



Vitamin D

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Vitamin D is an essential prohormone that is largely synthesised in the skin through exposure to ultraviolet B (UVB) sunlight.

Although foods such as fatty fish, egg yolks, mushrooms, beef liver, cod liver oil and fortified dairy products contain vitamin D, recommended daily requirements are difficult to obtain from diet alone. Vitamin D has a well established role in the musculoskeletal system, supporting calcium homeostasis, bone mineralization, and general skeletal health. More recently, vitamin D is becoming known for its influence on the immune system and inflammatory disease. In particular, there is a growing interest in the role of high-dose vitamin D in respiratory infections.

PREPARATIONS: Vitamin D2 (ergocalciferol) and D3 (cholecalciferol) are commonly used for supplementation and fortification, and are formulated into tablets, capsules, oral spray, chews, cod liver oil, liquids and drops in varying doses.

ACTIVE CONSTITUENTS: Vitamin D is an inactive compound that is hydroxylated in the liver to 25-hydroxyvitamin D (25(OH)D), the main

circulating vitamin D in the body. A second hydroxylation in the kidneys yields the active form, 1,25 dihydroxycholecalciferol (calcitriol).

MEDICAL CLAIMS: Vitamin D is thought to have a beneficial function in respiratory infections and lung function. It is hypothesised that vitamin D decreases inflammation through inhibition of NF-κB-pathways, and induces antimicrobial peptides that offer protection against microbial pathogens. Use has also been promoted in dementia, obesity, multiple sclerosis, hypertension and diabetes.

EVIDENCE: Results from randomised controlled trials are inconsistent. Findings from a recent systematic review and meta-analysis suggest that 25(OH)D concentrations were more strongly associated with lower acute respiratory tract infections (ARTI) than upper ARTI, with significant associations between serum concentration and both risk and severity of ARTI – although the link was stronger with severity. Evidence suggests a greater risk of infections with 25(OH)D levels below 50 nmol/L, with supplementation of most

Summary message

Studies suggest that vitamin D may play a role in the prevention of acute respiratory tract infections in adults and children but identifying the optimal 25(OH)D concentration below which supplementation is beneficial is difficult due to lack of consistency in study reporting. Current evidence suggests supplementation is of most benefit in patients with a 25(OH)D concentration less than 37.5 nmol/L, and should be prescribed in people who are unable to increase levels through exposure to direct sunlight or diet. Sustained and prolonged intake of high dose vitamin D is associated with headaches and gastrointestinal disturbances with risks for toxicity, which could prove fatal. People at greatest risk for toxicity include those with chronic kidney disease and hyperparathyroidism. Drug interactions may occur with cholestyramine, corticosteroids, antiepileptics, orlistat, statins and diuretics.

Herbal medicines are a popular health care choice, but few have been tested to contemporary standards. **POTION OR POISON?** summarises the evidence for the potential benefits and possible harms of well-known herbal medicines.

benefit in levels less than 37.5 nmol/L, but studies have not been able to indicate an optimal concentration of 25(OH)D.

In children under 5, a 2016 Cochrane review did not yield strong evidence in support of vitamin D in preventing ARTIs. However, trials have shown some benefit. In healthy pre-school children (mean age 2.7 years), high dose (2000 IU/day) vitamin D supplementation over 4-8 months reduced incidence of all strains of influenza by 50% compared with the standard-dose (400 IU/day) group but did not reduce upper ARTI severity, frequency of GP visits or antibiotic prescribing. In one study, 1200 IU/day reduced median durations for fever, cough and wheezing in infants 3–12 months, and in another, reduced the incidence of Influenza A but not Influenza B in school-aged children. A single oral vitamin D3 dose of 100,000 IU did not lead to reduction in duration of hospital stay, mortality, paediatric intensive care admission or complications when compared to standard therapy for children aged < 5 who were hospitalized with ARTI.

Inconsistencies in reporting may be due to differing vitamin D doses and regimens, baseline 25(OH)D concentrations, and study design. The studies showed significant heterogeneity and evidence of publication bias and it is possible that benefits are over-estimated.

ADVERSE EFFECTS: Sustained high levels of 25(OH)D are associated with headaches and gastrointestinal disturbances. Severe intoxication causes hypercalcaemia, which may lead to vascular or soft tissue calcification, over-calcification of bones, kidney stones, acute kidney injury and cardiac arrhythmias. Symptoms of toxicity include nausea, vomiting, loss of appetite, dry mouth, metallic taste, constipation, muscle or bone pain, muscle weakness and abdominal pain. Toxic levels in children can result in growth restriction. People with hyperparathyroidism and chronic kidney failure are at increased risk for toxicity.

DRUG INTERACTIONS: Medications that interfere with vitamin D absorption or metabolism include orlistat, cholestyramine, corticosteroids, antiepileptics and anti-tuberculosis medications. Statins and diuretics can increase vitamin D levels.

Key references

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