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Guidelines in focus

Zinc supplementation in the treatment of anorexia nervosa

Suplementação com zinco no tratamento da anorexia nervosa

*Associação Brasileira de Nutrologia (Brazilian Association of Nutrology)**

Projeto Diretrizes da Associação Médica Brasileira, São Paulo, SP, Brazil

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Description of the evidence collection method

Articles from the MEDLINE/PubMed databases were reviewed using the PICO search strategy with the following key words: ("Anorexia Nervosa"[Mesh] AND ("Zinc"[Mesh] OR "Zinc Sulfate"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Prognosis"[Mesh] OR "therapy" [Subheading])

Degree of recommendation and strength of evidence

- A: Experimental or observational studies of higher consistency.
- B: Experimental or observational studies of lesser consistency.
- C: Case reports (non-controlled studies).
- D: Opinions without critical evaluation, based on consensuses, physiological studies, or animal models.

Objective

This guideline aims to provide healthcare professionals with insight into the nutritional recommendations for zinc in the treatment of patients with anorexia nervosa. Treatment should be individualized according to the reality and experience of each professional, as well as the clinical conditions of each patient.

Introduction

Zinc

Zinc is an essential component of metalloenzymes in the organism, and plays an important role in gene transcription regulation. It is absorbed in the small intestine, stored in larger quantities in the liver, prostate, pancreas, and the central nervous system, and is mostly excreted in the feces, but also in urine and sweat¹ (D). The best sources of bioavailable zinc are described in Table 1.

Table 2 shows the recommended daily allowance (RDA)³ (D) and maximum dose (upper limit [UL])⁴ (D) of zinc.

Zinc deficiency can cause growth cessation in children, hypogeusia, immunological alterations, and night blindness;

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Table 1– Zinc content in foods (100 mg)² (D).

| Food | mg% |
|---|-----|
| Semi-skimmed milk | 0.5 |
| Hard-boiled egg | 1.3 |
| Cooked dried peas | 1.0 |
| Cooked white beans (after soaking in water) | 1.0 |
| Cooked chickpeas (after soaking in water) | 1.2 |
| Cooked lentils | 1.4 |
| Cooked soybeans | 1.4 |
| Tofu | 1.0 |
| Cooked lupini beans | 1.5 |
| Cooked rice | 0.6 |
| Raw brown rice | 1.4 |
| Whole-wheat flour | 3.0 |
| Cooked spaghetti | 0.3 |
| Mixed-grain bread | 0.8 |
| Rye bread | 1.3 |
| Oatmeal flakes | 4.5 |
| Raw spinach | 0.9 |
| Cooked cauliflower | 0.5 |
| Toasted cashew nuts | 5.7 |
| Pine nuts | 6.5 |
| Walnuts | 2.7 |

in its more severe forms, it can also cause hypogonadism, dwarfism, and olfactory loss of neural origin¹ (D).

Anorexia nervosa

Anorexia nervosa (AN) is characterized by severe weight loss and intentional use of exceedingly restricted diets, in an uncontrolled search for thinness, a gross distortion of body image, and alterations in the menstrual cycle^{5,6} (D). These eating disorders are illnesses that particularly affect female adolescents and young adults, leading to marked nutritional, psychological, and social impairment, as well as increased morbidity and mortality⁵ (D).

The criteria are summarized in Table 3, which compares the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) with those of the International Statistical Classification of Diseases and Health Related Problems, 10th revision (ICD-10)⁶ (D).

1. Is there an association between serum zinc levels and anorexia nervosa?

Clinical studies in patients with AN have shown a strong association between the disease and low serum zinc levels, and low rates of urinary zinc excretion, which demonstrates a deficiency of this micronutrient in these patients⁷ (A)^{8,9} (B).

Recommendation

Serum zinc levels should be assessed in patients with AN, since they may be low.

Table 2 – Zinc consumption according to age range and gender.

| Population | Age range | RDA | UL |
|------------|-----------------|-------|-------|
| Infants | 1 to 3 years | 3 mg | 7 mg |
| Children | 4 to 8 years | 5 mg | 12 mg |
| Males | 9 to 13 years | 8 mg | 23 mg |
| Males | 14 to 18 years | 11 mg | 34 mg |
| Males | 19 to +70 years | 11 mg | 40 mg |
| Females | 9 to 13 years | 8 mg | 23 mg |
| Females | 14 to 18 years | 9 mg | 34 mg |
| Females | 19 to 70+ years | 8 mg | 40 mg |

RDA, recommended dietary allowances; UL, tolerable upper intake level.

2. Does the degree of serum zinc deficiency influence the clinical picture of anorexia nervosa?

The severity of zinc deficiency is associated with greater weight deficits and long periods of disease duration, as well as with higher levels of depression and anxiety in patients with AN⁷ (A). There is also a similarity between symptoms caused by AN and those resulting from zinc deficiency, such as weight loss, changes in appetite, and sexual dysfunction⁹ (B).

Recommendation

Zinc deficiency may contribute to exacerbate the clinical picture of AN by aggravating weight loss, as well as increasing the duration of the disease and of the process of depression.

3. How can zinc influence the nutritional status of patients with anorexia nervosa?

Zinc participates in the mechanisms of smell and taste perception, and the regions in the central nervous system and sensory receptors that perceive and interpret the pleasures of eating are very rich in zinc¹⁰ (D). The reduced food intake and consequent malnutrition that characterize patients with AN lead to such deficiency^{8,9} (B), in addition to low zinc-content diets and purging episodes, which impair zinc absorption⁷ (A)⁸ (B).

Thus, the acquired zinc deficiency may contribute to the chronicity of alterations in eating behavior, perpetuating the major disorder⁸ (B), which results in a vicious cycle of nutrient deficiency and loss of enjoyment in eating, linked to loss of smell and taste¹⁰ (D).

