ZINC FOR THE COMMON COLD (Review) Singh M, Das RR



BACKGROUND

- Rhinovirus
- One of the most widespread illnesses
- A leading cause of visits to the doctor, absenteeism froms chool and work
 - Adults: 2-4 episodes annually
 - Children: 6- 10 colds a year
- Complications: otitis media, sinusitis and exacerbations of reactive airway diseases
- In the United States
 - \$7.7 billion per year.
 - \$2.9 billion on over-the-counter drugs and another \$400 million on medicines for symptomatic relief
 - 1/3 patients: received antibiotic prescription, which has implications for antibiotic resistance
 - work loss: \$20 billion per year

BACKGROUND

- No proven prevention or treatment.
- Zinc :
 - Inhibits viral replication
 - Stabilises cell membranes
 - Prevents histamine release
 - Inhibits prostaglandin metabolism
- Zinc has been tested in trials for treatment of the common cold

OBJECTIVES

Zinc:

- Efficacious in reducing the incidence
- Severity and duration of common cold symptoms.

METHODS

- 15 RCTs (5 trials children 1-16 age)
- 1360 participants, comparing zinc with placebo
- Types of interventions
- Therapeutic trials: interventions commenced within three days of participants developing common cold symptoms for a period of five or more consecutive days.
- Prophylactic trials: intervention commenced and continued throughout the cold season for at least five months.

METHODS

- Primary outcomes
- Duration of symptoms
- Severity of symptoms
- 3. Incidence of the common cold
- Secondary outcomes
- Proportion of participants symptomatic after three, five or seven days of treatment
- Time to resolution of individual symptoms: cough, nasal congestion, nasal drainage and sore throat
- Change in individual severity symptom scores: cough, nasal score
- School absence (days)
- 5. Antibiotic use
- Adverse events

- 996 participants in the therapeutic trials
- 394 in the preventive trials

A. Primary outcomes

1 Duration of cold symptoms

	Intervention			Control			5	Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Kurugol 2006a	4.7	0.8	97	5.3	0.7	97	18.0%	-0.80 [-1.09, -0.50]	•		
Kurugol 2007	5.5	1.97	60	6.5	1.97	60	17.5%	-0.50 [-0.87, -0.14]	•		
Macknin 1998	8.5	2.85	125	8.5	2.85	124	18.2%	0.00 [-0.25, 0.25]	•		
Petrus 1998	4.4	1.4	52	5.1	2.8	49	17.4%	-0.32 [-0.71, 0.08]	•		
Prasad 2000	4.5	1.6	25	8.1	1.8	23	14.7%	-2.08 [-2.80, -1.37]	-		
Prasad 2008	4	1.04	25	7.12	1.26	25	14.2%	-2.66 [-3.43, -1.88]	*		
Total (95% CI)			384			378	100.0%	-0.97 [-1.56, -0.38]	•		
Heterogeneity: Tau2 =	0.48; C	hi²= 6		10 5 0 5 10							
Test for overall effect: Z = 3.22 (P = 0.001)									-10 -5 0 5 10 Favours intervention Favours control		

- Ten studies : 762 participants
- Zinc: significant reduction (P = 0.001), within 24 hours of the onset of symptoms.

2. Severity of cold symptoms

	Intervention			Control			Std. Mean Difference		Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Kurugol 2006a	0.2	4.92	97	0.4	5.9	97	24.0%	-0.04 [-0.32, 0.24]	•	
Kurugol 2007	0.3	4.64	60	0.7	6.97	60	22.2%	-0.07 [-0.43, 0.29]	*	
Petrus 1998	1.41	0.29	52	1.5	0.28	49	21.3%	-0.31 [-0.71, 0.08]	_ *	
Prasad 2000	2.7	2	25	5.4	1.9	23	15.5%	-1.36 [-1.99, -0.73]	-	
Prasad 2008	3.45	5	25	5.61	2.5	25	17.0%	-0.54 [-1.10, 0.03]	-	
Total (95% CI)	259 254						100.0%	-0.39 [-0.77, -0.02]	•	
Heterogeneity: Tau ² =	0.13; C		-10 -5 0 5 10							
Test for overall effect:	Z = 2.05	Favours intervention Favours control								

- Five studies : significant difference between two groups (P = 0.04)
- Formulations and time of administration of zinc differed among the studies

