

A Case Series: Zinc Deficiency as a Potential Contributor to Oral Dysgeusia

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Abstract

Oral dysgeusia is relatively common, and may be caused by a number of factors. Zinc is a trace element that is critical for many enzymatic activities inside the body. Zinc deficiency is one of the causes of oral dysgeusia. The purpose of this study was to report three cases of oral dysgeusia. Haematological investigation revealed reduction in serum zinc level in all patients. They were prescribed with zinc supplement. Symptoms improved after a month of oral zinc supplementation. Zinc supplement appears to restore oral disturbance due to zinc deficiency and idiopathic taste disorders. However, we still cannot rule the placebo effect.

Keywords: Oral Dysgeusia; Taste Disorders; Zinc Deficiency; Zinc Supplement

Abbreviations: GP: General Practitioner; BMS: Burning Mouth Syndrome

Introduction

Nutritional problems are dependent on an individual's ability to access (aging, finances and refrigeration), eat (oral health), absorb (gastrointestinal disorders) and store food nutrients (demand for nutrients vs. supply). Zinc is an important trace element that is necessary for many biochemical functions, including enzyme activities, maintenance of the structural integrity of proteins and regulation of gene expression [1]. In general, zinc deficiency can cause problems of integumentary, gastrointestinal, central nervous system, immune, skeletal, and reproductive systems [2]. Moreover, zinc deficiency has been associated with disturbance of special senses including vision, taste and smell [3]. Several studies have suggested that oral dysgeusia may be one of the important symptoms of zinc deficiency [4-9].

Case reports

Case 1

In August 2014, an 80-year-old female was referred by her medical general practitioner (GP) to the Oral Medicine Clinic (School of Dentistry, Dunedin, New Zealand) for evaluation and treatment of recurrent fissures and uncomfortable tongue of five

months duration. The patient described changes in her tongue that she pointed to as being fissured areas. She described the condition as being intermittent burning sensation on the dorsal surface of her tongue bilaterally, although it was never completely asymptomatic. On the visual analogue scale, the burning sensation was 6 out of 10. She had no history of xerostomia. She was treated with nystatin oral drops and oral itraconazole, however her medical GP had no positive swabs to confirm the diagnosis of oral candidosis. Medically, she had hypertension, gastroesophageal reflux disease, and asthma, and her medication were amlodipine, bendroflumethiazide, pantoprazole, fluticasone propionate inhaler and Symbicort inhaler (budesonide and eformoterol fumarate) respectively. She had experienced adverse reaction to spironolactone, candesartan cilexetil and cilazapril. She had no history of mental health issues. On examination there was no lymphadenopathy in the submental, submandibular and cervical region. Cranial nerve examination was unremarkable. Intraoral examination was normal, other than her tongue, which showed evidence of tooth ridging laterally and fissuring with evidence of geographic tongue on the dorsal and lateral surface of tongue. Salivary flow test was normal. A tongue smear test revealed no evidence of Candida infection. Laboratory

investigations showed normal complete blood count, serum B12 and folate, and iron studies. However, she was low in serum zinc 8.7 μ mol/L (normal 10.0-17.0 μ mol/L). Therefore, we prescribed 50mg zinc sulphate capsule daily to this patient for two months, and encouraged her to have zinc-rich diet. At the six weeks review appointment, her serum zinc was 11.6 μ mol/L and patient reported her symptoms had improved significantly after two weeks zinc supplement. At three months review, no taste disturbances were reported.

