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A Study on the Relationship between Hypocapnia and Febrile Seizure at Hazrat Rasool Hospital in Iran during a Three-Year Period of 2013-2015

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Abstract

Aim: The recent studies have reported hypocapnia as an effective factor in febrile seizure. Since this problem has been overlooked in Iran, this paper aims to determine the relationship between hypocapnia and febrile seizure through a case-control study.

Method: The statistical population consists of children with simple fever or febrile seizure examined in Hazrat-Rasool Hospital during a three-year period of 2013-2015. We divided the children into case group (children with febrile seizure) and control group (children with simple fever). We also investigated the role of sex, age, family history and BMI in febrile seizure and hypocapnia. The data was collected by checklist based on inclusion and exclusion criteria. We compared the case and control groups using efficient statistical methods.

Results: We selected 83 children, out of which 44 children suffered from febrile seizure and 39 children had simple fever. 84.1% of the case group and 59.0% of the control group suffered from hypocapnia. The comparison of two groups produced P=0.011, which confirmed the significant relationship between febrile seizure and hypocapnia. The statistical analysis of the variables of sex, age, family history and BMI produced P-value>0.05, which confirmed the lack of relationship between the aforementioned variables and febrile seizure.

Discussion and Conclusion: The results of this research are in line with the previous studies, which indicate that hypocapnia is an important etiological factor in febrile seizure. It is recommended that further studies be made on this subject.

Keywords: Hypocapnia; Hazrat-Rasool hospital; Febrile seizure

Introduction

Febrile seizure is one of the most common convulsions among children [1-3]. According to the literature, 14 per 1,000 children experience the reoccurrence of febrile seizure during the first 24 hours, with a relative similarity between males and females [4]. While febrile seizure is often benign and self-limiting [5], child convulsion is a horrible experience for many parents [6]. Some researchers have reported the reoccurrence of febrile seizure in 30-40% of the cases [7].

Researchers have proposed various methods for preventing febrile seizure based on different theories. For example, Eda Özaydın and Dr. Bidabadi have confirmed the relationship between iron deficiency anemia and febrile seizure and Dr. Norouzi has confirmed the relationship between relative hyponatremia (below 135 meg/L) and febrile seizure [8-10]. The review of literature indicates that hypocapnia is an effective factor in febrile seizure. In the US, Wirrell examined 12 children with absence convulsion and investigated their CO_2 level. He reported that hypocapnia was responsible for convulsion in 67% of the cases [7]. Berg et al. examined 428 American children who had experienced fever and convulsion for one time. They reported that only 33.4% of the children suffered from the reoccurrence of fever and convulsion without a trigger such as hypocapnia, which was significantly higher than the cases with a specific trigger. In other words, where a specific trigger existed, prevention of the reoccurrence of fever and convulsion was more possible [11].

Thomas et al. conducted an empirical study and found that the brain axons which were sensitive to heat and triggered convulsion experienced lower stimulation threshold than other axons did under hypocapnia conditions [12]. Xiao-Fan Yang et al. investigated the role of CO_2 inhalation in the suppression of convulsion among children. They reported that deep and fast breath could result in respiratory alkalosis by CO_2 exhalation, which is mainly used to confirm the absence of epilepsy. The present paper aims to determine the role of medical carbogen inhalation (including 5% of CO_2 and 95% of O_2) in the suppression of fever and convulsion. According to the results, the presence of 5% of CO_2 in medical carbogen significantly suppressed hyperventilation-related convulsions [13].

Kilicaslan et al. examined 18 children with fever and convulsion in Turkey and compared them with 18 children with fever who had no convulsion. They found that the group with fever and convulsion had lower CO_2 level in ABG compared to the control group, which was explained by hyperventilation [14].

Marzuk et al. conducted a study on the relationship between hypocapnia and febrile seizure. According to Marzuk, while febrile seizure is the most common convulsion among children,

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the information on its development mechanism is insufficient. He investigated venous blood gases in children with convulsion to determine whether secondary hypocapnia was associated with fever-related hyperthermia. He reported that a significant difference existed between blood PH and PCO_2 of children with febrile seizure and control group. But there was no significant difference between blood PHs of children with simple and complicated febrile seizure. Children with complicated febrile seizure had lower PCO_2 than children with simple febrile seizure had. Furthermore, a significant relationship existed between the length of convulsion and PCO_2 value [1]. Since this problem has been overlooked in Iran, this paper aims to determine the relationship between hypocapnia and febrile seizure through a case-control study. In doing so, we examined the children with simple fever or febrile seizure in Hazrat-Rasool Hospital during a three-year period of 2013-2015.

