The Prescribing of Zinc in Family Medicine

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Abstract

Zinc is a trace mineral that is required by the human body. Despite testing being readily available in the Middle East, zinc deficiency and its management is poorly understood within the family medicine model. Diagnosis can be difficult because manifestations can vary from mild to severe symptoms. We must exercise caution due to co-existing alternative mineral deficiencies. Understanding the difference between acquired and genetic deficiencies can guide treatment. This paper will focus on diagnosing and treating symptoms of zinc deficiency within the community setting.

Keywords:zinc, zinc deficiency,severe symptoms, treatment

Background

Zinc is a fundamental antioxidant in the function of enzymes and transcription factors. The micronutrient plays an important role in development, immunity, protein synthesis, taste, smell, skin and hair health. The link between zinc deficiency and the myriad signs and symptoms is currently not well understood and we suggest that is why zinc deficiency is often overlooked, especially in primary care [1].

Zinc deficiency can be delineated into two aetiologies: congenital and acquired.

Acrodermatitis enteropathica is the rare autosomal-recessive genetic disorder that causes severe zinc deficiency and affects fewer than 1 in 500,000 people globally. It typically presents in infancy with vesicular dermatitis, malabsorptive diarrhoea, chronic infections and failure to thrive [2].

Acquired zinc deficiency can be further dichotomised into nutritional and metabolic causes. Nutritional deficiency is prevalent in least developed countries where diets may have reduced quantities of zinc, as well as foodstuffs that inhibit zinc absorption: phytates, oxalates and clay. More developed countries tend to consume more meat which is rich in zinc, as well as having zinc fortification in common staple foods. Notwithstanding, metabolic conditions such as end-organ disease and HIV may reduce the level of zinc found in plasma and serum, as well as frailty and iatrogenic factors such as thiazide diuretics. Another factor to consider is that significant alcohol consumption impacts nutritional zinc levels, which is more prevalent in the developed world [3] [4].

Figure 1: Acrodermatitis enteropathica [5]

Epidemiology

It is estimated approximately 17% of the global population are at risk from zinc deficiency. This further increases to 30% in South Asia, with a similar number in the Arab World. It is estimated that there is degree of zinc deficiency in approximately 2 billion people in developing areas; those most at risk are children and the elderly [6].

There is limited data on zinc deficiency in the Middle East. Studies on school children revealed low dietary intake of zinc. In a further study it showed that it may be common in type 2 diabetic patients because of their hyperglycaemia and polyurea [7] [8].

Symptoms

Diagnosis of zinc deficiency tends to be delayed due to the gross overlap of non-specific symptoms, especially within the time-pressured environment of family medicine. Suspicion should remain high in high-risk groups, such as: end-organ damage; haemoglobinopathy; iatrogenic risk (hydrochlorothiazide, penicillamine, ethambutol, among others); elderly >65 years; alcohol excess; vegan diet. Symptoms vary depending on severity of the deficiency, with multiple organ systems affected:

Table 1: Signs and Symptoms of Zinc Deficiency [9]

Mild	Moderate	Severe
Stomatitis	Chronic kidney disease	Bullous or pustular dermatitis
Weight-loss	Chronic liver disease	Diarrhoea
Altered testosterone and sperm count	Growth retardation including osteopenia/osteoporosis	Hair-loss
Altered sense of taste	Delayed gonadal development	Recurrent infections
	Skin reactions	Immunodeficiency
	Anorexia	Mood changes
	Delayed wound healing	Neurological symptoms

