

Trace minerals and the immune system – Impacts on the use of immune modulators and vaccine response

Lourens J. Havenga, BVSc

Chief Executive Officer, Multimin USA Inc. Fort Collins, CO 80528, lourens@multiminusa.com

Abstract

The functions of trace mineral-dependent enzymes impact every aspect of the complex immune response. This includes, but is not limited to, the chemical components (interferon and interleukin), the innate cellular functionality (neutrophil and macrophage) as well as the acquired immune response (T-cell and B-cell functionality). Disease management relies significantly on the use of vaccines and more recently on non-specific immune modulators. Understanding the role of the different minerals will enable practitioners to identify when and how trace mineral supplementation may be required for optimal immune function.

Key words: trace minerals, innate immunity, acquired immunity, vaccine

Résumé

Les fonctions d'enzymes qui dépendent d'oligo-éléments influencent toutes les facettes d'une réponse immunitaire complexe. Cela inclut les composantes chimiques (interféron et interleukine), les réponses cellulaires innées (neutrophiles et macrophages) de même que les réponses immunitaires acquises (lymphocytes T et B). La régie de la maladie compte énormément sur l'utilisation des vaccins et plus récemment sur les modulateurs immunitaires non-spécifiques. Une bonne compréhension du rôle des différents minéraux permettra aux praticiens d'identifier quand et comment un supplément d'oligo-éléments sera nécessaire pour favoriser une réponse immunitaire optimale.

The production of reactive oxygen species is central to the immune system.^{19,20} Not only are these molecules used to destroy phagocytosed antigen via the respiratory burst, but they are also produced by each cell during normal cellular respiration.^{11,13,15} During an immune response, cellular division and differentiation is increased significantly, hence the requirement for antioxidants to deal with the reactive oxygen species is significantly increased. The key enzymes dealing with reactive oxygen species in bovine are glutathione peroxidase (selenium dependent), catalase (iron dependent), and superoxide dismutase (manganese, zinc and copper dependent).^{10,11,13,15} During oxidative stress, when antioxidant levels are inadequate, cells suffer protein denaturation, DNA

and/or RNA damage, and cell membrane damage due to reactive oxygen species.¹¹

In a normal functional innate immune system, diapedesis, phagocytosis, and the respiratory burst are critical in dealing with ingested antigenic material by macrophages and neutrophils.^{12,13} Selenium deficiency significantly depresses diapedesis, while copper status influences phagocytosis.^{12,13} Selenium, copper, zinc, and manganese all impact the respiratory burst and the management of the reactive oxygen species produced during the burst.^{4,10,11}

Following vaccine administration, under optimal conditions, antigen is transported to regional lymph nodes by antigen presenting cells.^{7,8} T-cell and B-cell activation, multiplication, and differentiation follows, resulting in memory, cell-mediated protection, and humoral protection.^{9,14} In the presence of selenium, zinc, and copper imbalances, several pathways are disrupted, resulting in poor cell-mediated and/or humoral responses.^{3,5} Recent research has also indicated an impact on population dynamics, with fewer animals in the populace mounting adequate responses when experiencing trace mineral imbalances.^{6,16}

Several trace mineral supplementation options are available to address these imbalances.^{1,2,6,19,20} Oral supplementation needs to be provided for an extended time to correct imbalances^{19,20} and, where antagonists are present in large quantities, correcting these imbalances may be delayed even further. It has also been shown that cattle experience a decrease in serum zinc, copper, and selenium concentrations after vaccination due to the different trace minerals playing an active role in different pathways of the acquired immune response and disease prevention.¹

Evaluating the trace mineral status of receiving cattle is very difficult because most cases do not show obvious signs of deficiency, and deficient animals will be more susceptible to health challenges and will often be less efficient in feed conversion, weight gain, and carcass quality.^{6,18,19,20} Furthermore, cattle recently shipped to feed yards or stocker operators show significant variation in intake in the first 10 days post-arrival.²⁰ Stress factors such as vaccination, weaning, and transport exacerbate these trace mineral imbalances.²⁰ With the use of injectable trace minerals oral feed intake is not a rate-limiting factor, as each individual animal is injected.¹⁷ Injectable trace minerals also quickly bolster the trace mineral status of incoming cattle, even in the presence of antagonists in the feed and water.^{1,2,17,18}

Acknowledgement

Acknowledgement of conflict of interest: Dr. Lourens Havenga is the CEO of Multimin USA Inc., the developer and supplier of the injectable trace mineral product, Multimin® 90.

