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SUSHMA PALMER, DSC

*Central European Center for Health and the Environment (CECHE) Washington, D.C.*

# Zinc and the Common Cold: Are We Close to a Cure?

SHERIF B. MOSSAD, MD

*From the Department of Infectious Diseases, Cleveland Clinic Foundation, Cleveland, Ohio, USA*

The common cold is one of most frequent ailments affecting humans. In spite of the dramatic impact of such illness on our lives, scientists have not been able to achieve a cure. Several nutritional adjustments and supplements as well as a variety of pharmacological agents have been tried with not much success. The two most common supplements assessed in this regard are ascorbic acid and zinc.

The role of zinc in human nutrition has long been established.<sup>1</sup> The daily recommended dietary allowance for zinc is 15 mg. Zinc is involved in many biochemical functions related to protein synthesis, spermatogenesis, and platelet reactivity and plays a crucial role in maintenance of vigorous cellular immunity<sup>2</sup> and the prevention of certain types of cancer.<sup>3</sup> The causes of zinc deficiency include malnutrition, alcoholism, malabsorption, liver cirrhosis, chronic renal disease, extensive burns, the use of chelating agents such as penicillamine for Wilson's disease, and certain genetic disorders such as sickle cell disease and acrodermatitis enteropathica.<sup>4</sup> The highest content of zinc in our diet is in meat products, including beef and chicken.<sup>5</sup> Certain populations in developing countries suffer from the consequences of nutritional zinc deficiency.<sup>6</sup> In the Western world, however, certain subgroups of the population, such as adolescents, pregnant

women, and nursing home residents, are at risk for the same problem.<sup>7</sup> In addition, the intentional avoidance of red meat by some individuals increases the risk of zinc deficiency.<sup>8</sup> The clinical manifestations of zinc deficiency include growth retardation, male hypogonadism, delayed wound healing, bullous dermatitis, diarrhea, and intercurrent infections.<sup>4</sup> Administration of zinc in therapeutic doses (150 mg/d) to patients with sickle cell anemia significantly reduced irreversible sickling and helped healing of skin ulcers, but resulted in neutropenia due to induction of copper deficiency.<sup>9</sup> This has suggested a role for zinc therapy in patients with Wilson's disease.<sup>10</sup>

Several studies have demonstrated that zinc prevents the formation of viral capsid proteins, thereby inhibiting *in vitro* replication of several viruses, including herpes simplex virus,<sup>11</sup> foot and mouth disease virus,<sup>12</sup> poliovirus,<sup>13</sup> and rhinovirus.<sup>14</sup> Other mechanisms by which zinc might affect the common cold include preventing rhinovirus from binding to the tissue surface protein intracellular adhesion molecule type 1,<sup>15</sup> stabilizing cell membranes,<sup>16</sup> inhibiting prostaglandin metabolism,<sup>17</sup> and inducing interferon gamma production.<sup>18</sup> Well designed studies in the literature on the role of zinc in the treatment of common cold have had conflicting results.<sup>19-25</sup> Never-

theless, zinc gluconate glycine lozenges, when started within 24 h of the onset of symptoms of common cold, significantly reduced the duration of illness in general and had a clear therapeutic effect on most of the individual symptoms.<sup>26</sup> The most common side effects were nausea and bad taste reactions. This study had certain limitations, the most important of which is lack of microbiologic documentation of infection or cure. In the later study, patients were instructed to take one zinc lozenge every 2 h while awake, *i.e.*, about eight lozenges per day, but actually took only five; raising concerns about compliance with such therapy.

Whether zinc may exert its therapeutic effect on colds by correcting a subclinical zinc deficiency in certain people remains to be determined. Long-term surveillance studies for potential efficacy and toxicity are needed before widely accepting such therapy. If adopted, zinc might potentially be used by every human being for therapy of a very common illness.

## REFERENCES

1. Prasad AS. Importance of zinc in human nutrition. *Am J Clin Nutr* 1967;20:648
2. Good RA, Lorenz E. Nutrition and cellular immunity. *Int J Immunopharmacol* 1992;14:361
3. Hansen MA, Fernandes G, Good RA. Nutrition and immunity: the influence of diet

Correspondence to: Sherif B. Mossad, MD, Cleveland Clinic Foundation, Department of Infectious Diseases, Mailstop S-32, 9500 Euclid Avenue, Cleveland, Ohio, 44195-5066.

