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USE OF ZINC IN THE TREATMENT OF ACUTE DIARRHEA IN CHILDREN: LITERATURE REVIEW

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ABSTRACT

Objective: To evaluate the effectiveness of zinc supplementation in the treatment of acute diarrhea in children, focusing on reducing severity, and duration and preventing new episodes. Methods: This is a literature review, using the Google Scholar, PUBMED, Scielo, and LILACS databases together with information from Manuals and Guides of the World Health Organization and Ministry of Health, obtaining 24 articles. Bibliographic Review: Acute diarrhea, characterized by three or more liquid bowel movements in 24 hours, is one of the main causes of infant mortality, especially in developing countries. Several studies show zinc supplementation as an effective measure in reducing the duration and severity of diarrheal episodes in childhood, in addition to preventing recurrences. In addition, its use appears to decrease the frequency and duration of bowel movements and reduce hospitalizations. In addition to its use in acute diarrhea, there appear to be benefits in cases of pneumonia and malaria. Although effective, mild adverse effects, such as vomiting, reduce treatment adherence, and further studies are needed to assess the minimum dose required. Conclusion: Zinc supplementation, recommended by the WHO since 2004, reduces the severity and duration of diarrhea in children. However, research is possible to improve the dose and minimize adverse effects.

Keywords: Acute Diarrhea. Zinc. Child Health.

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INTRODUCTION

Acute diarrhea is defined as the occurrence of three or more semi-liquid or liquid bowel movements within the last 24 hours. According to the World Health Organization (WHO, 2005), diarrheal disease can be classified into three categories: acute watery diarrhea (lasting up to 14 days with significant fluid loss), acute bloody diarrhea (blood in stools with intestinal mucosal damage), and persistent diarrhea (lasting 14 days or more). Diarrhea lasting more than 30 days is considered chronic.

Acute diarrhea is the leading cause of death in children under 5 years of age. In Brazil, there is a significant mortality rate among children due to this condition. In regions with limited access to basic sanitation and healthcare, these infections are more frequent and recurrent (SAMPAIO et al., 2013).

Some symptoms may accompany diarrhea, such as fever, nausea, vomiting, and abdominal pain, exacerbating dehydration. Due to the magnitude of the problem, various therapies have been used to reduce the severity of the disease in low- and middle-income countries. Among these therapies, zinc supplementation has been increasingly implemented.

Micronutrients such as zinc, copper, and magnesium are essential for enzymatic reactions, immune response, and cellular replication. Without these micronutrients, individuals become more susceptible to infections and immune disorders. Zinc, a mineral, has been used for several years as a supplemental therapy to reduce gastrointestinal losses and, consequently, the severity of episodes, as well as to decrease the duration and risk of recurrence in subsequent months. Zinc deficiency has been associated with immune system insufficiency and persistent diarrhea (SAMPAIO et al., 2013).

Some countries have already implemented zinc supplementation in diarrhea management following the WHO's recommendation in 2004. However, the use of zinc is not yet effectively widespread. In Kenya, zinc was adopted as part of the essential medicines kit available in healthcare units to facilitate population access (FEIKIN et al., 2014).

Children are the highest-risk group for gastrointestinal infections due to their increased exposure to infectious agents during development, especially in childcare settings such as daycare centers and schools. These infections irritate the intestinal

mucosa, impairing the absorption of nutrients essential for biological growth, as well as neurological and immune development in these children (MACÊDO et al., 2010).

Children in developing countries, in particular, often suffer from zinc nutritional deficiencies. This may be related to the high incidence of diarrhea in these regions (LIMA e DIAS, 2010).

The role of zinc in the body is not fully understood, but its use has been shown to increase the absorption of electrolytes and water by the intestines. Additionally, zinc has anti-inflammatory functions in the intestinal villi mucosa, potentially regenerating the epithelium affected by diarrhea. This leads to an increase in the number of enzymes in the microvilli, improving digestion and nutrition (ARAÚJO, 2014).

Studies on zinc treatment have demonstrated a reduction in the number of diarrheal episodes and their severity. Beyond these benefits, some studies have shown a relationship between dietary zinc adaptation and cognitive development. Despite the importance of these studies for child health, they remain scarce in Brazil (BORGES et al., 2007).

