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Incidence and clinical picture of upper respiratory infection in children receiving zinc supplement

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KEYWORDS *upper respiratory infection; zinc supplementation; under five children*

ABSTRACT *The National Household Health Survey (1995) reported that the prevalence of upper respiratory infection (URI) in Indonesia was found 25.3% for all ages and 47.1% for the under five children. Reports of studies on the effect of zinc in the reduction of respiratory infection stated inconsistent results. The objective of this community base study is to evaluate the effect of zinc as the attempt to reduce the incidence of URI. We have studied the effect of daily supplementation of 10 mg elemental zinc in a double blind, randomized, controlled trial consisting of 37 children (zinc group) and 36 children (control group) of 6 months - 5 years old. The distribution of preparation and monitoring of morbidity were performed regularly once a week along 2-month study period. During the 2-month study (February-April 2001) we found 24 URI cases in the zinc group and 24 cases in the control group. Time series analysis concerning the incidence and severity of the zinc group showed a negative slope (Yt: a – bx), while the placebo group showed a positive slope (Yt: a + bx). The evidence and severity of URI in zinc groups within the 1st and 2nd months showed significant different, while it was not in the control group. The study obviously showed the benefit of zinc supplementation in the reduction of URI as showed by negative slope in the time series analysis, and significant decreased of the incidence and the severity of URI in zinc group. There was no side effect of zinc supplemented noted. We suggest, therefore regular zinc supplementation to the diet of the children in the low economic level community are needed.*

Upper respiratory infection (URI) in Indonesia is a major problem in terms of morbidity. A National Health Survey conducted by the Ministry of Health Republic of Indonesia was found the incidence URI in under five children at 47.1% (Dep. Kes. R.I., 1997). As a base line data for the 5-year program entitled Health for Children at RW 03 Kamal Village by the Year 2005, the survey of health profile of under five children was conducted and we found that the incidence of URI was 48%, followed by 40% under-nutrition, 12% skin infection, diarrhea and tuberculosis in 11% each, anemia and worm infection in 8% and 5% respectively (Widagdo, 2001 and Widagdo *et al.*, 2002). URI does not significantly contribute to the mortality in children, but it can be a burden to the community in term of social and economical aspects (Bahl and Bahn, 2000). Several reports have stated that the cause of URI mainly is virus, and in as much as 15% is β-hemolytic streptococcus (Herendeen and Szilagy, 2000).

Zinc is a micro-mineral needed in minute amount for the purpose of optimal life. The food rich in zinc such as meat, kidney, liver, milk, and beans, is digested and absorbed in the intestinal mucous membrane, and the total amount of zinc in the body is 0.0033% of total body mass (Gordon *et al.*, 1981). The blood zinc level is influenced by several conditions and it may be lower than normal such as in diarrhea (Naveh *et al.*, 1982 and Castilo-Duran *et al.*, 1988). Clinical manifestation of inadequate blood zinc level can be classified into three categories. Marginal or mild deficiency is a borderline state in which the signs occur only in conjunction with other stressors such as rapid growth. The clinical sign of moderate category is reduced blood zinc level, retarded growth and depressed immune response, while the severe category may due to nearly incomplete absorption of zinc in diet and is manifested as dermatitis and anorexia (Prasad, 1988).

Zinc deficiency is caused by multi factors, i.e. inadequate intake of zinc of any reasons such as poverty, vegetarian, anorexia, and prolonged infusion, gastrointestinal disorders such as diarrhea, pancreatitis, short bowel syndrome, and various diseases such as pneumonia, tuberculosis, meningitis, and nephrotic syndrome (Arlette, 1983).

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Zinc supplementation has been used with significant result in the treatment of diarrhea in children (Sazawal *et al.,* 1995, Hidayat, 1997, and Nova *et al.,* 1997). It has been also reported that the administration of zinc successfully reduce the incidence of diarrhea (Widagdo, 2002, Shankar and Prasad 1988 and Black, 1998), but inconsistent result was reported when zinc supplementation was used in the prevention of respiratory infection (Ruel *et al.,* 1997 and Sazawal *et al.,* 1998).

The purpose of this community-based study is to evaluate the effect of zinc supplementation in the attempt to reduce the high incidence of URI in Indonesia.

