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Clinical Reviews

THE MANAGEMENT OF CHILDREN WITH GASTROENTERITIS AND DEHYDRATION IN THE EMERGENCY DEPARTMENT

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□ **Abstract—Background: Acute gastroenteritis is characterized by diarrhea, which may be accompanied by nausea, vomiting, fever, and abdominal pain. Objective: To review the evidence on the assessment of dehydration, methods of rehydration, and the utility of antiemetics in the child presenting with acute gastroenteritis. Discussion: The evidence suggests that the three most useful predictors of 5% or more dehydration are abnormal capillary refill, abnormal skin turgor, and abnormal respiratory pattern. Studies are conflicting on whether blood urea nitrogen (BUN) or BUN/creatinine ratio correlates with dehydration, but several studies found that low serum bicarbonate combined with certain clinical parameters predicts dehydration. In most studies, oral or nasogastric rehydration with an oral rehydration solution was equally efficacious as intravenous (i.v.) rehydration. Many experts discourage the routine use of antiemetics in young children. However, children receiving ondensetron are less likely to vomit, have greater oral intake, and are less likely to be treated by intravenous rehydration. Mean length of Emergency Department (ED) stay is also less, and very few serious side effects have been reported. Conclusions: In the ED, dehydration is evaluated by synthesizing the historical and physical examination, and obtaining laboratory data points in select patients. No single laboratory value has been found to be accurate in predicting the degree of dehydration and this is not routinely recommended. The evidence suggests that the majority of children with mild to moderate dehydration can be treated successfully with oral rehydration therapy. Ondansetron (orally or intravenously) may be effective in decreasing the rate of vomiting, improving the success rate of oral hydration, preventing the need for i.v. hydration, and preventing the need for hospital admission in those receiving i.v. hydration. © 2010 Published by Elsevier Inc.**

□ **Keywords—pediatric; dehydration; gastroenteritis; rehydration; antiemetics**

INTRODUCTION

Acute gastroenteritis (AGE) is an illness characterized by acute diarrhea, which may or may not be accompanied by nausea, vomiting, fever, and abdominal pain. Gastroenteritis is a relatively common diagnosis for pediatric patients presenting to the Emergency Department (ED). Worldwide, diarrhea causes 1.4–2.5 million deaths per year (1,2). In children under the age of 5 years, diarrhea is responsible for as many as 150,000 hospitalizations (approximately 10% of hospitalizations in children between 1 and 5 years of age) and 3.7 million physician visits annually in the United States (3,4). Es-

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timated costs of caring for these patients in the hospital and outpatient setting exceed 2 billion dollars annually.

A common reason for hospitalization in children with acute gastroenteritis is greater degrees of severity of dehydration or mild dehydration accompanied by social factors. It is important to differentiate the child with gastroenteritis and dehydration from the child with a more sinister cause of vomiting such as an intra-abdominal catastrophe, an inborn error of metabolism, pyelonephritis, or diabetic ketoacidosis. The presence of diarrhea is generally a reassuring historical finding in these patients. However, diarrhea does not exclude other conditions such as appendicitis. Patients with acute gastroenteritis may have abdominal pain and diffuse abdominal tenderness as well as increased bowel sounds. Other examination findings such as distention, peritoneal signs, or localized tenderness are rare in children with gastroenteritis and should lead the clinician to consider other diagnoses. After the diagnosis of gastroenteritis has been determined, the emergency physician must make several management decisions such as whether to obtain laboratory data, how best to rehydrate the child, and if an antiemetic agent should be administered. This article will discuss the available evidence regarding the assessment of dehydration, methods of rehydration, and the utility of antiemetics in the child presenting with acute gastroenteritis.

METHODS

A literature review was conducted for all published articles relevant to the assessment of dehydration, the utility of laboratory studies in the evaluation of dehydration, oral rehydration therapy (ORT), and the use of antiemetics in pediatric medicine. The search was conducted over a 40-year period from 2006 back to 1966. Limits used in the PubMed search included all children 0 to 18 years of age and articles written in the English language. Search terms that were used were "pediatric," "dehydration," "oral rehydration therapy," "gastroenteritis," and "antiemetics." Further, the reference list for each article was examined and additional relevant articles were reviewed. Articles and abstracts were included if they concerned a human study that met one or more of the following criteria: assessment of dehydration, rehydration therapy, the use of antiemetics in patients < 16 years of age diagnosed with acute gastroenteritis. The articles and abstracts were reviewed for patient age, inclusion and exclusion criteria, method of rehydration, antiemetics used, adverse reaction to antiemetics, and hospital admission rates in children administered antiemetics.

