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Research Notes

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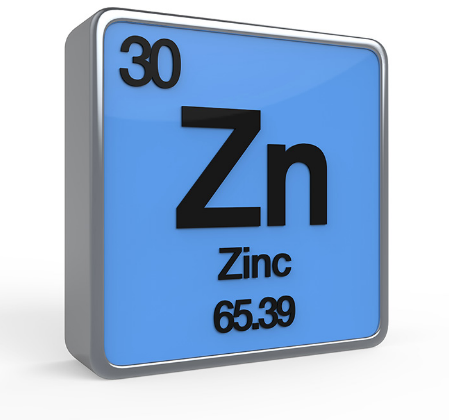
The Role of Zinc in the Immune System



Many nutrients are involved in making sure the immune system functions properly. Some minerals that are involved include selenium, copper, magnesium and zinc. Zinc's role in immunity has been studied extensively. In this Research Note, we are going to examine some of the recent research involving zinc and the immune system.

To help understand zinc's role in the immune system, it is helpful to review the essentiality of zinc in the body. Zinc is a nutrient whose essentiality in humans was first demonstrated by Prasad[1]. Subsequently, it has been shows to be part of the active center of more than three hundred enzymes. It is also essential for growth through DNA replication, RNA transcription, cell differentiation, and apoptosis[1].

Given the multitude of its physiological roles, zinc is homeostatically controlled in the body. There are two main protein families that are primarily responsible for zinc homeostasis. The first group are fourteen importer proteins which designated as the SLC39A1-A14 proteins and called ZIP proteins. Physiologically, the ZIP proteins import zinc into the cytosol from extracellular spaces or from intracellular compartments. The second group is the exporter proteins which are designated SLC30A1-A10 and called ZnT proteins. These ZnT proteins are responsible for transporting zinc out of the cytosol[2]. Both families or groups of proteins are distributed throughout the body. Other zinc protein players include metallothionein and albumin.

> **Zinc has been shows to be part of the active center of more than three hundred enzymes.**

Essential for T-cell development

Zinc has been shown to be essential for the proper T-cell development. T-cells or T-lymphocytes are a type of white blood cell that is of key importance to the immune system and is at the core of adaptive immunity – the system that tailors the body's immune response to specific pathogens. T-cells mature and differentiate in the thymus. During zinc deficiency, the thymus cannot adequately product thymulin. Thymulin binds to high affinity receptors and causes differentiation and promotes T-cell function, including cytotoxicity, suppressor function and interleukin production[3]. A recent publication suggests that thymulin expression is sensitive to zinc adequacy in animals. In this study, rats were fed zinc at either 5 or 25 ppm in their diets. Five ppm represents approximately 20% of an adequate intake. They found that the rats on 5 ppm zinc diet had 62% less thymulin than those fed 25 ppm zinc[4].

Zinc has further interactions with T-cells. Interleukin-2 (IL-2) is a cytokine predominantly secreted by activated T-cells. When IL-2 binds to its receptor, it causes a zinc flux. Zinc is released from zincosomes and lysosomes and is linked to the activation of the ERK1/2 pathway [5]. ERK1/2 is a member of a protein kinase superfamily that can mediate cell proliferation and apoptosis (cell death)[6].

Essential for B-cell function

Zinc may also be essential to B-cell function. B-cells (lymphocytes) are a type of white blood cell whose principle function is to secrete antibodies. Acute zinc deficiency causes an overall reduction in B-cell numbers [4]. One possible mode of function may be in the interaction of ZIP10 proteins and B-cells. Some data suggests that ZIP10 and the B-cell receptor are linked together to promote antigen sensing. Furthermore, zinc deficiency has been shown to increase apoptosis (cell death) in B-cells[5]. In a practical sense, vaccination effectiveness is dependent on the formation of antibodies to the antigen, but if the person is zinc deficient, there may be reduce effectiveness due to reduced B-cell activity.

