills and that stations checklists contained the standard questions/ answers in order to avoid bias in putting marks.

Concerning the rules for the examination which were established by the Department of Surgery, it appears to be consistent with the rules of Petrusa[14] and Talal [15] who pointed that for reasons of confidentiality, students must be in the examination area before the actual examination. They also need to be kept in spacious rooms under supervision to avoid contact between the different groups via mobile telephones. Because of the parallel lines of stations, time keeping is very important. A 6-minute period per station is usually sufficient to organize the movement of the students.

In regard to the analysis of self-administered questionnaire, it appeared that the majority of students expressed their acceptability and satisfaction with the structure of the stations as

more than one third of students felt that OSCE stations information and time were adequate. These findings were different from the study of Abdulla[13] in Basrah who reported that student who were satisfied with OSCE formed only 20.4% whereas 48% of students stated that the duration of station was adequate. Regarding the use of standardized patients, 58% of Basrah students accepted the use of such patients while 82.1% of our students responded that the information given in the clinical station was clear.

CONCLUSION

Data of this study showed that overall student's perception, satisfaction and acceptability of OSCE were encouraging. Proper preparation by OSCE committee in the Department, the cooperation of the Department members and the availability of the requirements had a great deal to do with this success. A timely feedback on the performance of the candidates after applying the standards of OSCE was a fact that we learned through this experience.

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REFERENCES

1. Ilic D. Assessing competency in evidence based practice: strengths and limitations of current tools in practice. BMC Med Educ [online]. 2009 [cited 2009 Dec 16]; 9:53. Available from http://www.biomedcentral. com/1472- 6920/9/53.

2. Harden RM, Stevenson M, Downie WW, Wilson GM. Assessment of clinical competence using objective structured examination. Br Med J 1975; 1(5955): 447-451.

3. Hatem HA, Objective Structured Clinical Skill Examination (OSCE) Medical Journal of Babylon2010: 7 (1-2): 29-30.

4. Abdulla MA, OSCE: things to be said. Bas J Surg 2010; 16: 30.

5. Bora Sh, Heah Th, Thakor Sh: OSCE for Medical and Surgical finals. New York: Oxford University Press; 2005.

6. Al-Youzbaki D B. Developing a communication skills training program for the undergraduate medical students. Mosul, Iraq: Mosul, Medical College, Mosul University; 2005.

7. Van der Vleuten C. The assessment of professional competence: developments, research and practical implications, Adv in Health Sci Edu 1996; 1: 41-67.

8. Wilkinson TJ, Newble DI, Wilson PD, Carter JM, Helms RM. Development of a three centre simultaneous objective structured clinical examination. Med Educ 2000; 34(10): 798-807.

9. Burton L N, Birdi K. Clinical Skills for OSCEs .2nd ed. UK: Informa healthcare; 2006.

10. Rekany A J, Al-Dabbagh S A. Validity and reliability of OSCE in evaluating practical performance skills of interns in emergency Medicine. Duhok Med J 2010; 4(2):21-29.

11. Davis MH. OSCE: the Dundee experience. Med Teach 2003; 25(3): 255-261.

12. Carraccio C, Englander R. The objective structured clinical examination: a step in the direction of competency-based evaluation. Arch Pediatr Adolesc Med 2000; 154(7): 736-741.

13. Abdulla M. A students perception of objective structured clinical examination (OSCE) in surgery at Basrah College of Medicine Bas J Surg, 2012; 18: 345

14. Petrusa ER. Taking standardized patient-based examinations to the next level. Teaching and learning in Medicine 2004; 16:98-110.

15. Bakhsh TM, AL Kashgari RH, Sibiany AM, Al-Mashat FM, Meccawy AA, Al Thubaity FA and AlJohary A A: Running OSCE for a Large Group of Students: Experience of the Surgical Department, King Abduaziz University, Faculty of Medicine. JKAU Med Sci 2005; 12:43-52.

Candida colonization in neonates admitted to neonatal intensive care unit (NICU) in Mosul

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ABSTRACT

Background: *Candida* species are important nosocomial pathogens in the newborns, particularly among the preterms. Colonization of the neonatal skin and gastrointestinal tract is the first step in the pathogenesis of invasive Candidiasis. Colonization of the infant occurs early in life and this is affected by a variety of common practices in the neonatal intensive care unit (NICU).

Objective: To determine colonization of *Candida* species in neonates admitted to NICU in Mosul city, and to identify the possible risk factors for colonization.

Patients and methods: A case series study was conducted in a Al Khansaa Teaching Hospital in Mosul city between September 2012 to March 2013. Fifty neonates who were admitted for several causes and stayed in the hospital for seven or more days were included in the study. Sterile cotton tipped swabs from oral, rectal and umbilical areas of each neonate were collected within 24 hours of admission, day five, day seven or thereafter when the neonate was discharged from hospital. Swabs were smeared on the surface of plates of Sabourauds glucose agar. Data was analyzed using Students "t" test, Chi-square test and Fisher's exact test wherever necessary.

Results: *Candida* colonization was seen in 70% of patients at different sites and times of samples collection. Colonization was more common in males than females. From the colonized neonates, 60% were full term and 40% were premature, and 74% had normal birth weight and 26% had low birth weight. Acquisition of *Candida* occurred in 63% of neonates within the first 24 hrs and by day five 94% of neonates were colonized. The remaining 6% were colonized after fifth days of admission. Male sex, normal birth weight and signs of vaginal candidiasis in the mother were found to be significant risk factors for neonatal colonization.

Conclusion: *Candida* colonization was seen in 70% of the study sample. Male neonates were colonized more often than females. Male sex, normal birth weight and signs of maternal vaginal candidiasis were significant risk factors for neonatal colonization with *Candida*.

Keywords: Candida colonization, neonates, intensive care, Mosul.

مستعمرات المبيضات لدى الأطفال حديثي الولادة الراقدين في وحدة الطفل الخديج في الموصل

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الخلاصة

المقدمة: تعتبر الإصابة بالمبيضات للأطفال الحديثي الولادة والخدج من الأمراض المهمة التي قد يصاب بها الطفل في المستشفى.أن تعشش المبيضات في الجلد والجهاز الهضمي يعتبر خطوة أولى لإنتشار الإصابة بالمبيضات إلى بقية أعضاء الجسم.

الأهداف: تهدف هذه الدراسة لمعرفة مدى تعشش المبيضات في الأطفال حديثي الولادة والخدج وكذلك لتحديد عوامل الخطورة للإصابة.

