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Original article

Incidence and characteristics of norovirus-associated benign convulsions with mild gastroenteritis, in comparison with rotavirus ones

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Abstract

Background and purpose: Rotavirus was detected in 40–50% of patients with benign convulsions with mild gastroenteritis (CwG) before the rotavirus vaccine was introduced in late 2000. However, the rate of rotavirus positivity has decreased since 2010 while the prevalence of norovirus has gradually increased. We investigated the incidence of norovirus-associated CwG during a recent 3-year period and additionally compared the characteristics of norovirus-associated CwG with those of rotavirus-associated CwG.

Methods: The medical records of CwG patients admitted to our hospital between March 2014 and February 2017 were reviewed, including the results of stool virus tests. For comparing norovirus- and rotavirus-associated CwG, data obtained between March 2005 and February 2014 that included sufficient numbers of patients with rotavirus-associated CwG were additionally reviewed. Data were collected on clinical characteristics (age, sex, seasonal distribution, enteric symptoms, and the interval to seizure onset), seizure characteristics (frequency, duration, type, and electroencephalographic findings), and laboratory findings.

Results: CwG was diagnosed in 42 patients during the 3-year study period. Stool viruses were checked in 40 (95.2%) patients and were detected in 32 (80.0%) patients. Norovirus genogroup II was detected in 27 (67.5%) of the 40 patients, rotavirus was detected in 3 patients, and adenovirus was detected in 2 patients. In total, 140 CwG patients were enrolled between March 2005 and February 2017. The patients with norovirus-associated CwG ($N = 44$) and rotavirus-associated CwG ($N = 26$) were aged 18.66 ± 5.57 and 19.31 ± 7.37 months (mean ± standard deviation), respectively ($P > 0.05$). Norovirus-associated CwG was less prevalent than rotavirus-associated CwG during spring (13.6% vs. 34.6%, $P = 0.04$), while the prevalence of both types of CwG peaked during winter (63.6% and 46.2%, respectively). Vomiting was more prevalent in norovirus- than rotavirus-associated CwG (97.7% vs. 80.8%, $P = 0.02$) and the interval between enteric symptom onset and seizure onset was shorter in norovirus-associated CwG (2.00 ± 1.06 vs. 2.58 ± 1.21 days, $P = 0.04$). Most cases in both groups had seizures that lasted for less than 5 min (95.5% vs. 92.3%). Clustered seizures seemed to occur more frequently in the norovirus group (79.5% vs. 57.7%), although with borderline significance ($P = 0.05$). Posterior slowing was observed more frequently in norovirus-associated CwG (34.9% vs. 11.5%, $P = 0.03$).

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Conclusion: The most common viral pathogen of CwG was norovirus during the analyzed 3-year period, with an incidence of 67.5%. In comparison with rotavirus-associated CwG, norovirus-associated CwG was less frequent during spring, more frequently seen with vomiting, had a shorter interval from enteric symptom onset to seizure onset, and more frequently showed posterior slowing in electroencephalography.
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Keywords: Benign convulsions; Gastroenteritis; Norovirus; Rotavirus; Children

1. Introduction

Benign convulsions with mild gastroenteritis (CwG) refer to afebrile infantile seizures with symptoms of acute gastroenteritis without any other conditions that trigger seizures (e.g., hypoglycemia, electrolyte imbalance, and cerebrospinal fluid abnormalities) [1,2]. Since CwG was firstly described in 1982 by the Japanese clinician Morooka [1], it has been frequently reported in East Asian countries such as Japan, South Korea, Taiwan, and Hong Kong, and was recently also reported in western countries [2–14]. Although CwG presents as clustered seizures in infancy or early childhood (usually between the ages of 3 months and 3 years), it is known to have a benign prognosis that does not involve either recurrence or disability [3].

Rotavirus was the most common enteric pathogen detected in patients with CwG, reportedly being present in 40–50% of patients before 2010 [4–7]. The adoption of rotavirus vaccinations with a vaccination rate exceeding 50% resulted in the decreasing rate of rotavirus positivity, and instead the incidence of norovirus has increased [7,15,16]. Our previous study that compared data between period I (March 2005 to February 2010) and period II (March 2010 to February 2014) found that the rate of rotavirus-antigen positivity decreased from 40.5% (15 of 37 tested CwG patients) to 16% (8 of 50 tested CwG patients). In contrast, the rate of norovirus-antigen positivity increased from 22.2% in period I (2 of 9 rotavirus-negative CwG patients) to 71.4% in period II (15 of 21 rotavirus-negative CwG patients who underwent a stool virus panel test) [7]. The report of Kim et al. covering a similar period showed a positivity rate of 63% for norovirus in 46 patients with CwG [17]. Kawano et al. compared the clinical characteristics between 9 patients with norovirus-positive CwG and 30 patients with rotavirus-positive CwG before 2010, but there is still a shortage of data comparing the incidence and characteristics of norovirus- and rotavirus-associated CwG [5].

In this study we investigated the incidence of norovirus-associated CwG during a recent 3-year period and compared the characteristics of norovirus-associated CwG with those of rotavirus-associated CwG while additionally reviewing our previous data between March 2005 and February 2014 when the incidence of rotavirus was higher.

2. Subjects and methods

We retrospectively analyzed the medical records of CwG patients between the ages of 3 months and 3 years who were admitted to Chonnam National University Hospital (CNUH) from March 2014 to February 2017. CwG was defined as follows based on previous studies: (1) afebrile seizures accompanied by acute gastroenteritis symptoms; (2) no hypoglycemia, electrolyte imbalance, or cerebrospinal fluid abnormalities; (3) normal development; (4) normal or only mildly abnormal electroencephalography (EEG) findings; and (5) normal brain imaging findings. Patients who had recurrent seizures during the subsequent 6 months or were later diagnosed with epilepsy were excluded. Applying these criteria resulted in 42 CwG patients being enrolled (Fig. 1).

To assess the performance rate of stool virus tests and the types of viruses detected from CwG patients during a recent 3-year period, three different stool virus test results were reviewed: (1) a stool rotavirus antigen test in CNUH using the latex agglutination method; (2) a stool virus panel test performed by the Health and Environment Research Institute of Gwangju (HERIG), which detects norovirus, astrovirus, and sapovirus using DNA (deoxyribonucleic acid) sequencing by the polymerase chain reaction (PCR) and detects adenovirus and rotavirus with an enzyme immunoassay first and then confirms the results with PCR sequencing; and (3) a stool multiplex PCR test with the Seeplex® kit (Seegene Inc., Seoul, Korea) detecting norovirus, rotavirus, adenovirus, and astrovirus that was introduced to Korea in 2012 and has been available in our hospital since late 2013. When the test results for rotavirus in a patient were inconsistent, we referred to the PCR test results since PCR sequencing is more accurate than the latex agglutination method.

For comparing between norovirus- and rotavirus-associated CwG, we additionally included our previous data obtained from March 2005 to February 2014 when rotavirus-associated CwG was prevalent [7]. Four of the 102 patients who were subjects in our previous study

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