

Essential Metals - Zinc

A Physician's Perspective on "Zinc Issues and Update"

Discussant - Ian M. F. Arnold
M. D., M.Sc., FRCPC, FCBOM
May 6, 2008

Introduction:

The author was requested to provide a short (5 minute) discussion on zinc following the keynote presentation on zinc by Dr. Craig Boreiko. In preparation for the discussion, the role of a discussant was reviewed and it was noted that it has been defined, somewhat whimsically, by Karl Weick¹ from the University of Michigan who notes:

- *"You'll get none of the papers in advance.*
- *At the session there will be no time left for you to make your comments.*
- *If there is time left, you'll be introduced as the person who will pull all of this together.*
- *The audience wants you to sit down so they can ask their questions.*
- *It's fun to do because you have a chance to spot connections and you don't have to scramble to write a quasi-paper during the December holidays to get a slot at the annual meeting."*

Within the limited time available to the discussant, the paper that follows takes a brief look at a public source of information on zinc followed by a short overview of recent research on both zinc deficiency and excess zinc intake - opposing ends of the U-shaped dose response curve. Some tentative conclusions are then drawn with respect to opportunities for future direction.

A Public Perspective:

To the general public, zinc seems to enjoy a very positive image as a health booster and health promoter. A search of recent titles reveals that "YouTube" is an excellent source for some brief, but well written, articles on the benefits of zinc supplementation - as well as numerous articles relating zinc to both pyrotechnics and music groups. Some sample titles and the discussant's comments on their content follow:

"Zinc 101" - An excellent overview of the value of zinc;

"Ejaculation - lose up to 3mg of Zinc" - Overall, a balanced view on zinc requirements from Dr. Brett, with an obviously catchy title.

"The Importance of Zinc in Bodybuilding Nutrition" - A good series of slides on the positive impact of zinc on bodybuilding;

Zinc Deficiency:

The population health impacts of zinc deficiency and the improvements seen on treatment are obvious. Two recent papers clearly demonstrate that this end of the U shaped dose response curve is, generally, well understood.

In a meta-analysis of the effects of oral zinc used for the treatment of acute and persistent diarrhoea, Lubacik² et al noted that the administration of supplemental zinc effectively reduces "the duration and severity of acute and persistent diarrhea". They note further, and this is an area for potential further research, that "the mechanisms by which zinc exerts its antidiarrheal effect have not been fully elucidated."

In another recent paper by Khan³ et al, zinc therapy for children with diarrhoea was evaluated from a safety perspective. Although they noted that "A significant proportion of infants and children may experience vomiting or regurgitation", they authors went on to add that this only occurred, "usually once, following the administration of the first dose of zinc" and added that: "This is a transient phenomenon that did not impact on continuation of treatment with zinc."

While the mechanisms of uptake may not be fully understood, these articles, as do many others, indicate that zinc deficiency is a well defined problem and that the solution lies with zinc supplementation when diets are deficient in this essential nutrient.

Elevated Zinc Intake:

At the upper end of the U shaped dose response curve, the impacts of elevated zinc intake appear to be more difficult to define.

In a recent case control study from Italy by Gallus⁴ et al, the authors noted that: "We found a direct association between high zinc intake and prostate cancer risk, particularly for advanced cancers. Our findings allow one to exclude a favourable effect of zinc on prostate carcinogenesis."

On the other hand, in a report on a study of patients with zinc supplementation used for the treatment of macular degeneration (published in Urology in February of 2007),

Johnson⁵ et al noted that: "There was no increase in prostate or other cancers with zinc supplementation" and goes on to conclude that: "Zinc supplementation at high levels results in increased hospitalizations for urinary complications compared to placebo. These data support the hypothesis that high dose zinc supplementation has a negative effect on select aspects of urinary physiology".

"Metal Balance":

It does not seem clear how the interaction between (trace) metals affects the balance of these materials and the impact of this "metal balance" on disease. A recent paper by Sparks⁶ et al using spontaneously hypercholesterolemic Watanabe rabbits, cholesterol-fed beagles and rabbits, PS1/APP transgenic mice¹ showed that:

- "In contrast to the effects of copper, we found that aluminum- or zinc-ion-supplemented distilled water did not have a significant effect on brain Ab accumulation in cholesterol-fed rabbits."

