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Correlation between serum zinc level and simple febrile seizure in children

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Abstract

Background Simple febrile seizure is the most common form of seizure which occurs during childhood period. Zinc, one of microelements in human body, has an important role in central nervous system formation.

Objectives To find out serum zinc level in simple febrile seizure patients and the correlation between serum zinc level and simple febrile seizure.

Methods This cros-sectional study was conducted at R. D. Kandou Hospital, Tingkat III Teling Hospital and Pancaran Kasih Hospital, Manado on April 5th – June 15th, 2009.

Results Diagnosis for febrile without seizure patients were 12 with acute respiratory tract infection (ARI), 6 dengue hemorrhagic fever (DHF), 6 acute diarrhea without dehydration and 1 ARI with DHF, while simple febrile seizure were 19 ARI, five acute diarrhea without dehydration and one ARI with DHF. There were no significant differences of age, gender and nutritional status in two groups. Family history of febrile seizure, febrile period and body temperature in two groups were significantly different. Mean serum zinc level in simple febrile seizure and febrile without seizure were 8.83 μmol/l and 13.72 μmol/l, respectively. Mean serum zinc level in simple febrile seizure children with seizure period <5 minutes, 5-<10 minutes and 10-15 minutes were 10.27 (SD 0.25) μmol/l, 9.02 (SD 0.81) μmol/l and 6.90 (SD) 0.98 μmol/l, respectively.

Conclusions There is correlation between serum zinc level and simple febrile seizure. The lesser serum zinc level, the longer duration of seizure occurs in simple febrile seizure. **[Paediatr Indones. 2010;50:326-30]**.

Keywords: *febrile, seizure, zinc*

Seizure is a paroxysmal motor activity which last for several moments and originated from abnormal electrical generation inside the brain.[1] Febrile seizure is the most common form of seizures among all children's neurological problems; commonly affect children under 5 years of age.[2,3] The incidence of febrile convulsion is 2–5% of all children.[3] The peak onset is age 18 to 22 months, where in most case, febrile seizure most often occurs at the age of 6 months to 3 years. Boys have a higher incidence than girls.[4] Simple febrile seizure itself is a form of seizures that often occurs during childhood. Simple febrile seizure has a good prognosis, but the simple febrile seizure is a sign of an acute infection occurs in the child's body.[1,3] Zinc, which is the largest component of metalloenzyme is an essential micronutrient that can be found in almost every cell.[5] Decline serum zinc level in simple febrile seizure patients is suggested secondary due to other causes. Zinc which is one of microelements in human body has an important role in central nervous system formation. Defeciency in zinc activates receptor N-methyl-D-aspartate, which causes a febrile seizure.[6,7] This leads

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to estimates that these neurotransmitter systems are also modulated by zinc.[8]

Recently, studies reveal that low serum zinc level has contribution in the occurrence of simple febrile seizure. Of all these results show that zinc plays a role in the occurrence of febrile seizure. Research on the decline serum zinc level in children with simple febrile seizure is still very limited, so the authors wanted to determine the correlation between serum zinc level and simple febrile seizure in children. The aim of this study was to find out serum zinc level in simple febrile seizure and the correlation between serum zinc level and simple febrile seizure in children.

Methods

This is a cross sectional study to find out the association between serum zinc level and simple febrile seizure in children. It was held at R. D. Kandou Hospital, Tingkat III Teling Hospital, and Pancaran Kasih Hospital Manado from April 5th 2009 until June 15th 2009.

We included children of aged 6 month to less than 5 years with simple febrile seizure with no decrease of consciousness after seizure, no recurrent seizures within 24 hours and parents or guardians signed the informed consent. We excluded subjects who experienced acute diarrhea with dehydration, chronic diarrhea, malnutrition, electrolyte imbalance, sepsis. Children aged of 6 months to less than 5 years with fever but without seizure and without malnutrition served as controls.

