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Clinical Characterization of Gastroenteritis-Related Seizures in Children: Impact of Fever and Serum Sodium Levels

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Abstract

Gastroenteritis-related seizures have increasingly gained attention in recent years. Most cases follow a brief, benign course with very few episodes of seizure recurrence and without development of epilepsy. Published reports usually do not make a distinction between febrile and afebrile patients, and most authors include only nonfebrile convulsions in their reported series. This study evaluated the impact of fever in children presenting with seizures during a mild gastroenteritis episode and found that the presence or absence of fever did not affect seizure characteristics or duration. However, mild hyponatremia affected some seizure features, particularly seizure duration, as hyponatremic children sustained more prolonged seizures than patients with normal serum sodium levels, irrespective of body temperature.

Keywords

gastroenteritis, seizure, hyponatremia

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Seizures occurring in the setting of acute gastrointestinal infection have long been recognized as a complication of shigellosis[1-3] and campylobacter gastroenteritis.[4,5] In recent years, convulsions during an episode of acute viral (or presumed viral) gastroenteritis have been increasingly reported.[6-10] Frequently, rotavirus has been the causal agent described, although norovirus has also been identified.[11-14] Rarely, sapovirus, adenovirus, and coxsackievirus have been detected.[14]

The association of seizures with mild gastroenteritis was recognized for several years in the far East,[14,15] and only recently has it gained the attention of Western medical literature.[9,10] Regarding the distinction between febrile and afebrile patients, lack of a clear definition is apparent, as most authors included only nonfebrile convulsions in their reported series whereas a minority of reports have considered febrile seizures during gastroenteritis to be part of the condition.[6,9,10,14-16] Hence, the aim of this study was to evaluate whether the presence or absence of fever in children presenting with seizures during a mild gastroenteritis episode has any influence on the clinical features of this condition.

Methods

A retrospective analysis was performed on all cases of gastroenteritis-related seizures in children admitted between April 2005 and July 2010 (Baskent University Hospital, Ankara, Turkey) and between May 2007 and July 2010 (Meir Medical Center, Kfar-Saba, Israel). Data gathered included demographic information on all patients, body temperature on admission, and presence of vomiting in addition to diarrhea. General physical examinations as well as neurological status were noted. Regarding seizure symptoms, type of seizure and its duration were obtained as well as electroencephalogram results when applicable. Laboratory data collected included complete blood count, serum chemistry, and urinalysis. Reports of stool culture and stool rotavirus assay (where available) were also recorded. Data on family history of epilepsy or febrile seizures were sought, and neurological outcome of the patients was established for up to 13 months following

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the convulsive episode. The study was approved by the local institutional review board.

Results

Forty-four children (25 females, 19 males) with seizures during gastroenteritis were detected. Their age ranged from 3 to 108 months (mean, 31 months; median, 25 months). All presented with diarrhea, and 24 (55%) sustained vomiting episodes. Fever, defined as body temperature greater than 38°C, was detected in 26 children (59%).

The neurological examination was normal in all cases (all patients were alert on admission). The vast majority (86%) sustained generalized tonic–clonic seizures. Among the remaining 6 children, 3 had hypomotor seizures, 2 experienced complex partial seizures, and 1 had a simple partial event. Seizure duration, as reported by parents or caregivers, lasted from several seconds to 20 minutes, although in most cases the attack lasted less than 3 minutes. Seven of the 44 children (16%) sustained a second seizure within 24 hours of the first one. All second events were brief, none lasting more than 5 minutes, and resolved spontaneously.

Twenty children (45%) had hyponatremia (defined as serum sodium level <135 mmol/L) on presentation (mean, 131.8 mmol/L; range, 126-134 mmol/L). Of those presenting with hyponatremia, 14 (70%) were also febrile. Most (67%) of the afebrile children had normal serum sodium levels. The mean duration of the seizure among normonatremic and hyponatremic patients was 1.9 and 6.4 minutes, respectively. Thus, those diagnosed with hyponatremia at presentation were much more likely to have a prolonged seizure ($P = .003$), irrespective of body temperature.

Of the patients with prolonged seizures (>5 minutes), all 6 were female and all sustained a generalized tonic–clonic seizure. Four patients were febrile and 2 afebrile at presentation. Interestingly, all 6 patients also had hyponatremia (mean 130.7 mmol/L). Of note, no significant difference in age, sodium level, and seizure duration could be found when we compared the febrile and afebrile groups.

Stool culture was negative for *Shigella*, *Salmonella*, and *Campylobacter* in all 21 Israeli patients. Rotavirus was not routinely tested for at Meir Hospital but was sought in all 23 Baskent University Hospital cases, detected only in 2 patients. No seasonality was noted, and presentations occurred evenly throughout the year.