Case 2

In February 2015, a 32-year-old female was referred by her general dentist to the Oral Medicine Clinic for evaluation and treatment of a seven months history of recurrent oral candidosis. She had an ectopic pregnancy and was treated with a single dose of methotrexate. Since then, she apparently had developed oral candidosis, and described lack of taste and intermittent burning sensation on the dorsal surface of her tongue bilaterally. She described the burning sensation was 5 out of 10 on visual analogue scale. She had tried a number of treatments including antifungal medications from the medical GP, probiotics and a change of diet. However, none of these treatments had relieved her symptom. Finally, she met a Naturopath who advised her that the oral candidosis could be the reaction with the mercury in the amalgam and suggested replacement of amalgam restorations. Medically, she was on no medication and had no known allergies. She had no history of mental health issues. On examination, there was no lymphadenopathy on submental, submandibular and cervical region. Cranial nerve examination was unremarkable. Intraoral examination was normal. Salivary flow test was normal. A tongue smear test revealed no evidence of Candida infection. Laboratory investigations showed normal complete blood count, serum B12 and folate, and iron studies. However, she was slightly low in serum zinc 9.9 μ mol/L (normal 10.0-17.0 μ mol/L). Therefore, we prescribed 50mg zinc sulphate daily for two months, encouraged her to have zinc-rich diet. At the review appointment six weeks later, her serum zinc was 12.4 μ mol/L and she reported symptoms had improved significantly after 7 days zinc supplement. No taste disturbances were reported at the three months review appointment.

Case 3

In April 2017, a 46-years-old female was referred by her medical GP to the Oral Medicine Clinic for evaluation and treatment of one-year history of an uncomfortable mouth. She described reduction in her saliva, lack of taste, intermittent burning sensation and changes in her tongue that she pointed to as being white-coated areas. She described the burning sensation was 7 out of 10 on visual analogue scale. Medically, she was fit and healthy. She had no history of mental health issues. On examination, there was no lymphadenopathy in the submental, submandibular and cervical region. Cranial nerve examination was unremarkable. Intraoral examination was normal. Un-stimulated and stimulated salivary

flows were within normal limits. A tongue smear test revealed no evidence of Candida infection. Laboratory investigations showed normal complete blood count, serum B12 and folate, and iron studies. However, she was low in serum zinc 8.0 μ mol/L (normal 10.0 -17.0 μ mol/L). A report was sent to her Medical GP. Her Medical GP therefore prescribed her 50mg zinc sulphate capsules daily for three months. At the review appointment six weeks later, her serum zinc was 12.6 μ mol/L and she reported symptoms had improved significantly after two weeks. No taste disturbances were reported at the four months review.

Discussion

Table 1: Zinc content of foods (NZ nutrition foundation).

Foods Rich in Zinc	Zinc (mg)
1 raw oyster	1.5
1 cup smoked mussels	4.1
1 grilled rump steak	8.0
1 roast chicken breast	1.9
1 wholegrain bread roll	0.8
1 cup cooked chickpeas	1.4
10 roasted peanuts	1.2
1 tablespoon pumpkin seeds	1.1
¼ cup edam cheese	1.0
1 cup reduced fat milk	1.0

Table 2: Clinical manifestations of zinc deficiency.

Anorexia
Smell and taste disorders
Growth impairment
Reproductive dysfunction
Wound healing impairment
Impotence
Depression, apathy
Jitteriness
Photophobia, nyctalopia, blepharitis
Cutaneous lesion
Nail hypoplasia
Hair loss
Diarrhea
Immunodeficiency

Zinc is an important trace mineral for normal growth, the immune system, nervous system development and pregnancy [10]. Zinc is found in many food sources (Table 1). Zinc deficiency may lead to a wide range of signs and symptoms (Table 2). The causes of zinc deficiency are summarized in Table 3. In general, zinc deficiency is mainly caused by malnutrition, lower food intake, medication, availability of food, and gastrointestinal disorders [11-16]. Zinc deficiency is defined as the serum or plasma zinc level is below 10.7 μ M (70 μ g/dl) (16). Zinc deficiency is a major health issue

in the world. An estimated 20.5 - 25% of the world's population is at risk of inadequate zinc intake [17,18]. Although zinc deficiency in developed countries is not a common problem, the elderly are still at high risk due to several factors [19-21]. A study from Australia and New Zealand revealed that many adolescent girls had inadequate dietary intake of zinc, and this may lead to problems in growth, immune and cognitive function, work capacity, sexual maturation, pregnancy and bone mineralization [22]. In addition, a New Zealand study [23] found younger male children were at risk of suboptimal zinc status, which was consistent with other studies [24], and pacific school and Māori children had higher prevalence of low serum zinc concentrations [25]. However, lower zinc intake appears to be more significant in developing countries. A South African study showed low zinc dietary intakes and serum zinc concentrations in elderly persons [11].

