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The Effect of Zinc Sulfate on Duration of Common Cold Symptoms in Children

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ABSTRACT

At the age of 1-7 years, the common cold is prevalence among children. It usually happens 6 to 7 times a year among children. An effective and safe drug is needed to reduce the duration of common colds symptoms in children and reduce subsequent complications. In some studies, zinc sulfate has showed an antiviral effect and immune enhancing activity. Therefore, this study was designed to evaluate the efficacy of zinc sulfate in duration of colds' symptoms in children. In this study, 112 children with common cold who are between 6-7 years old divided into two groups. Case group received zinc sulfate within 10 days and Control group didn't receive this drug. The symptoms like rhinorrhea and nasal obstruction, cough, sneezing, fever and duration of illness were checked out in both groups by questionnaire. In children with common cold, a significant decrease was observed in the mean duration of rhinorrhea, cough and nasal obstruction. Compared to the group that didn't receive zinc sulfate, the zinc group had shorter mean duration of sneezing and fever. The mean duration of illness in patients who had received the zinc sulfate was significantly less than the other group. No side effect was observed in subjects received zinc sulfate. Based on our result, zinc sulfate can be administered with other supportive treatments of common cold, for reduction of symptoms duration and complications in children.

Key words: Cold symptoms, Common cold, Zinc Sulfate.

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1. INTRODUCTION

Common cold, also known as a cold, is a viral disease characterized by runny nose and nasal congestion and mild fever or no fever and usually without systematic manifestations. Clinical symptoms of common cold usually appear after the first two or three days of viral infection and include nasal drip and nasal congestion and sore throat, and sometimes nonproductive cough. Cold usually lasts about a week, however, in 10% of cases it takes up to two weeks (1). Often a change occurs in the color or consistency of nasal discharge, which does not represent sinusitis or bacterial infection. Examination of nasal mucosa may indicate swollen blades and nasal erythematous (1). Common cold is the most common disease in children. Cold in early childhood occurs 5-7 times per year, compared with adults 2-4 times per year (2). Among etiologic factors of the disease, hundreds of different species of viruses are the factors that about 90 percent cause upper respiratory

infection. The viruses can enter the body through mucous membranes of the nose or eyes (2). According to the symptoms caused by common cold, the disease creates numerous problems for children and their families such as weight loss and probability of having secondary bacterial infections by creating restlessness and interference in nutrition. Zinc is one of the essential supplements affecting child's optimal physical growth, cognitive development and immune function (3-7). Several studies have found some anti-viral effects in children taking zinc supplements. Approximately one fourth of the people in the world are at risk of zinc deficiency especially those in sub-Saharan Africa (8). Some other clinical studies have shown that zinc significantly reduced the duration of cold treatment and the local application of Zinc Sulfate is effective in reducing the duration of symptoms (9, 10). Counseling before taking the drug is recommended (11, 12). Various studies have been conducted to evaluate the effect of Zinc Sulfate in pneumonia, respiratory infections and improving

cold symptoms without serious side effects (13-16). In some studies Zinc can reduce the severity and duration of the symptoms (15). By reducing the duration of cold symptoms in children, we can avoid some complications of common cold if drugs are effective and safe. This study was designed to investigate the effect of Zinc on duration of cold symptoms in children. It should be noted that this study has not been done in our country despite the high prevalence and importance of the disease.

2. MATERIALS AND METHODS

This study was a single-blind clinical trial type (Iranian Registry of Clinical Trials: IRCT138903184056N2) with randomized control. The samples were selected from children with colds (without being infected with respiratory diseases).

2.1. Inclusion criteria

Patients were children 1-7 years old with a common cold diagnosed by a pediatrician, without receiving antibiotics. Local symptoms were sore throat, stuffy nose, runny nose, cough, sneeze and systemic symptoms were defined as headache, muscle ache, and chilliness. Parent's patients, who were briefed in advance and signed the consent declaration prior to any study-related procedures, were recruited for the study. Anonymity was guaranteed and information on subjects was kept confidential. Subjects were free to withdraw from the study at any time without prejudice to further treatment.