MATERIALS AND METHODS

The study was designed as a double blind, randomized, controlled community trial at RW 03 Kamal village, a low socioeconomic suburban area of West Jakarta, commencing from February 2001 until April 2001.

The total population of Kamal village is 5.841 peoples including the under five as much as 462 children. The village has three community service posts, which is locally known as "posyandu". Once a month the under-five children regularly visit the post for health monitoring. Each post usually cover around 75-100 visitors. The parents were widely informed about the study and then kindly asked to give their written consent if they were eager for joining the study.

Then one hundred children selected at random, were enrolled to be the participant of the study. They were divided into treatment and control groups each consisting of 50 children. Thirteen in treatment and fourteen in control group were excluded from analysis because of contracting disease other than URI and incomplete participation in the study.

Two formulations, zinc supplement and placebo were used in liquid preparation which is similar in color and taste were weekly prepared and coded by Pharmaceutical Division of Pediatric Department Trisakti Medical Faculty. The zinc preparation consists of 10 mg elemental zinc as zinc sulfate and saccharine in quantum sates, while the placebo preparation contained only saccharine. The amount of saccharine is adjusted to get the similar taste and color of both solutions. Every day the child belongs to zinc group and control group should take a teaspoonful syrup containing 10 mg zinc sulfate and placebo syrup respectively. During the 1-month study period every week (on Monday) each participant will be received one bottle containing 35 ml syrup of zinc sulfate or placebo solutions. Two field workers were trained sufficiently to assist the study. Their job is door-to-door to distribute the solutions, to collect the previous bottle, and to check the volume of solution taken by the participant. The workers also should interview the mother weather the child get fever, cough, nasal discharge, and other complaints along the previous week. If one or more of the symptoms present, then the child is advised to visit the post on the following day for physical examination by the junior staff of Pediatric Department. The participant will be excluded from the study analysis, if: a). within the third day of the study they contracted URI, b). they did not take the solution as much as ≥ 2 times in a week, or ≥ 8 times along the study, and c). the solution was not tolerated of any reasons, and d). they were associated with other serious diseases.

On the day of enrollment, the junior staffs collected the demography data, base line data of anamnesis and physical examinations. The field assistants collected the data about the taken solution, complaints along a week before as stated by mother, and data taken whenever the participant have contracted from any disease. All data were recorded in the prepared form and logbook. The demography data consists of name, gender, birth date, parent education and occupation, and address. The anamnesis covers mainly the complaint of any disease especially fever, cough, runny nose, and sore throat. The physical examinations include body weight and height, temperature, heart rate, respiratory rate, nasal flaring, runny nose, respiratory difficulty, cyanosis, tonsils, pharyngeal wall, chest retraction, and pulmonary signs. The diagnosis of URI was made based on the presence of fever, cough and or runny nose. Episode of URI were defined as period in which the child started to have fever, cough and or runny nose until the illness disappeared. A child with high fever, increased respiratory rate of more than the rate for age, and chest retractions indicates the diagnosis of acute lower respiratory infection (ALRI), is not further analyzed. All data were noted in the available form. The data from both groups were analyzed descriptively, and inferentially applying the appropriate formula. The significant difference of the variables tested was defined on the confidence degree of 95% with $p < 0.05$.

RESULTS

Base line data of both groups were not significantly different as stated by the gender: $\chi 2$

0.66, p>0.25, age: Z 0.88, p>0.20, body weight: Z 0.47, p>0.20, height: Z 0.68, p >0.20, and nutrition: $\chi 2$: 1.20, p>0.25 (Table 1). During the 2-month study, we found 24 cases of URI in 37 children of zinc group and 24 cases in 36 children of placebo group, which is statistically not significant difference in incidence (χ^2 = 0.03, p>0.05). Time series analysis of the weekly evidence of zinc group showed a negative slope (a = 4.3 and b = -0.3), while the placebo group showed a positive slope (a = 1.5 and b = +0.3). The evidence and duration of fever, cough and runny nose in zinc group also demonstrated negative slope, while in placebo group showed positive slope (Table 2). Analysis of the incidence and the severity of URI in zinc and control groups in the first month was not significant different, while in the second month was significant different (Table 3). Table 4 shows the evidence of URI during the 2nd month in zinc group declined significantly as compared to the 1st month, while it was not in the placebo group. The evidence and duration of fever, cough and runny nose were also significantly lower in the 2nd month rather than in the 1st month. In the mean time the control group showed the contrary result as compared to the zinc group. There were no remarkable harmful effects of zinc supplementation, although two children have stated that the preparation was unpleasant but still tolerated.

