Hypervitaminosis

Description

Vitamins are readily available and sold in many different formulations and a wide variety of retail outlets. The food industry occasionally supplements foods with vitamins. Vitamins can be taken in excess and problems from hypervitaminosis, although uncommon, do occur.

Studies have shown that antioxidant supplements, including vitamin A and vitamin E, do not possess preventative effects and may be harmful with unwanted consequences to our health, especially in well-nourished populations. The optimal source of antioxidants seems to come from our diet, and not from antioxidant supplements in pills or tablets. Vitamin A and vitamin E supplements may even increase mortality.[1, 2]

However, vitamin D3 seems to decrease mortality in elderly people living independently or in institutional care.[3]

Vitamin C supplementation has not been shown to reduce the incidence of colds in the general population. Regular supplementation trials have shown that vitamin C reduces the duration of colds, but this was not replicated in therapeutic trials.[4]


Vitamin A is present as fatty-acid esters in food sources such as liver, kidney, and milk, and as provitamin A carotenoids in plants, usually as beta-carotene. High intake of beta-carotene (hypercarotenaemia) can colour the skin yellow, sparing the eyes (in contrast to jaundice where the sclera are also yellow).

The body stores excess amounts of vitamin A, primarily in the liver. Although excess preformed vitamin A can have significant toxicity, large amounts of beta-carotene and other provitamin A carotenoids are not associated with major adverse effects. The features of hypervitaminosis A depend on the size and timescale of the excess intake. Hypervitaminosis A following sudden, massive intake of vitamin A causes acute toxicity. More sustained intake of excess vitamin A leads to increased intracranial pressure (pseudotumour cerebri), dizziness, nausea, headaches, skin irritation, pain in joints and bones, coma, and even death.

Although hypervitaminosis A can be due to excessive dietary intakes, the condition is usually a result of consuming too much preformed vitamin A from supplements or therapeutic retinoids. Tissue levels may take a long time to fall after supplements are stopped and the resulting liver damage is not always reversible.

Excess intake of preformed vitamin A and some topical synthetic retinoids (eg, isotretinoin and etretinate) can cause congenital birth defects, including malformations of the eye, skull, lungs, and heart. Women who might be pregnant should therefore not take high doses of vitamin A supplements.

Unlike preformed vitamin A, beta-carotene is not known to be teratogenic. Even large doses of supplements of beta-carotene or diets with high levels of carotenoid-rich food for long periods are not associated with toxicity. The most significant effect of long-term, excess beta-carotene is carotenoderma, a harmless condition in which the skin becomes yellow-orange, which can be reversed by stopping ingestion of beta-carotene.

However, beta-carotene supplements, with or without retinyl palmitate, taken for 5-8 years have been associated with an increased risk of lung cancer and cardiovascular disease in current and former smokers and in men occupationally exposed to asbestos.

Pregnant women should not exceed their recommended intake of 600 micrograms/day. High doses of vitamin A can be teratogenic. Toxicity from vitamin supplements has been reported in children.[8]
Acute hypervitaminosis A
This occurs after large overdosage of the vitamin. This can occur with unusual dietary intake such as, for example, ingestion of polar bear liver, which has a very high vitamin A content. Symptoms include:

- Headache
- Abdominal pain
- Nausea or vomiting
- Lethargy
- Visual changes
- Impaired consciousness

Other features suggestive of raised intracranial pressure, such as bulging fontanelle (in an infant), papilloedema and diplopia, may also occur.

Chronic hypervitaminosis A
This requires in excess of 50,000 units/day for more than three months. Symptoms often include bone pain and bony swelling due to increased bone resorption and periosteal bone formation, often associated with hypercalcaemia. Other symptoms can be quite nonspecific:

- Scaly seborrhoeic eczema
- Patchy hair loss
- Stomatitis
- Loss of appetite
- Nausea
- Vomiting
- Malaise
- Hepatosplenomegaly
- Liver failure
- Raised intracranial pressure

Children can present with craniotabes, irritability, failure to thrive, decreased appetite and pruritus. Craniotabes is abnormally soft bones of the skull and is unrelated to tabes dorsalis.

Complications include:

- Hypercalcaemia.
- Hypercalciuria and renal stones.
- Benign intracranial hypertension.

Vitamin A may be associated with increased bone fragility and an increased risk of fractures but current evidence is inconclusive.[7]

Investigation

- FBC.
- U&E, especially if there is vomiting.
- LFTs.
- Ca++. Dual-energy X-ray absorptiometry (DEXA) scan for bone density in chronic intoxication.

Management
Stop the supplements. If there are changes in mental state, admission to hospital is required.