Recommendation

The nutritional status of patients with AN may be directly influenced by zinc deficiency, as it contributes to the alterations in eating behavior through the senses of smell and taste.

Table 3 – Diagnostic criteria for nervous anorexia.

| DSM-IV | ICD-10 |
|--|---|
| 1. Refusal to maintain weight within the normal minimum range for age and height; for instance, weight loss, leading to maintenance of body weight below 85% of the expected, or failure to gain the expected weight during the growth period, leading to a body weight less than 85% of the expected 2. Intense fear of gaining weight or becoming fat, even though the patient is underweight 3. Disorders in the way one experiences his/her own weight, size, or body shape through self-evaluation; denial of underweight severity 4. With regard specifically to women, the absence of at least three consecutive menstrual cycles, when the opposite is expected to occur (primary or secondary amenorrhea). A woman is considered as having amenorrhea if her periods occur only after the use of hormones, such as estrogen administration | a) Weight loss or, in children, lack of weight gain, and body weight is maintained at least 15% below the expected level b) Weight loss is self-induced by avoiding consumption of "fattening foods" c) There is a distortion in body image in the form of a specific psychopathology of fear of becoming fat d) A prevalent endocrine disorder involving the hypothalamic-pituitary-gonadal axis is observed in women, presenting as amenorrhea, and in men as loss of sexual interest and potency (an apparent exception is the persistence of vaginal bleeding in anorexic women who are receiving hormone replacement therapy, most commonly taken as contraceptive pills) |
| Type: | Comments: |
| – Restrictive: there are no episodes of binge-eating or purging (self-induced vomiting, use of laxatives, diuretics, enemas) – Purgative: there are episodes of binge eating and/or purging | If onset is prepubertal, the sequence of puberty events is delayed or even arrested (growth ceases; in girls, the breasts do not develop and there is primary amenorrhea; in boys, the genitals remain prepubertal). With recovery, puberty is often achieved normally, but menarche is delayed. The following aspects confirm the diagnosis, but are not essential elements: self-induced vomiting, self-induced purging, excessive exercising, and use of appetite suppressants and/or diuretics |
| DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4 th edition; ICD-10, International Statistical Classification of Diseases and Health Related Problems, 10 th revision. | |

4. Is zinc supplementation indicated in patients with anorexia nervosa?

Oral supplementation with zinc as an adjuvant to traditional dietary and psychological therapy was a hypothesis tested for the treatment of AN, based on the coincidence of signs and symptoms of this disorder and zinc deficiency, in addition to biochemical evidence of this deficiency in anorexic patients⁸ (B).

A controlled study showed a two-fold higher rate of BMI increase and an improvement in brain neurotransmitters, including gamma-aminobutyric acid (GABA) in the group receiving zinc supplementation as an adjuvant disease treatment¹¹ (A).

Recommendation

Zinc supplementation should be encouraged in the treatment of AN.

5. What is the impact of zinc supplementation on the nutritional status of patients with anorexia nervosa?

The most important and more frequent finding in oral supplementation with zinc was the increase in weight gain^{11,12}

(A)^{13,14} (B)¹⁵ (C)¹⁶ (D) and the increase in muscle mass index (MMI)^{11,12} (A). The increase in weight gain was due to the improvement in appetite, taste, and increased food intake, in addition to the improvement of pancreatic exocrine function and intestinal absorption¹⁵ (C).

Recommendation

Zinc supplementation may promote an increase in muscle mass and improve appetite in patients with AN.

6. What is the impact of zinc supplementation on the nervous system of patients with anorexia nervosa?

Zinc supplementation decreases the biochemical signs of zinc deficiency, such as low concentrations of zinc in serum and urine, increasing their levels¹⁴ (B). There is also evidence that zinc supplementation corrects abnormalities related to neurotransmitters, such as GABA metabolism and alterations in the amygdala. Both usually appear altered in AN patients, and are related to the physiopathology of the disease. This correction eventually brings clinical benefits to these patients¹¹ (A).

It was observed that zinc supplementation also contributes to improvement of depression and anxiety states, which are often elevated in patients with AN⁷ (A)¹⁶ (D).

Recommendation

Zinc supplementation can prevent abnormalities related to neurotransmitters and reduce levels of depression and anxiety.

7. Is there any contraindication to zinc supplementation in patients with anorexia nervosa?

Oral supplementation with zinc demonstrated no significant side or adverse effects^{7,11,12} (A)¹⁴ (B), and it presents low toxicity at the recommended doses¹² (A)¹⁵ (C)¹⁶ (D).

Recommendation

There is no evidence of side effects that might prevent zinc supplementation.

8. What is the recommended dose for oral supplementation with zinc?

Dose determination for oral supplementation with zinc remains quite heterogeneous and are the subject of debate.

Among these different determinations, the following are indicated for oral supplementation:

- 14 mg of elemental zinc^{11,12} (A), or
- 15 mg of elemental zinc¹⁵ (C), or
- 45 mg of elemental zinc¹³ (B), or
- 50 mg of elemental zinc⁷ (A), or
- 60 mg of elemental zinc, twice a day¹ (D).

Elemental zinc in 25 to 50 mg, in three daily doses¹⁷ (D), and oral administration of 14 mg of elemental zinc daily for two months in all patients with AN must be indicated as routine¹¹ (A).

Recommendation

Preventively, 15 mg of elemental zinc must be administered. In cases in which zinc deficiency is demonstrated (biochemical methods), the drug dose must vary between 15 and 20 mg of elemental zinc daily, for a minimum period of two months.

Conflicts of interest

The authors declare no conflicts of interest.

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