Convulsion following gastroenteritis in children without severe electrolyte imbalance

Ziaaedin Ghorashi[1], Nariman Nezami[2], Hassan Soltani-Ahari[1], Sona Ghorashi[2,3]

[1]Department of Pediatrics, Tabriz University (Medical Sciences), [2]Young Researchers Club and [3]Tabriz Islamic Azad University Faculty of Medicine, Tabriz, Eastern Azerbaijan, Iran

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Three to five million children from among one billion with gastroenteritis die annually worldwide. The etiologic agent in developed countries is viral in 15-60% of cases, while in developing countries, bacteria and parasites are frequently reported as the etiologic factors. Neurologic signs including convulsion are seen in some cases of diarrhea. This study aimed to investigate the etiology, risk factors and short-term prognosis of gastroenteritis with convulsion. During a case-control study, 100 patients with gastroenteritis were enrolled into the case and control groups on the basis of convulsion or no convulsion development, respectively. This study was conducted in Tabriz Children's Hospital from March 2004 to March 2007. The age of patients ranged from 2 months to 7 years, and the groups were age- and sex-matched. Body temperature (BT), severity and type of dehydration, stool exam and culture, past history of convulsion in the patient and first-degree relatives, electrolyte imbalance, and short-term prognosis were studied and compared. The mean weight of groups was not different, while the frequency of fever at the time of admission, past history of febrile convulsion in first-degree relatives and severity of dehydration were significantly higher in the case group ($p<0.001$). The BT of the case group on admission was higher than in the control group (39.01 ± 0.80 vs. $37.52\pm0.67^{o}C$; $p<0.001$). Past history of febrile convulsion in the patient, shigellosis and antibiotic usage were also significantly higher in the case group ($p=0.025$, $p=0.014$ and $p=0.001$). Convulsion mostly occurred in mild gastroenteritis accompanied with fever and positive history of febrile convulsion in first-degree relatives. History of febrile convulsion in the patient and shigellosis were associated with development of convulsion in patients with gastroenteritis. No significant electrolyte imbalance was observed in patients with gastroenteritis experiencing febrile convulsion.

Key words: convulsion, gastroenteritis, febrile convulsion, shigella.

Diarrheal diseases are one of the leading causes of morbidity and mortality in children worldwide, causing one billion episodes of illness and 3-5 million deaths annually[1]. In the United States each year, 20-35 million episodes of diarrhea occur among the 16.5 million children younger than five years of age, resulting in 220,000 hospitalizations and 300-400 deaths[1]. In another study, in 13% of children younger than five years old who were hospitalized, the discharge diagnosis was diarrhea[2]. Children in developed countries commonly acquire rotavirus and enterovirus, such that rotavirus infection accounts for 15-60% of cases of acute diarrhea in these countries[1,3]. Alterations in consciousness, including seizures, delirium and coma, occur during some cases of diarrhea[4]. Occasionally, in shigellosis and Campylobacter infection diarrhea, convulsion occurs at the onset of fever[2].

Today, the pathogenesis of convulsion in shigellosis is unknown, and with or without fever, dehydration, hypocalcemia, and hyponatremia, convulsion occurs in diarrheal disease[4]. In Khan et al.'s[4] study, 83,402 children

with diarrhea presented to the treatment center for care, and 6,290 were admitted. Shigella was isolated in 13.7% of patients, and 3% of them had a documented seizure[4]. In a study of 14 children with viral gastroenteritis without severe dehydration or electrolyte imbalance, convulsions occurred 1-8 times per child and the duration of convulsion was reported as 2-10 minutes[5].

Since Tabriz Children's Hospital is a referral center in Northwest Iran, this study was designed to determine the etiologic agent, frequency of seizures, possible risk factors, and short-term prognosis of patients admitted with gastroenteritis.

Material and Methods

This case-control study was carried out in Tabriz Children's Hospital from March 2004 to March 2007. During this period, 37,224 patients were admitted, 4,181 (11.2%) of them with gastroenteritis. Among them, 57 (0.2%) patients with diarrhea aged 2 months to 7 years had convulsed; 7 cases were omitted because of incomplete information. Fifty patients with diarrhea and convulsion were enrolled in the case group regarding duration of convulsion, number of convulsions, use of anticonvulsant drug, and short-term prognosis during hospitalization. Fifty patients with gastroenteritis with the same characteristics but who had not convulsed were included randomly as a control group. The age and gender of the two groups were matched. Duration of hospitalization, body temperature (BT) on admission, type and degree of dehydration, stool exam and culture, sodium, potassium and calcium levels, blood sugar, white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), antibiotic used, history of febrile convulsion in the patient and first-degree relatives, and outcome were studied and compared. Since the patients in the case group had convulsion less than 1 hour before referring to the hospital and/or developed convulsion within 2 hours after admission to the hospital, BT on admission can be considered as BT at the time of convulsion. BT higher than 38.2°C was considered as fever, and WBC count normality was determined according to the Rudolph ranges[6].