METHODOLOGY

This is a descriptive study, specifically an integrative literature review, aimed at evaluating the efficacy of zinc supplementation in the treatment of acute diarrhea in children, focusing on reducing severity, and duration, and preventing new episodes. To obtain the articles, the following databases were used: Google Scholar, PUBMED (Medical Publications), Scielo (Scientific Electronic Library Online), LILACS (Latin American and Caribbean Literature in Health Sciences), along with information from WHO and Ministry of Health manuals and guidelines.

RESULTS

Scientific articles published in Portuguese, English, and Spanish were selected, resulting in 35 articles on the use of zinc in acute diarrhea. After reviewing them, 24 materials were chosen for the development of this article.

DISCUSSION

The WHO and the Ministry of Health (MS) already recommend the use of zinc in diarrheal episodes, reporting that this measure can prevent future episodes. However,

despite recommendations from major institutions, few studies in this area prove its efficacy (BRANDT et al., 2015).

In 2004, this recommendation began based on studies showing that zinc use shortens the duration of acute diarrhea and prevents new episodes in the 2 to 3 months following its use.

The study by Bhutta et al. (1999) was one of the studies used by the WHO to support zinc supplementation. This study evaluated the effects of zinc supplementation in preventing diarrhea and pneumonia through a meta-analysis of randomized clinical trials in children from developing countries. The trials analyzed were those that provided oral supplementation of this mineral, with at least half the recommended daily dose for children under five years of age. The results in children who used zinc showed a reduction in the incidence and prevalence of diarrheal disease by 18% and 25%, respectively, compared to the control group. Additionally, it demonstrated a 41% reduction in the incidence of pneumonia compared to the control group.

The article by Sazawal et al. (1995) was another study used as a basis for the current WHO recommendation. This study evaluated the supplementation of 20 mg of zinc in children in India through a randomized clinical trial. The results showed a 23% reduction in the risk of diarrhea in children who received supplementation. Furthermore, it was observed that the earlier zinc was used, the faster the likelihood of recovery from the condition.

The study by Black et al. (2019) showed that the treatment of diarrhea with oral rehydration solution (ORS), zinc, antibiotics for dysentery, and treatment of persistent diarrhea, along with the rotavirus vaccine, accounted for 49.7% of the reduction in diarrhea mortality from 1980 to 2015. Additionally, it showed that despite proven benefits and a global recommendation made in 2004, therapeutic zinc coverage remains very low in some developing countries.

Zinc is an essential micronutrient for the body's homeostasis. This mineral acts as a mediator in various enzymatic reactions, as well as in the regulation of inflammatory cells, immune response, and stimulation of protein synthesis. In the article by Farthing et al. (2013), zinc deficiency is associated with immune system suppression and the prevalence of periodic diarrhea.

This micronutrient acts in the pathophysiology of acute diarrhea by accelerating the tissue regeneration of intestinal cells, particularly enterocytes, which recover their

function of absorbing water and salts, reducing the duration of diarrhea and its complications. Additionally, zinc regulates immune system cells, stimulating the regeneration of the intestinal mucosa, which acts as a defense barrier (BRITO et al., 2016).

The study by Lukacik et al. (2008) conducted a meta-analysis of the effects of oral zinc in the treatment of acute and persistent diarrhea. The results showed that the average duration of diarrhea was significantly shorter with zinc use compared to placebo, and it was effective in reducing mortality. However, there was a significant increase in vomiting in patients who received zinc therapy.

In the meta-analysis by Lamberti et al. (2013), studies from 1980 to 2012 on the use of zinc during acute diarrhea in hospitals across various countries were reviewed. This research found that the duration of diarrhea decreased after oral zinc supplementation. The results showed that diarrheal episodes were 4% shorter in children treated with zinc compared to those who received a placebo. In hospitalized children, the duration of hospitalization decreased by 37% in those supplemented with zinc. Additionally, the frequency of stools decreased by 6%.

This study also found that zinc use reduced the duration of fever, stool production, and the frequency of bowel movements. It was concluded that supplementation with this mineral was able to reduce the morbidity and mortality of acute diarrhea in children under five years of age, both inside and outside China. In agreement with the study by Lukacik et al. (2008), an increase in the frequency of vomiting was observed.

According to the clinical trial by Sampaio et al. (2013), the incidence of acute diarrhea in the test group, which received a daily sachet with added zinc and micronutrients for 90 days, was 14.7%. In the control group, which received the supplement without zinc for 90 days, it was 19.1%. Thus, the test group showed a lower risk of developing diarrhea than the control group, but this result was not statistically significant. However, regardless of the group, the study showed a lower risk of developing diarrhea in individuals over 24 months of age. Additionally, there was no significant difference in the duration of diarrheal episodes between the two groups. In the test group, the maximum duration of diarrhea was 6 days, and in the control group, it was 5 days.