In an unpublished pathologic post-mortem study comparing human AD brain specimens to non-AD controls, the author⁷ has advised that there was no correlation observed between aluminum levels and tau or Ab pathologies while significantly increased correlations were observed with zinc and significantly decreased correlations found with copper.

Workplace impacts:

Despite the well known impacts of zinc and its role in "metal fume fever", problems continue to be reported as demonstrated by this recent report from Japan by Miyazaki⁸ et al in 2006. The key aspects are noted below:

"A 55-year-old man with a 3-year occupational history of welding was admitted for repeated episodes of fever, cough and dyspnea after inhalation of smoke while welding galvanized steel. . . . symptoms and signs disappeared spontaneously only when he ceased welding . . . hypersensitivity pneumonitis caused by zinc fumes. "

Interestingly, differences exist in defining workplace limits⁹:

- OSHA PEL final rule limits zinc oxide dust - 10 mg/m³ (total); 5 mg/ m³ (respirable); OSHA PEL final rule limit for zinc oxide fume is 5 mg/m³. PEL for zinc oxide fume is 5 mg/m³.
- The ACGIH TLV for zinc oxide is 2 mg/m³ (respirable fraction) with a Short Term Exposure Limit (STEL) of 10 mg/m³ (respirable fraction).

Conclusions:

While this is only a brief overview, limited by the 5 minutes allowed to the discussant, some tentative conclusions may be drawn:

- The deficiency tail of the u shaped curve appears to be well defined and the benefits of zinc supplementation at reasonable levels appear to be equally well understood and documented - both in the public realm and in the scientific literature.
- The upper end of the u-shaped curve, however, is more difficult to define and study results appear to be somewhat contradictory. This is an area where further research to understand the mechanisms of action, uptake, and transport may assist in better determining whether health impacts, such as those related to the potential for carcinogenic and neurologic effects, do, in fact, even exist.
- The question of interaction between zinc and other trace metals and the state of "metal balance" may also play a crucial role in determining health. It is possible that the roles played by essential and non-essential metals and their possible interactions may explain, in part, the apparent contradictory results found in the medical literature.
- There also seems to be a need to better define workplace exposure levels and to improve workplace occupational health practices.

References:

1. Karl Weick, University of Michigan <http://www.fgvsp.br/iberoamerican/how1.htm>
2. Lukacik M. Thomas RL. Aranda JV, A meta-analysis of the effects of oral zinc in the treatment of acute and persistent diarrhea, Pediatrics. 121(2):326-36, 2008 Feb.;
3. Khan AM. Larson CP. Faruque AS. Saha UR. Hoque AB. Alam NU. Salam MA, Introduction of routine zinc therapy for children with diarrhoea: evaluation of safety, Journal of Health, Population & Nutrition. 25(2):127-33, 2007 June,
4. Gallus S. Foschi R. Negri E. Talamini R. Franceschi S. Montella M. Ramazzotti V. Tavani A. Dal Maso L. La Vecchia C., Dietary zinc and prostate cancer risk: a case-control study from Italy, European Urology. 52(4):1052-6, 2007 Oct.

5. Johnson AR. Munoz A. Gottlieb JL. Jarrard DF, High dose zinc increases hospital admissions due to genitourinary complications, Journal of Urology. 177(2):639-43, 2007 Feb.
6. Sparks, D L. Friedland, R. Petanceska, S. Schreurs, B G. Shi, J. Perry, G. Smith, M A. Sharma, A. Derosa, S. Ziolkowski, C. Stankovic, G., Trace copper levels in the drinking water, but not zinc or aluminum influence CNS Alzheimer-like pathology, Journal of Nutrition, Health & Aging. 10(4):247-54, 2006 Jul-Aug.2.
7. Personal communication - Delacourte, A. et al - Inserm U422, 1 Place de Verdun, 59045 Lille cedex
8. Miyazaki H. Hirata T. Shimane S. Morita S. Chihara K. Enomoto N. Suda T. Chida K., A case of hypersensitivity pneumonitis caused by zinc fume (in Japanese, abstract in English), Nihon Kokyuki Gakkai Zasshi. 44(12):985-9, 2006 Dec.
9. <http://www.teckcominco.com/DocumentViewer.aspx?elementId=115440&portalName=tc>. (2006)