المرضى وطرائق العمل: دراسة تتبعيه أجريت في مستشفى الخنساء التعليمي للأطفال للفترة من أيلول/ ٢٠١٢ لغاية آذار / ٢٠١٣. تمت دراسة خمسون طفلا أدخلوا لوحدة الطفل الخديج أثناء تلك الفترة لأسباب مرضية مختلفة وبقوا في المستشفى لمدة سبعة أيام أو أكثر. تم أخذ مسحات لغرض زرع المبيضات من فم وقاعدة السرة والجهاز الهضمي لجميع المرضى خلال اليوم الأول للدخول، اليوم الخامس واليوم السابع أو عند خروج المريض وأرسلت العينات الى المختبر لغرض الزراعة.

النتائج: لوحظ أن ٧٠% من الأطفال مصابين بتعشش المبيضات في أنحاء مختلفة من الجسم، وإن الأطفال الذكور معرضين للإصابة أكثر من الإناث كما لوحظ أن نسبة الإصابة للأطفال مكتملي النمو ٦٠ % بينما إصابة الأطفال غير مكتملي النمو بلغت ٤٠%. كما لوحظ أن نسبة الإصابة للأطفال الذين كانت أوزانهم كاملة (٢,٥ كيلوغرام أو أكثر) بلغت ٧٤ %. إكتسب ٦٣ % من الأطفال الإصابة خلال ٢٤ ساعة الأولى من دخول المستشفى، و ٩٤% خلال الأيام الخمسة الأولى والباقي ٦ % بعد اليوم الخامس للدخول. أظهر البحث أن عوامل الخطورة كانت الأطفال الذكور وزن الولادة ٢,٥ كيلوغرام أو أكثر ووجود أعراض لإصابة الأم بمبيضات المهبل أثناء الحمل.

الإستنتاج: كانت نسبة إصابة الأطفال المشاركين بالبحث بتعشش المبيضات ٧٠ %، الأطفال الذكور معرضين للإصابة أكثر من الإناث. أما عوامل الخطورة للإصابة بالمرض فهي الطفل الذكر، الوزن الكامل أثناء الولادة ووجود أعراض لإصابة الأم الحامل بمبيضات المهبل.

الكلمات المفتاحيه: مستعمرات المبيضات، أطفال حديثي الولادة، وحدة العناية المركزة، الموصل.

INTRODUCTION

Candida species are significant nosocomial microorganism in the neonate, especially in the preterm. The first step in Candida invasion is colonization of the gastrointestinal tract (GIT) and skin of neonates.[1] *Candida albicans* is the commonest detected species in colonized or infected neonates. During the last years colonization and infection with other candida species has increased dramatically especially among premature infants.[2,3] This has been attributed to the use and duration of broad spectrum antibiotics therapy,[4] technology advancement of life supporting systems, relative immunodeficiency in the neonates,[5,6] colonization of maternal vagina and Candida ability to live on environmental surfaces.[7]

Infant colonization by candida occurs early in life due to routine daily works in the neonatal intensive care unit (NICU). Neonatal fungal infections are associated with substantial mortality and morbidity.[8]

Risk factors of *Candida* colonization or infection are preterm neonates who need invasive and aggressive diagnostic and therapeutic procedures, congenital anomalies, prior antibiotic therapy, necrotizing enterocolitis and gastrointestinal tract diseases. Prior colonization is the major risk factor for candida infection.[9]

Most neonatal candidiasis is endogenously acquired through prior colonization of different parts of the neonatal body. Other studies suggested that some outbreaks of candidiasis were caused by nosocomial infection in NICU.[10]

In general, the first step towards severe infection is *Candida* colonization, which lives as normal flora in the intestine.[11-13] Actually, Wey *et al*[14] during the 1980s, recognized *Candida* colonization as an independent risk factor for candidemia. In fact, colonization of multiple sites is an improtant risk factor for invasive fungal infection in severely ill neonates and the density of colonization could be a predictive value for the diagnosis of systemic candidiasis,[15–17] indeed its difficult to recognize between infection and colonization.[18] *Candida* colonization can present in 5–50% of neonates and an invasive infection can develop in 5–30% of colonized patients.[19,20] The death risk in neonates with distinct Candida colonized body sites is similar to that of neonates with proven invasive infection.[20]

Aim of the study:

1- To determine colonization of *Candida* species in neonates admitted to NICU in Mosul city.
2- To detect the possible colonization risk factors.

PATIENTS AND METHODS

A case series study was conducted at Al Khansaa Teaching Hospital in Mosul city in the period from September 2012 to March 2013. A total of 50 neonates (premature and full term) who were admitted for several causes and stayed in the

hospital for 7 or more days were included in the study. All of them were kept in incubators and received antibiotics (ampicillin and aminoglycosides or ampicillin and third generation cephalosporin).

Specimens collection: Swabs from rectal, oral and umbilical areas of each neonate were collected within 24 hours of admission, 5th, 7th day or after that when the patient was discharged from hospital.

Collection of samples were done by using sterile cotton swabs after moistening them with sterile saline and all samples were processed to the laboratory within 30 minutes of collection. Swabs were smeared on the surface of plates of Sabourauds glucose agar which were incubated for 48 hours at 37 C°. All samples that yielded yeast colonies were proceeded further for the identification of C*andida* species and positive results were indicated by positive Germ tube test &/or API Candida test (Biomieux).

Collection of blood samples from the neonate and vaginal swabs from the mother were not part of the study.

In neonates, information about I) intake of antibiotics, steroids, blood transfusion or exchange, II) type of feeding III) associated disease or anomaly, IV) birth weight, and V) sex, were recorded. And in mothers I) site of delivery, II) gestational age, III) type of delivery, IV) duration of rupture of membrane, V) signs of vaginal candidiasis, and meconium stained liquor were noted and recorded.

Data was analyzed using Students "t" test, Fisher's exact test and Chi-square test wherever necessary.

RESULTS

The total number of patients included in the study was 50, (28 males and 22 females). *Candida* colonization was seen in 35 (70%) of the patients at different sites and times of samples collection.

Table 1 showed the characters of colonized neonates. Colonization was detected in 23 (65%) males and 12 (35%) females with male: female ratio of 1.9:1. From the colonized neonates, 21 (60%) were full term and 14 (40%) were premature. Twenty six (74%) of the colonized neonates had normal birth weight while 9 (26%) had low birth weight.

Table 2 showed the date and site of colonization. Among the colonized neonates acquisition of *Candida* occurred in 63% of them within the first 24 hrs and by day five 94% of neonates were colonized. The remaining 6% were colonized after fifth days of admission.

Regarding site of colonization, colonization of one site was seen in 19 (54%) of patients, and in two sites were seen in 16 (46%) of patients. The maximum colonization was in the mouth (66%) followed by the rectum (57%) and the umbilicus (20%). However earliest colonization i.e., within 24 hrs was that of the umbilicus (71%).