The study by Feikin et al. (2014), randomized 16 Kenyan villages (1,903 eligible children) to receive a 10-day cycle of zinc and oral rehydration solution (ORS) at home and 17 villages (2,241 eligible children) to receive ORS at home but zinc-only at the health unit, evaluated whether the incidence of diarrhea and acute respiratory disease decreased in villages with home zinc use. This clinical trial found that 6.1% of children still had diarrhea in villages with home zinc use, compared to 5.6% in the comparison villages. Thus, there was no significant difference in the reported incidence of diarrhea, as well as febrile and more severe episodes. There was also no difference between the village groups in hospitalization rates and all-cause mortality. The reasons for this outcome were likely the small number of children receiving zinc in the community, study design limitations, and surveillance biases.

However, diarrheal episodes in zinc villages resulted in less frequent use of antimalarials and antibiotics. Children with diarrhea and reported fever in zinc villages (approximately two-thirds of diarrheal episodes) received an antimalarial less frequently (17.8%) than in comparison villages (23.5%).

According to Walker and Walker (2014), the efficacy of zinc in treating diarrhea is 23%, and it may also reduce the mortality rate caused by diarrhea in children aged 1 month to 4 years. Some other studies also show that this supplementation reduces the incidence of diarrhea for 2 to 3 months and shortens the duration of prolonged diarrhea by 25%.

The study by Imdad et al. (2023) evaluated the effects of zinc supplementation on preventing morbidity and mortality and promoting growth and development in children aged six months to twelve years. It analyzed 96 randomized clinical trials conducted in 34 different countries, mostly in low- or middle-income countries. It was shown that zinc supplementation made little or no difference in all-cause diarrhea mortality but reduced mortality from lower respiratory tract infections and malaria. However, despite not showing an effect on morbidity, preventive zinc supplementation was effective in reducing the incidence of diarrhea.

The WHO recommends a dosage of 10 mg/day for children under 6 months of age and 20 mg/day after 6 months of age, for 10 to 14 days. However, some studies have shown intolerance to this dosage.

Lazzerini and Wanzira (2016) conducted a literature review of only randomized clinical trials that compared oral zinc supplementation with a placebo in children aged

one month to five years with acute or persistent diarrhea, including dysentery. This study concluded that in areas where the prevalence of zinc deficiency or malnutrition is high, zinc may be beneficial for children aged six months or older. The evidence showed that in children over six months of age, zinc therapy reduced the average duration of diarrhea and the average number of children with diarrhea by the seventh day. Additionally, zinc therapy did not show serious side effects in any age group, although it reported a higher risk of vomiting in both age groups.

Finally, the study concluded that in children under 6 months of age, the evidence did not demonstrate an effect of zinc on the average duration of diarrhea or the number of children still experiencing diarrhea on the seventh day. Furthermore, there was no benefit from zinc therapy in well-nourished children and areas with a low risk of zinc deficiency.

In search of an alternative to minimize the adverse effects of vomiting during zinc therapy, Dhingra et al. (2012) conducted a randomized, double-blind clinical trial. The objective was to evaluate whether lower doses of zinc could reduce this side effect without compromising the efficacy of diarrhea treatment. The standard dose recommended by the WHO is 20 mg/day for children over 6 months, but this study tested doses of 5 mg and 10 mg/day.

The proportion of children whose diarrhea lasted more than five days was 6.5% in the 20 mg group, 7.7% in the 10 mg group, and 7.2% in the 5 mg group. Compared to the standard dose of 20 mg, the lower doses were equally effective in treating diarrhea and resulted in fewer cases of vomiting. Vomiting within 30 minutes of zinc administration occurred in 19.3% of the 20 mg group, 15.6% of the 10 mg group, and 13.7% of the 5 mg group, with significant reductions in the 10 mg group.

Therefore, the use of zinc in acute diarrheal episodes is currently a recommended measure, with numerous studies demonstrating its benefits. However, there is still a gap regarding the correct dosage, recommended age for use, and potential side effects.