Table 3: The causes of zinc deficiency.

<p>Impairment of oral intake or absorption of zinc</p>	<p>Dietary restriction Eating disorder Primary biliary cirrhosis Chronic liver disease Chronic kidney disease Pancreatic dysfunction Inflammatory bowel diseases Ingestion of drugs with metal-chelating activity</p>
<p>Increase in excretion of zinc</p>	<p>Burn injury Diabetic ketoacidosis Chronic renal disease Chronic diarrhea Sickle-cell disease Hyperhidrosis</p>

High prevalence of zinc deficiency was found in children belonging to low socioeconomic index in India and Mexico [26,27]. In China, approximately 100 million people suffered from zinc deficiency, particularly those persons living in rural areas [28]. Moreover, diseases and medications, such as angiotensin-converting-enzyme inhibitors and diuretics can alter zinc status, and causes excessive urinary zinc excretion [13,28-31]. In particular, serum zinc levels were significantly reduced in captopril-treated patients over three months [13]. Furthermore, phytic acid that mainly presents in the plant tissue, particularly bran and seeds, can reduce the absorption of zinc in the gastrointestinal tract, thus leading to increased faecal excretion of zinc [32]. Signs of zinc deficiency, including low zinc in plasma, taste disturbance and low plasma activity of thymulin may be associated with diabetes [33-36]. Low dietary zinc intakes and serum zinc level are also found to be correlated with subclinical atherosclerosis [37]. Serum zinc concentration has been widely used to assess zinc deficiency. However, several factors, including

cancer, acute stress and inflammation can modify serum zinc level [38-41]. For example, a case report of Cronkhite-Canada syndrome demonstrated taste disturbance with normal range of plasmatic zinc levels recovered after zinc therapy [8]. Another report showed zinc supplement improved symptoms of taste disturbance patients that had normal serum zinc level [42]. Therefore, it has been suggested oral dysgeusia can occur even when serum zinc level is in the normal range [43].

Zinc Deficiency and Oral Dysgeusia

Taste is one of the five major senses in humans. There are five elements of taste perception: saltiness, sourness, bitterness, sweetness, and umaminess. The gustaoception is based on the detection of chemical simulants by the taste buds in the oral cavity. Taste buds are mainly located on the tongue, but they are also found on the soft palate, upper oesophagus and epiglottitis. The taste buds are innervated by the seventh, ninth and tenth cranial nerves. In general, gustaoception and olfaoception are considered less important than ophthamoception, audioception, and tactioception. However taste disturbance can affect the quality of life, lead to social and work related issues and, in extreme cases, may be associated with life-threatening problems [44-47]. Oral dysgeusia can be defined as a distortion of the gustaoception or persistent abnormal gustatory sensation in the absence of gustatory stimulation [48-50]. Patients with oral dysgeusia often complain of bitter, sour, or metallic sensation on the tongue, and may be associated with ageusia, which is lack of taste, and hypogesusia, which is the decrease of taste sensation. The taste disorder can be considered as one of the symptoms of neurological derangement [21]. The main causes of taste disorders are summarized in Table 4. Among these causative factors, drug-induced taste disorder and zinc deficiency are the most common [51].

Table 4: Causes of taste disorders.