2.2. Exclusion criteria

Patients were excluded if parents disagreed with continue to participate in the study.

2.3. Study visits and treatment schedule

A total of 120 children with colds were selected that referred to the pediatric clinic of Amir Kabir Hospital located in Makazi province, Iran. This study was carried out during one year. Patients were divided into two equal

groups for a randomized block design:

The treatment group (56 children): all patients received Zinc-Sulfate (Syrup zinc sulphate each measure contains: zinc as sulphate 1mg kg⁻¹ (5mg 5ml⁻¹) once per day after a meal for 10 days. The treatment group (56 children): all patients received zinc sulfate (Razak laboratories, Tehran-Iran). Syrup zinc sulphate each measure contains zinc as sulphate 1 mg kg⁻¹ (5mg 5ml⁻¹) once per day after a meal for 10 days. The control group (56 children): all patients did not receive the drug (zinc sulfate). The questionnaires were completed by parents during 10 days (duration of the symptoms) and they referred to the pediatric clinic and delivered the questionnaires after 10 days. The other drugs which the study population used has just been as nose drop (sodium chloride), children cold syrup, liquid diphenhydramine (if cough), syrup acetaminophen or ibuprofen (if fever). The patients in control group did not know the other group received a new treatment. After obtaining written consent from parents, data collection forms were delivered to them and they were given the necessary training to complete the questionnaire. Likewise, the study was conducted until the completion of the sample size. After completing the sample size, data was collected via questionnaires and the results were then analyzed using the SPSS statistical software SPSS18 (SPSS Inc, Chicago, IL, USA) and p<0.05 was considered statistically significant. Descriptive findings were presented in the form of average and standard deviation and analytical findings by t-test and Mann-Whitney U. It is important that the principles of medical ethics, at all stages of the study were respected and the patients have benefited from other treatments and study was approved by the Medical Ethics Committee.

3. RESULTS AND DISCUSSION

In this study, the average age of the samples (112 people) was 2.93±0.99. There was no significant difference according to age between the two groups (Table 1).

Table 1. The standard deviation and average age of children with colds referring to the pediatric clinic of Arak's Amir Kabir Hospital

Group	Mean(age)±SD	The Minimum Age	The Maximum Age	Number
A	2.90 ± 1.01	1.5	7	56
B	2.97± 0.99	1.3	5	56
Total	2.93±0.99	1.3	7	112

P-value=0.2

The minimum and the maximum age in the treatment group were 1.5 and 7 years, respectively, and in the control group that was 1.5 and 5 years. In the total sample (n = 112), 35 patients (31.3%) were male and 77 patients (68.8%) were female. In the treatment group (56 samples),

19 of the samples were boys (33.9%) and 37 were girls (66.1%). In the control group (56 samples), 16 of the samples were boys (28.6%) and 40 were girls (71.4%) (Table 2).

Table 2. Number and percentage of children with colds referring to the pediatric clinic of Arak's Amir Kabir Hospital by gender

Group	The number of boys (Percent)		The number of girls (Percent)	
	Number	Percent	Number	Percent
A	19	33.9%	37	66.1%
B	16	28.6%	40	71.4%
Total	35	31.3%	77	68.8%

The average duration of fever in treatment group was 2.82 ± 2.14 and this amount in control group was 5.02 ± 2.74 (Mann-Whitney U, $p= 0.0001$) (Odds ratio 0.56). As a result, duration of fever showed a significant difference between the two groups. The average duration of the

disease in the treatment group was 6.63 ± 1.71 . The average duration of disease in the control group was 7.95 ± 1.58 (Mann-Whitney U, $P= 0.0001$). Thus in terms of duration of disease, there was a significant difference between the two groups (Table 3) (Odds ratio 0.83).