When the PubMed search for the three sub-topics included in this manuscript was performed using the combinations of the search terms listed above, the following numbers of articles were found: assessing dehydration (n = 299), oral vs. intravenous rehydration in the ED (n = 352), and the use of antiemetics in children with gastroenteritis (n = 118). Articles and abstracts were then considered based on applicability to one or more sub-topics. Articles deemed by the authors to be relevant to the use of antiemetics in children were appraised for inclusion based on relevance to the topic. The following numbers of investigations were ultimately included: assessing dehydration and the role of laboratory studies (n = 30), oral vs. intravenous rehydration in the ED (n = 24), and the use of antiemetics in children with gastroenteritis (n = 15). A hierarchy based on quality was not assigned.

DISCUSSION

Assessing Dehydration and the Role of Laboratory Studies

Clinical assessment of the degree of dehydration done quickly and accurately in infants and young children with gastroenteritis often determines patient treatment and disposition. Certain clinical signs and symptoms can help quantify the degree of dehydration (Table 1) (5,6). The clinical history in a child who presents to the ED with vomiting or diarrhea should assess the onset, frequency, quantity, and character (i.e., the presence of bile, blood, or mucous) of the vomiting and diarrhea. The history should also include weight before illness, recent oral intake (including breast milk and other fluids and food), urine output, and associated symptoms, including fever or changes in mental status. The past medical history should identify underlying medical problems, history of other recent infections, medications, and human immunodeficiency virus status.

Porter et al. determined that parental report of historical details and physical signs (emesis, diarrhea, fluid intake, urine output, ill appearance, weak cry, sunken fontanelle, sunken eyes, decreased tears, dry mouth, and cool extremities) related to dehydration have a predictive value for abnormal physiologic states and the outcome of hospital admission (8). The authors found parental reported data to have a greater sensitivity (range 73–100%) than specificity (range 0–49%) for the prediction of dehydration of 5% or greater. Further, the likelihood of significant dehydration was decreased by a history of normal fluid intake, normal urine output, and normal tearing state, whereas a sunken fontanelle and decreased tear production were associated with hospital admission.

The physical examination should include an accurate body weight, temperature, heart rate, respiratory rate, and blood pressure. The gold standard for diagnosis of

Table 1. Symptoms Associated with Dehydration

Symptom	Minimal or No Dehydration (< 3% Loss of Body Weight)	Mild to Moderate Dehydration (3–9% Loss of Body Weight)	Severe Dehydration (> 9% Loss of Body Weight)
Mental status	Well; alert	Normal, fatigued or restless, irritable	Apathetic, lethargic, unconscious
Thirst	Drinks normally; might refuse liquids	Thirsty; eager to drink	Drinks poorly; unable to drink
Heart rate	Normal	Normal to increased	Tachycardia, with bradycardia in most severe cases
Quality of pulses	Normal	Normal to decreased	Weak, thready, or impalpable
Eyes	Normal	Slightly sunken	Deeply sunken
Tears	Present	Decreased	Absent
Mouth and tongue	Moist	Dry	Parched
Breathing	Normal	Normal; fast	Deep
Skin fold	Instant recoil	Recoil in < 2 s	Recoil in > 2 s
Capillary refill	Normal	Prolonged	Prolonged; minimal
Extremities	Warm	Cool	Cold; mottled; cyanotic
Urine output	Normal to decreased	Decreased	Minimal

Adapted from Ref (5): Duggan C, Santosham M, Glass RI. The management of acute diarrhea in children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep 1992;41(No. RR-16):1–20.
Adapted from Ref (6): World Health Organization. The treatment of diarrhoea: a manual for physicians and other senior health workers. Geneva, Switzerland: World Health Organization, 1995. Available at http://whqlibdoc.who.int/publications/2005/9241593180.pdf.
Adapted from Ref (7): King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep 2003 Nov 21;52(RR-16):1-16.

dehydration is measurement of acute weight loss. A patient's true pre-illness weight is rarely known in the acute care setting; as such, an estimate of fluid deficit is made based on clinical assessment. Thus, historically, the measurement of dehydration has been based on several clinical variables scaled into three categories. There are two classification scales for estimating fluid deficit. The first is derived from the 1992 recommendations of the Centers for Disease Control and Prevention (CDC) and the 1996 guidelines of the American Academy of Pediatrics (AAP) (5,9). In this classification system, a patient's degree of dehydration is subdivided into mild (3–5% fluid deficit), moderate (6–9% fluid deficit), and severe dehydration (≥ 10% fluid deficit) (5,10). The second classification system was defined by the 1995 manual by the World Health Organization and the 2001 guidelines of the European Society of Paediatrics titled, "Gastroenterology, Hepatology and Nutrition" (6,11). This classification system divides patients into no signs of dehydration (< 5 %), some signs of dehydration (5–10%), and severe dehydration (> 10%) (6,11). This estimate is employed to determine the need for therapy and the type of therapy to be administered (6,7,11).