Statistical Package for the Social Sciences software package for Windows version 13 (SPSS Inc., Chicago, IL, USA) was used to analyze the obtained data. Results are expressed as mean ± standard deviation (SD). Independent sample t-test and Fisher exact test/chi-square test were applied to compare the data between two groups. A p value <0.05 was considered significant.

Results

The mean ages of the case and control groups were 2.34±1.67 years (5 months-7 years) and 2.43±1.62 years (5 months-6.5 years), respectively. The male/female ratios in the case and control groups were 25/25 and 24/26, respectively. Mean weights of the case

Table I. Comparison of Clinical and Laboratory Findings Between the Case and Control Groups

Variables	Unit	Groups: Case (Mean ± SD)	Groups: Control (Mean ± SD)	P value
Duration of hospitalization	day	3.87±2.83	2.94±1.57	>0.05
BT on admission	°C	39.01±0.80	37.52±0.67	<0.001
Na^+	mEq/L	137.26±9.36	138.58±6.15	>0.05
K^+	mEq/L	4.41±0.65	4.39±0.47	>0.05
BS	mg/dl	109.00±33.62	98.60±17.06	>0.05
Ca^{2+}	mg/dl	8.73±1.10	8.94±0.68	>0.05
WBC count	/mm^3	11736.00±7454.89	8974.00±3460.73	0.02
ESR	mm/1st hour	20.76±13.69	16.12±13.14	p>0.05
CRP	+	1.02±1.16	0.58±0.92	0.04

BT: Body temperature. BS: Blood sugar. WBC: White blood cells. ESR: Erythrocyte sedimentation rate. CRP: C-reactive protein.

and control groups were 11.66±4.21 and 11.69±3.49 kg, respectively (p>0.05). Table I shows the clinical and laboratory findings of both groups. WBC count was significantly higher in the case group (p=0.020), but the number of patients with high WBC count was not different between the case and control groups (23 vs. 17 patients, respectively; p>0.05). The mean BT on admission in the case group was significantly higher than in the control group (Table I) and fever (BT≥38.2°C) was significantly more frequent in the case group (46 vs. 7 patients; p<0.001).

The frequency of dehydration by type and degree is demonstrated in Figures 1A and 1B. The case group primarily had mild dehydration (p<0.001), while moderate dehydration was significantly more frequent in the control group (p<0.001). Five patients in the case group had hypocalcemia (calcium <7.2 mg/dl), while none of control group developed hypocalcemia.

Table II shows the result of stool exam and culture in both groups. The frequency of shigellosis in the case group was significantly higher than in the control group (p=0.014). Twenty-four (48%) patients in the case group underwent antibiotic therapy, while 8 (16%) patients of control group received antibiotic (p=0.001).

There was a positive history of febrile convulsion in 9 of the case group and 2 of the control group (p=0.025). History of febrile convulsion in first-degree relatives was positive in 22 and 3 patients in the case and control groups, respectively (p<0.001). Duration of convulsion in the case group was 5.72±6.52 minutes and number of convulsions ranged from 1 to 5, with a mean of 1.30±0.74.

Cerebrospinal fluid was obtained in 16 patients of the case group, and the results were normal. Electroencephalography (EEG) was done in 9, and only 1 was abnormal. In 3 cases, computerized tomography scan was done, and 1 case had cerebral atrophy.

Two of the patients in the case group died. One had hypernatremia and the second patient was referred with disseminated intravascular coagulation (DIC). In both of the patients who died, shigella was grown in the stool culture.