Table 3. The standard deviation and average duration of symptoms of the common cold in the Zinc group and the control group in children with colds referring to the pediatric clinic of Amir Kabir Hospital in Arak in 2007

Duration of symptoms	Case group	Control group	Odds ratio	Confidence interval	p-Value
The average duration of congestion and runny nose	5.07±1.96	6.23±2.33	0.81	0.2-2.6	0.005
The average duration of cough	4.13±2.46	5.7±2.9	0.72	0.2-2.5	0.003
The average duration of sneezing	5.09±1.93	6.16±2.16	0.82	0.27-2.4	0.007
The average duration of fever	2.82±2.14	5.02±2.74	0.56	0.1-2.3	0.001
The average duration of disease	6.63±1.71	7.95±1.58	0.83	0.3-2.3	0.001

In this study, side effects were not observed in any of the samples. Therefore, t test showed that there was not any significant difference between the two groups. The average duration of congestion and runny nose, cough, sneeze, fever and the total duration of disease in both groups have shown in Table 3. The averages show a significant difference between the two groups as specified in the Table 3. In some studies, Zinc supplements for children have anti-viral effects. In other clinical studies, zinc sulfate significantly reduces duration of a cold. Also, some studies have shown that local application of zinc sulfate is effective in reducing the duration of symptoms; but the specific mechanisms that cause these clinical effects are unknown (17). An inconsistent evidence from a meta-analysis suggests that oral zinc administration reduces the duration and severity of common cold in adults (18). Side effects such as nasal stinging and burning were more common in treatment group than placebo group (19). Using oral zinc supplements was associated with an increased risk of adverse events such as bad taste and nausea (risk ratio 1.24, 95% CI 1.05 to 1.46). It is unclear why oral zinc treatment seems to benefit adults more than children (18, 19). Due to the positive charge, ionized Zinc tends to bind to the cells which are the junction of viruses and for this reason prevents the connection, proliferation and invasion of the virus in cell (17). The function of 3C protease, the virus that is a key enzyme for virus transcription, is controlled by Zinc. Ionized Zinc by vasoconstriction property in the nasal mucosa epithelial cells causes reducing tissue edema, inflammation and mucus secretion (17). As well as zinc increases the host response to a variety of infections and it plays an important role in the homeostasis of the immune system (15). According to the results of the two groups who were similar in terms of age and sex distribution, with a significant difference, duration of congestion and runny nose, cough, sneezing, fever in children with colds used zinc is lower than the patients who did not take zinc. In the treatment group, the children with colds used zinc, with a significant difference, had a reduction in the total duration of disease compared to the control group. In this study, side effects were not observed in any of the samples. Some

studies in other countries, have examined the effect of zinc sulfate on recovery of common cold symptoms in children. The results showed that zinc reduced the duration of symptoms in the patients. In none of these studies examined the effect of zinc on each of the symptoms of a cold individually, but the effect of the drug was studied on total duration of the disease (13, 14, 20, 21). In Miller's study, 50 patients with common cold were treated with zinc sulfate. The proportion of symptoms duration in the treatment group to the control group was 4.4 to 7.6 days (20), however, in our study each of the symptoms in patients was evaluated separately and associated with total duration of common cold. Barret also showed the role of zinc-sulfate to control the proliferation of rhino viruses (21). Another study suggested that high doses of zinc can reduce the severity of the symptoms and shorten the duration of colds (22). Administration of zinc in the form of intranasal zinc gluconate in the first 24 hours is effective in reducing the severity of the symptoms and it has not side effects (23). In the laboratory conditions as shown zinc inhibits the respiratory syncytial virus and can play a role in preventing RSV infection (17). In a study in Turkey, disease duration and nasal symptoms were similar in both groups (6 days); but the severity of symptoms especially nasal symptoms was lower in the treatment group (24). Brown also did not observed harmful side effects in using zinc compounds (pills, syrups, nasal gels). He reported mild side effects like headache, dry mouth or throat, changes in taste and irritation of the nose and mild gastrointestinal effects but considering its utility, using zinc compounds is recommended for the common cold (9). On the other hand, some studies including Chang in Australia showed vitamins and zinc have been effective, alone or in combination with other drugs in improving hospitalized patients with lower respiratory symptoms. Of course, this study involves hospitalized patients with lower respiratory infection which is different from our study on outpatients and upper respiratory tract infection (13). In Burman study, unlike the present study, there was no difference for clinical symptoms of colds in both groups (16). Blungia in a double-blind clinical trial study did not observed the positive effects of zinc gluconate nasal spray