<p>Physiological</p>	<p>Atrophy of oral epithelium Increase degrees of atrophy and fibrosis of acini of the salivary gland Reduction of taste buds</p>
<p>Diseases</p>	<p>Local: Dental Caries, periodontal diseases, candidosis, erythema migrans, fissure tongue, glossitis, dermatoses, denture faults Systemic diseases: Stroke, Alzheimer's disease, Parkinson's disease, Depression, Diabetes mellitus types 1 and 2, Hypo/hyperthyroidism, Chronic renal failure, Acute and chronic liver disease, cirrhosis, Sjögren's syndrome, irritable bowel syndrome, Gastroesophageal reflux disease, Hiatus hernia, Inflammatory bowel diseases, HIV</p>
<p>Iatrogenic</p>	<p>Drugs Chemotherapy/radiotherapy</p>
<p>Nutrition deficiencies</p>	<p>Iron deficiency, Folate/Vitamin B12 deficiency, Zinc deficiency</p>
<p>Allergy</p>	<p>Food and additives allergy</p>

Zinc plays a significant role in the taste perception, as zinc deficiency in healthy persons can cause taste disturbance [52]. Zinc is found in high concentration in taste buds [53]. Although the primary role of zinc in dysgeusia is unknown, but it has been suggested that zinc is a cofactor of an enzyme that involves in alkaline phosphatase activity in the membrane of taste bud. Moreover, zinc might influence gustin concentration by direct or indirect interacting carbonic anhydrase VI, which may affect the production of taste buds [50,54]. It has been suggested that zinc deficiency decrease the rate of taste buds proliferation and regeneration [55,56]. Another observation from zinc deficient rats showed lower carbonic anhydrase activity on tongue epithelium and submandibular gland [57]. Therefore, zinc deficiency may induce changes in the number, size, and structure of the taste bud cells, as well as decreases in the nerve sensitivity [57,58].

Zinc supplement can improve the symptoms of taste disorders that are caused by zinc deficiency and idiopathic taste disorders [7,42]. A study in Europe showed zinc supplement (30mg daily over 6 months) improved salt taste acuity in persons over the age of 70 years [20]. A randomized clinical trial revealed zinc supplement (20mg/day over 3 months) appeared to have beneficial effects on general gustatory function and general mood compared to the control group [50]. The recommended daily zinc supplement (25-100mg) appears to be an effective treatment for taste dysfunction [59]. After zinc supplementation, the serum zinc levels remains constant and this may due to the fact that zinc is transported into cells [60].

Psychological Factors

Several studies have shown that patients suffer from psychological disorders, such as mood disorders and anxiety disorders have higher risk than general population in developing unexplained somatic symptoms [61,62]. Psychogenic oral-facial dysaesthesia such as burning mouth syndrome (BMS) is an unpleasant burning, pricking sensation with no obviously organic causes [63]. Study has been suggested that psychological factors play an important role in the aetiology of BMS, however the exact relationship remains unclear. A number of medications have been tried to reduce the symptoms of BMS patients. Selective serotonin reuptake inhibitors found to be the most effective drugs for BMS [64]. A Cochrane review has shown that cognitive behavioral therapy can also reduce BMS symptoms [65]. These implied BMS might belong to somatoform pain disorders. In addition, one study found the acute stress event could set off the BMS in patients who have pre-existing psychological factors [66]. All patients denied any mental health problems, with clearly reduction in serum zinc in this case series. However, given that psychogenic factors, such as anxiety and depression are important in oro-facial dysaesthesia in which dysgeusia is often also reported the placebo effect of the provision of zinc supplementation maybe a source of bias [67].

Conclusion

Adequate serum zinc level is critically important for human health. Since zinc is involved in numerous enzymatic activities, it could affect taste through its role in those biochemical reactions. Zinc supplement appears to restore oral disturbance due to zinc deficiency and idiopathic taste disorders. However, we still cannot rule the placebo effect. Long-term review of these patients is recommended.

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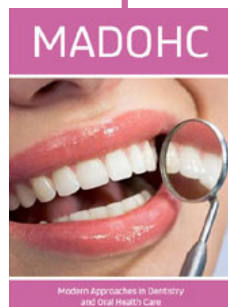
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