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Treating Cyclic Vomiting Syndrome in the Emergency Department: Sooner Appears Better

Cyclic vomiting syndrome (CVS) is a complex disorder of gut-brain interaction characterized by repeated cyclic or sporadic episodes of extreme nausea, severe vomiting, and retching occurring as often as every 5 minutes. The formation of the Cyclic Vomiting Syndrome Association in 1993 spurred current progress in characterizing the phenotype, uncovering potential mechanistic pathways, and improving acute and preventative management. The North American Society of Pediatric Gastroenterology, Hepatology and Nutrition Consensus Statement in 2008 and the American Neurogastroenterology and Motility Adult Guidelines in 2019 have helped guide diagnostic and treatment approaches.[1,2] From the vantage point of 2020, CVS is recognized as a disorder that affects adults as well as children, one with multiple comorbidities, and one composed of distinct endophenotypes. Despite this progress, the widest remaining knowledge gap is how to best treat acute episodes.

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In this volume of *The Journal,* Abdulkader et al report a retrospective, single-center analysis of 209 children with CVS seen over a 3-year period and address the disposition—whether to send home or be admitted to the hospital—of pediatric patients with CVS who received acute treatment in the emergency department (ED).[3] Underscoring the high medical morbidity, nearly one-quarter (23%) used the ED: 14% used it 1-2 times, 3% between 3 and 5 times, and 7% more than 5 times! Remarkably, nearly two-thirds (62%) of those seen during 152 ED visits required admission to the hospital for continued therapy. Using univariable and multivariate analyses, factors predictive of subsequent hospitalization included male sex, younger age, a more than 24-hour delay from the onset of symptoms to ED presentation, and longer wait times from ED presentation to antiemetic administration. The prehospital use of rescue medications, time delay in administration of intravenous saline boluses, and numbers of antiemetics administered were not predictive of hospitalization. It is noteworthy that the difference in delayed dispensing of antiemetics between the hospitalized and discharged groups was approximately one hour, suggesting that even a brief delay could have a significant impact! Prior

CHS	Cannabinoid-hyperemesis syndrome
CVS	Cyclic vomiting syndrome
ED	Emergency department

The author serves as a consultant for Takeda (early drug development, Clinical Outcomes Assessment Advisory Board) and Section Editor, *Pediatric Gastroenterology.* The author declares no conflicts of interest.

https://doi.org/10.1016/j.jpeds.2020.12.066

home treatment was not systematically recorded in the charts and that variable could have delayed either departure to the ED or repeat dosing of the same antiemetic. The main clinical takeaways were that delayed intervention of more than 24 hours after the onset of the CVS episode and delayed administration of antiemetics in the ED were associated with hospitalization, and conversely, that earlier intervention might avert subsequent admission, consistent with observations by clinicians experienced in treating CVS.

Children with CVS are high users of ED care; 50% require intravenous therapy, of which 28% require it for each episode totaling a median of 10 times in a separate survey of ED usage.[4,5] Because the presenting symptoms of affected children with CVS are similar to that of other acute illnesses, many of these children are understandably misdiagnosed as having gastroenteritis, and the recurring pattern may go unrecognized. In fact, a salient and simple screening question asked in the clinic, urgent care or ED settings—"Have you had similar vomiting attacks before?"—can uncover the characteristic pattern of recurring stereotypical episodes, which if 3 or more, will ultimately be diagnosed as CVS in 88% of cases. Yet, even if an outside diagnosis of CVS had been established, 80%-88% of patients or caregivers noted that the diagnosis was not recognized in the ED.[5] Such problematic interactions in some EDs impel many patients with CVS to avoid them, despite their capability to attenuate symptoms and restore hydration. At a macro level, the cost of acute care is substantial. In an adult cohort, the average per visit cost of ED care was $2880, with a total cost of $377 000 for 1 institution. The national annual estimates of hospitalization costs for adult patients with CVS was $200 million.[6]

There is a dearth of evidence for effective acute treatment of CVS. The North American Society of Pediatric Gastroenterology, Hepatology and Nutrition Consensus Statement recommended intravenous fluids with electrolytes and 10% dextrose, antiemetics, analgesics, and sedation. These recommendations were based on expert experience and opinion. In a systematic review, Gui et al found only 6 applicable case series on acute management, none addressing the same agent administered by the same route.[7] They concluded that ondansetron use had the most quantitative and qualitative support. Yet, even ondansetron has limited efficacy; it mildly attenuates the vomiting, but seldom aborts an episode, and rarely lessens the unrelenting nausea during CVS episodes. But, perhaps if administered earlier during the ED visit, it may forestall impending hospitalization.