3. Incidence of common cold

	Intervention		Control			Risk Ratio	Risk		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Rando	om, 95% CI	
Kurugol 2006b	121	281	160	281	48.8%	0.76 [0.64, 0.90]	-		
Vakili 2009	170	480	310	480	51.2%	0.55 [0.48, 0.63]			
Total (95% CI)		761		761	100.0%	0.64 [0.47, 0.88]	•		
Total events	291		470						
Heterogeneity: Tau ² =	0.05; Chi	² = 8.39	, df = 1 (F	3%	0.1 0.2 0.5	1 2	5 10		
Test for overall effect:	Z= 2.76 (P = 0.00	06)			Favours intervention	Favours cor		

- two studies
- > Zinc : reduced the incidence (P = 0,006)

B. Secondary outcomes

- Proportion of participants symptomatic after three, five or seven days of treatment
- Three, five days
 - Three studies : 340 participants.
 - No significant difference
- Seven days
 - Five studies : 476 participants.
 - Significant difference between the intervention and control group

2. Time to resolution of individual cold symptoms

- 5 studies.
- 1) Time to resolution of cough
- 2) Time to resolution of nasal congestion
- 3) Time to resolution of nasal drainage
- 4) Time to resolution of sore throat
- > significantly shorter in the intervention group

- 3. Change in individual severity symptom scores
- Change in cough symptom score: Mean cough score
 - 2 studies: lower in the control group statistically significant (P = 0.2)
 - 1 study: significant decrease in the intervention group (P < 0.00001)

- Change in nasal symptom score
 - 4 studies : the mean nasal score
 - 1 study : lower in the control group, statistically significant
 - 1 study : decrease (not significant) in the intervention group
 - 2 studies : no difference between the two groups

- Change in throat symptom score
 - 2 studies : the mean throat score
 - 1 study : lower in the intervention group statistically insignificant
 - ▶ 1 study : decrease in the mean throat score (not significant) in the intervention group

4. School absenteeism

- Three trials.
- Two preventive trials: zinc were absent for fewer days from school (P = 0.03)
- One <u>therapeutic trials</u>: zinc were less likely to be absent than placebo (P = 0.12).

5. Antibiotics use

- Two trials
- More likely in placebo than in zinc (P < 0.00001)</p>

6. Adverse events

- Ten trials
- > Bad taste and nausea: higher in the zinc group.
- No significant difference between the 2 groups : constipation (P = 0.17), diarrhea (P = 0.08), abdominal pain (P = 0.25), dry mouth (P = 0.09) and oral irritation (P = 0.50)

DISCUSSION

Results

- Quality of the evidence
 - Generally of good quality, with a lowrisk of bias
- Agreements and disagreements with other studies or reviews

Zinc for the common cold

Marshall I (2000)

OBJECTIVES:

The objective of this review was to assess the effects of zinc lozenges for cold symptoms.

MAIN RESULTS:

- Seven trials: 754 cases
- Describe the duration, incidence and severity of respiratory symptoms.
- Two trials: reduced the severity and duration of cold symptoms.

REVIEWER'S CONCLUSIONS:

- > Evidence inconclusive.
- There was significant potential for bias
- further research is required to substantiate these findings.

DISCUSSION

- The important changes in this updated review
 - Significant reduction in the duration and severity of common cold symptoms.
 - Duration of individual cold symptoms was also significantly reduced
 - The syrup and tablet preparation of zinc is better tolerated than lozenges.
 - Reduces incidence, school absenteeism and prescription of antibiotics

AUTHORS'CONCLUSIONS

Implications for practice

- Zinc:
 - > therapeutic :
 - > reduced the duration
 - severity of common cold symptoms
 - > prophylactic :
 - > reduced the incidence
 - > school absence
 - > antibiotic use in healthy children
- Beneficial for high-income countries. Cannot be applied low-income countries
- Included healthy participants, not evidence in participants at risk
- Caution: not all formulations may be effective (especially lozenges)

AUTHORS'CONCLUSIONS

Implications for research

1. Asthmatic children:

- Cold episodes is a common risk factor for acute asthma exacerbations.
- The results would be more meaningful for them.

2. Low-income countries:

The assumption is that in these countries zinc deficiency may be prevalent and the results may be far more impressive.

THANK YOU!