

## Zinc Therapy for the Common Cold: Another Look

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. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 2000;133:245-52.

### Study Overview

**Objective.** To determine if zinc lozenges can reduce symptom duration in adults affected by the common cold.

**Design.** Randomized, double-blind, placebo-controlled trial.

**Setting and participants.** Fifty volunteers recruited from the Detroit Medical Center, Detroit, Michigan. Study subjects were medical students, graduate and undergraduate students, staff, and employees at Wayne State University who were 18 years or older. Participants were selected if they had had cold symptoms for 24 hours or less and had at least 2 of the following symptoms: cough, headache, hoarseness, muscle ache, nasal drainage, nasal congestion, scratchy throat, sore throat, sneezing, and fever.

**Intervention.** Participants received lozenges containing 12.8 mg of zinc acetate or placebo. Lozenges had the same weight, aspect, color, texture, taste, and packaging. Subjects were instructed to allow 1 tablet to dissolve in their mouths every 2 to 3 hours until symptoms resolved. No other cold medications were taken during the study.

**Main outcome measures.** The primary outcome was duration of cold symptoms. Scores for 10 subjective cold symptoms (listed above) were also measured. Secondary outcomes included plasma zinc and proinflammatory cytokine levels. Participants were asked to keep a logbook to rate the severity of their symptoms on a scale from 1 to 3 and to fill out a questionnaire on side effects.

**Main results.** Compared with the placebo group, the zinc group had a shorter mean overall duration of cold symptoms (4.5 days versus 8.1 days;  $P < 0.01$ ), nasal discharge (4.1 days versus 5.8 days;  $P < 0.001$ ), and cough (3.1 days versus 6.3 days;  $P < 0.001$ ). At 3.8 days, 50% of the patients in the treatment group were well; in the placebo group, 50% were well at 7.7 days. At baseline, the average severity index was higher in the treatment group. On a scale with a maximum score of 12, the mean score was 10.8 in the zinc group and

8.9 in the placebo group ( $P = 0.002$ ). The side effect rate was similar except for a higher incidence of mouth dryness (72% versus 26%) and constipation (24% versus 0%) in the zinc-treated group. Proinflammatory cytokine levels were not statistically different between the 2 groups. At the beginning of treatment, zinc levels were normal in both groups; after therapy, there was a change in the mean zinc level, which was higher in the treatment group but still within normal limits.

### Conclusion

When taken at symptom onset, zinc lozenges were associated with reduced duration and severity of cold symptoms. The mechanism of action is unclear. No difference in the proinflammatory cytokine levels of study participants was detected.

### Commentary

Several studies have been conducted to determine if zinc lozenges would shorten the duration of the common cold. Some of these trials suggest benefits [1-6], while other trials showed no symptom improvement [7-10]. In their study, Prasad and colleagues tried to address methodologic problems seen in past research. This study was very well conducted. The authors took great care in making sure that they had a proper blinding, which was not the case in the previous studies. Because zinc lozenges seem to have a bitter taste, investigators tried to make the placebo and zinc lozenges taste the same. However, it appears that this may not have been accomplished successfully. To ensure that blinding was adequate, patients were asked which kind of tablet (zinc or placebo) they thought they were taking. An editorial in the same issue by Desbiens points out that 3.5 times as many patients in the zinc group guessed correctly that they were taking zinc. This obviously could have affected study results, since measurements of symptoms were subjective.

Prasad et al's study is unique because of the authors' attempt to measure cytokine levels, the theory being that zinc may have an effect on the immune response to the common cold. When these secondary data were examined, there was a trend for the plasma cytokines to be lower in the treatment group; however, the differences were not significant

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( $P > 0.2$ ). One explanation could be that the sample size was too small. Another problem may have been that cytokine levels in the placebo group were measured 3 days after they were measured in the treatment group; ideally, levels should have been taken at the same time. One significant finding was the magnitude of effect: symptom duration was shortened by 3 days in the treatment group. However, the administration of the lozenges (every 2 hours while awake until symptoms resolve) is quite cumbersome. Side effects were not negligible and were similar to those reported in previous studies on zinc lozenges. Finally, analysis of demographic data showed that study patients' average age was 36 years. There were few smokers (25%), and few participants had allergies (10%). This means that study results probably cannot be applied to elderly patients or to those with multiple comorbidities. Because the authors examined only symptoms and because no viral cultures were performed, Prasad and colleague's study does not indicate whether zinc has any antiviral effect. Further studies should also be conducted to determine the mechanism of action in zinc lozenges.

#### Applications for Clinical Practice

In the office, when asked about the efficacy of zinc lozenges, physicians can advise patients that if they take this medication as prescribed it will probably reduce the duration of symptoms by 3 days. Patients should be informed that they will have a 72% chance of experiencing some dry mouth and a 24% chance of becoming constipated. At this time, it remains unclear if this type of therapy can be used safely in patients with multiple comorbidities or if it can be taken with other medications.

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