Table 1. Demography data of the children

No	Specification	Zinc supplement group (N: 37)	Control group (N: 36)	Statistics
1	Male	14	17	$\chi 2$:0.66
	Female	23	19	p > 0.25
2	Age (mo)	28.1±13.4 (6-53)	28.3±12.7(6-58)	Z: 0.08, p > 0.20
3	Weight (kg)	11.4±2.1 (8-17)	10.8±1.9 (5-15)	Z: 0.47 p > 0.20
4	Height (cm)	84.1±8.9 (66-105)	82.9±7.6 (64-97)	Z: 0.64 p > 0.20
5	Normal nutrition	28	23	$\chi 2$: 1.20
	Under nutrition	9	13	p >0.25

Table 2. Regression Analysis of Weekly Evidence of URI

No	Spec'tion	Group	W-1	W-2	W-3	W-4	W-5	W-6	W-7	W-8	Statistics
1	URI:										
	Evidence	Zn	2	5	3	5	4	1	1	2	Y=4.3-0.3X
		Control	0	1	5	3	4	3	2	3	Y=1.5+0.3X
2	Rhinorrhoe										
	Evidence	Zn	2	4	3	4	3	1	1	1	Y=3.9-0.4X
		Control	0	1	4	2	3	3	2	3	Y=0.9+0.3X
	Duration	Zn	8	18.8	12	19.3	13	1	2	2.2	Y=15.5-1.6X
		Control	0	5	13	4.8	12	15.1	14	11	Y=2.2+1.6X
3	Cough										
	Evidence	Zn	2	4	3	4	4	0	0	1	Y=4.2-0.4X
		Control	0	1	5	3	4	3	1	2	Y=1.9+0.9X
	Duration	Zn	8	22.8	10	27.5	16	0	0	4.3	Y=20.8-2.2X
		Control	0	5	16	6.96	8.8	15.1	7	9	Y=4.7+0.1X
4	Fever:										
	Evidence	Zn	1	5	1	5	0	1	1	1	Y=3.2-0.3X
		Control	0	1	3	3	3	2	1	2	Y=1.3+0.1X
	Duration	Zn	1.25	13.9	3	23.8	0	1.08	2	2.1	Y=10.4-1.0X
		Control	0	2	8	5.83	7	4.99	0.2	2.5	Y=3.8+0.01X

Table 3. Comparison of URI in zinc and control groups each in the 1st and 2nd month

No	Specifications		Month	Zinc group (n37) Number(X±SD)	Control group (n36) Number(X±SD)	z	p
1	URI:						
		Evidence	I	1.55 ± 0.67	1.18± 2.22	0.97	> 0.50
			II	1.31 ± 1.41	3.00 ± 0.82	6.28	< 0.001
2	Runny Nose:						
		Evidence	I	1.44 ± 0.62	1.75 ± 1.71	1.02	> 0.20
			II	1.50 ± 1.00	2.75 ± 0.50	1.92	< 0.10
		Duration	I	6.29 ± 3.34	5.75 ± 5.44	0.16	> 0.50
			II	4.44 ± 5.51	12.73 ± 1.77	8.7	< 0.001
	Cough						
		Evidence	I	1.50 ± 0.67	2.25 ± 2.22	1.94	< 0.10
			II	1.25 ± 1.89	2.50 ± 1.29	3.31	< 0.002
		Duration	I	5.68 ± 3.73	7.03 ± 6.76	1.05	> 0.20
			II	4.97 ± 7.36	9.98 ± 3.52	3.73	< 0.001
	Fever						
		Evidence	I	1.29 ± 0.47	1.75 ± 1.50	1.76	< 0.10
			II	0.75 ± 0.50	2.00 ± 0.82	7.84	< 0.001
		Duration	I	3.46 ± 2.90	3.94 ± 3.60	0.63	> 0.50
			II	1.29 ± 0.98	3.68 ± 2.97	4.59	< 0.001

