ORIGINAL REPORT

Lack of Correlation between Plasma Neuropeptide Y and Typical and Atypical Febrile Seizures

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Abstract- It is known that neuropeptide Y which is widely distributed throughout the central nervous system is able to prevent seizures in animals. There are limited studies about the role of neuropeptide Y in febrile seizures. This study was conducted to evaluate the association between plasma neuropeptide Y level and febrile seizures in children. Seventy six patients with typical and atypical febrile seizures (each group 38 patients) and 38 sex and age matched control subjects were enrolled. The mean plasma levels of neuropeptide Y in typical and atypical febrile seizures were 90.60±28.01 and 97.34±41.27 pmol/l respectively. This value in control group was 88.94±32.66 pmol/l. There was no significant differences between groups regarding plasma neuropeptide Y level (*P*=0.532). Also, there was no significant difference in comparison with case groups (*P*=0.40). This study revealed that there is no association between plasma neuropeptide Y and febrile seizures.

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Keywords: Febrile seizures; Neuropeptide Y

Introduction

Febrile seizures are seizures that occur in febrile children between the ages of 6 and 60 months. In this type of seizure the patient does not have central nervous infection (such as meningitis or encephalitis), metabolic disturbance (such as inborn error of metabolism and electrolyte imbalance) and history of afebrile seizures. Febrile seizures are classified into typical and atypical. Typical febrile seizures last for less than 15 min, are generalized and occur once in a 24-hours period, whereas atypical febrile seizures are prolonged (>15 min), focal, or occur more than once in 24 hours (1-3). Despite of several studies, the actual causes of febrile seizures are not known (4,5). Studies about the role of plasma neuropeptide in febrile seizures are rare. Results obtained in these studies are controversial (6,7). Neuropeptide Y is a 36-amino acid peptide made by neurons throughout the brain and by other secretory cells of the body (8). It is believed that neuropeptide Y which is distributed throughout the central nervous system, including the hippocampus, can prevent seizures attack in animals (9-11). So, this study was conducted to investigate the relationship between plasma neuropeptide Y level and typical and atypical febrile seizures in children.

Materials and Methods

This prospective case-control study was conducted at Qazvin Children Hospital affiliated to Qazvin University of Medical Sciences (Iran) in 2011. Qazvin Children Hospital is the only referral hospital for children in Qazvin province. Case groups (76 patients) were selected consecutively from children who were admitted to the hospital following typical and atypical febrile seizures. The control group comprised 38 febrile children without seizure. The age of all patients was between 6 and 60 months. The sample size was calculated to provide 95% confidence coefficient and 80% power in statistical analysis (6).

Inclusion criteria's for the febrile seizures groups were: 1. fever ≥38ºC, 2. Existence of typical febrile seizures criteria's (generalized seizure and seizure

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lasting less than 15 min), 4. Existence of atypical febrile seizures criteria's (focal seizure, seizure lasting more than 15 min and repeated seizures more than once within 24 h) (2,3). Patients with central nervous system infections (such as meningitis, encephalitis), electrolyte imbalance, neurologic deficit and afebrile seizure were excluded. The control group included healthy children without seizure who were visited in hospital clinic due to mild febrile illness without any intervention. Children in all groups were matched in terms of sex, age and fever severity. Weight and body temperature (axillary) were measured according to standard methods (3). In all groups, 4 ml blood were taken from the peripheral vessel and then plasma was obtained by centrifugation for 5 min at 3,000 rpm at 4°C and then poured into an acid-washed tube and stored in the refrigerator at -70°C until for the neuropeptide Y assay . Blood samples were taken from the cases groups within 3 days after a seizure (6). All parents were given information about the research method in a simple language. The children were included in the study when their parents agreed and signed the informed consent form. The study was approved by the ethical committee of the research department in the Qazvin University of Medical Sciences (Project No: 232). The plasma concentration of plasma neuropeptide Y was measured by radioimmunoassay with plasma neuropeptide Y Kit (IBL, Germany, Hamburg, Cat.-No: ED 291). To improve accuracy, all measurements of plasma neuropeptide Y were double checked. For statistical investigation, Chi-square test and analysis of variance (ANOVA) was used to compare the variables between case and control groups and also, Tukey's post-*hoc* test for comparison of plasma neuropeptide Y level between groups. *P*-value less than 0.05 was considered statistically significant.