Three patients were previously diagnosed with epilepsy. All 3 had short seizures and a normal serum sodium level upon admission. Two other patients had a history of febrile convulsions prior to their reported event, and their temperature was indeed high during the seizure.

An electroencephalogram was performed in 18 patients, of whom 14 (78% of those done) had a normal recording. In the 4 abnormal studies, 3 depicted left and 1 showed bilateral centroparietal sharp waves. All 3 epileptic children had undergone an electroencephalogram study—it was interpreted as normal in 2 of them.

Four patients received phenobarbital therapy after their seizure—3 of them because of abnormal electroencephalogram findings and 1 because of a prolonged seizure (10 minutes).

During the follow-up period (2-54 months), only 1 of the 41 nonepileptic patients (2.4%) experienced 1 afebrile seizure unassociated with gastroenteritis. An electroencephalogram test performed following the second event was normal.

Discussion

Seizures occurring in children suffering from acute gastroenteritis have been recognized for several decades. The first report on this association probably belongs to Morooka,[17] who described this condition in the Japanese medical literature in 1982. Since then, it has mostly been reported in East Asian countries. The condition was first recognized in the Western hemisphere only in the mid-1990s,[18] and as recently as 2004, it was considered "virtually unknown outside Asia."[19] Given this geographic distribution, a genetic predisposition for this disorder has been suggested. However, attempts to identify a specific channelopathy have not been successful.[16] Still, Sakai et al[20] described a single family in which multiple members have endured benign seizures in infancy, either with or without gastroenteritis. Hence, genomic mutations rendering a child more prone for these seizures can exist in some cases. Despite the different ethnic backgrounds of Israeli and Turkish patients, no significant difference was found in age, seizure type, seizure duration, the presence of fever or hyponatremia at presentation or the recurrence of seizures after admission.

As previously mentioned, there is lack of agreement on whether to consider febrile cases as part of the syndrome. Published reports in recent years vary in their inclusion or exclusion of febrile patients among their series.[6,7,21-23] Therefore, we felt that an analysis of the impact of fever on the clinical features of gastroenteritis-related seizures, comparing afebrile and febrile cases, could help establish whether the 2 conditions should be considered separately or as a single entity.

We did not detect any significant difference in age, serum sodium level, and seizure duration when we compared the febrile and afebrile groups. Likewise, no difference was found in the propensity for events taking place during the cold seasons in which rotavirus infections are more prevalent. This may arise from the small number of patients in each group, as this phenomenon is rather infrequent. Still, perhaps in the context of acute mild gastroenteritis, the presence or absence of fever does not hold much significance for the development of seizures.

In our series, mild hyponatremia appears to play a role in the symptoms of gastroenteritis-related seizures. When comparing hyponatremic and normonatremic patients, we found that those with low serum sodium levels on presentation were on average younger and had longer seizures. No increased risk for seizure recurrence was noted. Although seizures are a known manifestation of hyponatremia (especially if severe), most series on

gastroenteritis-associated convulsions have not reported significant rates of hyponatremia.[3,6,21] However, Motoyama et al[10] found statistically significantly lower serum sodium and chloride levels among patients with benign convulsions during rotavirus gastroenteritis compared with patients with gastroenteritis without convulsions. Thus, the possibility that mild hyponatremia can lower seizure threshold in some children with mild gastroenteritis, irrespective of body temperature, needs to be explored more thoroughly.

Some reports in the 1990s suggested that low sodium serum levels at presentation in children with febrile seizures were associated with higher seizure recurrence during the same febrile illness.[24,25] However, in recent years the validity of this association has been questioned.[26] Regardless of sodium levels or fever, convulsions associated with gastroenteritis have recently been associated with lower recurrence rates.[27] The low recurrence rate found in our study may be attributable to a small cohort, as other investigators have reported a slightly higher rate.[28]

In summary, the presence or absence of fever in the setting of seizures during mild gastroenteritis did not affect seizure characteristics or duration in our series. Thus, febrile cases probably can be included in future descriptive series of gastroenteritis-related seizures. However, relatively low sodium serum levels appear to affect some seizure features, particularly their duration, as hyponatremic children sustained more prolonged seizures than patients with normal serum sodium levels irrespective of body temperature.

Note

This work was performed in the child neurology units of Meir Medical Center, Kfar Saba, Israel, and Baskent University Hospital, Ankara, Turkey.

Author Contributions

EZ and NW are the main authors. NW is the corresponding author. EZ wrote the first draft. FA, SM, MH-G, PM, SS, and BO contributed to the work and participated actively in this study.

Declaration of Conflicting Interests

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Ethical Approval

The study was approved by the local Institutional Review Board and the need for informed consent was waived.

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