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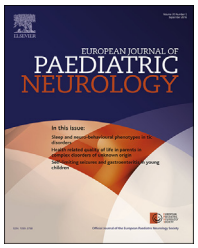

Review Article

Benign convulsions in children with mild gastroenteritis

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ABSTRACT

Background: Benign convulsions with mild gastroenteritis (CwG) is a clinical condition characterized by convulsions occurring in otherwise healthy children, usually in the absence of fever and in the presence of mild acute gastroenteritis. Until now, CwG had not been fully recognized as an epileptic syndrome, and several aspects of this condition are not clearly defined, especially its pathogenesis.

Methods: The main aim of this paper is to discuss after the review of the literature what is known about CwG to facilitate its recognition and treatment.

Results: CwG is a benign condition that has several clinical and prognostic similarities with febrile seizures. The disease occurs in infants and in children who are 1 month to 3 years old, during the winter and early spring when rotavirus and norovirus are circulating. In most cases, seizures follow gastrointestinal symptoms. In a minority of patients, the seizures and gastrointestinal symptoms occur before or simultaneously with the development of diarrhoea. Even if convulsions are mostly described as generalized tonic-clonic, the ictal recordings have always demonstrated a focal origin. Electroencephalography, lumbar punctures, and radiological examinations are not useful because they are normal in these patients; and when alterations are present, they disappear in a relatively short time. Only prolonged seizures, which are usually not common, require antiepileptic treatments in the acute phase.

Conclusion: Knowledge of CwG characteristics is essential for paediatricians to avoid useless hospitalization, examinations and, above all, drug administration, as the drugs have potential side effects.

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Contents

1. Introduction

Acute gastroenteritis (AGE) is a very common and clinically important disease in paediatrics. It is the third most common cause of death in children <5 years of age in the developing world.[1] In patients living in industrialized countries, only a few deaths from AGE occur, but the disease has a considerable impact on the health system and the quality of life of children and their families.[2] In a number of cases, AGE is associated with convulsions.[3] Several factors may explain the development of seizures in subjects with AGE (Table 1). Electrolyte abnormalities and dehydration due to the severe loss of electrolytes and water in stools or vomitus may induce neurological symptoms.[4] A high fever (>39 °C) that sometimes accompanies diarrhoeal syndromes may induce convulsions, particularly in infants and toddlers who are highly susceptible to febrile stimuli due to the immaturity of their central nervous system (CNS).[5] Infectious pathogens or fragments of these pathogens may breach the blood–brain barrier and cause significant CNS damage, leading to seizures.[6] Finally, in patients with a disease called benign convulsions with mild gastroenteritis (CwG), convulsions may be observed. This clinical condition, identified more than 30 years ago[7] and that was later repeatedly reported,[8–22] has been defined as a syndrome characterized by afebrile convulsions occurring in otherwise healthy children with mild AGE who do not have central nervous system infections, dehydration, or electrolyte imbalances and who have a benign prognosis.[23] Based on these characteristics, it has been suggested that CwG might be termed as situation-related seizures and are classified as an epileptic syndrome within benign infantile seizures in the classification set by the International League Against Epilepsy (ILAE).[24] However, until now, CwG has not been fully recognized as an epileptic syndrome by ILAE.[25] On the other hand, several aspects of this condition are not clearly defined, especially its pathogenesis. The main aim of this paper is to discuss what is known about CwG to facilitate its recognition and treatment.

2. The epidemiology and pathogenesis of CwG

The epidemiologic characteristics of CwG can help us understand which factors are potentially associated with the development of this disease and suggest, at least for some of the cases, its pathogenesis. CwG has been described in children aged 1 month to 6 years, and the disease peaks in 1- to 2-year-olds. This finding seems to indicate that, in terms of febrile seizures (FS), an immature CNS may favour the occurrence of CwG.[26] Moreover, although some cases have been reported in Europe[17,27] and America,[18,21,28,29] CwG has been more frequently described in East Asian countries, mainly in Japan, South Korea, Taiwan and Hong Kong where it occurs in approximately 1% of all AGE cases.[8–16] This finding suggests that the genetic characteristics of the host may play a role in the development of CwG. However, most of the CwG cases occur during the winter and early spring months. This is the period of the year during which viruses, such as rotavirus (RV),[30] norovirus (NV),[31] and adenovirus,[32] have the largest circulation and are the most common cause of AGE in temperate countries. Enteric viruses have been detected in a number of stool specimens from children with CwG.[8–16] Consequently, we cannot exclude the fact that these infectious agents might induce seizures by directly stimulating the CNS. A number of findings, unfortunately only for RV, support this hypothesis. Before the introduction of RV vaccines, RV was the most common virus associated with CwG in all of the studies.[12,33] Moreover, RV antigens and RV RNA have been detected in the cerebrospinal fluid (CSF) of a number of children with AGE,[34,35] and an association between meningitis, meningoencephalitis, acute cerebellitis, flaccid paralysis, and Reye or Reye-like syndrome and RV AGE has been repeatedly reported.[36–39] In some cases, the CNS lesions in children with RV AGE and seizures have been found to be reversible as evidenced in cases with transient lesions in the splenium of the corpus callosum[40–42] or transient bilateral basal ganglia lesions.[43] Finally, particular attention has been paid to NSP4, the RV enterotoxin that causes brain damage. NSP4 is a glycosylated protein that is important for viral replication, morphogenesis, and pathogenesis.[44] During AGE, NSP4 is responsible for intestinal secretion by altering calcium

Table 1 – Factors associated with seizure development in subjects with acute gastroenteritis.

Factors
Electrolyte abnormalities and dehydration
High fever (>39 °C)
Infectious pathogens or fragments of these pathogens
Unknown factors