Patients were taken randomly. History taking and physical examination were held by the authors. Data collected include anamnesis form of the name, gender, age, duration of fever, duration of seizure, family history of simple febrile seizure and history of present illness. Physical examination of body weight, body height, physiological reflexes, pathological reflexes, and meningeal signs were generally checked and recorded. Laboratory examination of blood samples were taken by an experienced officer. Venous blood was taken for routine blood test (malaria slide, hemoglobin, hematocrit, white blood cells and platelets), serum zinc in all patients and serum electrolytes (serum sodium, potassium and calcium) only on simple febrile seizure group patients. Blood samples was taken as many as 4 ml, 0.5 ml of blood was inserted in the Ethylene Diamine Tetra Acetate (EDTA) tube for routine blood test, 1.5 ml in a 3 ml disposable syringe for serum electrolyte test and the remaining 2 ml of blood in the other disposable tube without EDTA for the examination of serum zinc levels.

Fever was defined as axillary body temperature greater than or equal to 37.5 degrees Celsius, which is measured using a digital thermometer with a precision 0.1 degrees Celsius for 1 minute. Duration of fever was estimated in hours based on parents report. Duration of seizure was measured in minutes, based on parents or guardians observations. Simple febrile seizure was febrile seizure which lasted brief, less than 15 minutes, general tonic and/or clonic, generally stopped itself, no neurological abnormalities post ictal, without focal movement and does not recurrent within 24 hours.[12,13] Familiy history of simple febrile seizure was history of parents or siblings who have experienced simple febrile seizure. Acute respiratory infections were respiratory tract infections from upper respiratory tract and its adnexa to lung parenchymal, which lasted less than 14 days, marked by fever, sore throat, dyspnea, cough, runny nose, rough breathing sound.[14-16] Dengue hemorrhagic fever was diagnosed based on WHO criteria.[17,18] Acute diarrhea is watery defecation more than three times a day, with or without blood and/or mucus in the feces, lasted no more than 1 week.[19,20] Electrolyte disturbances was disturbances in the levels of serum sodium, potassium and calcium, either increase or decrease levels.[21] Nutritional status was determined based body weight compared to body height patients plotted on the CDC curve according to their age and sex.[22]

Data analyses were performed by using SPSS version 15.0. Descriptive analysis was used for children characteristics, logistic regression analysis and correlation coefficient Spearman rho to find out the correlation between serum zinc level and simple febrile seizure in children. To find out the correlation between serum zinc level and duration of seizure, simple regression analysis was performed. P values of <0.05 were considered significant.

Results

There were 25 children with febrile without seizure and 25 children with simple febrile seizure. The cause of

fever was described in **Table 1**. Subjects characteristics were shown in **Table 2**. Simple regression analysis shows there was a significant correlation between serum zinc level and duration of seizure (P<0.001) and there was also a strong correlation between those variables **(Figure 1 and Table 3)**.

Table 1. Patient diagnosis

Diagnosis	Simple febrile seizure (n=25)	Febrile without seizure (n=25)
ARI	19	12
DHF	0	6
Acute diarrhea without dehydration	5	6
ARI + DHF	1	1
Jumlah	25	25

ARI = acute respiratory tract infection; DHF = dengue hemorrhagic fever

Table 2. Characteristics of patients in both groups

	Simple febrile seizure (n=25)	Febrile without seizure (n=25)	P
Sex			
Boys	16	16	
Girls	9	9	
Age, yr			
Mean (SD)	1.98 (1.00)	2.27 (1.27)	
Nutritional status			
Moderate malnutrition	11	12	
Normal nutrition	11	11	
Overweight	2	2	P = 0.006
Obese	1	0	
Family history			
Parents	7	3	
Siblings	1	0	
Others relatives	1	1	
Parents + siblings	3	0	
None	13	21	P = 0.004
Duration of fever			
<24 hr	16	6	
≥24 hr	9	19	P = 0.013
Body temperature, °C			
Mean (SD)	39.01 (0.56)	38.64 (0.45)	
95% CI	38.78 to 39.24	38.46 to 38.83	P < 0.001
Zinc serum level, µmol/l			r_s = 0.867
Mean (SD)	8.83 (1.23)	13.72 (0.45)	
95% CI	8.33 to 9.34	12.84 to 14.59	
Duration of seizure, n			
<5 minutes	3		
5-<10 minutes	18		
10-15 minutes	4		

