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Original Article

Influence of zinc on severity of common cold in children

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Abstract

Background Symptomatic treatment of common cold in children does not reduce the duration and severity of disease. Since zinc has been used to enhance cellular and humoral immunity, it has the potential to reduce the severity of the common cold. However, the effects of zinc on the common cold have been inconclusive. The use of zinc to treat cold symptoms deserves further studies.

Objective To determine the effect of zinc supplementation on the severity of the common cold in children.

Methods We performed a randomized, double-blind, controlled trial in children aged 3-5 years who were diagnosed with a common cold at primary health care centers in Gedongtengen, Umbulharjo I and Kotagede II, Yogyakarta. Subjects were collected by consecutive sampling and their parents were interviewed. Severity of illness was categorized as mild, moderate or severe.

Results One hundred fourteen patients with common cold were divided into 2 groups of 57 subjects each. One group received zinc supplementation while the other group received a placebo. Subjects with fever received additional paracetamol. After 7 days of treatment, there were no significant differences in clinical improvement in the zinc group (80.7%) compared to that of the placebo group (78.9%), P=0.83.

Conclusion The severity of the common cold in children aged 3-5 years was not significantly different in those who received zinc supplementation compared to placebo. **[Paediatr Indones. 2012;52:324-8]**.

Keywords: *common cold, severity, zinc, children*

Common cold is an acute, viral respiratory tract infection.[1,2] Cold symptoms are caused by the body's immune response against viral infection.[3] In Indonesia, common cold has been estimated as the reason for 40%-60% of visits to primary health care centers and 15%-30% visits to outpatient facilities in hospitals.[4] The prevalence of common cold in Yogyakarta was found to be 59.4% in 2006.[5] Ninety-four percent of the patients with common colds who visit a doctor get prescriptions for antibiotics, cough medicines, or symptomatic treatments. These medicines are of little benefit in treating the common cold and potentially cause side effects.[6] There is still no standard therapy for the common cold. Good immune status is required to eliminate the virus in order to avoid complications.[7]

Zinc is a micronutrient needed for growth, development, and good immune function. Zinc plays a role in the inflammatory process by inhibiting viral interactions with intercellular adhesion molecule-1 (ICAM-1), inhibiting viral replication, stabilizing and protecting cell plasma membranes, as well

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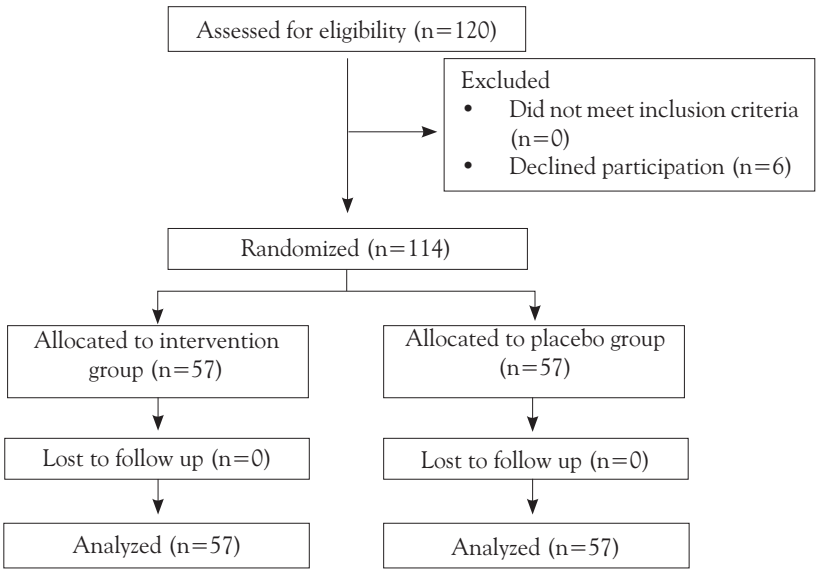
as disrupting and inhibiting the release of pro-inflammatory mediators.[3,6,8]

In Kurugöl et al's randomized, controlled trial on the effects of zinc on the common cold, zinc had a significant effect in reducing the duration and severity of colds.[9] However, Godfrey *et al*. reported inconsistent effects of zinc on cold severity.[10] Since the evidence for the effects of zinc on the common cold have been inconclusive, a further study is needed.

