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Zinc Deficiency, Excess and Supplementation

The role of zinc in the body

Zinc is an essential trace element and has a number of roles and functions in the human body.

- It is an essential component/cofactor for more than 300 enzymes involved in the synthesis and metabolism of carbohydrates, lipids, proteins, nucleic acids and other micro-nutrients.
- It stabilises cellular components and membranes and so is important for cell and organ structure and integrity.
- It is essential for cell division and is needed for normal growth and development during pregnancy, childhood and adolescence.
- It is involved in DNA synthesis and the process of genetic expression.
- It is important for immune function (both cellular and humoral immunity).
- It is involved in wound healing and tissue repair.
- It is needed for the senses of taste and smell.

How much zinc?

- Zinc is found in all body tissues and fluids and the total body zinc content is estimated at 2 g (30 mmol).^[1]
- Approximately 60% of the total body zinc content is found in skeletal muscle and 30% in bone mass.^[1]
- The choroid of the eye and prostatic fluid have high concentrations of zinc.
- Plasma zinc represents approximately 0.1% of total body zinc content.^[1]
- Zinc is absorbed in the small intestine and is excreted via the kidneys, skin and intestine (in faeces).
- There are no body stores of zinc and so daily intake of zinc is needed to maintain adequate body levels.
- The recommended daily zinc intake (reference nutrient intake) for an adult man in the UK is 9.5 mg.^[2]
- The recommended daily zinc intake for an adult woman in the UK is 7 mg.^[2]
- The Food Standards Agency and the Department of Health in the UK advise that intake of zinc should not exceed 25 mg per day.^[3]

Dietary sources of zinc

Zinc rich foods:

- Red meat and poultry (these are the main sources of zinc for many).^[3]
- Oysters, crab, lobster and other shellfish (oysters contain more zinc per serving than any other food).^[4]
- Pulses, nuts and legumes.
- Wholegrain cereals.
- Fortified breakfast cereals.
- Dairy products such as cheese.

Note that phytates in wholegrain bread, cereals, legumes and some other foods inhibit zinc absorption and so affect the bioavailability of zinc from plant foods.^[4]

Zinc deficiency

Risk factors^[4]

- Inadequate diet.
- Gastrointestinal diseases including ulcerative colitis, Crohn's disease, short bowel syndrome and chronic diarrhoea.
- Chronic liver disease.
- Chronic kidney disease.
- Alcoholism (decreases zinc absorption and increases urinary zinc excretion).
- Sickle cell disease.
- Diabetes.
- Pregnancy and breast-feeding.
- Vegetarian diet.
- People taking large amounts of iron supplementation (iron can interfere with zinc absorption).

Presentation

This depends on the severity of zinc deficiency.

- Anorexia, lethargy, diarrhoea.
- Growth restriction (delayed bone maturation).
- Impaired immune function and susceptibility to infection.

Severe cases can lead to:^[5]

- Delayed sexual maturation, impotence, hypogonadism and hypospermia.
- Alopecia, dermatitis, paronychia.
- Intellectual disability, impaired nerve conduction and nerve damage.
- Weight loss.
- Macular degeneration.
- Impaired taste and smell.
- Impaired wound healing.

Investigations

- Diagnosis may be difficult to confirm because plasma and serum zinc levels do not necessarily reflect cellular zinc status.
- Clinical signs and effects of zinc deficiency may be present with normal laboratory values.^[4]
- Clinicians need to have a high index of suspicion, particularly if risk factors are present.

Management

- This is based on both treatment of any underlying cause and zinc supplementation.
- Dietary advice should also be given.

Acrodermatitis enteropathica^[6]

- Acrodermatitis enteropathica can either be inherited or acquired.
- The acquired form can arise in people with a zinc-deficient diet.
- The inherited form is a rare autosomal recessive disorder leading to failure to generate a transport protein that enables zinc to be absorbed in the intestine:^[7]
 - Symptoms usually begin after an infant is weaned from breast milk.
 - It presents with a characteristic pustular rash over the mucocutaneous junctions, particularly around the mouth and around the anus and genital areas.
 - Hair loss, nail dystrophy, failure to thrive and severe diarrhoea are also features.
 - Atrophy of the brain cortex can lead to irritability and emotional disturbances.
 - Secondary bacterial and fungal infections may also occur.
 - Treatment is with zinc supplements.^[8]
 - If treated early, most of the symptoms are reversible and usually leave no sequelae.
 - Therapy is lifelong and total compliance is essential.

Zinc excess and zinc toxicity

Risk factors

- Zinc may accumulate in acute kidney injury.^[5]
- Those with haemochromatosis may absorb larger amounts of zinc.^[5]
- Various pesticides contain zinc salts.
- Compounds used to make paints, rubber and dyes may also contain zinc.