Prognosis
Mortality is rare. Once identified, the prognosis is good. The yellow coloration of skin will reverse with time.
Hypervitaminosis D

Vitamin D toxicity can cause nonspecific symptoms such as anorexia, weight loss, polyuria, and heart arrhythmias. More serious effects include raised blood calcium leading to urinary tract stones and also vascular and tissue calcification, causing damage to the heart, blood vessels and kidneys. Excessive sun exposure does not result in vitamin D toxicity because the sustained heat on the skin is thought to degrade previtamin D3 and vitamin D3 as it is formed. \[^8\]

Long-term intake of high-dose supplements has been shown to be associated with an increased risk of adverse health effects, with an increase in all-cause mortality, greater risk of some cancers (eg, pancreatic), greater risk of cardiovascular events, and more falls and fractures in the elderly. \[^8\]

**Presentation**

Most symptoms occur because of secondary hypercalcaemia with increased bone resorption and hypercalciuria. Features of hypercalcaemia include polyuria, polydypsia, vomiting, anorexia, lethargy, dehydration, constipation, hypertension, tetany and seizures.

The traditional description of hypercalcaemia is *stones, bones and groans*. Hypervitaminosis D is also recognised as a cause of depression. In children it can result in dental enamel hypoplasia and focal pulp calcification.

**Investigations**

Serum calcium and phosphate and 25 hydroxy-vitamin D and 1,25 dihydroxy-vitamin D levels.

**Management**

Stop the supplements and treat the cause. Bisphosphonates such as pamidronate may be used to treat hypercalcaemia. Glucocorticoids are occasionally used for a short while in severe cases of vitamin D intoxication.

**Complications**

Complications may include nephrolithiasis, nephrocalcinosis (calcium oxalate and calcium phosphate are radio-opaque stones), calcinosis of the joints and periarticular tissues, and chronic kidney disease.

**Prognosis**

Renal disease is usually reversible if recognised early.

Hypervitaminosis E

Vitamin E is present in a great many foods, particularly vegetable oils, unprocessed cereal grains, nuts and seeds. There is no evidence of any adverse effects from consuming vitamin E in food. However, high doses of alpha-tocopherol supplements can affect blood clotting, inhibit platelet aggregation and cause haemorrhage. Studies have also shown an increase in all-cause mortality associated with vitamin E supplements. \[^9\]

Supplementation with vitamin E may also significantly increase the risk of prostate cancer among healthy men. \[^10\]

**Symptoms**

Bruising and bleeding with increased prothrombin time is mediated by the inhibition of vitamin K-dependent carboxylase, and reversed by administering vitamin K. Platelet thromboxane production is also reduced. Some studies have also reported fatigue, weakness, headache and gastrointestinal upset. Impaired immunity with secondary necrotising enterocolitis has been observed in premature infants given vitamin E to prevent retrolental fibroplasia.

**Management**

Stop the supplements. Consider vitamin K if prothrombin time is prolonged.

Hypervitaminosis B6

High intakes of vitamin B6 from food sources have not been reported to cause adverse effects. However, long-term use of supplements can cause severe and progressive sensory neuropathy with ataxia. The severity of symptoms is dose-dependent and the symptoms usually stop when the supplements are discontinued. Other adverse effects of excessive vitamin B6 intake include painful skin rashes, photosensitivity, nausea and heartburn. \[^11\]

**Symptoms**

Excessive doses damage sensory nerves. This can cause:

- Paraesthesia in the hands and feet.
- Difficulty walking (poor co-ordination, "staggering").
- Reduced sensation to touch, temperature, and to vibration.
- Tiredness.
Management
Stopping the vitamin B6 resolves symptoms unless irreversible nerve damage has already occurred.

Prevention
Toxicity from excess of vitamins A and D and, exceptionally, vitamin E, can occur but it is important not to exaggerate the risk. However, the belief that vitamins are good, therefore lots of vitamins are even better is inaccurate and simplistic. There has been an explosion of interest in vitamin supplementation and a great deal of interest in nutritional medicine. This may help to inform on better diets and better dietary supplementation. It is important for doctors to be informed and to be able to identify misinformation, harmful diets and potentially harmful misuse of vitamin supplements.

Further reading & references
5. Vitamin A; National Institutes of Health (USA)
6. Vitamin B6; National Institutes of Health (USA)
7. Vitamin C; National Institutes of Health (USA)
8. Vitamin D; National Institutes of Health (USA)
9. Vitamin E; National Institutes of Health (USA)
11. Vitamin B6; National Institutes of Health (USA)

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