Table 4a. Comparison of the evidence and reduction of URI in zinc group

No	Group Specification		Month	Mean ± SD	Changes of mean	Statistics
I	**Zinc (n: 37)**					
1	URI:					
		Evidence	I	1.55±0.67	↓19%	Z: 5.16
			II	1.31±1.41		P<0.01
2	Runny Nose:					
		Evidence	I	1.44±0.62	↓19%	Z: 7.69
			II	1.50±1.00		P<0.01
		Duration	I	6.29±3.34	↓4%	Z: 7.97
			II	4.44±5.51		P<0.01
3	Cough:					
		Evidence	I	1.50±0.67	↓22%	Z: 5.73
			II	1.25±1.89		P<0.01
		Duration	I	5.68±3.73	↓5%	Z: 6.18
			II	4.97±7.36		P<0.01
4	Fever:					
		Evidence	I	1.29±0.47	↓24%	Z: 5.79
			II	0.75±0.50		P<0.01
		Duration	I	3.46±2.90	↓4%	Z: 5.38
			II	1.29±0.98		P<0.01

Table 4b. Comparison of the evidence and reduction of URI in control group

II	**Control (n: 36)**				
1	URI:				
	Evidence	I	1.18±2.22	↑9%	Z: -1.9
		II	3.00±0.82		P>0.05
2	Runny Nose:				
	Evidence	I	1.75±1.71	↑12%	Z: -3.37
		II	2.75±0.50		P<0.01
	Duration	I	5.75±5.44	↑3%	Z: -7.29
		II	12.73±1.77		P<0.01
3	Cough:				
	Evidence	I	2.25±2.22	↑3%	Z: -0.58
		II	2.50±1.29		P>0.20
	Duration	I	7.03±6.76	↑1%	Z: -2.32
		II	9.98±3.52		P<0.05
4	Fever:				
	Evidence	I	1.75±1.50	↑3%	Z: -0.88
		II	2.00±0.82		P>0.20
	Duration	I	3.94±3.60	↓1%	Z: 0.34
		II	3.68±2.97		P>0.20

DISCUSSION

The study of the influence of zinc supplementation in the incidence of URI is the integral part of a 5-year master program entitled "Health for Children at Kamal Village by the Year of 2005", a sustainable program of The Service to Community developed by the Child Health Department which is coordinated by The Board of the Service to Community, Trisakti University. This program consists of 5 yearly sub-programs, i.e. nutrition improvement, disease treatment, prevention / immunization, optimal growth and development, and healthy environment (Widagdo, 2001).

Disease profile of the children at Kamal as the base line data of the program showed that URI was the disease number one with 48% incidence followed by malnutrition, diarrhea as the number 2 and 3 with the incidence of 20% and 15% respectively (Widagdo *et al.,* 2002). Upper Respiratory Infection is mainly due to many types of viruses, and β-hemolytic streptococci can be isolated in only 15% of cases (Naveh *et al.,* 1982). Prevention of URI, in general is far more desirable than treatment, and the vaccine is now under development for use globally. These vaccines will be not limited to the prevention of bacterial infections but also includes of viral infection (Monto, 2000). Therefore the focus of preventive measure is directed to the improvement of general condition mainly the nutrition.

The studies performed in Palembang, South Sumatra (Nova *et al.,* 1997), and Koesnadi, (1995) in Central Java disclosed that the zinc deficiency was significantly found in children with under nutrition. The other studies found the low plasma zinc in children with diarrhea and various infections (Hidayat, 1997 and Nova *et al.,* 1997).

Since the education, and income of the people living in this village is still low, then the consumption of meat, fish and other sources of zinc with high price, is also quite low. In the mean time the health profile showed the high incidence of under nutrition, diarrhea and various infections (Arlette, 1983). It can be assumed that most children at the community have the varying degree of inadequate level of blood zinc.

The study in India showed the reduction of 45% in the incidence of acute lower respiratory infection in 298 zinc supplementation children as compared to 311 children of control group (Sazawal *et al.,* 1998). On the other hand, a study in Guatemala reported the result that the prevalence of respiratory infection was not significantly different between 145 children of zinc supplementation group of against 44 children of placebo group (Ruel *et al.,* 1997)..