Table 3 showed the risk factors that lead to *Candida* colonization, it is clear from this table that male sex, normal birth weight and signs of vaginal candidiasis in the mother were found to be significant risk factors. However colonization in neonates was seen more frequently in those with normal vaginal delivery, non-breast milk feeding and delivery at hospital, but the differences were not statistically significant.

Table 1. Characters of colonized neonates.

Patents character	No= 35 (100%)
♀	12 (35%)
♂	23 (65%)
Full term	21 (60%)
premature	14 (40%)
LBW	9 (26%)
NBW	26 (74%)

Table 2. Date and site of colonization.

Colonization	Time			Total
	24 hr	5 days	>5 days	
Number of colonization	22 (63%)	11 (31%)	2 (6%)	35
Cumulative colonization	22 (63%)	33 (94%)	35 (100%)	-
Mouth	13 (57%)	7 (30%)	3 (13%)	23 (66%)
Umbilicus	5 (71%)	2 (29%)	0 (0 %)	7 (20%)
Rectum	12 (60%)	7 (35 %)	1 (5 %)	20 (57%)

Table 3. Risk factors for Candida colonization.

Factor	Candida positive n=35		Candida negative n=15	
	No.	%	No.	%
1-Gestational age				
premature	14	(40)	10	(66.7)
full term	21	(60)	5	(33.3)
2-Birth weight				
≥2.5 kg	26	(74)*	6	(40)
<2.5 kg	9	(26)	9	(60)
3-sex				
Male	23	(65)*	5	(33.4)
Female	12	(35)	10	(66.6)
4-Mode of delivery				
NVD	19	(54)	13	(87)
CS	16	(46)	2	(13)
5-PROM				
Yes	10	(29)	5	(33.4)
no	25	(71)	10	(66.4)
6-Use of steroid				
Yes	5	(15)	3	(20)
no	30	(85)	12	(80)
7-Meconium aspiration				
Yes	14	(40)	4	(27)
no	21	(60)	11	(73)
8-Signs of vaginal candidiasis				
Yes	24	(69)*	14	(93.4)
no	11	(31)	1	(6.6)
9-Mode of feeding				
Breast	7	(20)	7	(47)
Others	28	(80)	5	(53)
10-Place of delivery				
Home	8	(22)	3	(20)
Hospital	27	(78)	12	(80)
11-Blood or exchange transfusion				
Yes	8	(23)	3	(20)
No	27	(77)	12	(80)
12-Congenital anomalies				
Yes	12	(34)	3	(20)
No	23	(66)	12	(80)

*P value < 0.05 (statistically significant).

DISCUSSION

Disseminated candidiasis is an significant cause of neonatal morbidity and mortality and candida colonization is the early step in the pathogenesis of invasive candidiasis.[1]

Neonatal colonization by *Candida* was 70% in this study, and this is nearly similar to that in Virginia (60%)[21] but higher than that reported from India (34%)[1] and Italy (18%).[22] This variation may be due to difference in intensity of routine antifungal antiseptic measures and difference in the environments.

Colonization of male neonates was more than female in this study, and this is in agreement with a study done in India.[1] Colonization of full term and normal birth weight neonates were more frequent than premature and low birth weight babies in our study and this is different from other studies done in India[1] and North Carolina,[23] which showed no statistical difference between prematurity and birth weight. And this difference may be due to small sample size in our study.

It is noted that neonatal candida colonization occurs during the first few hours of life.[2, 24] In the present study colonization was recognized with in the first 24 hours of admission in 63% of cases.

Oral (66%) and rectal colonization (57%) were the commonest sites and this is comparable to other studies.[1,25] Colonization of GIT occurs predominantly during the first week of life,[2,26] and it can serve as a reservoir from where the *Candida* can spread and this may be due to poor local colonization resistance particularly if there is a breach in mucosal lining.[27]

The significant risk factors observed in our study were signs of vaginal candidiasis in the mothers, male sex and normal birth weight. The frequency of colonization in neonates was higher in those who were delivered normally through vaginal canal than those delivered by Cesarean intervention and the fact that earliest colonization was that of the oral mucosa (probably colonization during vaginal delivery) signifying that mothers with vaginal candidiasis are important source of neonatal candidiasis.[1] Male sex was a significant risk factor in the present study and which is similar to that reported from India.[1] In regard to normal birth weight as a risk factor, found in this study, others did not report similar result.[1, 28] They showed that low birth weight is a risk factor for neonatal colonization which may be attributed to small sample size in our study.

CONCLUSION

Candida colonization was seen in 70% of the studied neonates. Male neonates were colonized more often than females. Male sex, normal birth weight and signs of maternal vaginal candidiasis were significant risk factors for neonatal colonization with Candida.

RECOMMENDATIONS

1- Monitoring of *Candida* colonization in hospitalized neonates is an important step to prevent disseminated infection.
2- Over use of steroid and antibiotics, should be avoided.
3- Screening of all pregnant women for the presence of *Candida*, irrespective of symptoms and treatment of them, is important to decrease colonization and prevent infection of the neonates.

