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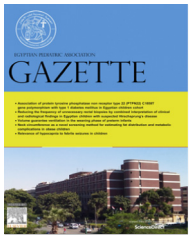

Relevance of hypocapnia to febrile seizures in children

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KEYWORDS

Febrile seizure;
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Abstract *Background:* Febrile seizure is the most common type of convulsion in children. However, there are scanty data on the mechanism of its development. The aim of this study was to evaluate the venous blood gas status in children with febrile seizures and to determine whether hypocapnia secondary to hyperthermia-induced hyperventilation was associated with febrile seizures in children.

Patients and methods: The study enrolled 43 individuals, twenty-two children with febrile seizures, together with 21 controls (children with febrile illness without seizures). Venous blood gases were determined in the febrile seizure group within 1 h and at 24 h after a seizure attack while, venous blood gases were measured once in the control group within 1 h after a febrile period.

Results: There were significant differences in mean blood pH and Pco_2 between the febrile seizure and control groups ($p < 0.001$). There was no significant difference in pH values between the children with complex febrile seizure and those with simple febrile seizure. However, children with complex febrile seizure had significantly lower Pco_2 within 1 h of seizure attack than those with simple febrile seizure. In addition, there was a significant correlation between duration of the seizure attack and Pco_2 value within 1 h of seizure.

Conclusion: The results of the present study confirmed the association between febrile seizure and hypocapnia and that supported the role of hypocapnia in the development of febrile seizures.

Introduction

Febrile seizure is one of the most common types of seizure in children aged between 5 months and 5 years and accounts for 30% of all childhood seizures.[1,2] This convulsion is considered as the response of immature brain of children to fever, without any intracranial infection or other defined cause.[3] Peak incidence of febrile seizures is at the age of 16–18 months.[4–8]

Most febrile seizures have a good prognosis. However, children with a simple febrile seizure have a risk of recurrence and an increased risk to develop epilepsy in 2.4–8.0% of affected children by adolescence.[9–13]

Simple febrile seizures mainly occur within the first 24 h of a febrile illness, last less than 15 min, only once during a febrile illness and don't show a focal pattern. In contrast, complex

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febrile seizures last longer than 15 min, occur more than once in one febrile episode and may have focal features.[11,13]

The pathophysiological link between fever and increased seizure susceptibility had been researched in rats. In the mouse models, hyperthermia causes hyperventilation with intracerebral hypocapnia (alkalosis) and seizures.[14–16]

Hyperventilation with subsequent respiratory alkalosis is known to induce epileptiform manifestations especially complex partial seizures and absence.[17]

In this study, we measured Pco_2 and pH values in children with febrile seizures to know whether hyperthermia with subsequent respiratory alkalosis was relevant to febrile seizures in children. This was the second study to compare between children with febrile seizures and those with febrile episodes but without seizures excluding the possibility of acidosis such as respiratory tract infection and gastroenteritis and this study could help in understanding the possible mechanism of febrile seizures in children.

Materials and methods

The study enrolled 43 children including, 22 children with a febrile seizure (defined as: seizures in children in association with fever of 38.0 °C or more without definitive evidence of neurological disorders, central nervous system infection, or metabolic abnormalities) admitted to the Pediatric Emergency department of the Cairo University Specialized Pediatric Hospital during the period from June 2013 to October 2014. Twenty-one age- and gender-matched children with febrile illness, but without convulsions, were assigned to the control group.

Inclusion criteria for patients with febrile convulsions: age ranged from 6 to 60 months, with convulsive seizure associated with fever of 38 °C or more. Children with definitive evidence of neurological illness, central nervous system (CNS) infection, metabolic abnormalities or poisoning were excluded from the study. Also none of the study populations (patients and controls) had gastroenteritis or lower respiratory tract infection to exclude the possibility of acidosis.

The study was approved by the ethics committee of Faculty of Medicine, Cairo University, and written informed consents were obtained from the parents of all participants.

For all participants, the cause of fever was determined by detailed history and complete physical examination.

For patients with febrile seizures, duration of febrile seizures, history of previous febrile seizures, family history of febrile seizure, and the type of seizures (simple febrile seizure or complex febrile seizure) were recorded.

Venous blood gases were measured in children with febrile seizures within 1 h and at 24 h after seizure attack, while they were measured only once in the control group within 1 h after a febrile period.

Normal values in pediatric age group for pH were defined from 7.35 to 7.45 and for Pco_2 35–45 mmHg.

Statistical analysis

Pre-coded data were entered into the Statistical Package of Social Science Software program, version 21 (SPSS) to be statistically analyzed. Data were summarized using mean, standard deviation for quantitative variables and frequency and percentage for qualitative ones. Comparison between groups was performed using Mann Whitney and Kruskal Wallis tests for quantitative variables and Chi square or Fisher's exact test for qualitative ones. Spearman correlation coefficients were calculated to explore the association between different quantitative variable. p values less than 0.05 were considered statistically significant, and less than 0.01 were considered highly significant.

Graphs were used to illustrate some information.

Results

The study included 22 children with febrile seizures, 12 females and 10 males. Their mean age was 19.3 ± 11.7 months. 40.9% of our cases had family history of febrile seizures and 72.7% of the cases had past history of febrile seizures.

The control group included 21 children with febrile illness but without seizures, 11 females and 10 males. Their mean age was 20.3 ± 13.1 months.

The children in the febrile seizure group were diagnosed with tonsillitis (45.5%), otitis media (22.7%), urinary tract infection (18.2%) and pharyngitis (13.6%). Also, children in the control group were diagnosed with tonsillitis, pharyngitis, urinary tract infection and otitis media (47.6%, 28.6%, 19% and 4.8%, respectively), with no statistically significant difference between both groups.

There was no significant difference between the cases and control groups as regards mean temperature (39.1 ± 0.6, 38.9 ± 0.6, respectively), $p = 0.3$.

Sixteen children were diagnosed with simple seizure (72.7%) and 6 with complex febrile seizures (27.3%).

There were highly significant differences in mean blood pH and Pco_2 between the febrile seizure and control groups within 1 h after seizure ($p < 0.001$). At 24 h after seizure attack, there was a highly significant difference in mean blood pH while there was no significant difference in Pco_2 between the febrile

Table 1 Comparison between children with febrile seizure and control group as regards blood pH and Pco_2 values.

	Children with febrile seizure	Control group		p-Value[d]
	1 h[a]	24 h[b]	1 h[c]	
pH[e]	7.47 ± 0.06	7.42 ± 0.04	7.37 ± 0.03	< **0.001**[a,c&b,c]
Pco_2[e]	29.89 ± 2.98	36.01 ± 3.41	37.98 ± 3.90	< **0.001**[a,c] and 0.093[b,c]

[a] Values in patients with febrile seizures at 1 h.
[b] Values in patients with febrile seizures at 24 h.
[c] Values in control at 1 h.
[d] Significant p-value < 0.05, and highly significant p-value < 0.01.
[e] Values are mean ± standard deviation.