Differential Diagnosis

- Hypothyroidism – Can be difficult to differentiate clinically with zinc deficiency due to overlapping symptoms. Thyroid function testing is integral [10].
- Haematinic deficiency – Can co-exist with reduced zinc; full blood count and haematinic testing can be used to differentiate [10].
- Vitamin A & D deficiency – Can also co-exist with reduced zinc; vitamin testing can be used to differentiate [10].
- Depression – Many overlapping symptoms including low mood and anhedonia. This is a clinical diagnosis and zinc levels are normal [10].
- Atopic Dermatitis – Can be differentiated clinically from zinc deficiency as this does not cause hair loss. In addition, zinc deficiency typically presents with a cutaneous rash in an acral and peri-orifical distribution [11].
- Seborrhoeic Dermatitis – Can be differentiated clinically from zinc deficiency as this typically presents in the flexural distribution [11].
- Langerhans Cell Histiocytes – Can be differentiated clinically from zinc deficiency as this presents with a papulopustular rash in the napkin area [12].
- Bullous Disorders – Can be differentiated clinically from zinc deficiency as this can leave slow-healing wounds when the blisters burst [13].
- Human Immunodeficiency Virus – Can present with recurrent infections and skin rashes. Virology testing prudent.
- Malabsorption Symptoms (including Gluten Enteropathy) – Can present with abdominal pain/distension, bloating, vomiting and diarrhoea [11] [12].

Treatment

Dietary sources of zinc can be obtained from meat, dairy and seafood such as oysters and shellfish. Plant-based sources include whole grains, nuts and beans [14]. Prior to any zinc treatment, the underlying causes must also be addressed.

The National Institute of Health stipulate the daily intake of elemental zinc is as follows (measuring the minimum quantity of absorption to match the total excretion of endogenous zinc): [15]

Table 2: Daily Intake of Zinc [15]

Age	Male	Female
Birth to 6 months	2mg	2mg
7-12 months	3mg	3mg
1-3 years	3mg	3mg
4-8 years	5mg	5mg
9-13 years	8mg	8mg
4-18 years	11mg	9mg
Adults >18 years	11mg	8mg

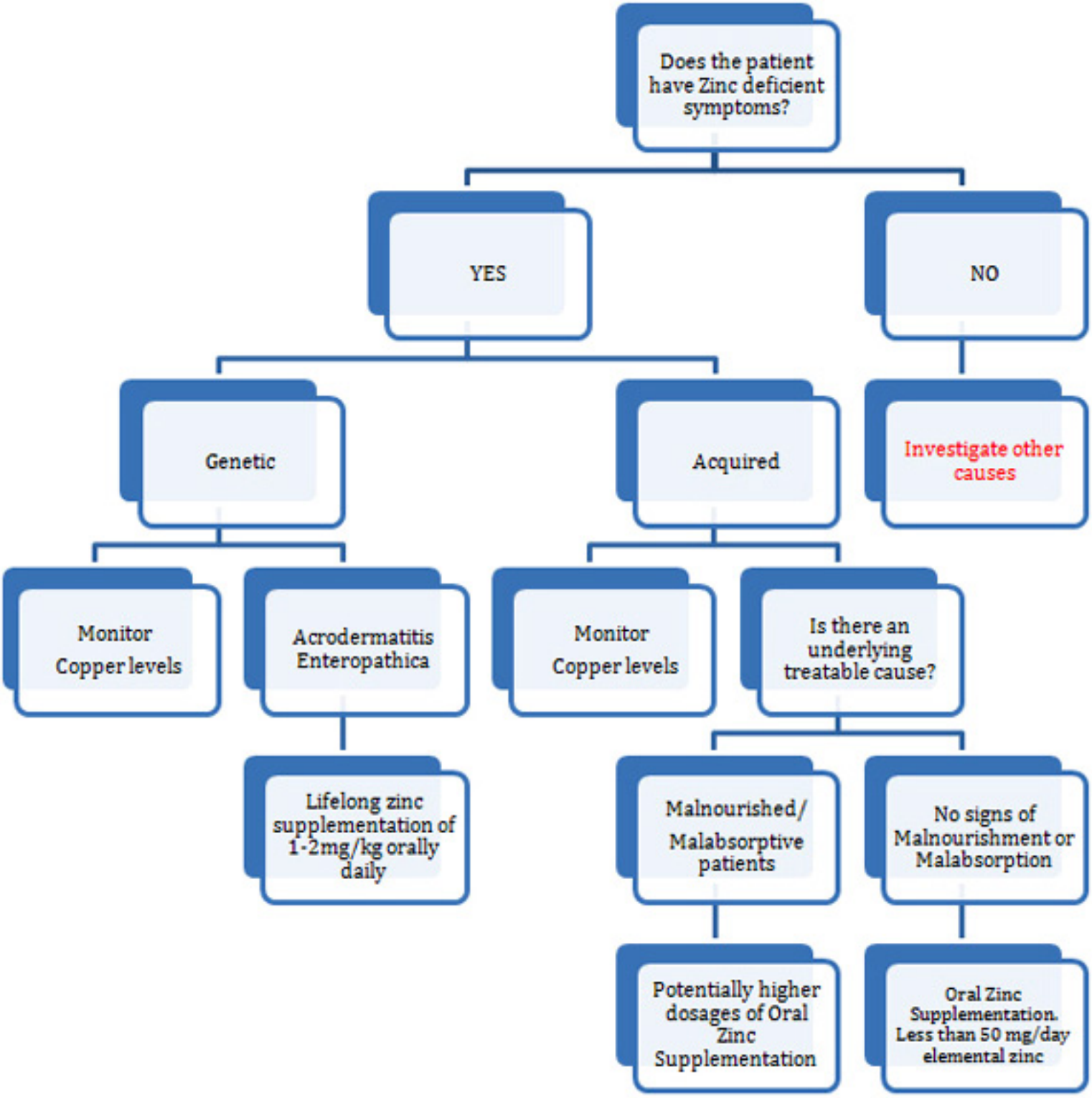
Higher doses may be required for malnourished/malabsorptive patients, pregnant or breastfeeding patients [15].