During the physical examination, the general condition of the patient should be assessed. Specifically, it should be noted if the child is listless, apathetic, or less reactive. Other important examination findings include the appearance of the eyes, including the degree to which they are sunken, the presence or absence of tears, and the condition of the lips and mouth. The rate and quality of respirations should be noted as they can be a clue to the presence of metabolic acidosis. Examination of the extremities should include an estimation of systemic perfusion and capillary refill time (12).

Dehydration assessment conventionally has been performed by evaluating clinical signs thought to be associated with dehydration, such as general appearance, tachycardia, abnormal radial pulse, sunken eyes, absent tears, dry mucous membranes, abnormal respirations, decreased skin elasticity, capillary refill > 2 s, and decreased urine output. It is important to note that the assessment of dehydration, by using such clinical parameters, is quite inaccurate and usually overestimates dehydration when tested against the standard of acute weight gain with rehydration (13). When studied, these individual findings have not been shown to be sensitive or specific predictors of the degree of dehydration. In general, individual findings in the studies generally had a low sensitivity and high specificity (14).

Gorelick et al. conducted a trial in which clinical signs of dehydration were assessed for their predictive value for dehydration in children by using weight gain after rehydration as a standard (14). They concluded that diagnosis of clinically important dehydration should be based on the presence of at least three of 10 clinical findings: decreased skin elasticity, capillary refill, general appearance, tears, respirations, mucous membranes, sunken eyes, radial pulse, tachycardia, urine output. Individual findings generally had a low sensitivity and high specificity (an exception was parental report of decreased urine output, which was found to be sensitive but not specific). The presence of any three or more of these signs had a sensitivity of 87% and a specificity of 82% for detecting a deficit of 5% or more. A subset of four factors (capillary refill > 2 s, absent tears, dry mucous

membranes, and ill general appearance) predicted dehydration as well as the entire set, whereas the presence of any two or more of these signs indicated a deficit of at least 5%. Interobserver reliability was good to excellent for all but one of the findings studied (quality of respirations).

Friedman and colleagues prospectively evaluated children < 3 years of age with gastroenteritis (12). Children were assessed for dehydration based on 12 clinical signs. Weight changes from pre- to post-rehydration were measured and used as the gold standard to measure the percentage of dehydration. The authors concluded that general appearance, eyes, mucous membranes, and tears had the most significant measurement properties for dehydration (12).

Steiner et al. systematically reviewed 13 studies (1246 patients) to determine the precision and accuracy of signs, symptoms, and laboratory testing for the evaluation of dehydration of children < 5 years of age (15). None of the investigation-fulfilled criteria were found to be of high methodologic value. The three most useful predictors of 5% dehydration were abnormal capillary refill time (likelihood ratio [LR] 4.1; 95% confidence interval [CI] 1.7–9.8), abnormal skin turgor (LR 2.5; 95% CI 1.5–4.2), and abnormal respiratory pattern (LR 2.0; 95% CI 1.5–2.7). Diagnostic accuracy was improved by the use of clinical score systems or the combination of findings. The authors advocate for use of the 1995 World Health Organization (WHO) and 2001 European Society of Paediatrics Gastroenterology, Hepatology and Nutrition guidelines that divide patients into categories of no signs of dehydration (< 3–5%), some signs of dehydration (5–10%), and severe dehydration (> 10%) (Table 1) (6,11).

Trials that have evaluated the correlation of clinical signs of dehydration with post-rehydration weight report that the first signs of dehydration are evident at 3–4% dehydration, with increasing clinical signs noted at 5% dehydration and signs of severe dehydration noticed at 9–10% dehydration (7,13,15). It is especially difficult to distinguish between mild and moderate dehydration because the first signs of dehydration appear at 3–4% dehydration, increase at 5% (the threshold for mild dehydration), and there is not another significant clinical difference until 9–10% (the threshold for severe) (7,16). Overall, the ability of clinical signs to predict the degree of dehydration (mild, moderate, or severe) is, at best, problematic. Employing the WHO classification groups mild to moderate dehydrated patients together; it eliminates the need to distinguish between them and allows for the fact that signs of dehydration might be apparent over a wide range of fluid losses.

Several laboratory studies have been proposed as a means to help predict the degree of fluid deficit. These include blood urea nitrogen (BUN), serum bicarbonate (CO_2) base excess, electrolytes, glucose, urine specific gravity, and end-tidal carbon dioxide.