REFERENCES

1. Mendiratta DK, Rawat V, Thamke D. Candida colonization in preterm baby admitted to neonatal intensive care unit in the rural setting. Indian J of medical microbiology 2006; 24(4):263-267.
2. Sharp AM, Odds FC, Evans EG. Candida strains from neonates in a special care baby unit. Arch Dis Child 1992; 67: 48-52. [PUBMED]
3. Singh K, Chakrabarti A, Narang A, Gopalan S. Yeast colonization and fungemia in preterm neonates in tertiary care centre. Indian J Med Res 1999; 110: 169-73.
4. Charles PE, Dalle F, Aube H, Doise JM, Quenot JP, Aho LS, *et al.* Candida spp. colonization significance in critically ill medical patients: a prospective study. Intensive Care Med. 2005 Mar; 31(3):393-400.
5. Phelps M, Ayliffe GA, Babb JR. An outbreak of candidiasis in a special care baby unit: The use of a resistogram typing method. J Hosp Infect 1986; 7: 13-20.
6. Burnie JP, Odds FC, Lee W, Webster C, Williams JD. Outbreak of systemic Candida albicans in intensive care unit caused by cross infection. BMJ 1985; 290: 746-748.
7. Pfaller MA. Epidemiology of candidiasis. J Hosp Infect 1995; 30: 329-338.
8. Kaguelidou F, Pandolfini C, Manzoni P, Choonara I, Bonati M, Jacqz-Aigrain E. European survey on the use of prophylactic fluconazole in neonatal intensive care units. Eur J Pediatrics. 2012 Mar; 171(3):439-445.
9. Klempp-Selb B. Rimek D.; Kappe R. Karyotiping of *Candida albicans* and *Candida glabrata* from patients with *Candida* sepsis. *Mycoses* 2000; *43*:159–163.
10. Singhi, S.; Rao, D.S, Chakrabarti, A. Candida colonization and candidemia in a pediatric intensive care unit. Pediatr. Crit. Care Med. 2008; *9*: 91–95.
11. Ruping M.J, Vehreschild J, Cornely O.A. Patients at high risk of invasive fungal infection: when and how to treat. *Drugs* 2008; *68*: 1941–1962.
12. Wey S.B, Mori M, Pfaller M.A, Woolson R.F, Wenzel R.P. Risk factors for hospitalacquired candidemia. A matched case-control study. *Arch. Int. Med*. 1989; *149*: 2349–2353.
13. Agvald-Ohman, C, Klingspor, L, Hjelmqvist, H, Edlund, C. Invasive candidiasis in long-term patients at a multidisciplinary intensive care unit: Candida colonization index, risk factors, treatment and outcome. *Scand. J. Infect. Dis*. 2008; 40:145–153.
14. Almirante B, Rodríguez D, Park B.J, Cuenca-Estrella M, Planes, A.M, Almela M, *et al.* Epidemiology and predictors of mortality in cases of Candida blood stream infection: Results from population-based surveillance, Barcelona, Spain, from 2002 to 2003. J. Clin. Microbial. 2005; *43*: 1829–1835.
15. Charles P.E, Dalle F, Aube H, Doise J.M, Quenot J.P, Aho L.S. Candida spp. colonization significance in critically ill medical patients: A prospective study. Intensive Care Med. 2005; *31*: 393–400.
16. Paphitou N.I, Ostrosky-Zeichner L, Rex J.H. Rules for identifying patients at increased risk for candidal infections in the surgical intensive care unit: Approach to developing practical criteria for systematic use in antifungal prophylaxis trials. Med. Mycol. 2005; 43: 235–243.
17. Petri M.G, Konig J, Moecke H.P. Epidemiology of invasive mycosis in ICU patients: A prospective multicenter study in 435 non-neutropenic patients. Intensive Care Med. 1997; *23*:317–325.
18. Slotman G, Shapiro E, Moffa S. Fungal sepsis: multisite colonization *versus* fungemia. Am. Surg. 1994; 60:107–113.
19. Heljic S, Hukic M, Dzinovic A, BabicM, Djozic M. 173 Fungal Colonization of Newborn in Neonatal Intensive Care Unit: A Prospective Study. Pediatric Research 2005; 58: 384–384.
20. Shireen Y Issa, Eman F Badran, Kamal F Akl, Asem A Shehabi1. Epidemiological characteristics of Candida species colonizing oral and rectal sites of Jordanian Infants. BMC Pediatrics 2011, 11:79.
21. David K, Boyle R, Hazen K. Fluconazol prophylaxis against fungal colonization and infection in preterm infants. Engl J Med. 2001; 345(23):1960-1966.
22. Paolo Manzoni P, Ilaria S, Hubert M. *et al*, Bovine Lactoferrin Prevents Invasive Fungal Infections in Very Low Birth Weight Infants: A Randomized Controlled Trial. Pediatrics 2012; 129(1):116.
23. Richard A, Randall G, Fisher Daniel K, Benjamin Jr, Kelly Ross, Ross E. When to Suspect Fungal Infection in Neonates: A Clinical Comparison of Bacteremia Candida albicans and Candida parapsilosis Fungemia With Coagulase-Negative Staphylococcal. Pediatrics 2000; 106(4):712-718.
24. Waggoner-Fountain LA, Walker MW, Hollis RJ, Pfaller MA, Ferguson JE 2nd, Wenzel RP, *et al*. Vertical and horizontal transmission of uniqe Candida species to premature newborns. Clin Infect Dis 1996; 22: 803-8.
25. Gagneur A, Sizun J, Vernotee E, de Parscau L, Quinio D, Le Flohic AM, *et al.* Low rate of Candida parapsilosis related colonization and infection in hospitalized preterm neonates: A one year prospective study. J Hosp Infect 2001; 48: 193-7.
26. Baley JE, Kliegman RM, Boxerbaum B, Fanarof AA. Fungal colonization in the very low birth weight infant. Pediatrics 1986; 78: 225-32.
27. Rippon JW. Candidiasis and the pathogenic yeasts.Medical Mycology. WB Saunders: Philadelphia; 1988. p. 532-81.
28. Eugene Leibovitz. Strategies for the Prevention of Neonatal Candidiasis. Pediatrics and Neonatology 2012; 53: 83-89.

Conservative treatment of acute appendicitis

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ABSTRACT

Objective: To define the value of Tamsulosin drug addition to antibiotics (Ceftriaxone and Metronidazole) in conservative treatment of nonperforated acute appendicitis.

Patients and methods: Prospective clinical study performed in Al-Jamhoory Teaching Hospital covering a period from Jan 2010 to Jan 2012. Formal consent from the patients and ethical approval were obtained. One-hundred and two patients including 74 males and 28 females, with age range of 17-45 years were admitted to the surgical unit number 3 complaining of acute appendicitis. Detailed clinical history was taken and clinical examination was carried out. All the patients had general urine examination (G.U.E), ultra sound (U.S) of the right iliac fossa and determination of serum c.reactive protein level. Those who had complicated appendicitis were excluded from the study. The patients were randomly divided into two groups A and B.

Group A: Fifty one patients were given 500 mg of Ceftriaxone and 500 mg Metronidazole, both I.V twice daily.

Group B: Fifty one patients were given the antibiotics regime plus Tamsulosin 0.4 mg orally once daily.

The patients who had good signs of response (decrease or disappearance of the abdominal pain, tenderness and rebound tenderness and return of appetite) in the first 24 hours of the treatment continued the treatment for further 5 days, if there was no good response immediate appendicectomy was done. There was follow up of discharged patients for 4 months.

Results: Group A: Forty-one patients out of 51 (80.39%) had a good signs of response (decrease or disappearance of the abdominal pain, tenderness and rebound tenderness and return of appetite) within the first 24 hours post presentation while 10 patients needed appendicectomy. Group B: Forty-nine patients (out of 51) 96.07% had good signs of response (decrease or disappearance of the abdominal pain, tenderness and rebound tenderness and return of appetite) within the first 24 hours post presentation and only 2 patients needed appendicectomy. Those who were discharged after conservative treatment were followed up for 4 months. Five patients in group A and 3 patients in group B had recurrence of symptoms and signs of acute appendicitis and appendicectomy was performed for them.

Conclusion: Tamsulosin added to antibiotics for treatment of acute appendicitis is safe and resulted in speedy recovery of the patients with reduced recurrence of the condition.

Keywords: Appendicitis, Conservative treatment.

