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The Relationship Between Febrile Convulsion and Acid-base Disturbances in Children

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ABSTRACT

Background and Aim: Febrile seizures (FS) represent the most prevalent type of convulsive events in children. This study sought to explore the association between febrile convulsions and acid-base disturbances in children.

Methods: This case-control study included 150 children aged 6 to 60 months with simple FS and 150 febrile children without seizures. Blood gas analysis was performed to measure pH, PCO_2, and base excess (BE) among the children admitted to Amir Kabir Hospital in Arak, Iran. Statistical analyses, including t-test, chi-square test, and Mann-Whitney test, were conducted using SPSS software, version 18.

Results: The two groups did not differ significantly in mean fever (case: 38.46±0.51 vs control: 38.45±0.59; P=0.48), pH (case: 7.49±0.06 vs control: 7.48±0.06; P=0.77), and BE (case: -2.58±3.03 vs control: -2.41±3.42; P=0.48). Although the mean arterial PCO_2 in the case group was 25.1±3.51 mm Hg, which was lower than the control group's 26±5.53 mm Hg, there was no statistically significant difference between the two groups.

Conclusion: The mean venous and arterial pH values did not differ significantly in febrile children with and without seizures. Although PCO_2 in pediatric patients with FS was lower than in the control group, this difference was not significant. However, due to the lack of evidence, we recommend further studies in the future.

Keywords: Seizures, Febrile, Acid-base Imbalance, Alkalosis, Respiratory, Children

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Introduction

Seizures associated with fever can be due to meningitis, brain abscess, encephalitis, undiagnosed epilepsy presenting with fever, or febrile seizures (FSs) [1]. FSs are the most widespread nervous system disorder in pediatric patients, with a prevalence of 2-5% among children [2]. FS is defined as a seizure that occurs in children between 6 months and 60 months of age, with a fever of 38 ˚C or above, without evidence of central nervous system (CNS) infection, metabolic disorders, or previous afebrile seizures [3]. FS is the most common type of seizure in children and is divided into two types: Simple and complex [1, 2]. The mechanism behind the association of fever and convulsions is still unknown; however, it is certain that many etiological factors play a role in causing this condition. The occurrence of fever alone does not lead to this type of convulsion; in other words, fever in these children is a necessary condition for convulsions, but it is not a sufficient condition [4].

pH changes are very important in controlling convulsive activity in the brain. According to studies, alkalosis is known to trigger convulsive activity in the human body. In this context, hyperventilation—an increase in breathing that reduces CO_2 pressure and causes respiratory alkalosis—is a standard method to induce absence seizures, partial complex seizures, and convulsive manifestations in humans. In contrast, convulsive activity is reduced by measures that decrease pH, such as exposure to high levels of CO_2 [5].

Given these factors and the fact that FS is one of the most common types of seizures in children, the present study aims to investigate the relationship between acid-base disorders, fever, and simple seizures in children.

Materials and Methods

In this case-control single-center study, 300 children aged 6 to 60 months were included, all treated between 2013 and 2014 at the Pediatric Clinic and Emergency Department of Amir Kabir Hospital in Arak, Iran. Written approval was obtained from the Ethics Review Committee of Arak University of Medical Sciences. Informed written consent was secured from the parents following a detailed explanation of the procedure. The demographic data and relevant history of the children were recorded. The patients were divided into two groups:

Case group: 150 pediatric patients with simple FSs; control group: 150 febrile children; without seizures.

The eligibility criteria for the case group included children aged 6 to 60 months with simple FSs, while the control group included febrile children without a history of seizures. The exclusion criteria included children with complex FSs, previous afebrile seizures, CNS infections, underlying neurological disorders, and a history of FSs or seizures during hospitalization for the control group.

Demographic variables and clinical parameters, including age, sex, body temperature, the cause of fever, and the history of FSs in a first-degree relative, were recorded for all participants. Body temperature was measured using a mercury thermometer in the axillary region [6]. Blood samples were collected from all children using heparinized syringes, and arterial blood gas (ABG) was analyzed by the blood gas analyzer OPTI CCA-TS (AVL, Model 995, Austria). The following parameters were measured: pH, partial pressure of PCO_2, and base excess (BE).

At the time of admission, a sample containing at least 0.5 cc of blood was taken from the children using heparin syringes. After placing the syringe containing the blood sample in an ice bag, it was sent to the hospital's diagnostic laboratory for the measurement of blood gas values. Samples with a partial pressure of oxygen (PO_2) greater than 60 mm Hg were considered arterial.

Standard reference ranges for blood gas parameters were defined as follows: For arterial blood, pH values ranged from 7.37 to 7.43, PCO_2 between 36 and 44 mm Hg, and BE from 22 to 26 mmol/L. For venous blood, normal values included pH between 7.32 and 7.38, PCO_2 ranging from 42 to 50 mm Hg and BE levels of 23 to 27 mmol/L [1].

Quantitative variables were analyzed using Mean±SD, while qualitative variables were analyzed using numbers and percentages. The student's t-test was employed to analyze quantitative variables, while qualitative variables were examined using the chi-square test. For variables that deviated from normal distribution, the Mann-Whitney U test was employed. All statistical procedures were conducted utilizing SPSS software, version 18. Moreover, a $P<0.05$ was considered statistically significant.

Results

Demography: The study included 300 children, divided into two groups: 150 pediatric patients with simple FSs, and 150 febrile patients without seizures. Table 1 shows the age and sex of the participants.

