



Zinc for the common cold— not *if*, but when

A new meta-analysis shows that zinc supplementation can reduce the duration and severity of a cold, if it's started early on.

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PRACTICE CHANGER

Advise patients to start taking zinc supplements (available as tablets, syrup, or lozenges) within 24 hours of the onset of a cold.¹

Singh M, Das RR. Zinc for the common cold. *Cochrane Database Syst Rev.* 2011;(2):CD001364.

STRENGTH OF RECOMMENDATION

A: Based on a meta-analysis of 13 randomized placebo-controlled trials.

ILLUSTRATIVE CASE

A healthy 31-year-old woman schedules a visit because of congestion and rhinorrhea. She tells you that her cold symptoms developed in the last day or 2 and asks for something to speed her recovery. What can you suggest?

Americans experience roughly 500 million episodes of noninfluenza-related viral respiratory tract infections annually (ie, common colds), or roughly 2.5 episodes per person each year. The total economic burden of the common cold is nearly \$40 billion annually.²

Most cold remedies offer little relief

We've all cared for patients with cold symptoms. And despite the desire to help, many of us have been frustrated by the fact that there is no cure for the common cold, and most over-the-counter therapies offer little or no relief.

■ What about zinc? Zinc has been in and out of favor as a treatment for the common cold, based on contradictory findings, since the first randomized trial was published in 1984.³

A 1998 systematic review (which did not include a quantitative synthesis of data) suggested that zinc was beneficial in reducing the duration and severity of cold symptoms.⁴ A meta-analysis published in 2000 found that zinc was ineffective compared with placebo in reducing the likelihood that cold symptoms were present after 7 days.⁵ A meta-analysis published in June 2011 concluded that zinc lozenges reduce the duration of cold symptoms by 12% to 48%, but only at daily doses >75 mg.⁶

These conflicting results have made it difficult to recommend zinc to patients—until now.

STUDY SUMMARY

Zinc for colds? Cochrane review provides convincing evidence

The 2011 Cochrane review that's the focus of this PURL¹ addressed the question: Does zinc reduce the duration and severity of the common cold? The review also assessed zinc's ability to prevent colds, although only 2 studies focused on prevention.

The researchers included only randomized, double-blind, placebo-controlled trials in which oral zinc supplementation was used for ≥5 consecutive days for treatment or ≥5 months for prevention. Studies included patients of any age, taking any dosage and any formulation of zinc.

Primary outcomes included the duration of symptoms, the severity of symptoms, and the incidence of the common cold in preven-

tion studies. Secondary outcomes included the proportion of patients symptomatic after 3, 5, and 7 days of treatment, the time to resolution of individual symptoms (eg, cough), change in individual symptom scores, school absences, antibiotic use, and adverse effects.

Thirteen therapeutic trials and 2 prevention trials met the inclusion criteria. These studies, all of which were judged to be of high quality with a low risk of bias, had a total of 996 patients in the therapeutic trials and 394 patients in the prevention trials. Participants ranged in age from 1 to 65 years.

Therapeutic trials. In general, therapeutic studies included lozenges containing 10 to 24 mg zinc gluconate, with one lozenge taken every 1 to 4 hours during the day for 3 to 7 days. In one therapeutic trial that enrolled only children ages 1 to 10, the intervention group took zinc sulfate syrup (15 mg bid) for 10 days. In 11 of the 13 therapeutic studies, treatment began in the first 24 hours of symptoms; in the remaining 2, it began within 48 hours of symptoms.

Ten studies reported on duration of symptoms; 6 of them were similar enough to allow for pooling of results. The pooled results showed that patients who took zinc had a shorter duration of cold symptoms (0.97 days; 95% confidence interval [CI], -1.56 to -0.38), compared with those on placebo. Pooled results from 5 trials revealed that zinc significantly reduced the severity of symptoms by a standard effect size of 0.39 (95% CI, -0.77 to -0.02), which is considered a small to moderate effect.

Prevention trials. In one prevention trial, which included only children ages 6½ to 10 years, those in the intervention group took one 10-mg zinc sulfate tablet 6 days a week for 5 months. In the other trial, children in the intervention group took 15 mg zinc sulfate syrup daily for 7 months.

Pooled results from these 2 studies revealed that daily zinc supplementation substantially reduced the incidence of colds. The incident rate ratio (the number of children who developed colds while taking zinc compared with the number who developed colds while on placebo) was 0.64 (95% CI, 0.47-0.88). In the original trials, one study found a difference of 0.5 colds (1.7 in the con-

trol group vs 1.2 in the intervention group) per season, and the other found a difference of 1.8 colds per season (3.15 in the control group vs 1.37 in the intervention group).

WHAT'S NEW

Evidence of zinc's cold relief properties is conclusive

This Cochrane review provides convincing evidence from 13 randomized placebo-controlled trials that taking zinc soon after the onset of symptoms of the common cold significantly reduces both the duration and severity of symptoms. Zinc supplements are widely available over the counter, so you can recommend that patients take zinc the next time they develop a cold.

In addition, 2 prevention trials found that zinc can reduce the incidence of colds in children, whether it is taken as a syrup or in tablet form. There have been few trials of zinc for prophylaxis of the common cold, and no previous meta-analyses included preventive studies.⁷ This Cochrane review substantiates the effectiveness of zinc for prophylaxis of the common cold in young children.

However, children need to take zinc daily for prophylaxis, which may be inconvenient. Long-term safety information is not yet available. Given these considerations, parents may choose to wait for additional evidence about safety before considering daily prophylaxis.

CAVEATS

Adverse effects, long-term use may create problems

In this meta-analysis, side effects from zinc were common. The 2 most frequently reported were bad taste (pooled odds ratio [OR], 2.64; 95% CI, 1.91-3.64) and nausea (pooled OR, 2.15; 95% CI, 1.44-3.23). When you recommend zinc, warn your patients about these adverse effects. The side effects are not severe, so patients can decide for themselves whether the benefit of a reduction in cold duration is worth the downside of nausea and a bad taste in the mouth.

It is also important to note that the trials included in the meta-analysis enrolled healthy children and adults ≤65 years old.



Do you recommend that patients take zinc to reduce the duration and severity of cold symptoms?

- Yes, frequently
- No, but I plan to do so
- No; the side effects are unpleasant
- Other _____

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Whether zinc benefits people with chronic illnesses (eg, chronic obstructive pulmonary disease) who develop colds is unknown.

Prolonged elevated serum zinc levels can interfere with copper metabolism, and the adverse effects of long-term use of zinc as prophylaxis are unknown. The trials included in the meta-analysis took place in relatively affluent countries in which zinc deficiency is uncommon. It is not known what impact zinc supplementation would have on people in poor countries.

Of the 15 studies included in the meta-analysis, 10 received support from pharmaceutical companies, 4 received support from foundations, and one received support from both.

CHALLENGES TO IMPLEMENTATION

When to talk to patients about zinc

Most patients do not seek medical care for colds. Those who do typically present only af-

ter having symptoms for several days, and it is not clear whether zinc supplementation has the same beneficial effects when started after the first 24 hours.²

Thus, you may have few opportunities in the office to recommend zinc for patients with colds, for whom there is evidence of immediate benefit. More likely, you'll need to incorporate a zinc recommendation into your overall advice about colds.

Zinc is available over the counter in various forms and dosage. After recommending zinc, you may be confronted with the question of which dose, brand, and formulation is best—a question which, unfortunately, remains unanswered. **JFP**

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