## **Complementary Medicine**

An evidence-based review of alternative therapies



# Zinc for the Common Cold?

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any patients take zinc as a treatment for the common cold. What is the evidence that it works?

A review conducted by Garland, et al concluded that zinc gluconate lozenges "may be effective in decreasing the duration and severity of cold symptoms." This review included eight trials (n = 620)and found four with positive results and four with negative results.1

## *Positive trials*

Eby, et al conducted a randomized, controlled trial (RCT) for patients with cold symptoms of less than three days. Twenty-eight patients were given placebo and 37 patients were given two zinc gluconate tablets containing 23 mg of elemental zinc initially and then one tablet every two wakeful hours until symptoms had disappeared. Eleven per cent of patients treated with zinc became asympto- the zinc-treated group experienced less severe matic within 12 hours. After 24 hours, 22% of symptoms by day four of the study compared to patients were asymptomatic. None of the patients in the placebo group were asymptomatic during this timeframe. By the conclusion of the trial (seven days later), 86% of patients in the zinctreated group were asymptomatic, compared to 46% of placebo-treated patients. The trial had poor methodological quality because of an initial difference in severity between groups at baseline and the high drop out rate.<sup>2</sup>

In a RCT by Mossad, et al, 50 patients with cold symptoms lasting  $\leq 24$  hours were given one zinc gluconate lozenge containing 13.3 mg of elemental zinc every two hours, while awake, for as long as their cold symptoms were present. The median duration of symptoms in the zinc-treated group was

4.4 days compared to 7.6 days in the placebo group. Zinc-treated patients had a lesser duration of:

- Coughing
- Headache Nasal congestion
- Hoarseness • Sore throat
- Nasal drainage

The authors concluded that zinc gluconate lozenges decreased the duration of symptoms in patients with the common cold.<sup>3</sup>

Another RCT by Prasad, et al assessed the effect of one zinc acetate lozenge containing 12.8 mg of elemental zinc every two hours to three hours in 25 patients who were experiencing signs and symptoms of the common cold for  $\leq 24$  hours. Patients in the zinc-treated group experienced colds of shorter duration compared to those in the placebo-treated group (4.5 days vs. 8.1 days). Half of the patients in the zinc-treated group were asymptomatic within 3.8 days compared to 7.7 days in the placebo-treated group. Patients in patients in the placebo-treated group. The authors concluded that zinc acetate lozenges are effective in decreasing the duration and severity of symptoms of the common cold.4

McElroy, et al conducted a retrospective chart review of zinc gluconate glycine lozenges for the common cold in children ages 12 years to 18 years. Children were given four lozenges of zinc gluconate glycine daily if they were experiencing at least two signs and symptoms of a common cold on the same day. A year later, prophylactic zinc lozenges containing 13.3 mg of elemental zinc were given to the study participants, along with the symptomatic treatment, if required. The colds treated with zinc were shorter than those that were

not treated with zinc. Prophylaxis with zinc gluconate glycine lowered the incidence of colds in the non-prophylaxis and prophylaxis periods. The authors concluded that the use of zinc gluconate glycine lozenges was effective in decreasing the duration of cold symptoms, as well as in decreasing the number of colds. This study was neither blinded, nor randomized, therefore, further research is needed to support these results.<sup>5</sup>

A RCT by Hirt, *et al* gave 108 patients zinc gluconate nasal gel while 105 patients received a placebo. The gel was to be applied as one spray into each nostril every four hours for as long as symptoms were present. The zinc nasal gel was found to decrease the duration of cold symptoms compared to the placebo-treated group. The average time to resolution of all symptoms was 2.3 days in the zinc-treated group and nine days in the placebo group. The authors concluded that zinc gluconate nasal gel is effective in reducing the duration of symptoms of the common cold.<sup>6</sup>

### Negative trials

Smith, et al, in a RCT, gave 86 college-aged students with upper respiratory tract infections an initial dose of four zinc gluconate lozenges containing 11.5 mg of elemental zinc, followed by two lozenges every two wakeful hours for seven days or 24 hours after the last symptom had subsided. There was no difference in the duration of symptoms of the common cold between groups. There was a decrease in the severity of symptoms on days four to seven of zinc treatment; however, the clinical effect and significance of this decrease was small. The authors concluded that zinc gluconate lozenges were minimally effective in decreasing the severity of symptoms and ineffective in terms of decreasing the duration of symptoms of the common cold.7

Farr, *et al* inoculated two groups of patients with rhinovirus. In the first trial (n = 32), two zinc

gluconate lozenges containing 23 mg of elemental zinc were given initially, followed by one lozenge every two hours, to a maximum of eight doses per day. Each lozenge was given 36 hours after inoculation with rhinovirus Type 39 and continued for five days. In the second trial (n = 41), zinc was initiated two hours after inoculation with rhinovirus Type 13 and continued for seven days. The authors concluded that zinc gluconate lozenges were not effective at decreasing the rate of viral shedding or in decreasing the severity, or duration of symptoms of the common cold.<sup>8</sup>