العلاج التحفظي لإلتهاب الزائدة الدودية الحاد

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الخلاصة

الهدف: بيان فائدة إضافة عقار التامسوليسين إلى المضادات الحيوية في علاج إلتهاب الزائدة الدودية التحفظي.

طريقة العمل: دراسة مستقبلية أجريب في المستشفى الجمهوري التعليمي في الموصل من ك٢ ٢٠١٠ الى ك٢ ٢٠١٢. شملت ١٠٢ مريض ومريضة مصابون بإلتهاب الزائدة الحاد, قسم المرضى بطريقة عشوائية إلى مجموعتين.

مجموعة أ: أعطيت المضادات الحيوية، المجموعة ب: أعطيت المضادات الحيوية وعقار التامسوليسين.

النتائج: تم متابعة المرضى خلال الأربع والعشرون ساعة الأولى من قبل جراحين يجهلون تماما تبعية المريض إلى مجموعة من المجموعتين.
المجموعة أ:- واحد وأربعون مريض ومريضة من مجموع ٥١ مريض ٨٠,٣٩% أظهروا إستجابة جيدة للعلاج خلال الأربع وعشرون ساعة الأولى من بدء العلاج (إختفاء الآلام في البطن وعودة الشهية للطعام) بينما إحتاج ١٠ مرضى لعملية بتر الزائدة.
المجموعة ب:- تسع وأربعون مريض ومريضة من مجموع ٥١ مريض ٩٦,٠٧% أظهروا إستجابة جيدة للعلاج في الأربع وعشرون ساعة الأولى من بدء العلاج وإحتاج مريضان فقط إلى عملية بتر الزائدة. جرت متابعة المرضى الذين شفوا بعد العلاج التحفظي لمدة أربع أشهر لظهور علامات إلتهاب الزائدة الدودية وكان هناك خمسة مرضى في المجموعة أو ثلاثة مرضى في المجموعة ب ممن عانوا من الرجعة وأجريت لهم عملية بتر الزائدة.
الإستنتاج: إضافة عقار التامسوليسين إلى المضادات الحيوية في علاج إلتهاب الزائدة التحفظي أظهر نتائج جيدة وقلة عدد المرضى الذين عانوا من عودة المرض.
الكلمات المفتاحيه: إلتهاب الزائده الدودية، العلاج التحفظي.

INTRODUCTION

In spite of the progress in surgical practice, acute appendicitis is still considered as one of the most common surgical emergencies and appendicectomy is still the most frequent procedure performed.[1,2] Pathogenesis of acute appendicitis is multifactorial including infection and obstruction. There has been dramatic reduce in acute appendicitis since the use of antibiotics,[3,4] so it became feasible to treat acute appendicitis conservatively.[5]

In this study, Tamsulosin is used for the first time in combination with antibiotics in conservative treatment of the non-complicated acute appendicitis. Tamsulosin is an alpha 1A-receptor blocker which relaxes smooth muscles. It is primarily used in the treatment of prostatic hypertrophy. It's main side effect is dizziness. I think that Tamsulosin causes relaxation of the appendicular muscle which enhances the drainage and relieves the intramural pressure of the inflamed appendix. Hence, it gave better results if given with antibiotics in the treatment of nonperforated appendicitis than antibiotics alone.

PATIENTS AND METHODS

From Jan 2010 to Jan 2012, 102 adult patients complaining from non-complicated acute appendicitis were admitted to the surgical unit number 3 in Al-Jamhoory Teaching Hospital in Mosul. they were 74 males and 28 females. Full history was taken and thorough clinical examination was done. All of the patients were sent for G.U.E, white blood cell (WBC) count, serum c-reactive protein and ultra sound U.S. of the abdomen.

Consent from the patients and ethical approval from the ethical committee were obtained.

The patients were randomly divided into two groups.

Group A:- The patients were treated conservatively with antibiotic only (Ceftriaxone 500mg I.V twice daily with Metronidazole 500mg I.V twice daily).

Group B:- Were given the same antibiotic of group A plus Tamsulosin 0.4mg orally once daily.

The patients in both groups were monitored blindly by separate surgeons in our unit in the first 24 hours of the treatment for signs of response to the treatment (decrease or disappearance of the abdominal pain, tenderness and rebound tenderness and returning of appetite). Those who showed these signs of response were maintained on the treatment for 5 days. Those who had no signs of recovery in the first 24 hours, appendicectomy were done for them immediately. Four months follow up for those who were discharged from the hospital was carried out.

RESULTS

Group A:

Forty one patients out of 51 (80.39%) showed good response (decrease or disappearance of the abdominal pain, abdominal tenderness and rebound tenderness and returning of appetite) in the first 24 hours of treatment with the antibiotics while ten patients showed no such signs. Appendicectomy was performed for them.

Group B:

Forty-nine patients out of 51 (96.07%) showed good signs of response and recovery and only 2 patients needed appendicectomy.

Table 1 shows the number of patients with recovery in the first 24 hours in both groups.

Good response of the patients in both groups in relation to time table in the first 24 hours of the conservative treatment showed clearly that the response to the treatment started earlier in group B than those in group A and the final result is much better in group B than in group A as demonstrated in **Table 2**.

Good appetite returned after 10-16 hours from the commencement of the conservative treatment in 44 patients in group B while 38 patients in group A did so.

Patients with high c.reactive protein level (4 mg/dL) (10 patients in group A and 2 patients in group B) showed high index of failure of the conservative treatment in the first 24 hours (persistent and increase of the abdominal pain, tenderness, and rebound tenderness). Also the recurrence rate of acute appendicitis after 4 months of follow up is noted to be high in patients with high c.reactive protein level.

Recurrence of signs and symptoms of acute appendicitis after 4 months of follow up occurred in 5 (9.8%) patients from group A, 3 (5.9%) patients in group B, and all were operated upon immediately.

Ultra sound (US) examination of the abdomen showed no calcification in the appendix. No mortality was recorded in both groups.

Table 1. Number of patients recovered within the 1st 24 hours of treatment.

Group	No of recovered patients	No of patients needed operation	Percentage
Group A	41	10	80.39%
Group B	49	2	96.07%

Table 2. number of patients recovered in both groups in relation to the time table in the first 24 hour of the treatment.