Research Methodology

The statistical population consists of children with simple fever or febrile seizure examined in Hazrat-Rasool Hospital during a three-year period of 2013-2015. We divided the children into case group (children with febrile seizure) and control group (children with simple fever). Based on the research objective, we determined the following hypotheses:

H1: Hypocapnia is associated with febrile seizure

Ha1: *Age is an effective factor in the prevalence of hypocapnia with febrile seizure.*

Ha2: *Sex is an effective factor in the prevalence of hypocapnia with febrile seizure.*

Ha3*: BMI is an effective factor in the prevalence of hypocapnia with febrile seizure.*

Ha4: *Family history is an effective factor in the prevalence of hypocapnia with febrile seizure.*

Inclusion and exclusion criteria are shown as below:

Inclusion criteria

1. Between the age of 6 months and 6 years
2. Rectal temperature of above 38 or axillary temperature of above 38.3
3. Convulsion

Exclusion criteria:

1. CNS inflammation/infection
2. Congenital or acquired CNS anomaly
3. Electrolyte disorders (hypocalcemia hyponatremia and hypoglycemia)
4. Intoxication
5. Chronic background disease: Chronic cardiac, renal and pulmonary diseases
6. Convulsion without prior fever
7. Malignity
8. Movement disorder: chorea, tremor, tics
9. Acute severe dehydration

The above criteria were applied by the checklist (Table 1).

Hypocapnia is the main and dependent variable of the research. Based on PCO_2 definition, the nominal variable was lower than 35 mmHg. We investigated the relationship between febrile seizure and hypocapnia and the impact of sex, age, family history and BMI on hypocapnia.

Considering the type of variable, we assessed and compared the variables using independent t-test, Mann-Whitney test and parametric tests.

Comparative tests

Comparative tests are used to study the impact of a nominal variable on a quantitative variable. These tests can be divided into parametric and non-parametric groups. The normality of quantitative variable is determined to select the proper test. If the normality is confirmed, parametric tests are used. Independent t-test is used when the qualitative variable has two levels. Non-parametric tests are used when the qualitative variable is normal. Mann-Whitney test is used for qualitative variables with two levels. In these tests, H_0 indicates the lack of difference between two groups. In other words, qualitative variable does not affect the quantitative variable. If P-value is greater than 0.05, H_0 is rejected. In other words, qualitative variable affects the quantitative variables.

Row	Variables	Type of Variables					Definition	Measurement Method	Scale
		Independent	Dependent	Continuous	Nominal	Rating			
1	Age	✓	-	✓	-	-	The age of the individual	Checklist	Year
2	Sex	✓	-	-	✓	-	The observed sexual phenotype	Observation	Male/ Female
3	BMI	✓	-	✓	-	-	Weight divided by height square	Checklist	Kg/m^2
4	Family History	✓	-	-	✓	-	History of fever and convulsion in first degree relatives	Checklist	+/-
5	Fever and Convulsion	✓	-	-	✓	-	Fever and convulsion as the main complaint of the patient	Checklist	+/-
6	Hypocapnia	-	✓	-	✓	-	CO_2 of lower than 35 mmHg in VBG	VBG	+/-

Table 1: Definition of variables.

Results

We selected 83 children, out of which 44 children suffered from febrile seizure and 39 children had simple fever. We divided the children into 4 age groups.

Table 2 contains the frequency percentage of each age group in case and control groups.

As you can see in Table 2, the highest frequency belongs to the age group of 1-2 years who constitutes 33.3% of the samples (28 children). The next highest frequencies belong to the age groups of 0.5-1 and 2-4, who constitute 29.6% and 25.3% of the samples respectively (24 and 21 children). Therefore, children with the age of below 4 years constitute most of our samples.

Table 3 shows the frequency of family history. As you can see, the majority of samples lack family history.

As you can see in Table 4, the presence of hypocapnia has the highest frequency in case group (84.1%) and control group (59%).

As you can see in Table 5, the group with febrile seizure has lower CO_2 level than control group.

We computed the mean scores of variables in two groups, as shown in Table 6.

We investigated the relationship between hypocapnia and nominal variables of sex, convulsion and family history using Chi-Square and Fischer tests. Table 7 represents the results for the relationship between sex and hypocapnia.