- on autoimmunity and the role of zinc in the immune response. *Annu Rev Nutr* 1982;2:151
4. Prasad AS. Clinical, endocrinological and biochemical effects of zinc deficiency. *Baillieres Clin Endocrinol Metab* 1985; 14:567
  5. Halsted JA, Smith Jr. JC, Irwin MI. A conspectus of research on zinc requirements of man. *J Nutr* 1974;104:345
  6. Prasad AS, Miale Jr. A, Farid Z, Sandstead HH, Schultert AR. Zinc metabolism in patients with the syndrome of iron deficiency anemia, hepatosplenomegaly, dwarfism and hypogonadism. *J Lab Clin Med* 1963;61:537
  7. Sanstead HH. Zinc nutrition in the United States. *Am J Clin Nutr* 1973;26:1251
  8. Yokoi K, Alcock NW, Sanstead HH. Iron and zinc nutriture of premenopausal women: associations of diet with serum ferritin and plasma zinc disappearance and of serum ferritin with plasma zinc disappearance. *J Lab Clin Med* 1994;124:852
  9. Prasad AS, Brewer GJ, Schoemaker EB, Rabbani P. Hypocupremia induced by zinc therapy in adults. *JAMA* 1978; 240:2166
  10. Brewer GJ, Hill GM, Prasad AS, Cossack ZT, Rabbani P. Oral zinc therapy for Wilson's disease. *Ann Intern Med* 1983; 99:314
  11. Gordon YJ, Asher Y, Becker Y. Irreversible inhibition of herpes simplex virus replication in BSC-1 cells by zinc ions. *Antimicrob Agents Chemother* 1975;8:377
  12. Firpo EJ, Palma EL. Inhibition of foot-and-mouth disease virus and procapsid synthesis by zinc ions. *Arch Virol* 1979;61:175
  13. Ratka M, Lackmann M, Ueckermann C, Karlins U, Koch G. Poliovirus-associated protein kinase: destabilization of the virus capsid and stimulation of the phosphorylation reaction by zinc. *J Virol* 1989; 63:3954
  14. Geist FC, Bateman JA, Hayden FG. In vitro activity of zinc salts against human rhinoviruses. *Antimicrob Agents Chemother* 1987;31:622
  15. Novick SG, Godfrey JC, Godfrey NJ, Wilder HR. How does zinc modify the common cold? Clinical observations and implications regarding mechanism of action. *Med Hypotheses* 1996;46:295
  16. Marone G, Findley SR, Lichtensein LM. Modulations of basophil histamine release by zinc. *J Allergy Clin Immunol* 1979; 65:171
  17. Kelley RW, Abel MH. Copper and zinc inhibit the metabolism of prostaglandin by the human uterus. *Biol Reprod* 1983; 28:883
  18. Salas M, Kirchner H. Induction of interferon gamma in human leukocyte cultures stimulated by zinc. *Clin Immunol Immunopathol* 1987;45:139
  19. Eby GA, Davis DR, Halcomb WW. Reduction in duration of common cold by zinc gluconate lozenges in a double-blind study. *Antimicrob Agents Chemother* 1984;25:20
  20. Al-Nakib W, Higgins PG, Barrow I, Batstone G, Tyrrell DAJ. Prophylaxis and treatment of rhinovirus colds with zinc gluconate lozenges. *J Antimicrob Chemother* 1987;20:893
  21. Godfrey JC, Sloan BC, Smith DS, Turco JH, Mercer N, Godfrey NJ. Zinc gluconate and the common cold: a controlled clinical study. *J Int Med Res* 1992;20:234
  22. Farr BM, Conner EM, Betts RF, Oleske J, Minnefor A, Gwaltney Jr. JM. Two randomized controlled trials of zinc gluconate lozenges therapy of experimentally induced rhinovirus colds. *Antimicrob Agents Chemother* 1987;31:1183
  23. Douglas RM, Miles HB, Moore BW, Ryan P, Pinnock CB. Failure of effervescent zinc acetate lozenges to alter the course of upper respiratory tract infection in Australian adults. *Antimicrob Agents Chemother* 1987;31:1263
  24. Smith DS, Helzner EC, Nuttall Jr. CE, et al. Failure of zinc gluconate in treatment of acute upper respiratory tract infections. *Antimicrob Agents Chemother* 1989;33: 646
  25. Weismann K, Jakobsen JP, Weismann JE, et al. Zinc gluconate lozenges for common cold. *Dan Med Bull* 1990;37:279
  26. Mossad SB, Macknin ML, Medendorp SV, Mason P. Zinc gluconate lozenges for treating the common cold: a randomized, double-blind, placebo-controlled study. *Ann Intern Med* 1996;125:81