Is intranasal zinc effective and safe for the common cold? A systematic review and meta-analysis

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CRD summary
This well-conducted review concluded that there may be some benefit from zinc for symptoms of a common cold in adults, but the results for symptom relief at day three were not significant; there may be a risk of loss of the sense of smell. The authors overall conclusions reflect the evidence presented and are likely to be reliable.

Authors' objectives
To evaluate the effectiveness of intranasal zinc used to treat a common cold.

Searching
MEDLINE, EMBASE and the Cochrane Register of Controlled Trials (CENTRAL) were searched up to 2007; search terms were reported. There were no language restrictions. Study authors were contacted to locate unpublished studies.

Study selection
Eligible studies were randomised controlled trials (RCTs) that assessed the effectiveness of intranasal zinc compared with placebo in reducing severity and duration of common cold symptoms at day three of treatment. Trials that evaluated intranasal zinc as a prevention were excluded.

All of the included trials were conducted in adults who had naturally occurring colds. The nasal sprays were zincum gluconicum or zinc gluconate 2.1mg daily or zinc sulphate 0.044mg daily. The sprays were used for 10 days or until all symptoms were resolved.

Two reviewers independently selected the studies, with any disagreements resolved by discussion.

Assessment of study quality
The authors assessed trial quality for method of randomisation, concealment of allocation, blinding, follow-up and outcome measure criteria.

Data extraction
Outcomes (resolution of symptoms, symptom score and days to resolution of symptoms) were extracted from each trial to calculate risk ratios and 95% confidence intervals (CIs). Trial authors were contacted to obtain missing data.

Three reviewers independently extracted the data, with any disagreements resolved by discussion.

Methods of synthesis
The trials were pooled using fixed-effect and random-effects analyses. Heterogeneity was assessed using $\hat{I}^2$. Subgroup analysis was conducted by the dose of zinc.

Results of the review
Three RCTs were included in the review (451 participants). Methods of randomisation and allocation concealment were adequately reported in one trial, partially addressed in one trial, and unclear in the third trial. All trials were double-blinded.

Two of the RCTs reported a statistically significant benefit of intranasal zinc in the resolution of symptoms at day three. One trial reported an improvement in total symptom score at day one ($p=0.002$).

The pooled risk ratio for any symptoms persisting at day three favoured intranasal zinc compared with placebo, but the results were not statistically significant using a random-effects analysis (risk estimate 0.62, 95% CI 0.18 to 2.19; $\hat{I}^2=99\%$; three RCTs).
Subgroup analysis of the two high dose zinc studies for any symptoms at day three (using a fixed-effect model) showed a significant improvement in favour of zinc compared with placebo (RR 0.43, 95% CI 0.35 to 0.53).

Adverse events, including nasal stinging and burning, were more common in the treatment group in one of the trials. The two other trials did not demonstrate significant differences in adverse events between treatment groups.

Authors' conclusions
There may be some benefit from zinc for symptoms of a common cold in adults, but the results for symptom relief at day three were not significant. There are some unquantified concerns about permanent anosmia (loss of sense of smell) following the use of intranasal zinc.

CRD commentary
The review question and inclusion criteria were clear for intervention, comparators, study design, and outcomes. Attempts to identify all the relevant studies were undertaken. Measures were taken to minimise error and bias throughout the review process.

The quality of included trials was assessed and incorporated into the discussion. Comprehensive details of the included trials were provided. Appropriate methods were used to pool the results and to investigate statistical and clinical heterogeneity.

This was a well-conducted review, and the authors overall conclusions reflect the evidence presented and are likely to be reliable.

Implications of the review for practice and research
The authors stated that the prevalence of permanent anosmia would need to be established as a side effect before widespread and routine use of zinc could be recommended.

Funding
Not stated.

Bibliographic details

PubMedID
20690364

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Intranasal; Adolescent; Adult; Common Cold /drug therapy; Female; Humans; Male; Middle Aged; Trace Elements /administration & dosage /pharmacology; Young Adult; Zinc /administration & dosage /pharmacology

AccessionNumber
12010006740

Date bibliographic record published
30/03/2011

Date abstract record published
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.