References

1. Arthington JD, Havenga LJ. Effect of injectable trace minerals on the humoral immune response to multivalent vaccine administration in beef calves. *J Anim Sci* 2012; 90:1966-1971.
2. Arthington JD, Moriel P, Martins PGMA, Lamb GC, Havenga LJ. Effects of trace mineral injections on measures of performance and trace mineral status of pre- and post-weaned beef calves. *J Anim Sci* 2014; 92:2630-2640.
3. Bonaventura P, Benedetti G, Albarède F, Miossec P. Zinc and its role in immunity and inflammation. *Autoimmun Rev* 2015; 14:277-285.
4. Bonham M, O'Connor JM, Hannigan BM, Strain JJ. The immune system as a physiological indicator of marginal copper status? *Br J Nutr* 2002; 87:393-403.
5. Cerone SI, Sansinanea AS, Streitenberger SA, Garcia MC, Auza NJ. The effect of copper deficiency on the peripheral blood cells of cattle. *Vet Res Commun* 1998; 22:47-57.
6. Chirase NK, Hutcheson DP, Thompson GB, Spears JW. Recovery rate and plasma zinc and copper concentrations of steer calves fed organic and inorganic zinc and manganese sources with or without injectable copper and challenged with infectious bovine rhinotracheitis virus. *J Anim Sci* 1994; 72:212-219.
7. Ellermann-Eriksen S. Macrophages and cytokines in the early defense against herpes simplex virus. *Virology* 2005; 2:59.
8. Ellis J, West K, Cortese V. Effect of maternal antibodies on induction and persistence of vaccine-induced immune responses against bovine viral diarrhoea virus type II in young calves. *J Am Vet Med Assoc* 2001; 219:351-356.
9. Forthal DN. Functions of antibodies. *Microbiol Spectr* 2014; 2:AID-0019-2014. doi: 10.1128/microbiolspec.AID-0019-2014.
10. Haase H, Rink L. Multiple impacts of zinc on immune function. *Metalomics* 2014; 6:1175-1180.
11. Klotz LO, Kroncke KD, Buchczyk DP, Sies H. Role of copper, zinc, selenium, and tellurium in the cellular defense against oxidative and nitrosative stress. *J Nutr* 2003; 133:1448S-1451S.
12. Maddox JF, Aherne KM, Channa Reddy C, Sordillo KM. Increased neutrophil adherence and adhesion molecule mRNA expression in endothelial cells during selenium deficiency. *J Leuk Biol* 1999; 65:658-664.
13. Minatel L, Carfagnini JC. Copper deficiency and immune response in ruminants. *Nutr Res* 2000; 2010:1519-1529.
14. Nobiron I, Thompson I, Brownlie J, Collins ME. DNA vaccination against bovine viral diarrhoea virus induces humoral and cellular responses in cattle with evidence for protection against viral challenge. *Vaccine* 2003; 21:2082-2092.
15. O'Dell BL. Interleukin-2 production is altered by copper deficiency. *Nutr Rev* 1993; 51:307-309.
16. Palomares RA, Hurley DJ, Bittar JHJ, Saliki JT, Woolums AR, Moliere F, Havenga LJ, Norton NA, Clifton SJ, Sigmund AB, Barber CE, Berger ML, Clark MJ, Fratto MA. Effects of injectable trace minerals on humoral and cell-mediated immune responses to bovine viral diarrhoea virus, bovine herpes virus 1 and bovine respiratory syncytial virus following administration of a modified-live virus vaccine in dairy calves. *Vet Immunol Immunopath* 2016; 178:88-98.
17. Pogge DJ, Richter EL, Drewnoski ME, Hansen SL. Mineral concentrations of plasma and liver after injection with a trace mineral complex differ among Angus and Simmental cattle. *J Anim Sci* 2012; 90:2692-2698.
18. Richeson JT, Kegley EB. Effect of supplemental trace minerals from injection on health and performance of highly stressed, newly received beef heifers. *Prof Anim Sci* 2011; 27:461-466.
19. Spears JW. Micronutrients and immune function in cattle. *Proc Nutr Soc* 2000; 59:587-594.
20. Tomlinson DJ, Socha MT, DeFrain JM. Role of trace minerals in the immune system, in *Proceedings*. Penn State Dairy Cattle Nutrition Workshop 2008; 39-52.