Table 1. Demographic results

Variables	Mean±SD/No. (%)	
	Case Group (n=150)	Control Group (n=150)
Age (m)	19.96±12.15	19.96±10.9
Sex (boy/girl)	102(68)/48(32)	94(62.7)/56(37.3)

Table 2. Comparison of temperature, PH, PCO_2, BE between the groups

Variables	Mean±SD	
	Case Group (n=150)	Control Group (n=150)
Temperature (°C)	38.46±0.51	38.45±0.59
PH	7.49±0.06	7.48±0.06
PCO_2 (mm Hg)	25.1±3.51	26±5.53
BE (mM)	-2.58±3.03	-2.41±3.42

Table 3. Comparison of acid-base disturbances between the groups

Variables	No. (%)	
	Case Group (n=150)	Control Group (n=150)
Respiratory alkalosis	105(70)	100(66.7)
Mixed respiratory alkalosis and metabolic acidosis	45(30)	50(33.3)

Comparison of key variables

Temperature: Table 2 shows that the temperature was similar in both groups of participants (P=0.48). The mean temperature in the FS group was 38.46±0.51 ˚C, while in the control group, it was 38.45±0.59 ˚C.

PH: The mean pH was similar in both groups (FS group: 7.49±0.06 vs control group: 7.48±0.06, P=0.77) (Table 2).

PCO_2: As shown in Table 2, the FS group had a lower mean PCO_2 (25.1±3.51 mm Hg) compared to the control group (26±5.53 mm Hg). However, this comparison showed a non-significant difference (P=0.1).

BE: No statistically significant difference was observed in the BE mean values (P=0.48) between the case group (-2.58±3.03 mM) and the control group (-2.41±3.42 mM) (Table 2).

Acid-base disturbances (Table 3)

Respiratory alkalosis: 7 Seventy percent (n=105) of the FS group and 66.7% (n=100) of the control group had respiratory alkalosis. Mixed respiratory alkalosis and metabolic acidosis: Thirty percent (n=45) of the FS group and 33.3% (n=50) of the control group had this acid-base distribution. The distribution of acid-base disorders showed no statistically significant variation between the groups, as determined by the chi-square test (P>0.05).

Discussion

In summary, although the cases of respiratory alkalosis in the group of children with FSs were higher than in the control group, no significant difference was observed. The results demonstrated no significant difference in mean arterial pH or PCO_2 levels between pediatric patients with FSs and febrile children without seizures. Although the FC group exhibited lower mean PCO_2 levels (25.1±3.51

mm Hg) compared to the controls (26±5.53 mm Hg), this difference did not reach statistical significance (P=0.1). The difference between the average body temperature and blood pH between the two groups of children was not significant. In other words, our study found no relationship between respiratory alkalosis and FS.

Two clinical studies have been conducted by Schuchmann et al. in 2011 [5] and Kilicaslan et al. in 2014 [7], aimed at investigating the relationship between hypocapnia and the occurrence of FSs. Schuchmann et al. analyzed 433 children (213 with FSs and 220 with febrile gastroenteritis without seizures) and reported significantly higher blood pH (7.46±0.04 vs 7.31±0.03; P<0.001) and lower PCO_2 (29.5±5.5 mm Hg vs 37.7±4.3 mm Hg; P<0.001) in the FS group. The outcomes of this study revealed that the most common cause of fever in children with FS is upper tract infection, at 74.2% [5], in contrast to our findings, where gastroenteritis (50%) predominated.

Kilicaslan et al. conducted a case-control study that included 18 children with FSs as the case group and 18 febrile children without seizures as the control group, examining the relationship between hypocapnia and the occurrence of FSs. In this study, venous blood gas analysis was performed for the two groups of children. Similar to our research, the findings indicated that no statistically significant difference was found in the mean blood pH between the two groups of children [7]. However, contrary to our findings, the mean PCO_2 was significantly lower in the FS patients than in the control group. According to this study, FS is significantly associated with systemic respiratory alkalosis.

In addition to the differing sample sizes and differences in blood sampling site (venous blood in the study by Kilicaslan et al. [7]), another reason for the discrepancies between our findings and those of the two studies, as well as the differences between those two studies themselves, could be attributed to the fact that our study only examined children with simple FSs. In contrast, the two similar studies investigated the relationship between respiratory alkalosis and PCO_2 levels in a group of patients with fever and seizures, more than half of whom had complex FSs.

Based on the studies examining the relationship between acid-base disorders and FSs, the association between respiratory alkalosis and the stimulating role of hypocapnia in the development and progression of FSs is plausible. However, due to the lack of evidence and the controversy among the studies, it is recommended that more clinical and laboratory studies be conducted in the future to reach a definitive conclusion regarding the validity of the hypothesis concerning the use of CO_2 prophylaxis in pediatric patients with FSs.

One limitation of our investigation include the exclusion of patients with complex FSs. A comparative analysis of acid-base disturbances among pediatric patients with simple FSs, complex FSs, and febrile children without seizures could strengthen the conclusions. We recommend that subsequent studies evaluate the association between acid-base imbalances and the type of FSs.

Conclusion

Our study found no statistically significant difference in mean blood pH and PCO_2 levels between febrile children with and without seizures. While PCO_2 levels in pediatric patients with FS were lower than those in the control group, no significant statistical distinction was found. However, due to the lack of evidence, further studies are recommended in the future.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Review Board of Arak University of Medical Sciences, Arak, Iran (Code: 14-141-91).

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Authors' contributions

The authors equally participated in the study's conceptualization, methodology, data gathering, analysis, interpretation of findings, and writing of the manuscript. All authors endorsed the final version for publication.

Conflict of interest

The authors declared no conflict of interest.

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