CONCLUSION

The use of zinc should be considered in the treatment of acute diarrhea in children aged 6 months to 5 years, especially if malnourished or at risk of zinc deficiency. The benefits extend beyond diarrhea prevention and reduction of episodes, also showing promise in

respiratory tract infections and potential benefits in malaria, a diseases with high incidence in underdeveloped and developing countries. Despite the advantages of its use and well-established recommendations by global and national organizations, more studies are needed on dosage to minimize side effects such as nausea and vomiting, as well as its efficacy in children under 6 months of age.

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REFERENCES

1. Araújo, C. M. A. (2014). Tratamento da diarreia aguda [Dissertação de Mestrado, Universidade Fernando Pessoa].

2. Bhutta, Z. A., et al. (1999). Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries: Pooled analysis of randomized controlled trials. The Journal of Pediatrics, 135(6).

3. Black, R., et al. (2019). Drivers of the reduction in childhood diarrhea mortality 1980–2015 and interventions to eliminate preventable diarrhea deaths by 2030. Journal of Global Health, 9(2).

4. Borges, C. V. D., et al. (2007). Associação entre concentrações séricas de minerais, índices antropométricos e ocorrência de diarreia entre crianças de baixa renda da região metropolitana do Rio de Janeiro. Revista de Nutrição, 20.

5. Brandt, K. G., et al. (2015). Diarreia aguda: manejo baseado em evidências. Jornal de Pediatria, 91(1), 36–43.

6. Brito, B. B. O., et al. (2016). Uso de zinco em casos de diarreia aguda em crianças. Journal of Medicine and Health Promotion, 1, 355–364.

7. Dhingra, U., et al. (2012). Effect of reduced zinc dose on vomiting in children with acute diarrhea: A randomized clinical trial. The Lancet, 379, 1230–1238.

8. Dhingra, U., et al. (2020). Lower-dose zinc for childhood diarrhea – A randomized, multicenter trial. The New England Journal of Medicine, 383, 1231–1240.

9. Farthing, M., et al. (2013). Acute diarrhea in adults and children. Journal of Clinical Gastroenterology, 47, 12–20.

10. Feikin, D. R., et al. (2014). Village-randomized clinical trial of home distribution of zinc for treatment of childhood diarrhea in rural western Kenya. PLoS ONE, 9(5).

11. Imdad, A., et al. (2023). Zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years. Cochrane Database of Systematic Reviews, 3(3).

12. Lamberti, L. M., et al. (2013). Oral zinc supplementation for the treatment of acute diarrhea in children: A systematic review and meta-analysis. Nutrients, 5(11).

13. Lazzerini, M., & Wanzira, H. (2016). Oral zinc for treating diarrhea in children. Cochrane Database of Systematic Reviews, 12(12).

14. Lima, R., & Dias, J. (2010). Gastroenterite aguda. Nascer e Crescer: Revista do Hospital de Crianças Maria Pia, 19(2).

15. Lukacik, M., et al. (2008). A meta-analysis of the effects of oral zinc in the treatment of acute and persistent diarrhea. Pediatrics, 121, 326–336.

16. Macêdo, E. M. C., et al. (2010). Efeitos da deficiência de cobre, zinco e magnésio sobre o sistema imune de crianças com desnutrição grave. Revista Paulista de Pediatria, 28(3).

17. Sampaio, D. L. B., et al. (2013). Suplementação de zinco e outros micronutrientes através do uso de sprinkles: Impacto na ocorrência de doença diarreica e infecções respiratórias em crianças institucionalizadas. Jornal de Pediatria, 89(3).

18. Sazawal, S., et al. (1995). Zinc supplementation in young children with acute diarrhea in India. The New England Journal of Medicine, 333, 839–844.

19. Sociedade Brasileira de Pediatria. (2009). Avaliação nutricional da criança e do adolescente: Manual de orientação. Departamento de Nutrologia.

20. Sociedade Brasileira de Pediatria. (2017). Diarreia aguda: diagnóstico e tratamento (Nº 1, Março).

21. Sociedade Brasileira de Pediatria. (2023). Diarreia aguda infecciosa (Nº 74, Junho).

22. UNICEF; WHO. (2009). Diarrhea: Why children are still dying and what can be done. United Nations Children's Fund.

23. Walker, C. L. F., & Walker, N. (2014). The Lives Saved Tool as a model for diarrhea mortality reduction. BMC Medicine, 12(70).

24. World Health Organization. (2005). The treatment of diarrhoea: A manual for physicians and other senior health workers (WHO/CAH/03.7).