Groups	4-10 hours	11-16 hours	17-24 hours	No response
Group A	6 Patients	20 Patients	15 Patients	10 Patients
Group B	12 Patients	29 Patients	8 Patients	2 Patients

DISCUSSION

In spite of all the medical progress acute appendicitis is still considered as one of the most surgical emergencies and appendicectomy is still the most frequent surgical procedure performed.[1, 2] In the United States nearly 300,000 appendicectomy is annually performed.[6] Nearly 50% of all emergency appendicectomies were performed on normal or mildly inflamed appendix.[7]

The advent of antibiotic use caused drastic reduction in both mortality and morbidity of acute appendicitis.[8] Hence, conservative treatment of non-complicated appendicitis became more popular.[9] In this study, Tamsulosin is added to the antibiotics regime (Ceftriaxone and Metronidazole). In conservative treatment of non-complicated acute appendicitis the use of this mixture yielded an excellent results in group B (96.07% recovery) versus (80.39% recovered in group A), similar results were seen in the study the Similes *et al*[10] On reviewing literature concerning the conservative treatment of acute appendicitis, I found that Tamsulosin had not been used before in the treatment of this condition, so this is the first time this drug is used in combination with antibiotics in the treatment of non-complicated acute appendicitis. Group B showed good response in relation to the time **Table**, 12 patients showed such signs in the first 10 hours versus 6 patients in group A.

Two patients in group B showed no response to the conservative treatment and 10 patients from group A showed the same results, so appendicectomy was carried out.

Regaining of appetite and feeling of well being is good in both groups. However, group B did better than group A (84.6% versus 73.07%) **Table 2**.

This study showed that elevated serum c-reactive protein level (4bmg/dl) plays a key role in predicting failure of the conservative treatment in the first 24 hours, which is also seen in the study the Liu *et al*[11] No calcified appendenicolith by US examination was detected in our patients so it has no role in the predication of failure of the conservative treatment contrary to the findings reported by others study.[11]

Recurrence of acute appendicitis 4 months after the first presentation was reported in 5.9% in group A compared to 9.8% in group B. High level of serum c-reactive protein at presentation has

predictive value of recurrence of acute appendicitis, comparable to other studies.[11,12]

Conservative treatment of acute appendicitis is safe because delaying of appendicectomy for 24 hours after presentation did not increase the rate of perforation or other complications as seen by others.[13-16]

Tamsulosin which is an alpha 1A-receptor blocker and smooth muscle relaxant can result in better drainage and relieveing the intra luminal pressure in the inflamed appendix. It has minimal side effect, (mild dizziness). Adding it to the antibiotics combination in the conservative treatment of non-complicated appendicitis will definitely lead to a better results than antibiotics alone.

REFERENCE

1. Liu CD, McFaden DW. Acute abdomen and appendix. In: Greenfield LJ, (ed) Surgery principles and practice, Philadelphia Lippincott-Raven, 1997. 1246-1261.
2. Tehrani H Y. petros JG, Kumar PR, *et al* Marker of sever eappendicitis. Asm surg. 1999; 65:453-455.
3. Ricci MA, Trevisani MF, Beck WC. Acute appendicitis: A five year review. Am surg. 1991; 57: 301-305.
4. Larner AJ. The aetiology of appendicitis Br J hosp Med 1988; 39:540-2.
5. Andersson RE, Petzold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. Ann Surg; 2007; 264:741-8.
6. Mason RJ. Surgery for appendicitis: is it necessary? Surg Infect (Larchmt) 2008; 9: 481-488.
7. Bijen C, Van den Broek W, Bijen A, Ruiter P, Gouma D. Implication of removing a normal appendix. Digestive Surgery 2003; 20(3): 215-221.
8. Gill BD, Jenkins JR. Cost effective evaluation and treatment of acute abdomen. SurgClin North Am, 1996; 76: 71-82.
9. Hansson J, Korner U, Khorram-Manesh A, Solberg A, Lundholm K. Randomized clinical trial of antibiotic therapy versus appendicectomy as primary treatment of acute appendicitis in unselected patients. Br J Surg; 2009; 96: 437-81.
10. Simillis C, Symeonides P, Shorthouse AJ, *et al* A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). Surgery; 2010; 147:818-829.
11. Liu K, Ahanchy S, Pisaneschi M, Lin I, Walter R. Can acute appendicitis be treated by antibiotics alone? Am Surg; 2007; 73: 1161-1165.
12. Tsai H, Shan Y, Lin P, Lin X, Chen C. Clinical analysis of the predicative factors for recurrent appendicitis after initial nonoperative treatment of perforated appendicitis. Am J Surg; 2006; 192: 311-6.
13. Shindoh J, Niwa H, Kawai K, ishiharai Y, Takabayashi N. Predictive factors for negative outcome in initial nonoperative management of suspected appendicitis. J GastroinestSurg; 2010; 14(2):309-14.
14. Abou-Nukta F, Bakhos C, Arroyo K, Koo Y, Martin J, Reinhold R. Effects of delaying appendicectomy for acute appendicitis for 12 to 24 hours. Arch Surg; 2006; 141: 504-7.
15. Colson M, Skinner KA, Punnington G. High negative appendicectomy rates are no longer acceptable. Am J surgint 2001; 174(6): 723-726.
16. Bachoo P, Mahomed A, Ninan R, Youngson G. Acute appendicitis: The continuing role for active observation. PediatrSurgInt 2001; 17(2-3): 125-128.

Evaluation of postoperative gum chewing role in stimulating bowel motility in colonic surgery

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ABSTRACT

Objective: Postoperative ileus (POI) after abdominal surgery is an inevitable consequence of various etiologies. It causes much discomfort to patients by resultant vomiting, abdominal distention, and prolonged hospital stay; thus, exploring efficient and cost effective solutions could reduce the patients' suffering and hospital stay. This study aimed to evaluate the effect of gum chewing on the duration of POI following colonic surgery.

Patients and methods: Ninety patients at Aljumhoory Teaching Hospital from October 2007 to October 2008, undergoing elective large bowel surgeries were randomly assigned to the study group (n=44) and the control group (n=46). Patients in the study group chewed gum 3 times daily for 20 minutes starting from the 1st postoperative day until the return of bowel function. The control group patients had standard postoperative treatment. All patients were assessed clinically and the data were collected using an inquiry forma for every patient.

Results: Study and control group patients were comparable at inclusion. The mean time for the passage of first flatus as well as the time for the first bowel movement was shorter significantly in the study group (by 20.4 hours, P=<0.01; by 22 hours, P=<0.01) respectively. The first feeling of hunger was also experienced earlier in study group cases (by 14.7 hours, P=<0.01). The postoperative hospital stay was shorter in the study group, but the difference was not significant (P=<0.1).

Conclusion: Early postoperative gum chewing significantly hastens the time of bowel function recovery following colonic surgery. Moreover, it is a cost-effective and well-tolerated treatment for POI.

Keywods: Postoperative colonic surgery, bowel motility, stimulation, evaluation,gum chewing.

دراسة تقويمية لدور مضغ العلكة في تحفيز حركة الأمعاء بعد عمليات القولون الجراحية

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الخلاصة

المقدمة: الشلل الأمعائي فيما بعد العمليات الجراحية هو نتيجة لايمكن تفاديها ولها أسباب مختلفة، ولأنها تسبب الكثير من المضايقات وعدم الراحة للمرضى بما تسببه من: تقيؤ، وإنتفاخ بطني، ومدة بقاء أطول في المستشفى، فإن حلا فعالا قد يقلل من هذه التبعات.