Our study revealed the benefit of a 2-month zinc supplementation, which significantly reduced the incidence of URI, and either the duration and severity of the disease. In fact, the time series analysis showed that the regression line of zinc group

crossing the placebo group in the 5th week period of zinc supplementation, whether it meant that the optimal effect of zinc supplementation occurred within the 5th week of administration, it needs further investigation. The difference result of these three studies may be due to the study design, sample size, the state of nutrition, blood zinc level, and the immune status of the children. There were also no side effects observed in this study, neither in the study reported by Sazawal *et al.,* (1998) in India and by Ruel *et al.,* (1997) in Guatemala.

CONCLUSION

This study obviously showed the benefit of zinc supplementation in the reduction of URI incidence as documented by the statistical calculation. The severity and the duration of the diseases were also significantly milder and shorter in the zinc group rather than in the control group. Based on the result of this study, then a regular zinc supplementation to the children diet in the community can be considered as the mean to minimize the incidence and the severity of upper respiratory infection.

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REFERENCES

Arlette JP 1983. Zinc and the skin. Ped Clin N Am. 30(3):583-96

Bahl R and Bhan MK 2000. Clinical management of acute respiratory infections in children. An Nestle 58:49-57

Black RE 1998. Therapeutic and preventive effects of zinc on serious childhood infectious diseases in developing countries. Am J Clin Nutr. 68(suppl):476S-9S

Castilo-Duran C, Vial P and Uauy R 1988. Trace mineral balance during acute diarrhea in infants. J Ped. 113:452-7

Departemen Kesehatan R.I 1997. Survei Kesehatan Rumah Tangga (SKRT) 1995. Badan Penelitian dan Pengembangan Departemen Kesehatan Republik Indonesia. Jakarta. 1995 hal 67-70

Gordon EF, Gordon RC and Passal DB 1981. Zinc metabolism: Basic, clinical, and behavioral aspects. J Ped. 99(3): 341-9

Herendeen NE and Szilagy PG 2000. Infections of the upper respiratory tract, in Behrman R.E., Kliegman R.M. and Jenson H.B. Nelson Textbook of Pediatrics 16th ed. Philadelphia; Saunders. 1261-6

Hidayat A 1997. The influence of zinc supplementation to acute diarrhea in under-five children. Abstract. Thesis. Jakarta. pp 12-19

Koesnadi D 1995. The relation between plasma zinc level and under-five nutrition status. BIKGM. 27:81-8

Naveh Y, Lightman A and Zinder O 1982. Effect of diarrhea on serum zinc concentrations in infants and chidren. J Pediatr. 730-2

Nova R, Bakri A and Ismail R 1997. The influence of oral zinc supplementation to the duration of diarrhea in infant acute diarrhea. Med J Sriw Univ. 29(1):20-8

Prasad AS 1988. Zinc in growth and development and spectrum of human zinc deficiency. J Am Coll Nutr. 7: 377-84

Monto AS 2000. Acute respiratory infections in childhood. Prospects for vaccine prevention. Annales Nestle. 58:66-73

Ruel MT, Rivera JA, Santiza M-C, *et al*. 1997. Impact of zinc supplementation on morbidity from diarrhea and respiratory infection among rural Guatemalan children. Pediatr. 99:808-13

Sazawal S, Black RE, Bhan MK, *et al*. 1995. Zinc supplementation in young children with acute diarrhea in India. N Engl J Med. 333:839-44

Sazawal S, Black RE, Jalla S, *et al*. 1998. Zinc supplementation reduces the incidence of acute lower respiratory infection in and preschool children. Pediatrics. 102:1-7

Shankar AH and Prasad AS 1998. Zinc and immune function: the biological basis of altered resistance to infection. Am J Clin Nutr. 68 (suppl): 447S-63S

Widagdo 2001. Health for children at RW 03 Kamal by the year 2005. A 5-year program of Service to Community. Darmasakti. 11:5-8

Widagdo, Mawardi H and Sidarta N 2002. The health profile of under-five children at Kamal village West Jakarta. 11th ASEAN Pediatric Conference. Bali. P 105

Widagdo 2002. Zinc supplementation reduces the incidence of diarrhea in children at Kamal village West Jakarta. Abstract. 11th ASEAN Pediatric Conference. Bali. p 105