The supplemental doses of elemental zinc vary due to the degree of variability between subjects and their degree of absorption. When one looks at understanding how much zinc is required in deficiency, one should utilise the 'no observed adverse effect level' (NOAEL).

It is the consensus from several studies that high doses of zinc supplementation can cause displacement of metal ions and therefore cause potential harm. A particular element that is relevant is copper. A measure of copper status or balance can determine the safe NOAEL. This has been determined for a healthy adult to be a value of 50mg/day of elemental zinc [16] [17].

Considerations of the route of supplementation include intestinal absorption and the mode of their nutritional intake. Parenteral zinc is rarely necessary, therefore oral zinc treatment is commonly used. Oral treatment dosage should be less than this NOAEL. Some common forms of supplementation including zinc sulphate, zinc acetate and zinc gluconate. Their bioavailability may vary significantly. Actual dosages of these supplements vary, but their elemental amounts usually are generally less than 50mg [18].

Figure 2: Treating Zinc Deficiency



Monitoring

Patients should be regularly monitored for their response to treatment and alleviation of symptoms. It is widely accepted that whilst on treatment most minerals should tested up-to every 3 months. Thereafter at least yearly monitoring is required. With Acrodermatitis Enteropathica treatment can be tailored individually by monitoring.

Zinc toxicity can be classified as acute and chronic. Acute toxicity (>200mg/day) can cause neurological and gastrointestinal symptoms, whereas chronic raised levels (50-150mg/day) may affect absorption, or the metabolism of copper and iron. It can also lead to atherosclerosis, genitourinary, cardiac and pancreatic complications. Rarely can excess dietary intake cause toxic zinc levels. [10] [15] [18].

Summary

Zinc is an essential component in the human body and deficiencies can produce a varying degree of symptoms. Many other conditions share similar signs which is why the diagnosis may prove challenging to clinicians. Although there is limited data on its prevalence in the Middle East, this will change with time. More awareness is required to allow for quicker diagnosis and more rapid treatment. There may be other associated mineral deficiencies alongside zinc. Treatment can be tailored and is usually safe, but monitoring is required.

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