In a RCT by Macknin, *et al*, 249 children in grades one through twelve were given either zinc gluconate glycine lozenges containing 10 mg of elemental zinc or placebo for the common cold. The authors concluded that zinc gluconate glycine lozenges were ineffective in treating the common cold in this patient population.<sup>9</sup>

Belongia, *et al* advised patients in a RCT to inhale two sprays of zinc sulphate nasal spray containing 0.12% of zinc sulfate; resulting in 0.011 mg of elemental zinc per dose, four times a day if they had symptoms of the common cold for < 24 hours. Participants were given a viral culture to determine that the symptoms were actually due to the common cold. No difference was observed in median time to resolution between the zinc and the placebo groups. The authors concluded that zinc sulfate nasal spray was ineffective in decreasing the duration or severity of symptoms of the common cold.<sup>10</sup>

A RCT by Eby, *et al* instructed patients to use a 10 mmol zinc gluconate nasal spray two times to three times every 15 minutes to 30 minutes while

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awake, in addition to one zinc orotate lozenge containing 37 mg of elemental zinc every two hours to three hours while awake. No difference in the duration of common cold symptoms was observed between the zinc and the placebo groups.<sup>11</sup>

#### Research variability

Citric acid, tartaric acid, mannitol and sorbitol have classically been added to zinc lozenges to improve palatability. However, citric acid and tartaric acid undergo chelation when combined with zinc and may result in the decreased effectiveness of the lozenges. The effects of mannitol and sorbitol on the effectiveness of zinc lozenges have yet to be concretely determined. Some practitioners blame the additives on the variability of the research.

## Adverse effects

#### GI complaints

GI complaints include nausea, abdominal pain/ dyspepsia, diarrhea, constipation and vomiting. In one trial, 20.4% of people experienced mild nausea. This occurs more often when zinc is ingested on an empty stomach and can be alleviated with concomitant ingestion of food.

### Nasal complaints

Nasal complaints with the use of zinc nasal spray or gel consist of nasal irritation, headache, bad taste, tingling/burning of nose and throat, nasal pain/discomfort, alterations in sense of smell and epistaxis/nosebleed.

### Oral complaints

Oral complaints comprise mouth irritation, sore mouth, unpleasant aftertaste, mouth sores, distortion of taste and dry mouth. In one study, 50% of participants experienced a sore mouth due to ingestion of zinc lozenges.

### Additional complaints

There have been case reports of jaundice, kidney disease, anemia and neutropenia. Copper deficiency has been reported with very high doses of zinc.

## Drug interactions

The following may decrease levels of zinc in the body:

- Amiloride Captopril
- Folic acid Thiazide diuretics

Zinc may decrease the absorption of fluoroquinolone antibiotics and tetracyclines.

## Conclusion

There is conflicting evidence for the use of zinc for the common cold.  $\mathbf{D}_{\mathbf{x}}$ 

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#### References

- 1. Garland ML, O'Hagmeyer K: The role of zinc lozenges in treatment of the common cold. Ann Pharmacother 1998; 32(1):63-9.
- Eby GA, Davis DR, Halcomb WW: Reduction in duration of common colds by zinc gluconate lozenges in a double-blind study. Antimicrob Agents Chemother 1984; 25(1):20-4.
- 3. Mossad SB, Macknin ML, Mendendorp SV, et al: Zinc gluconate lozenges for treating the common cold. Ann Intern Med 1996; 125(2):81-8.
- 4. Prasad AS, Fitzgerald JT, Bao B, et al: Duration of symptoms and plasma cytokine levels in patients with the common cold treated with zinc acetate. Ann Intern Med 2000; 133(4):245-52.
- McElroy BH, Miller SP: An open-label, single-centre, phase IV clinical study of the effectiveness of zinc gluconate glycine lozenges (Cold-Eeze) in reducing the duration and symptoms of the common cold in schoolaged subjects. Am J Ther 2003; 10(5):324-9.
- Hirt M, Nobel S, Barron E: Zinc nasal gel for the treatment of common cold symptoms: A double-blind, placebo-controlled trial. Ear Nose Throat J 2000; 79(10):778-82.
- Smith DS, Helzner EC, Nuttall CE, et al: Failure of zinc gluconate in treatment of acute upper respiratory tract infections. Antimicrob Agents Chemother 1989; 33(5):646-8.
- Farr BM, Conner EM, Betts RF, et al: Two randomized controlled trials of zinc gluconate lozenge therapy of experimentally induced rhinovirus colds. Antimicrob Agents Chemother 1987; 31(8):1183-7.
- Macknin ML, Piedmonte M, Calendine C, et al: Zinc gluconate lozenges for treating the common cold in children. JAMA 1998; 279(24):1962-7.
- Belongia EA, Berg R, Liu K: A randomized trial of zinc nasal spray for the treatment of upper respiratory illness in adults. Am J Med 2001; 111(2):103-8.
- 11. Eby GA, Halcomb WW: Ineffectiveness of zinc gluconate nasal spray and zinc orotate lozenges in common-cold treatment. Altern Ther Health Med 2006; 12(1):34-8.