Lecture title: Vitamins :Part 3

Lecturer Affiliation: Chapter Two

Summary:

Therapeutic uses (Niacin)

1. Prophylactically (20–50 mg/day oral) in people at risk of developing pellagra.

2. Treatment of pellagra—200 to 500 mg/day

in divided doses orally or parenterally. Striking improvement occurs in 1–2 days, but skin lesions take weeks to months. Nicotinamide is preferred, especially for injection, because it does not cause flushing and other side effects seen with nicotinic acid.

3. Hartnup's disease: in which tryptophan transport is impaired, and in carcinoid tumours which use up tryptophan for manufacturing

5-HT, need niacin supplementation

4. Nicotinic acid (not nicotinamide) has been used in peripheral vascular disease and as hypolipidaemic.

Adverse effects Nicotinic acid, in pharmacological doses, has many side effects and toxicities. Nicotinamide is innocuous.

4-Pyridoxine (vit B6)

Absorption and fate: All three forms of the vitamin are well absorbed from the intestine. They are oxidized in the body and excreted as pyridoxic acid. Little is stored.

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Physiological role and actions: Pyridoxine and pyridoxamine are readily oxidized to pyridoxal, which is then phosphorylated to *pyridoxal phosphate*—the coenzyme form. Pyridoxal dependent enzymes include transaminases and decarboxylases involved in synthesis of nonessential amino acids, tryptophan and sulfur containing amino acid metabolism, formation of 5-HT,dopamine, histamine, GABA and aminolevulinic acid (first step in the synthesis of haeme). High protein diet increases pyridoxine requirement. Pyridoxine has been shown to interact with steroid hormone receptors, but its clinical implication is not clear. Prolonged intake of large doses of pyridoxine can give rise to dependence, and mega doses (0.2–2.0 g/day) have been linked with sensory neuropathy. Otherwise, pyridoxine is free from pharmacological actions and side effects. However, suppression of lactation has been noted in nonsuckling postpartal women given high doses of pyridoxine: may be due to increased dopamine action on pituitary lactotropes.

Drug interactions

1. Isoniazid reacts with pyridoxal to form a hydrazone, and thus inhibits generation of pyridoxal phosphate. Isoniazid also combines with pyridoxal phosphate to interfere with its coenzyme function. Due to formation of hydrazones, the renal excretion of pyridoxine compounds is increased. Thus, isoniazid therapy produces apyridoxine deficiency state.

2. Hydralazine, cycloserine and penicillamine also interfere with pyridoxine utilization and action.

3. Oral contraceptives reduce pyridoxal phosphate levels in some women.

4. Pyridoxine, by promoting formation of dopamine from levodopa in peripheral tissues reduces its availability in the brain, abolishing the therapeutic effect in parkinsonism, but not when a peripheral decarboxylase inhibitor is combined with it.

5. 4-deoxypyridoxine is a vit B6 antagonist.

Deficiency symptoms Deficiency of vit B6usually occurs in association with that of other B vitamins. Symptoms ascribed to pyridoxine deficiency are—seborrheic dermatitis, glossitis, growth retardation, mental confusion, lowered seizure threshold or convulsions (due to fall in brain GABA levels), peripheral neuritis and anaemia.

Therapeutic uses

1. Prophylactically (2–5 mg daily) in alcoholics, infants and patients with deficiency of other B vitamins.

2. To prevent and treat (10–50 mg/day) isoniazid, hydralazine and cycloserine induced neurological disturbances. Acute isoniazid poisoning has been successfully treated with massive doses (in grams)of pyridoxine.

3. To treat mental symptoms in women on oral contraceptives (50 mg daily).

4. Pyridoxine responsive anaemia (due to defective haeme synthesis) and homocystinuria are rare genetic disorders that are benefited by large doses of pyridoxine (50–200 mg/day).

5. Convulsions in infants .