Tabel 3. Serum zinc level in simple febrile seizure patients based on duration of seizure occured

Duration of seizure	n	Mean	SD	CI 95%	Minimal	Maximal	F	P
<5 minutes	3	10,27	0,25	9,64 to 10,89	10,00	10,50	16,785	<0,001
5-<10 minutes	18	9,02	0,81	8,62 to 9,43	7,20	10,10		
10-15 minutes	4	6,90	0,98	5,34 to 8.46	5,60	7,80		
Total	25	8,83	1,22	8,33 to 9.34	5,60	10,50		

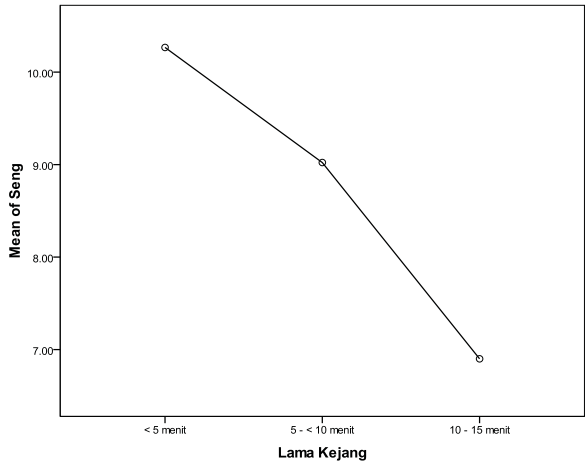

Figure 1. Serum zinc level based on duration of seizure occured in simple febrile seizure group

Discussion

From 50 subjects, mostly were diagnosed as acute respiratory tract infection (ARI). Tomoum et al[23] stated that infection was caused mostly by viral infection (60%) and manifest in gastroenteritis, ARI and non specific infection. Gender distribution in both group were not significantly different, similar with Ganesh et al[7] study. While Lestari[24] found that simple febrile seizure mostly occurred in boy (♂:♀= 18:13). Simple febrile seizure are mostly of occur at aged 18 month,[1,26,29] while some studies stated that it was occurred at aged 12 months to 4 years.[20,25] Based on this, we included only children under five year-old.

It is believed that simple febrile seizure is occurred as a combination between genetic and environment factors. Similar with Lestari,[24] we found that family history of febrile seizure and duration of fever associated with simple febrile seizure condition. In the other study, 24% children has family history of simple febrile seizure and 4% has a history of epilepsy in their family.[28] Livingston had said that seizure must occur in first 16 hours after onset of fever.[12] Body temperature also play a role in simple febrile seizure event. Nelson and Hirzt said that body temperature of 38°C or more was a risk factor.[29]

We found negative correlation between serum zinc level and simple febrile seizure event (r= 0.867, P< 0.001). Some studies also stated that serum zinc level in children with simple febrile seizure was lower than those without.[7,9,11] Zinc can modulate glutamic decarboxylase acid activity, an enzyme which has an important role in GABA synthesis. Zinc also has role in neurotransmitter like glutamic and their receptor. Zinc also facilitates inhibition effect of calcium on N-methyl-D-aspartate receptor which inhibits neuronal excitation activity. During hypozincemia, N-methyl-D-aspartate receptor is activated and febrile seizure occurs.[4,6,7] These conditions justify that neurotransmitter system is modulated by zinc. Zinc was also stimulating piridoxal kinase activity, an enzyme which can produce piridoxal from piridoxal phosphate. After that piridoxal can modulate glutamic acid decarboxylase activity and GABA synthesis.[6,7,30]

In our study, all subjects had have seizure duration less than 15 minutes. We found that the lower of serum zinc level, the longer duration of seizure occurs (P< 0.001). Sadleir et al[28] found that most children (about 87%) had seizure less than 10 minutes, while 9% had seizure lasted for 15 minutes. In conclusion, serum zinc level was associated with simple febrile seizure event and its duration.

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