Evidence for the predictive value of BUN in dehydrated children is mixed. Teach et al. studied a convenience sample of 40 children requiring intravenous fluid resuscitation (17). Laboratory variables of BUN to creatinine (Cr) ratio (BUN/Cr), CO_2, serum uric acid, serum anion gap, urine anion gap, venous pH, venous base deficit, urine specific gravity, and fractional excretion of sodium were individually assessed in a simple linear regression model with fluid deficit as the dependent variable. The authors found serum BUN/Cr and serum uric acid to be significantly associated with increasing fluid deficit ($r = 52$, $p = 0.0005$ and $r = 0.35$, $p = 0.03$, respectively). However, the sensitivity, specificity, and positive predictive value of these two laboratory studies for the detection of > 5 % fluid deficit were poor. Shaoul et al. retrospectively reviewed 300 pediatric cases (18). They found a BUN > 14.3 mmol/L in 5% of children who were not dehydrated, in 26% of children with mild dehydration, and in 38% of children with moderate dehydration. In this study, BUN concentration was found to be 95% specific for dehydration status. Creatinine concentration and mean pH were similar whether or not dehydration was present. In contrast, Bonadio et al. reported that the magnitude of BUN concentration was not an accurate method of assessing hydration status in children with dehydration due to gastroenteritis (19).

Other investigators have looked at serum bicarbonate level and base excess concentrations as predictors of dehydration in children. Narchi compared serum bicarbonate levels to clinical assessment of dehydration by emergency physicians (20). A serum bicarbonate concentration < 22 mmol/L was more common in children with severe dehydration. Although decreased bicarbonate concentrations occurred more frequently with increasing degrees of dehydration, the magnitude of bicarbonate reduction was not significantly different with increasing degrees of dehydration. The authors concluded that the decrease in bicarbonate concentration is not reflective of the severity of fluid deficit. Vega and Avner, and Ylimaz et al. evaluated the sensitivity of serum bicarbonate in predicting degree of dehydration by comparing pre- and post-rehydration weights in children (21,22). Vega and Avner found that a serum bicarbonate level < 17 mEq/L was 77% sensitive for moderate dehydration and 94% sensitive for severe dehydration. In Vega's investigation, when clinical impression was combined with a bicarbonate concentration of < 17 mEq/L, sensitivity for prediction of severe dehydration increased to 100%. The findings of Yilmaz et al. suggest that a serum bicarbonate level of < 15 mEq/L coupled with an elevated serum urea concentration may be a valuable adjunct to clinical evaluation in predicting the degree of

dehydration. However, in each of these studies, many children who were judged to have only mild dehydration by clinical evaluation or rehydration weight gain were found to have bicarbonate levels below the threshold chosen for calculation of the sensitivity. The specificity of a low bicarbonate levels as a predictor of degree of dehydration at the thresholds defined by these authors is very poor. Both investigations suggest that a bicarbonate concentration may be a useful adjunct to clinical evaluation in the assessment of dehydration.

Serum electrolytes alone may not be sufficiently sensitive or specific enough to predict the degree of dehydration, but they may yield other useful information. Wathen et al. prospectively investigated 182 patients with dehydration and found that 88 had an abnormal serum electrolyte value such as hypoglycemia 9.9%, hypokalemia 6%, and hypernatremia 3 % (23). However, it should be noted that Wathen and colleagues found that obtaining serum electrolytes changed management in 10.4% of cases (23).

Overall, in the vast majority of patients with uncomplicated AGE, serum electrolytes are not helpful in predicting degree of dehydration or determining appropriate management of the patient. The AAP recommends obtaining electrolytes in cases of AGE associated with altered mental status, moderate to severe dehydration, clinical signs of hypokalemia or hypernatermia, infants $<$ 6 months of age, and suspicious presentations (9,24).

Hypoglycemia may accompany dehydration. Several investigations have been performed in underdeveloped countries where, unlike developed countries, a bacterial pathogen is usually responsible for diarrhea causing dehydration, and the dehydration often occurs in children who are chronically malnourished. Hirschhorn et al. found 2% of Pakistani children between 1 and 6 years of age with dehydration secondary to gastroenteritis to be hypoglycemic (25). The majority had a bacterial pathogen as the etiology of their gastroenteritis. None of the children in the study was malnourished. Glyn-Jones found 7.9% of South African pediatric patients between 2 and 35 months of age with dehydration secondary to gastroenteritis to be hypoglycemic (26). Hypoglycemia was more common in the hypothermic and malnourished. Daral and colleagues determined 14% of Indian children ($<$ 3 months of age) presenting with dehydration from diarrhea to be hypoglycemic (27). Fifty-five percent of children had a bacterial pathogen isolated. Bennish et al., in the largest prospective investigation to date, found 4.5% of Bengali patients $<$ 15 years old admitted with diarrhea to be hypoglycemic (28). Sixty-five percent had a bacterial pathogen identified and 39% were malnourished. The children who were found to be hypoglycemic had longer fasting times, seizures (35%), and altered mental status. Huq et al. determined 11% of dehydrated children at their center in Bangladesh to be hypoglycemic (29). Seven percent were bacteremic and one-half to three-quarters of hypoglycemic patients were malnourished. Seizures and a higher mortality rate were found in the hypoglycemic children. The above data are of interest but are difficult to apply to dehydration in a developed nation where malnutrition and bacterial causes of diarrhea are less common.