and zinc orotate used in the treatment of common cold and it was not recommended due to the permanent loss of the sense of taste, which can be a complication of zinc (10). No side effects were observed in this study, but according to other issues, such a suggestion was given. In addition, the zinc type used in the study was different from the zinc in our study. In a study that Eby Gaetal done to investigate the effect of zinc in children with colds, one group used the zinc and mild side effects were noted in two samples include nausea, dry mouth and headache. These side effects were not observed in the placebo group. Therefore, there was no significant difference in terms of side effects between the two groups (11). However, in our study the placebo drug was not used in the studied patients. Fashner considered the common cold treatment in children and adults. As a result of the study, vapor rub, zinc sulfate, Pelargonium sidoides (geranium) extract, and buckwheat honey can improve symptoms in children. Also the prophylactic probiotics, zinc sulfate, nasal saline irrigation, and the herbal preparation Chizukit reduce the incidence of common cold in children (12). Zinc sulfate had no effect on the duration of cold symptoms. However, it appears to be effective in reducing the severity of the cold symptoms in healthy children (24). A review recently published in 2004, an overview of published articles through Medline (1980 – 2003), concluded that zinc was effective in reducing the duration and severity of symptoms of common cold (23). In low-income populations, micronutrient deficiencies is more prevalent; so using combined supplementations with zinc is recommended to decrease childhood morbidity and mortality (5, 7, 25-27). In a review by Marshall, it was concluded that zinc gluconate lozenges were effective in reducing the symptoms and duration of the common cold, but the side-effects and particularly bad taste might limit patient compliance (28). Thus, oral zinc formulations may shorten the duration of symptoms of the common cold. However, large high-quality trials are needed before definitive recommendations for clinical practice (18, 29, 30). One of the limitations in our study was the studied children were in the age group of 1-7 years and children are limited in expression signs and symptoms that may be due to side effects of drugs. However, if any of the symptoms described by patients, there will be more confidence. Other limitations were non-cooperation of parents in the child's medication because of side effects such as abdominal pain and lack of co-parents in terms of long-term use of drugs by children and lack of parents track to full recovery.

4. CONCLUSION

Zinc can be used as a complementary treatment of the common cold in children, due to the mild side effects and shorten the duration of symptoms of a cold virus. According to the obtained results and lack of special side effect while taking zinc and the availability and easy use of the drug, it can be used in conjunction with other supportive treatments to reduce the duration of symptoms

of common cold. Concurrent use of Zinc along with other necessary treatments can shorten the duration of symptoms of the disease and reduce the side effects caused by cold. Due to the age limitation in this study, we can examine a wider range of samples in the future. Since other studies have not been done in our country for effects of zinc on duration of cold symptoms in children. It is suggested that to investigate the possible side effects as well as confirm the findings in this study, further studies need to be done with a larger sample size, especially in the seasons of the outbreak, from autumn to spring.

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AUTHORS CONTRIBUTION

Parsa Yousefichaijan planned and carried out the study. Fatemeh Dorreh performed the clinical testing of the patients participating in the study. Mahdyieh Naziri performed the statistical analysis and helped to draft the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this paper.

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