Presentation

- Zinc toxicity may be acute or chronic.
- Acute toxicity (ingesting more than 200 mg/day of zinc) can cause:
 - Abdominal pain, nausea, vomiting and diarrhoea.^[4, 5]
 - Other reported effects - these include gastric irritation, headache, irritability, lethargy, anaemia and dizziness.^[9]
- Prolonged intake of zinc ranging from 50-150 mg/day can lead to:
 - Disturbance of copper metabolism, causing low copper status, reduced iron function, red blood cell microcytosis, neutropenia and reduced immune function.
 - It can also lead to reduced levels of high-density lipoproteins and so it has been suggested that excessive zinc intake may be atherogenic.^[5]
 - Excess zinc can also affect cardiac function and can impair the pancreatic enzymes amylase and lipase.^[5]

Investigations

- Blood zinc levels can be measured to assess toxicity.

Management

- Treatment is symptomatic.^[10]

Metal fume fever

- Inhalation of fumes containing zinc oxide may cause metal fume fever.
- Metal fume fever can also follow inhalation of fumes of copper, magnesium, aluminium, antimony, iron, manganese and nickel during welding, galvanising or smelting.^[10]
- Symptoms may occur within 3-10 hours of exposure and usually resolve within 1-2 days.
- Symptoms include cough, dyspnoea, sore throat, chest pain, headache, fever, rigors, myalgia, arthralgia and gastroenteritis.
- Management of metal fume fever includes removing the patient from exposure, oxygen as required, and symptomatic treatment for pain and fever.^[10]

Zinc supplements

- A number of different forms of zinc are available as supplements, including zinc sulfate, zinc gluconate and zinc acetate.^[4]
- Zinc supplements must be used with caution in view of the dangers of zinc excess and zinc toxicity.

Indications for zinc supplementation

These include:

- Proven zinc deficiency and zinc-losing conditions.
- Zinc acetate is used to treat Wilson's disease.^[9]
- Total parenteral nutrition regimens usually include trace amounts of zinc. If necessary, further zinc can be added to intravenous feeding regimens.
- Zinc supplementation may reduce the incidence and prevalence of pneumonia in children aged under 5. Most deaths from pneumonia occur in low-income countries.^[11]

Supplementation during acute diarrhoea in children

- In developing countries, acute diarrhoea in children is associated with high mortality rates.
- The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) recommend zinc supplementation for 10-14 days (20 mg twice daily; 10 mg twice daily for children aged under 6 months) in children with acute diarrhoea in such countries because studies have shown that this shortens the course of the diarrhoea. [12]

Supplementation as treatment for the common cold

- A Cochrane review found that zinc supplements may reduce the duration and severity of cold symptoms if they are taken within 24 hours of onset of the symptoms but caution was advised due to heterogeneity of the data.
- Lozenges containing at least 75 mg have been the most widely studied but their use needs to be balanced against side-effects of nausea and bad taste.
- No sufficient evidence was found to support prophylactic zinc supplementation for the common cold. [13]

Supplementation for age-related macular degeneration (AMD)

- The Age-Related Eye Disease Study (AREDS) was a large, randomised, placebo-controlled trial looking at the effect of high-dose antioxidant (beta-carotene, vitamin C and vitamin E) and zinc supplements on the development of advanced AMD in people who already had different degrees of AMD. [14]
- When both antioxidants and zinc were taken, the risk of developing advanced AMD was significantly reduced and visual acuity loss was reduced as well.
- Supplementation with zinc alone reduced the risk of advanced AMD in high-risk individuals but not in the total study population.
- Zinc supplementation alone did not have a significant effect on visual acuity loss.
- A Cochrane review also supported the use of antioxidant and zinc supplementation in those with AMD. [15]

Insufficient evidence for zinc supplementation

- There is not sufficient evidence to support zinc supplements for improved mental and motor development in children. [13]
- A Cochrane review concluded that oral zinc sulfate does not help the healing of arterial and venous leg ulcers. However, the authors noted that all studies included were small and at unclear risk of bias. [16]

Cautions

- Zinc may accumulate in acute kidney injury.
- Those with haemochromatosis may absorb larger amounts of zinc.
- Excess zinc supplementation can interfere with iron and copper absorption.
- It can also reduce magnesium and calcium absorption.

Interactions [4]

- Quinolone and tetracycline antibiotics may interact with zinc supplements, leading to reduced absorption of the supplement and the antibiotic.
- Zinc supplementation can reduce the absorption of penicillamine.
- Prolonged use of thiazide diuretics increases urinary excretion of zinc and so can reduce tissue levels.

Side-effects

- Irritability, headache, lethargy. [9]
- Unpleasant taste in the mouth.
- There have been reports of anosmia with intranasal zinc preparations. [17, 18]
- Gastrointestinal effects, including abdominal pain, dyspepsia, nausea, vomiting, diarrhoea, gastric irritation, and gastritis. [9] This is more likely when supplements are taken with little or no food.
- Prolonged use of high doses of zinc can result in deficiency of copper.

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