Reid and Losek undertook a retrospective investigation with a goal of estimating the prevalence of hypoglycemia among pediatric patients with dehydration in a developed nation (30). The authors reviewed the records of 196 children, older than 1 month of age and younger than 5 years of age. They reported that 18 children (9.2%) were hypoglycemic. The duration of vomiting was longer for the children with hypoglycemia (2.6 days, SD $\pm$ 1.5) than for those without hypoglycemia (1.6, SD $\pm$ 1.8; 95% CI 0.13–1.88). None of the hypoglycemic children was found to have an altered mental status or to be hypotensive. A second investigation by Reid et al. enrolled 184 children to identify variables associated with hypoglycemia (31). The authors found an association with female gender, neurologic symptoms of hypoglycemia, and a greater amount of vomiting vs. diarrhea to be more closely associated with hypoglycemia. However, these clinical variables did not have an adequate sensitivity or specificity to accurately predict which children with AGE were hypoglycemic. To date, a definitive investigation describing indications to obtain a rapid glucose in the dehydrated child does not exist. According to Reid and Losek, hypoglycemia is relatively common in children $<$ 5 years of age with dehydration from AGE (30). A reasonable approach would be to adopt a liberal policy on obtaining a rapid glucose, as the risks of obtaining one are low and it seems that identifying hypoglycemia in the dehydrated child based on clinical grounds alone is challenging.

The role of urine specific gravity to judge the dehydration status in the acute care setting is questionable. The reason for this is twofold. First, the dehydrated child often does not urinate until rehydration has begun. Second, as determined by investigations by Oppliger et al. and Popowski et al., the value of urine specific gravity tends to lag behind actual hydration status (32,33). Furthermore, the use of urine specific gravity in the neonate and young infant is unreliable, as the concentrating ability of the kidney does not reach adult values until approximately 1 year of age (34).

A study of 130 children with gastroenteritis comparing the use of end-tidal carbon dioxide monitoring to serum bicarbonate as a measure of acidosis showed that end-tidal carbon dioxide levels and serum bicarbonate concentrations were correlated linearly in bivariate analysis (10). The mean end-tidal carbon dioxide level for

patients who had a return visit (33.0 ± 4.0 mm Hg) was lower than the level for those who did not seek reevaluation (36.6 ± 3.6 mm Hg). The authors concluded that capnography offers an objective non-invasive measure of the severity of acidosis among patients with gastroenteritis.

In summary, no one laboratory value has been found to have great accuracy in predicting the degree of dehydration in children with gastroenteritis. Most experts recommend that routine laboratory studies, including serum electrolytes, to assess dehydrated patients with acute diarrhea are unnecessary (7,9). However, serum electrolyte levels may provide useful information about other abnormalities such as hypoglycemia, hypokalemia, and sodium abnormalities. Other laboratory studies such as a complete blood count, blood cultures, urine analysis, and urine culture should be obtained only if other pathology, such as sepsis or urinary tract infection, is suspected. Stool cultures are not routinely indicated in immunocompetent patients with diarrhea. The majority of domestically acquired cases of diarrhea are viral and, therefore, stool cultures are of low yield and will not likely change acute management. The presence of gross or occult blood in the stool may raise suspicion of a bacterial etiology, such as hemorrhagic *Escherichia coli, Shigella, Salmonella, Yersinia*, or *Campylobacter* species (35).

Oral vs. Intravenous Rehydration in the Emergency Department

Controversy exists as to the best route for rehydration of children who present to the ED with dehydration secondary to gastroenteritis. Although intravenous therapy (IVT) remains the therapy of choice for severely dehydrated patients, the AAP, CDC, European Society for Paediatric Gastroenterology and Nutrition, and the WHO all strongly support the use of oral rehydration therapy (ORT) as the first-line therapy for the treatment of mild to moderate dehydration (6,7,36,37). Despite this, ORT is still underutilized and used incorrectly in many EDs across the United States (38–42). Barriers to utilization of ORT include concern regarding the effectiveness of oral therapy, unfamiliarity with published guidelines, the perception that oral rehydration takes more time than intravenous hydration, the misperception that ORT is contraindicated with vomiting, and parental or referring physician preferences (38,39,43,44). There are few contraindications to ORT; these include patients with hemodynamic instability, suspected ileus (suggested either clinically by abdominal distension or absent bowel sounds, or if seen on radiography), or patients with impaired protective airway reflexes (45).