الهدف: تقييم فعالية ودور مضغ العلكة بعد العمليات الجراحية للقولون في تحفيز عملية رجوع الوظيفة للمعي مبكرا.

المرضى وطريقة العمل: هذه الدراسة المستقبلية ضمّت ٩٠ مريضا ممن أجريت لهم عمليات جراحية للأمعاء الغليظة، وتم توزيعهم عشوائيا إلى مجموعتين: المجموعة الأولى مجموعة مضغ العلكة، وضمت ٤٤ مريضا والمجموعة الثانية هي عدم مضغ العلكة، وضمت ٤٦ مريضا. تم تقييمهم جميعا سريريا بواسطة جمع المعلومات عن طريق إستمارة إستبيان لكل مريض

النتائج: كانت نسبة الإناث إلى الذكور هي ٢١:٢٤ و٢٠:٢٥، ومعدل أعمار المرضى هو ٥٦ سنة و٥١ سنة في المجموعة الأولى والثانية على التوالي. كانت الدواعي الجراحية كالتالي: سرطان القولون مع التوصيل المعوي ٢٩ مريضا، سرطان القولون مع تفويه القولون ١٦ مريضا، الإلتواء المعوي للقولون ١٥ مريضا وغلق تفويه القولون ٤٥ مريضا.

كان وقت أول شعور بالجوع أبكر بـ ١٤,٧ ساعة، ووقت أول خروج للريح أبكر بـ ٢٠,٤ ساعة، ووقت أول تغوّط أبكر بـ ٢٢ ساعة في المجموعة التي مضغت العلكة عن المجموعة الأخرى، وكان الفرق مؤثرا إحصائيا، وأما فيما يخص مدة البقاء في المستشفى فهي أقل بـ ٠,٨ يوما في المجموعة الأولى، لكن الفرق لم يكن مؤثرا إحصائيا.

الإستنتاجات: إن مضغ العلكة مبكرا بعد الجراحة يسرع من إسترجاع المعي لوظيفته، وبالتالي تحمل المرضى للطعام عن طريق الفم بصورة أبكر.

الكلمات المفتاحيه: بعد العمليات الجراحيه للقولون، حركة الأمعاء، تحفيز، تقييم، مضغ العلكه.

INTRODUCTION

Post operative ileus (POI) is a transient cessation of coordinated bowel motility after surgical intervention, which prevents effective transit of intestinal contents and/or tolerance of oral intake.[1] Primary POI occurs in the absence of any precipitating complication,[2] it is an inevitable response to surgical trauma.[1] Secondary POI occurs in the presence of a precipitating complications such as uremia and hypokalemia.[3]

The incidences of POI in different common abdominal surgeries are; 4.1% after abdominal hysterectomy, 6.2% after appendectomy, 14.9% after large bowel resection and 19.2% after small bowel resection.[4] The average time for resolution of POI after major abdominal surgery is 24 hours for small bowel surgery, 24- 48 hours for stomach surgery, and 48-120 hours for large bowl surgery.[5]

The manifestations and consequences of postoperative ileus include; delayed passage of flatus and stool, increased nausea and vomiting, delay in resuming oral intake with possible need for parenteral nutrition and wound healing, and delay in postoperative mobilization. In addition, POI increases the risk of other complications such as pulmonary complications. Prolonged hospitalization decreases patient satisfaction and increases health care cost.[6,7]

Conventionally, POI has been managed by gastric decompression by nasogastric (NG) tube, keeping the patient nil per mouth, and intravenous fluid supplementation until the ileus resolves and patient passes flatus.[8] However, very few improvements in the understanding of POI have been established in the past 100 years, and therefore therapies have changed minimally. In recent years, the use of gum chewing has emerged as a new and simple modality for decreasing POI. Chewing gum acts as sham feeding, potentially stimulating gastric and bowel motility through repetitive stimulation of the cephalic-vagal complex.[9] Recently, it has been proposed that hexitols present in sugarless chewing gums might also be playing a role in the amelioration of POI.[4]

The aim of this study was to assess the efficacy of the gum chewing after abdominal surgery especially in the return of bowel function.

PATIENTS AND METHODS

This is a prospective randomized study, included 90 patients with colonic surgeries, between October 2007 and October 2008 in the surgical ward of Al- Jumhoory Teaching Hospital. The surveyed patients were evaluated for the effectiveness of the sugarless gum chewing in alleviation of postoperative ileus following abdominal surgeries, especially involving the large bowel. The surgical operations included colon cancer (resection and anastamosis), volvulous of sigmoid, colon cancer (resection and colostomy), and closure colostomy.

The patients were divided into two groups:

Group 1: gum chewing (44) patients (24 males and 20 females).

Group 2: no gum chewing (46) patients (25 males and 21 females).

Mean age for group 1 was 56 years, and for group 2 was 51 years.

The gum chewing group started chewing sugarless gum (1 GM per stick) that does not contain hexitol, in the morning of the first postoperative day. Patients chewed one stick of gum three times daily: in the morning, afternoon and in the evening, for 20 minutes.

Postoperative analgesia (diclofenac sodium and tramadol injections) was given to all patients in both groups (75 mg & 50 mg twice daily) respectively tailored to the individual patients requirement.

The two groups were tested for:

1. Time at first flatus.

2. Time at first feeling of hunger.
3. Time at first bowel motion.
4. Duration of hospital stay.

Student-t test was used to perform statistical analysis where P<0.05 was considered statistically significant for all compared values.

RESULTS

All patients (90) of the two groups completed the protocol study until recovery of bowel. There were no difference in mean age and gender (the female: male ratio was (1:1.25) (No. 21:25) in the no gum group and (1:1.4) (No. 20:24) in the gum chewing group. **Table 1** showing all 90 patients with different surgeries, classified according to gender.

Table 2 showing mean time of duration of surgery and operative complication in all 90 patients.

All patients in the two groups started mobilization on the first postoperative day.

Table 3 showing different clinical characteristic in both group (gum chewing and control).

A part from three patients in the control group and one patient in the study group who had mild chest infections, there were no other complications.

Table 1. Types of colonic surgery used in the study & no. of patients in both groups according to sex.

Indication for surgery	Control group		Gum chewing group	
	Male	Female	Male	Female
Colon cancer (resection & anastamosis)	8	6	8	7
Volvulous of sigmoid	3	2	3	2
Colon cancer (resection & colostomy)	3	5	3	4
Closure colostomy	11	8	10	7
Total	25	21	24	20

Table 2. Intraoperative findings.