Results

In the typical febrile seizures group 27 patients were male and 11 were female. These values in atypical febrile seizures and control groups were 20, 18 and 17, 21, respectively (P=0.06). The minimum and maximum ages in case and control groups were 6 and 60 months, respectively. There were no statistically significant differences between the groups in terms of age and body temperature (P>0.05) (Table 1). The concentrations of plasma neuropeptide Y in typical and atypical febrile seizures were 90.60 ± 28.01 and 97.34 ± 41.27 pmol/l, respectively. This value in control group was 88.94 ± 32.66 pmol/l. There were no significant difference between typical (P=0.81) and atypical febrile seizures (P=0.32) with control group regarding plasma neuropeptide Y level. Also, there was no significant differences comparing case groups (P=0.40) (Tables 2, 3 and Figure 1).

Table 1. Comparison of variables in case and control groups.

Variables	Case groups		Control group	*P*
	Simple febrile seizures	Complex febrile seizures		
Age (mean ± SD month)	23.56 ± 13.29	24.771 ± 13.08	23.56 ± 13.29	0.90
Temperature (mean ± SD ºC)	38.63 ± 0.43	38.63 ± 0.57	38.53 ± 0.46	0.59

Analyzed by analysis of variance (ANOVA) test.

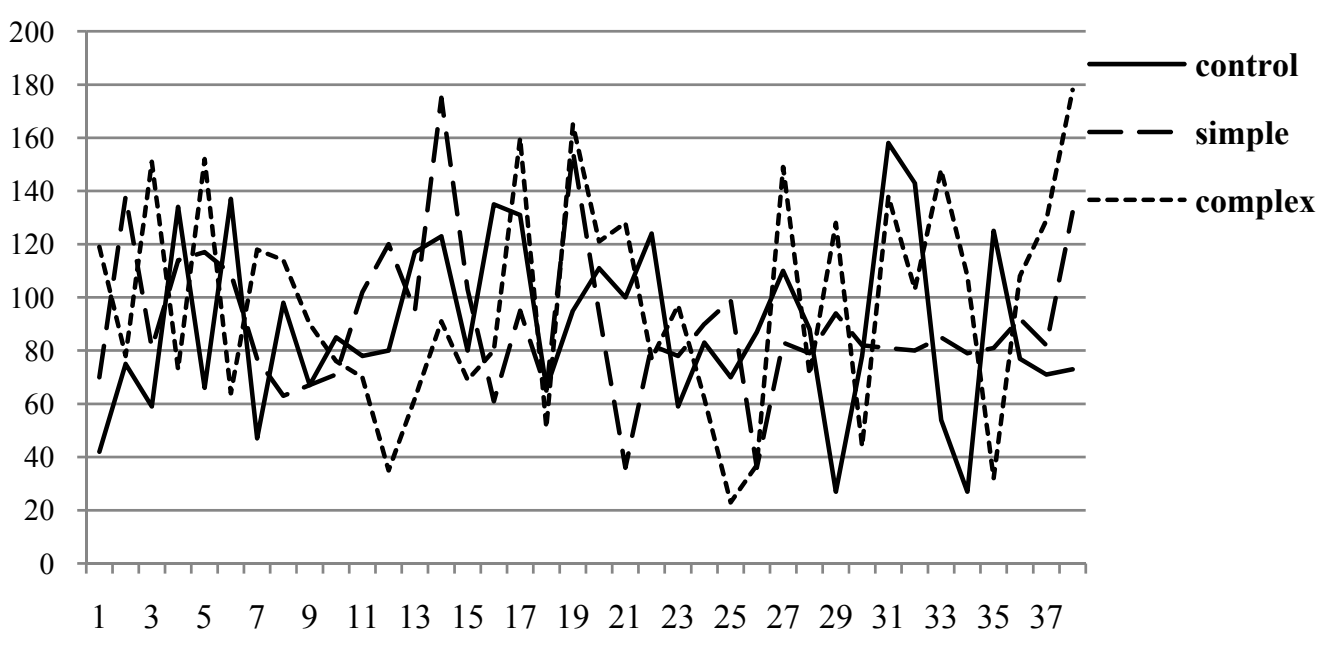

Figure 1. Comparison of plasma neuropeptide Y level between groups.

Lack of correlation between plasma neuropeptide Y

Table 2. Descriptive comparison of plasma Neuropeptide Y levels between groups.

Groups	n	Mean (pmol/l)	SD	Std error	95% confidence interval		Minimum	Maximum
					Lower bound	Upper bound		
Control	38	88.94	32.66	5.29	78.21	99.68	27	158
Typical febrile seizures	38	90.60	28.01	4.54	81.39	99.81	36	175
Atypical febrile seizures	38	97.34	41.27	6.69	83.77	110.90	23	178
Total	114	92.29	34.31	3.21	85.93	98.66	23	178

Table 3. Comparison of plasma Neuropeptide Y between groups.

Groups Plasma neuropeptide Y (mean ± SD pmol/l)	Groups Plasma Neuropeptide Y (mean ± SD pmol/l)	*P*
Control (88.94 ± 32.66)	Typical febrile seizures (90.60±28.01)	0.81
	Atypical febrile seizures (97.34±41.27)	0.32
Typical febrile seizures (90.60 ± 28.01)	Atypical febrile seizures (97.34±41.27)	0.40

Analyzed by Tukey's post-*hoc* test.

* $P < 0.05$ was considered statistically significant

Discussion