ORT is a form of enteral rehydration therapy. Oral rehydration solutions typically contain sodium, potassium, chloride, carbohydrates (typically glucose) and a base. The WHO recommends a reduced osmolarity solution for ORT. Table 2 lists the composition of commercial oral rehydration solutions and commonly consumed beverages (Gatorade and apple juice are not recommended as solutions for ORT but are included as they are commonly consumed). ORT has been the mainstay of treatment of dehydration caused by gastroenteritis in underdeveloped countries out of sheer necessity, given the overwhelming burden of diarrheal illness and lack of access to more advanced medical interventions, such as intravenous therapies. Oral rehydration therapy is a striking example of reverse technology transfer (i.e., technology developed and embraced by lesser developed countries that is now returning to more technologically advanced countries) (48). ORT is informally used to describe rehydration both by mouth and by nasogastric tube. Although more invasive than rehydration by mouth, rehydration via nasogastric tube is safe and effective and is an alternative route in children who cannot tolerate rehydration by mouth (49–51). Although not generally recommended for patients with severe dehydration, nasogastric hydration can serve as a temporizing method of hydration for children in whom intravenous or intraosseous access is difficult.

Table 2. Composition of Commercial Oral Rehydration Solutions and Commonly Consumed Beverages

Solution	Sodium (mEq/L)	Carbohydrate (g/dL)	Potassium (mE/L)	Chloride (mEq/L)	mOsm/kg H_2O
World Health Organization	90	2	20	80	310
Pedialyte	45	2.5	20	35	250
Rehydralyte	75	2.5	20	65	250
Infalyte	50	3	25	45	200
CeraLyte	70	4	20	60	220
Gatorade	21	5.9	2.5	1.7	377
Apple juice	0.4	11.9	26	—	700

Sources: Ref (46): Colletti JE. Diarrhea. In: Hendey GW, Hendry PL, Linden CH, Rosen CL, Schaider J, editors. Hardwood-Nuss' Clinical Practice of Emergency Medicine, 4th edition. Philadelphia: Lippincott Williams and Wilkins; 2005:1221.
Ref (47): Stone B. Fluids and electrolytes. In: Robertson J, Shilkofski N. The Johns Hopkins Hospital: The Harriet Lane Handbook, 17th edn. St. Louis, MO: Mosby; 2005.

Studies comparing enteral and intravenous rehydration therapy in mildly to moderately dehydrated children have reported numerous outcome measures. Some of these studies were performed in less-developed countries, and most compared these therapies in inpatients. Three studies of rehydration methods enrolled ED patients (51–53). One additional study compared patients receiving ORT in an ED holding area with ED patients and inpatients receiving IVT (54). The most relevant outcome measures for emergency physicians include therapy efficacy, time required for therapy, and adverse effects.

A recent systematic review compared the failure rate of enteral rehydration to rehydrate or maintain hydration after initial rehydration of dehydrated children to intravenous rehydration. This analysis found that the failure risk for enteral rehydration therapy was 4.9%, and was 1.3% for intravenous rehydration. For every 25 children (95% CI 14–100) receiving oral or nasogastric rehydration therapy, one would fail and require intravenous rehydration. However, for patients treated with the currently recommended WHO reduced osmolarity solutions, one patient out of 100 children would need i.v. fluid after failing enteral rehydration. The authors caution that these results may be applicable only to children with dehydration from diarrhea and not necessarily to children with gastroenteritis (i.e., vomiting and diarrhea), although the risk difference for trials between enteral rehydration and intravenous therapy that included children who had persistent vomiting was 4% (95% CI −5–13) compared to 0% (95% CI −3–3) for children enrolled in trials that excluded persistently vomiting patients (45). This enteral failure rate is similar to previously published failure rates reported in meta-analyses (55,56).

Most studies comparing ORT with IVT studied inpatients; however, a few studies have investigated ED length of stay based on rehydration methods. An equivalent percentage of children receiving ORT or IVT showed improvement in dehydration scores at 2 h (79% ORT vs. 80% IVT) and were successfully rehydrated at 4 h (55% ORT vs. 57% IVT; difference −1%; 95% CI −24–22%) (53). In one pediatric ED-based study, children receiving oral rehydration therapy had a shorter ED length of stay when compared to patients receiving IVT (225 min [SD 78 min] vs. 358 min [SD 160 min], respectively) (52). Nasogastric rehydration via continuous infusion was as efficacious as intravenous therapy in correcting moderately dehydrated patients at 3 h (51). Successful i.v. placement is frequently difficult in dehydrated children and may require multiple attempts, further delaying rehydration via the intravenous route (53).