Characteristics	Control group (n 46)	Gum chewing group (n 44)	P-Value
Mean (SD) duration of surgery in minutes	115 (50)	108 (39)	0.02
Intra operative complications	0	0	0

Table 3. The main outcome measures.

Characteristics	Gum Chewing group (n=44)	Control group (n=46)	p-value
Time for 1st bowel motion mean (SD) hr	52.6 (9.1)	74.6 (6.8)	<0.01
Time for 1st feel of hunger mean (SD) hr	48.9 (7.6)	63.6 (8.0)	<0.01
Time for 1st flatus mean (SD) hr	53.3 (8.0)	73.7 (6.5)	<0.01
Post-operative stay in hospital mean (SD) days	5.0 (2.7)	5.8 (2.6)	0.1

DISCUSSION

There was significant reduction in mean time for the first feeling of hunger postoperatively in the gum chewing group, (39) patients which was in the second postoperative day, while 30 patients in the control group experienced it in the third postoperative day (14.7 hours; P value=<0.01). This is similar to Asao *et al* study.[10] in which the time was (1.1day, p value=<0.01), but not to Rob Schuster et al study.[11] who found no significant difference in time for feeling of hunger between both groups (9.3 hours; P value=0.27).

There was significant decrease in mean time for first passage of flatus in gum chewing group (20.4 hours; P value<0.01). This result is comparable to Asao *et al*,[10] Schuster *et al*,[11] Chan *et al*,[12] Vasquez *et al*[13] and Kouba *et al*;[14] their results were: (1.1 days; p<0.01), (14.8 hours; P<0.05), (20.8 hours; P <0.0006) and (14 hours) and (0.5 day; p<0.001) respectively. On the other hand, Matros *et al*[15] finding was (7 hours; P =0.384), this may be attributed to how the gum was given, since they used the gum in combination with sips of clear fluid.

In our study there was a statistically significant shorter mean time for first bowel movement in gum chewing group (22 hours; P<0.01). Similarly Schuster *et al*[11] (26.2; P=0.04), Chan *et al* [12] (33.3 hours; P <0.0002), Vasquez *et al* 25 (25 hours),[13] and Kouba *et al*[14] 26 (0.7 day; p<0.01) reported comparable results. However, our outcome is different from that of Quah *et al*[16] (0.6 days) and Matros *et al*[15] in which there was no significant reduction in mean time for bowel motion.

From our data we found that there was statistically non-significant reduction in mean time for postoperative hospital stay (0.8 day; P value =0.1) **Table 3**. These results are consistent with those obtained in studies performed by Quah *et al* (1.71 days),[16] De Castro *et al* (1.3 day)[17] and a meta-analysis done by Purkayastha *et al* (3.27; P=0.23),[18] but not with that of Asao *et al*[10] which may be attributed to the use of laparoscopic colectomy in their study.

CONCLUSION

Gum chewing early in the postoperative period following colonic abdominal surgery significantly hastens time to bowel function and ability to tolerate feeding.

REFERENCES

1. Luckey A, Livengston E, Taché Y. Mechanisms and treatment of postoperative ileus. Arch Surg 2003; 138(2): 206-14.
2. Sarna SK. Cyclic motor activity; migrating motor complex. Gastroenterology 1985; 89(4): 894-913.
3. Sanjay M, Sham S, Pradeep T. Role of Gum Chewing on the Duration of Postoperative Ileus Following Ileostomy Closure Done for Typhoid Ileal Perforation: A Prospective Randomized Trial. Saudi J Gastroenterol 2012; 18(2): 111–117.
4. Delaney CP, Wolff BG. Postoperative ileus following bowel resection. ther. Clin risk manag 2008; 4(5): 913-917.
5. Livingston EH, Passaro EP. Postoperative ileus. Dig Dis Sci 1990; 35(1): 121-31.
6. Taché Y, Monnikes H, Bonaz B, Rivier J. Role of CRF in stress-related alterations of gastric and colonic motor function. Ann N Y Acad Sci 1993; 697: 233-43.
7. Kalff JC, Wolfgang HS, Simmons RL, Bauer AJ. Surgical manipulation of the gut elicits an intestinal muscularis inflammatory response resulting in postsurgical ileus. Ann Surg 1998; 228(5): 652-663.
8. Borody TJ, Quigley EM, Phillips SF, *et al*. Effects of morphine and atropine on motility and transit in the human ileum. Gastroenterology 1985; 89(3): 562-70.
9. Hocevar BJ, Robinson B, Gray M. Does chewing gum shorten the duration of postoperative ileus in patients undergoing abdominal surgery and creation of a stoma? J Wound Ostomy Continence Nurs 2010; 37(2): 140-6.
10. Asao T, Kuwano H, Nakamura J, Morinaga N, Hirayama I, Ida M. Gum chewing enhances early recovery from postoperative ileus after laparoscopic colectomy. J Am Coll Surg 2002; 195(1): 30-2.
11. Schuster R, Grewal N, Greaney GC, Waxman K. Gum chewing reduces ileus after open sigmoid colostomy. Arch Surg 2006; 141(2): 174-6.
12. Chan MK, Law WL. Use of chewing gum in reducing postoperative ileus after elective colorectal resection: a systematic review. Diseases of the Colon and Rectum 2007; 50(12): 2149-57.
13. Vásquez W, Hernández AV, Garcia-Sabrido JL. Is gum chewing useful for ileus after elective colorectal surgery? A systematic review and meta-analysis of randomized clinical trials. J Gastrointest Surg 2009; 13(4): 649-56.
14. Kouba EJ, Wallen EM, Pruthi RS. Gum chewing stimulates bowel motility in patients undergoing radical cystectomy with urinary diversion. Urology 2007; 70 (6): 1053-56.
15. Matros E, Rocha F, Zinner M, *et al*. Does gum chewing ameliorate postoperative ileus? Results of a prospective, randomized, placebo-controlled trial. J Am Coll Surg 2006; 202(5): 773-8.
16. Quah HM, Samad A, Neathey AJ, Hay DJ and Maw A. Does gum chewing reduce postoperative ileus following open colectomy for left-sided colon and rectal cancer? – a prospective randomized controlled trial. Colorectal Disease 2005; 8(1): 64-70.
17. D Castroa SM, van den Esschertb JW, van Heeka NT, *et al*. A systematic review of the efficacy of gum chewing for the amelioration of postoperative ileus. Dig Surg 2008; 25(1): 39-45
18. Purkayastha S, Tilney HS, Darzi AW, Tekkis PP. Meta-analysis of randomized studies evaluating chewing gum to enhance postoperative recovery following colectomy. Arch Surg 2008; 143(8): 788-93.

مجلـة طـب الموصـل

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الهيئة الاستشارية