Methods

We performed a randomized, double-blind, controlled trial in August 2009 to January 2010, on subjects with common cold received either zinc supplementation or placebo therapy. A pharmacist from an outside primary health care center held the key, so subjects and researchers were blinded until the end of the study. Diagnosis of common cold were based on cough and runny nose with clear or mucopurulent secretions of less than 10 days, with or without mild fever of <39ºC, good general condition and no thoracic abnormalities on physical examination. We included subjects aged 3-5 years who lived in Yogyakarta, suffered from the common cold for less than 2 days, had good general appearance, had parents willing to participate by signing the proxy consent and had an active phone number to maintain contact. Those suffering from a common cold with complications such as pneumonia, acute otitis media, sinusitis, exacerbation of asthma, as well as immunocompromised status such as HIV infection, malignancy or on steroid therapy for more than 4 weeks were excluded. Weight was measured by a nurse using weight scales and nutritional status was determined based on weight-for-age according to the WHO growth charts 2006.[11] Adherence to therapy was considered to be good if $\geq$ 85% of the zinc/placebo was taken. We defined exposure to smoke as exposure to cigarette smoke, kitchen smoke, or mosquito repellent smoke during the study. The study profile is shown in **Figure 1**.

The estimated required sample size was 114, calculated by unpaired categorical analysis with α=0.05 and β=0.20. Subjects were collected by consecutive sampling. The treatment group received zinc powder (1x20mg) for seven days, while control group received placebo powder. Any subject with fever received paracetamol. Subjects were assessed at primary health care centers on the 3rd and 7th days of treatment. Nurses assessed the cough, nasal symptoms, throat symptoms and systemic symptoms to determine severity of disease. We gave scores for each common cold symptom: 0-no symptoms, 1-mild symptoms, 2-moderate symptoms and 3-severe symptoms. After total scores were obtained, subjects were classified into 1 of 3 disease severities: mild if the total score was $\leq$ 4, moderate if >4 to 8, and severe if >8 to 12. Common cold severity and side effects of the therapy were recorded by parents or



nurses on study forms. The outcome of the study was the severity of the common cold. The condition was considered to be improved if there was a reduction of one degree or more compared to the prior assessment of severity.

The independent variable in this study was the therapy type; zinc or placebo. The dependent variable was severity of the common cold. Confounding factors were age, nutritional states, and initial degree of severity.

This study was approved by the Commission on Medical Research Ethics and Health, Gadjah Mada University Medical School. All subjects provided proxy consent, signed by their parents.

Data was analyzed with SPSS for Windows 15.0. The effectiveness of zinc compared with that of placebo therapy was analyzed by Chi-square test. Statistical significance was considered to be $P<0.05$.

Results

The 114 subjects were divided into two groups. Subjects in both groups had similar characteristics, as shown in **Table 1**.

The decrease in severity of cold symptoms is shown in **Table 2**. There was no significant difference between the two groups in the decrease of cold symptom severity ($P=0.83$).