We obtained a Chi-Square of P=0.154 using SPSS software, which indicated that no significant relationship existed between sex and hypocapnia in febrile seizure. We obtained a Fischer value of P=0.154 using SPSS software, which indicated that no significant relationship existed between family history and hypocapnia in febrile seizure. We obtained a Chi-Square of P=0.011 using SPSS software, which confirmed that a significant relationship existed between febrile seizure and hypocapnia. Age and BMI were the quantitative variables of this study. We investigated the impact of hypocapnia on the variables of age and BMI using independent t-test or Mann-Whitney Test (Tables 7 and 8).

Research hypotheses results

H1: Hypocapnia is associated with febrile seizure

Chi-Square test results confirmed the significant relationship between hypocapnia and febrile seizure.

Age Group	Febrile Seizure		Control	
	Number	Percentage	Number	Percentage
1-0.5	10	22.70%	14	35.80%
1-2	15	34.10%	13	33.30%
2-4	13	29.50%	8	20.50%
4-6	6	13.60%	4	10.80%
Total	44	100.00%	39	100.00%

Table 2: Frequency of age groups.

Family History	Group			
	Febrile Seizure		Control	
	Number	Percentage	Number	Percentage
No	34	77.30%	37	97.40%
Yes	10	22.70%	2	2.40%
Total	44	100.00%	39	100.00%

Table 3: Frequency of family history.

Hypocapnia	Group			
	Febrile Seizure		Control	
	Number	Percentage	Number	Percentage
No	7	15.90%	16	41.00%
Yes	37	84.10%	23	59.00%
Total	44	100.00%	39	100.00%

Table 4: Frequency of children with hypocapnia in two groups.

Febrile Seizure	Control Group	CO_2 Mean
28.4	33.4	

Table 5: Comparison of mean scores of hypocapnia in two groups.

Variables	Mean		
	Febrile Seizure	Control	Both Groups
PCO_2	28.4	33.4	30.7
Ph	7.41	7.39	7.4
HCO_3	20.6	21.7	21.1
BMI	16.7	16.6	16.6

Table 6: Means of variables separated by groups.

Variable	Statistic	P-value	Results
Age	-0.247	0.805	There is no significant relationship between age and hypocapnia.

Table 7: Mann-Whitney test results for the relationship between hypocapnia and age.

Variable	Statistic	P-value	Results
BMI	-0.213	0.832	There is no significant relationship between BMI and hypocapnia

Table 8: Independent t-test results for the relationship between hypocapnia and BMI.

Ha1: Age is an effective factor in the prevalence of hypocapnia with febrile seizure

The results indicated that no significant relationship existed between the age of children with hypocapnia and the age of children without hypocapnia.

Ha2: Sex is an effective factor in the prevalence of hypocapnia with febrile seizure

Fischer test results test indicated that no significant relationship existed between hypocapnia and sex.

Ha3: BMI is an effective factor in the prevalence of hypocapnia with febrile seizure

P-value>0.05 indicated that no significant relationship existed between hypocapnia and BMI.

Ha4: Family history is an effective factor in the prevalence of hypocapnia with febrile seizure, but its impact is not significant

Kilicaslan et al. conducted a study on febrile seizure in Turkey and reported that people with febrile seizure had lower CO_2 level in ABG than control group, which was explained by hyperventilation [14]. The result is in line with our findings. We concluded that the children with febrile seizure had lower CO_2 level than control group. Wirrell et al. reported that hypocapnia was responsible for recent convulsion of children in 67% of the cases [7]. Likewise, we found that febrile seizure was significantly associated with hypocapnia and the majority of febrile seizures were explained by low CO_2 level. Thomas et al. conducted an empirical study and found that the brain axons which were sensitive to heat and triggered convulsion experienced lower stimulation threshold than other axons did under hypocapnia conditions [12]. Likewise, the present paper confirmed the impact of hypocapnia on convulsion.

Recommendations

The results of this research are in line with the previous studies, which indicate that hypocapnia is an important factor in febrile seizure. It is recommended that further studies be made on this subject. According to the study of Xiao-Fan Yang et al. medical carbogen may be considered a prophylaxis against febrile seizure [13,14].

Discussion and Conclusion

Febrile seizure is a widespread problem. The recent studies have reported hypocapnia as an effective factor in febrile seizure. Since this problem has been overlooked in Iran, we conducted this study to determine the relationship between hypocapnia and febrile seizure through a case-control study. The statistical population consisted of children with simple fever or febrile seizure examined in Hazrat-Rasool Hospital during a three-year period of 2013-2015. We divided the children into case group (children with febrile seizure) and control group (children with simple fever). We also investigated the role of sex, age, family history and BMI in febrile seizure and hypocapnia.

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