Present study showed that there is no association between plasma neuropeptide Y and febrile seizures. Neuropeptide Y is widely distributed in the central nervous system. It has been documented that neuropeptide Y plays numerous physiologic roles including excitability, circadian rhythms, cardiovascular function and epilepsy (12). The significant role of neuropeptide Y in regulating seizure activity has been reported in several animal and human studies (13-19). Noè *et al.* reported that administration of neuropeptide Y gene to epileptic rat brain leads to a remarkable decrease in the seizure frequency and this effect was correlated with the neuropeptide Y over-expression in the hippocampus (13). The mechanism of this decrement of seizure attacks may be related to inhibitory action of the peptide on pre-synaptic glutamate release via activation of NPY-Y2 receptors on glutamatergic terminals (14,15). Other researchers have also shown that neuropeptide Y is able to reduce and control seizure attack in animal models (16-18). A similar result was obtained by the study of Furtinger *et al*. in patients with temporal lobe epilepsy (19). This author proposes that neuropeptide Y has a potent inhibitory effect on glutamate release. Ultimately this process can suppress seizures activity in epileptic patients (19). Unlike previous studies, studies in the field of febrile seizures are scarce and the results are controversial (6,7). Lin *et al.* showed that patients with atypical febrile seizures had significantly lower concentration of plasma neuropeptide Y than children with typical febrile seizures and control (6). They concluded that patients with inadequate neuropeptide Y inhibitory activity are more susceptible to atypical febrile seizures (6). In contrast, another report showed that there is no statistical difference between febrile seizures and control groups regarding plasma neuropeptide Y level (7). The results of our study were similar to this study. Since our patients did not have clinical indications for lumbar puncture, so we did not measure the neuropeptide Y concentration in cerebrospinal fluid, and this was limitation of our study. In conclusion, the present study did not show any significant difference in plasma neuropeptide concentration between patients with febrile seizures and control group. Thus, it seems that circulatory neuropeptide Y might not play a cause-effect role in this type of seizure.

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