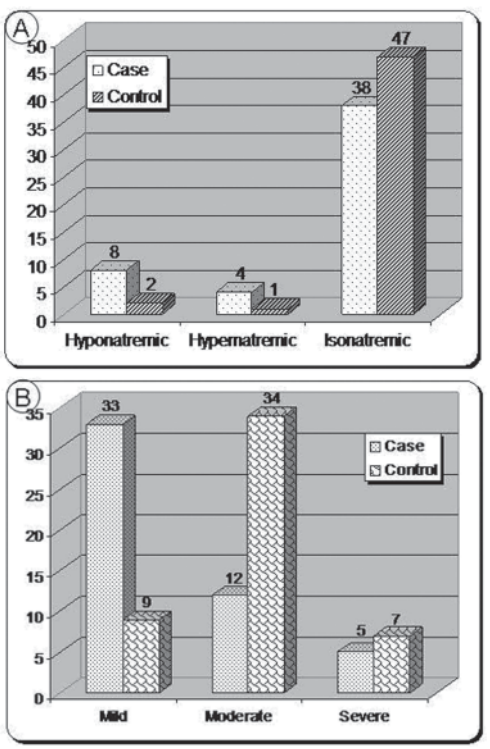

Fig. 1. A- Frequency of dehydration by type in the case and control groups. **B-** Frequency of dehydration by degree in the case and control groups.

Discussion

Convulsions with gastroenteritis are commonly observed in infancy and childhood, to the extent that it is a familiar phenomenon among pediatric neurologists and general pediatricians[7,8]. During the present study, 1.4% (57 of 4,181) of patients with gastroenteritis developed convulsion. Up to 5% of children in North America and Western Europe experience at least one episode of febrile seizure before six years of age[9]. Most of these seizures are self-limited and patients do not require treatment[10-12]. Some of the clinical features of gastroenteritis-induced convulsion are similar to those of febrile convulsions. Both are usually a brief, symmetrical generalized convulsion, and interictal EEG is usually normal[13].

In our study, patients who developed gastroenteritis-induced convulsion had higher BT than patients with gastroenteritis alone. Furthermore, frequency of previous history of febrile convulsion and positive family history of febrile convulsion were higher in the case group.

Table II. Results of Stool Examination and Stool Culture in Both Groups

Groups	Normal	Abnormal	WBC & RBC	Amebiasis	Giardia	Shigella	E. coli
Case	34	16	14	4	1	8	2
Control	40	10	7	1	0	2	0

WBC: White blood cells. RBC: Red blood cells.

One of the factors that may result in convulsion is degree of dehydration. There are several reports of convulsion with mild gastroenteritis from Japan[8,13,14]. Results of the present study also showed that the frequency of convulsion was significantly higher among patients with mild gastroenteritis.

In developing countries, shigellosis is associated with higher morbidity and mortality rates among children and could be accompanied with fever and convulsion[15]. Kavaliotis et al.[16] reported an approximately 16% convulsion rate in patients with shigellosis. Ashkenazi et al.[17] studied 153 children with shigellosis-induced convulsion. Thirty-six of them (23%) had a previous history of febrile convulsion, and 31 (20%) children had a positive family history of convulsive disorder. In the present study, prevalence of shigellosis in patients with convulsion was significantly higher than in patients without convulsion (p=0.014).

Different studies have reported various frequencies of central nervous system (CNS) involvement in children with acute rotavirus gastroenteritis: 2% in Germany[18], 2.6% in Japan[19], 3.7% in the United States[20], 5.4% in Taiwan[20], and 5.7% in Hong Kong[21]. In Weinstein's[22] study, 13 (7.2%) children with viral gastroenteritis presented with seizure, especially patients having rotavirus gastroenteritis. Wong[21] found a statistically significant association between encephalopathy and rotavirus infection versus no organism found, and rotavirus infection also had a higher risk of encephalopathy in comparison to that for bacterial gastroenteritis (relative risk=1.846). Although we did not determine viral etiology (due to technical limitations), convulsion was seen in some patients with negative stool culture.

One of the recognized complications of diarrheal disease in children is hypernatremic dehydration[23]; both hypernatremic dehydration itself, and complications of its management, have been associated with seizures, neurological insult and death[1,24,25]. Of the studied patients in the case group, 8% had hypernatremia and one of them died. The second patient who died during our study was referred with shock and DIC. In both patients who died, stool culture was positive for shigella. In Kavaliotis et al.'s[16] study, shock and DIC were reported in two cases with shigellosis.

In our study, all of the case and control group patients had normal cerebrospinal fluid analysis, and among nine EEGs performed, only one patient had abnormal findings, which was consistent with Ashkenazi et al.'s[17] report.

This is the first report from Iran studying convulsion association with gastroenteritis. Nevertheless, limitation in determining viral etiology resulted in the study of only a limited numbers of stool pathogens during the present study.

In conclusion, convulsion mostly occurred in cases of gastroenteritis with fever and a positive family history of convulsion in first-degree relatives. Those with shigellosis and previous history of convulsion are prone to develop convulsion. Electrolyte imbalance did not play a significant role in convulsion occurrence.

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