An additional challenge to the patient with CVS who seeks treatment in the ED is the association between episodic vomiting and intensive cannabis use first reported in 2004 in young adults and adolescents.[8,9] The 2016 Rome IV criteria newly classified this as cannabinoid-hyperemesis syndrome (CHS). From surveys of adult patients with CVS, cannabis use is widespread: 41% use it to quell anxiety or to prevent episodes.[10] However, young adult males who use recreational cannabis on a daily basis for a median of 6 years may experience CVS-like episodes. A review of 376 cases found that only one-sixth met the Rome IV criteria for CHS which could argue that many presumed to have CHS could instead have had CVS and should have been actively treated as such.[8] The proposed pathognomonic hot water bathing behavior during CHS episodes was observed in three-quarters of patients with CHS, but also in one-half of adult patients with CVS with no admitted cannabis exposure. We have observed this behavior in young children as well. Although the nature of the overlap between CVS and CHS remains controversial, the adult guidelines committee conjectured that CHS is likely to be a subtype of CVS triggered by frequent and prolonged high-dose cannabis use.[8] Owing to the current confusion between these 2 entities, the care of patients with CVS has been impacted. Once a patient with CVS admits to any level of cannabis use, they are readily stigmatized as cannabis abusers, told to cease their use, and may not receive established treatment for CVS.

The additional point of the report by Abdulkader et al is that it stratifies risks in patients with CVS similar to ongoing efforts in children with inflammatory bowel disease. Because CVS is a heterogeneous disorder with multiple endophenotypes (migraine, mitochondrial, catamenial), it may have different genetic profiles (mt 16519T + 3010A, nuclear RYR2) and comorbidities (anxiety, limited stamina, postural orthostatic tachycardia syndrome) that likely account for the variable treatment responses observed.[11] Further stratification will help to identify high-risk patients, such as those who are likely to have a more severe course and require step-up prophylactic therapy and repeated ED management.

What approaches might we foresee in the next iteration in ED management? There is a natural tension for patients with CVS and their families, especially with prior mixed experiences, about whether to seek needed care in the ED. Yet clearly, for those who have a known diagnosis and prior hospitalizations, earlier intervention with a prompt infusion of intravenous fluids followed by parenteral antiemetics, perhaps even before obvious signs of dehydration, is supported by the findings of Abdulkader et al. In the ideal scenario, a known patient would be quickly triaged, begun on intravenous therapy and antiemetics, and then fully evaluated. Knowing that ED approaches differ, partnering with the primary or subspecialist physician to imbed an approved CVS order set in the electronic medical record, either a general template or patient-specific one, would greatly facilitate care. Continued education of staff about CVS as well as patients on the benefits of earlier intervention would help create a more hospitable and responsive ED setting.

This study should stimulate us to consider further quality improvements to ED processes that could expedite care of patients with CVS to avoid subsequent admissions. This study also extends the forefront of risk stratification of these patients who are complex functional in order to help us provide optimized, individualized acute and prophylactic care. We certainly have a long way to go in improving acute treatment of children with CVS, but again, the sooner the better. ■

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When Measuring Is More Important than Measurement: The Importance of Measuring Diagnostic Errors in Health Care

Diagnostic errors are unacceptably prevalent and harmful,[1,2] yet they have received little attention in the field of patient safety.[3] Reasons for this include the lack of widespread awareness of the problem, the myriad and complex factors leading to diagnostic error, and the lack of clearly defined and generalizable measurement strategies for assessing the diagnostic process and its outcomes.[4] Furthermore, the diagnostic process reflects one of the core tasks of physicians, making diagnostic errors a sensitive topic to discuss, necessitating an open, nonpunitive safety culture.[5]

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More than 20 years ago, the publication of *To Err is Human*[6] started a culture change, and since the publication of the National Academies of Sciences, Engineering, and Medicine report on Improving Diagnosis in Health Care in 2015,[7] attention to diagnostic errors has increased. Increasing diagnostic safety is now, finally, considered a patient safety priority. Consequently, there has been significant progress in diagnostic safety in the last few years, including in the field of pediatrics. Specifically, there is better understanding of the incidence of diagnostic errors, curricular interventions to improve diagnosis education, and implementation of strategies to define and evaluate uncertainty in clinical medicine.[8-10]

In this volume of *The Journal*, Perry et al describe another important step forward in improving diagnosis in pediatric practice, not only for the initiative described, but also for the implications for the field.[11] In this editorial, we discuss the importance of the Diagnostic Error Index (DEI), describe its strengths and limitations, and make suggestions to further develop the DEI.

The Diagnostic Error Index

Perry et al describe a rigorous and impressive quality improvement (QI) project to develop an effective and efficient measure for diagnostic error.[11] In their large tertiary care children's hospital, the project team formed a multidisciplinary QI team representing different health care professionals, the Chief Medical Information Officer, and representatives of QI services. Pragmatically, they chose 5 existing data sources from which to identify potential diagnostic errors. Subsequently, the project team discussed those potential diagnostic errors and determined which could be confirmed. The DEI is defined as the number of confirmed diagnostic errors in 1 month.[11]

Drawing upon already reported diagnostic errors through a variety of existing systems makes the DEI efficient for use in

DEI	Diagnostic Error Index
QI	Quality improvement

0022-3476/$ - see front matter.
https://doi.org/10.1016/j.jpeds.2020.12.076