Table 1. Baseline characteristics of subjects

Characteristics	Zinc n=57		Placebo n=57	
Age, n (%)				
3-4 years	29	(51)	31	(54)
4-5 years	28	(49)	26	(46)
Sex, n (%)				
Male	26	(46)	25	(44)
Female	31	(54)	32	(56)
Nutritional status, n (%)				
Good	48	(84)	50	(88)
Undernourished	7	(12)	7	(12)
Overweight	2	(4)	0	0
Smoke exposure, n (%)				
Yes	36	(63)	41	(72)
No	21	(37)	16	(28)
History of common cold contact, n (%)				
Yes	17	(30)	18	(32)
No	40	(70)	39	(68)
Length of illness, n (%)				
1 day	27	(47)	32	(56)
2 days	30	(53)	25	(44)
History of allergy, n (%)				
Yes	15	(26)	17	(30)
No	42	(74)	40	(70)
Attends school, n (%)				
Yes	36	(63)	33	(58)
No	21	(37)	24	(42)
Adherence to therapy, n (%)				
Yes	56	(98)	56	(98)
No	1	(2)	1	(2)
Additional therapy (paracetamol) given, n (%)				
Yes	29	(51)	35	(61)
No	28	(49)	22	(39)
Initial severity, n (%)				
Mild	52	(91)	48	(84)
Moderate	5	(9)	9	(16)
Severe	0	0	0	0

Table 2. Subjects with decreased cold severity in the zinc and the placebo groups

Variable	Zinc group n = 57	Placebo group n = 57	P value*
Decreased severity status, n (%)			
Did not decrease	11 (19)	12 (21)	0.83
Decreased	46 (81)	45 (79)	

*Chi-square test

One subject in the placebo group was considered to be failed because he took antibiotics. We included this subject into group with did not decrease of severity of common cold. Secondary outcomes in terms of side effects (vomiting) occurred in 2 children in the zinc group and in 2 children in the placebo group (drowsiness). According to parents' and nurse's reports, all subjects received therapy with 100% compliance.

Discussion

Previous study showed that zinc administration reduced the severity and shortened the duration of common cold. The duration of common cold in subjects who were given zinc was less than 5 days.'[12-15] However, our results were in contrast to this previous study. The common cold is self limiting disease with symptoms generally remaining up to 7 days, and up to 14 days in 10% of cases.[16] In patients with a previous history of bronchial asthma, the common cold can be a trigger for asthma attacks. Thus reduction in the severity of common cold in children over time was expected.[17,18,19,20]

The difference in our results may have been due to insufficient zinc dosage. Previous studies have used varying doses of zinc. According to Eby, only zinc ions were shown to have anti-rhinovirus activity by inhibiting the normal cleavages by which the viral polypeptides are processed, inhibiting ICAM-1, increasing levels of interferon-gamma (IFN-γ), inhibiting the release of histamine and leukotrienes from basophils and mast cells, protecting the plasma cell membrane, and being useful in allergy treatment.[21] We used a lower dose of zinc than previous studies because the 20 mg once daily zinc dosage proved to be useful in other diseases. In addition, higher doses have been associated with adverse events.[22]

Another possible reason for a lack of difference in the effects of zinc and placebo may be due to the type of viruses causing colds in our subjects. Current evidence has shown zinc to have an anti-rhinovirus effect (30 to 50% of cases of common cold are caused by rhinovirus), but there has been no evidence that zinc inhibits other cold-causing viruses. There are more than 200 types of viruses that cause the common cold.[23,24] Furthermore, we gave zinc to patients with symptom duration of > 24 hours, whereas there is evidence that zinc provides benefits only if administered within the first 24 hours.[22]

A limitation of our study was that we did not perform intensive supervision after the treatment administration to both groups. Compliance to zinc administration was based on reporting by parents and families, hence, it is possible that the zinc was not taken regularly due to its unpleasant taste.

Co-intervention at home in the form of food and drink also were not explored. If the placebo group received more co-intervention than the zinc group, the results may have been influenced.[25,26] The duration of the common cold was not defined as well because the data was compiled only up to the seventh day of observation. In addition, we found that side effects were not significantly different between the two groups. However, since our subjects were young (3-5 years), they may not have been able to communicate their experience.

In conclusion, we found that 20mg of oral zinc supplementation once daily started in the first 48 hours of cold duration did not significantly reduce the severity of illness in children aged 3-5 years compared to a placebo. A further study needed to determine if a higher dosage of zinc and a different treatment duration can decrease the severity of the common cold.

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The authors declare that they have no conflict of interest in this research.

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