Essential for acute phase inflammatory response

Acute phase inflammation is a normal response in the immune system. Zinc has been shown to be essential to this process. In acute phase responses adequate zinc status is essential because zinc homeostasis is temporarily disrupted. Zinc is transferred from the serum into the organs causing a temporary hypozincemia. Mechanistically, it has been proposed that when inflammation starts, NF- B (Nuclear Factor kappa-light-chain-enhancer of activated B cells) activates the expression of the zinc importer ZIP8 which then attaches to the cellular membrane. This causes zinc to be imported into the cellular spaces which then acts as signals for other processes[2]. This temporary movement of zinc into the cellular spaces eventually is resolved and homeostasis is restored. Some have postulated that this movement may act as a danger signal to the body to react[5].

Essential to deal with oxidative stress

Zinc is also essential in helping to deal with oxidative stress in and to the body. In normal physiological conditions, cell will produce reactive oxygen species (ROS) as part of metabolic function. Additionally, there are external stresses such as radiation (sun), pollution, smoke, etc. All these produce ROS which can damage cellular structures and may lead to the development of some chronic diseases. Zinc is the co-factor in the Cu/Zn SOD (superoxide dismutase) enzyme complex. This enzyme complex catalyzes the detoxification of superoxide radicals into less harmful oxygen and hydrogen peroxide which the body can then eliminate through other enzyme systems[2].

Essential to the immune system

It is often said that the best offense is a good defense. This applies with the immune system. The body has an extensive physical defense in the epithelial lining of the lungs and gastrointestinal tract. Critical to maintaining the epithelial layers is to maintain the membrane barriers and the connecting proteins. Zinc deficiency has been shown to accelerate the degradation of E-cadherin and Beta-catenin in the alveolar epithelial lining[2]. Externally, the epidermis and dermal layers provide the same defensive function, and zinc is essential to the maintenance and repair of these layers. In addition to protection against ROS as previously discussed, zinc is an essential cofactor in enzyme systems that remove dead tissue and movement of keratinocytes involved in wound healing[2].

Having illustrated the essentiality of zinc to the immune system and its response to challenges, is there utility in boosting zinc consumption when the body is undergoing an immunological challenge? The answer is that it is dependent on the immunological challenge and the timing of the administration. In some challenges such as the prevention or treatment of diarrhea, zinc supplementation has been shown to be effective[1]. In some viral and bacterial infections, zinc supplementation used as a treatment has helped reduce severity of symptoms and/or aided in recovery from the infection. In other cases, it has not done anything. One of the viral infections most studied with zinc is the common cold. The results of these studies vary in effectiveness of zinc, and the effectiveness is dependent on timing of zinc supplementation within a narrow window of time from the first onset of symptoms[7].

It is difficult to impossible to determine when our bodies are going to be immunologically challenged. Thus, the best strategy is to ensure that zinc consumption is adequate so that our zinc status is optimized and primed to respond. To that end, zinc needs and availability are based upon age, sex, weight and phytate content of the diet[2]. One sub-population that is at particular risk for zinc deficiency is the elderly. It is estimated that approximately 30% of the elderly in industrialized nations are zinc deficient[5]. Vegetarians and vegan are also at risk due to high levels of phytate in the diet that binds zinc and makes it unavailable for absorption[2,5].

Conclusion

Zinc is a key nutrient for the proper and adequate immunological responses to daily challenges to the body. Adequate consumption of zinc from the diet on a daily basis is essential. In some cases, zinc supplementation can help maintain a healthy immune response and system.

References

1. *Overbeck S, et al. Arch Immunol. Ther. Exp. 2008;56:15-30.*
2. *Gammoh NZ and Rink L. Nutrients. 2017;9:624-649.*
3. *Maywald M, et al. Int J Mol Sci 2017;18:2222-2255*
4. *DiSilvestro RA, et al. Biol Trace Elem Res, 2020; https://doi.org/10.1007/s12011-020-02159-y*
5. *Wessels I, et al. Nutrients. 2017;9:1286-1329,.*
6. *6. Mebratu Y and Tesfaigzi Y. Cell Cycle 2009;8(8):1168-1175*
7. *7. Huliaz D. J Am Pharm Assoc 2004;44:594-603*

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