Guidelines in focus

Zinc supplementation in the treatment of anorexia nervosa

Suplementação com zinco no tratamento da anorexia nervosa

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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.

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.

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)2 (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;
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 higher levels of depression and anxiety in patients with AN\(^7\) (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 dysfunction\(^9\) (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 zinc\(^10\) (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 absorption\(^7\) (A)\(^8\) (B).

Thus, the acquired zinc deficiency may contribute to the chronicity of alterations in eating behavior, perpetuating the major disorder\(^8\) (B), which results in a vicious cycle of nutrient deficiency and loss of enjoyment in eating, linked to loss of smell and taste\(^10\) (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.
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 patients (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 treatment (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 absorption (C).

Recommendation
Zinc supplementation may promote an increase in muscle mass and improve appetite in patients with 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 (A, B) and the increase in muscle mass index (MMI) (C) and the increase in muscle mass index (MMI) (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 absorption (C).

Recommendation
Zinc supplementation should be encouraged in the treatment of 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 levels (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 patients (A).
It was observed that zinc supplementation also contributes to improvement of depression and anxiety states, which are often elevated in patients with AN. Zinc supplementation can prevent abnormalities related to neurotransmitters and reduce levels of depression and anxiety.

**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, and it presents low toxicity at the recommended doses.

**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, or
- 15 mg of elemental zinc, or
- 45 mg of elemental zinc, or
- 50 mg of elemental zinc, or
- 60 mg of elemental zinc, twice a day.

Elemental zinc in 25 to 50 mg, in three daily doses, and oral administration of 14 mg of elemental zinc daily for two months in all patients with AN must be indicated as routine.

**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.

**REFERENCES**

3. United States Department of Agriculture [accessed 22 Oct 2011]. Available from: http://www.iom.edu/Activities/Nutrition/SummaryDRIs/~/media/Files/Activity%20Files/Nutrition/DRIs/5_Summary%20Table%20Tables%201-4.pdf