In the systematic review comparing oral vs. intravenous rehydration, 33 children (95% CI 20–100) needed to be treated with i.v. fluid rather than oral or nasogastric rehydration to prevent one case of paralytic ileus. Phlebitis developed in 2.5% of patients who received IVT (45). Most ORT vs. IVT trials excluded patients with severe dehydration and shock. Not surprisingly, deaths in study patients were exceedingly rare and were reported exclusively in low-middle-income countries, and these deaths could not be directly attributed to the mode of rehydration therapy (45). In one trial, 1 patient developed a seizure 17 h after the onset of ORT, thought to be related to a rapid decrease in total osmolality (57). Other relatively minor complications (i.e., complications with nasogastric tube placement and multiple attempts at i.v. line placement) were reported as well (50,51,53).

There are limited cost-effectiveness data from the United States (54). One study demonstrated that rehydration through a nasogastric tube was less expensive than IVT (51). The cost of WHO oral rehydration solution in 2005 was $0.07 per liter (6). Patients who received ORT and IVT and were treated and discharged from the ED were equally likely to make an unscheduled return visit to the ED (52,53). Caregivers of patients who received ORT were at least as likely to be satisfied with their ED treatment when compared to those patients receiving IVT (52,53).

All of these studies discussed above enrolled patients who were dehydrated and had diarrhea, but there was some heterogeneity in the approach to children who had vomiting as well. Some studies included patients with significant vomiting, whereas others excluded these patients. Most studies excluded children $<$ 3 months of age. Although ORT is usually successful even in children who are vomiting, intractable or persistent vomiting may preclude successful ORT. Some children with carbohydrate malabsorption may develop worsening diarrhea with ORT, and ORT should be discontinued in children who have significant worsening of their diarrhea. However, there is no clear definition of ORT failure.

Treatment of dehydration consists of three components: rehydration, replacement of ongoing losses, and continuation of normal feeding. The method of rehydration therapy depends on the degree of dehydration; therefore, the degree of dehydration should be assessed before initiating therapy (see above). Patients with minimal or no dehydration need therapy directed at replacement of ongoing losses. For each watery stool, patients should be given 10 cc/kg body weight of oral rehydration solution (ORS) and for each episode of emesis, children should receive 2 cc/kg body weight of replacement fluid (7). Alternatively, children weighing $<$ 10 kg should receive 60–120 cc of ORS for each diarrheal stool or episode of emesis, whereas children weighing $>$ 10 kg should receive 120–250 cc of ORS for each event (7) (Table 3). Children who are breastfed should continue breastfeeding ad lib, whereas patients eating solids should continue

Table 3. Therapy Based on Degree of Dehydration

Degree of Dehydration	Rehydration Therapy	Replacement of Losses
No dehydration to minimal	None	< 10 kg: 60–120 mL oral rehydration solution (ORS) per vomiting or diarrheal episode > 10 kg: 120–240 mL ORS for per vomiting or diarrheal episode
Mild to moderate dehydration	ORS, 50–100 cc/kg body weight over 3 to 4 h ORS therapy is initiated with 5 cc (1 teaspoon) every 1 to 2 min If not improving with ORS, consider intravenous (i.v.) fluid therapy.	As above
Severe dehydration	0.9 normal saline or lactated ringers 20 cc/kg i.v. until mental status and perfusion improve, followed by 5% dextrose ½ normal saline i.v. at twice maintenance rates.	As above If unable to tolerate oral fluids, administer through nasogastric tube or administer 5% dextrose ½ normal saline with 20 mEq/L potassium chloride i.v.

Source: Ref (7): King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep 2003 Nov 21;52(RR-16):1–16.

to receive their usual diet, with the exception of eliminating foods high in simple sugars. Children should not be taking any diluted or special formula. Patients with mild to moderate dehydration should receive 50–100 cc/kg of ORS over 3–4 h, supplemented by fluids to replace ongoing losses (7) (Table 3). Patients should initially receive small amounts (e.g., 5–15 cc) of ORS every 5 min, increasing the volumes of ORT if tolerated (Table 4) (7). Patients should also continue to breastfeed or eat solids (with the exception of limiting foods high in simple sugars) normally.

Patients assessed to have severe dehydration should be resuscitated initially with Lactated Ringer's solution or normal saline intravenously to restore hemodynamic stability (58). The role of dextrose-containing solution in i.v. rehydration is unclear. Levy and Bachur studied whether the amount of i.v. dextrose administered to children with gastroenteritis and dehydration affected return visits warranting admission (59). The authors performed a case control investigation of children 6 months to 6 years of age who presented with acute gastroenteritis and dehydration. The investigation concluded that children who received more i.v. dextrose, independent of the fluid amount, were less likely to present for a return visit requiring admission. In patients receiving i.v. hydration for severe dehydration, oral rehydration should be initiated as soon as it is tolerated. Table 5 summarizes suggestions for treatment of acute gastroenteritis from the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (60). Indications for hospital admission are contained in Table 6.

The Use of Antiemetics in Children with Gastroenteritis

The third controversy in the treatment of children with acute gastroenteritis in the ED is whether or not to use antiemetics. In 1996, the AAP published practice guidelines discouraging the use of antiemetics in children < 5 years of age (9). Administration of antiemetics has been associated with adverse reactions, most commonly extrapyramidal side effects such as acute dystonic reactions

Table 4. Oral Replacement Therapy Dosing Based on Weight and Age

Age	Weight	Initial Dosing	Volume/h	First Advance	Next Advance
0–6 mo	8 kg	5 cc every 5 min	60 cc (10 cc/kg)	15 cc every 15 min	30 cc every ½ h
6–12 mo	10 kg	10 cc every 5 min	120 cc (10 cc/kg)	30 cc every 15 min	60 cc every ½ h
12–18 mo	12 kg	10 cc every 5 min	120 cc (10 cc/kg)	30 cc every 15 min	60 cc every ½ h
18–24 mo	13 kg	10 cc every 5 min	120 cc (10 cc/kg)	30 cc every 15 min	60 cc every ½ h
2–3 years	15 kg	10 cc every 5 min	120 cc (10 cc/kg)	30 cc every 15 min	60 cc every ½ h
3–5 years	20 kg	15 cc every 5 min	180 cc (10 cc/kg)	45 cc every 15 min	90 cc every ½ h
5–8 years	25 kg	15 cc every 5 min	180 cc (10 cc/kg)	60 cc every 15 min	90 cc every ½ h
8–10 years	35 kg	15 cc every 2 min	450 cc (10 cc/kg)	90 cc every 15 min	120 cc every ½ h
10–12 years	40 kg	15 cc every 2 min	450 cc (10 cc/kg)	90 cc every 15 min	120 cc every ½ h
12–15 years	50 kg	15 cc every 2 min	450 cc (10 cc/kg)	90 cc every 15 min	120 cc every ½ h

Courtesy of Mark Hostetler, MD, University of Chicago, Illinois.

Table 5. The Essential Pillars of Good Treatment of Acute Gastroenteritis

I. Use of oral rehydrating solution (ORS) for dehydration
II. Hypotonic solution (Na 60 mmol/L, glucose 74–111 mmol/L)
III. Fast oral rehydration over 3–4 h
  50–100 cc/kg maintenance plus:
    10 cc/kg for every watery stool
    2 cc/kg for every emesis
IV. Rapid realimentation with normal feeding (including solids) thereafter
V. Use of special formula is unjustified
VI. Use of diluted formula is unjustified
VII. Continuation of breast-feeding at all times
VIII. Supplementation with ORS for ongoing losses

Adapted from Ref (60): Szajewska H, Hoekstra JH, Sandhu B. Management of acute gastroenteritis in Europe and the impact of the new recommendations: a multicenter study. The Working Group on acute Diarrhoea of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2000;30:522–7.

and apnea. In one prospective investigation, the use of prochlorperazine was associated with akathisia in 16% of patients and dystonia in 4% of patients (61). Central nervous system depression manifesting as sedation and drowsiness may interfere with oral hydration and make it difficult to assess the child for changes in mental status (e.g., lethargy). These dystonic-like reactions and sedative effects are reported to occur more frequently in children and young adults than in older patients (62). It has been suggested by Kahn and colleagues that the use of antiemetics in infants with vomiting may be associated with Sudden Infant Death Syndrome (63,64). The Food and Drug Administration has required a black box warning on promethazine hydrochloride (65). This warning cautions against the use of promethazine in children $<$ 2 years of age due to the potential for fatal respiratory depression. Furthermore, the warning calls for exercising caution when administering promethazine to children aged 2 years or older and to avoid the concomitant administration of other medications with respiratory depression effects. Concern also has been raised that the use of antiemetics in children with emesis could possibly mask a more serious illness (66). It is important to note that the above-mentioned investigations were performed mostly with phenothiazine antiemetics before serotonin type 3 (5-hydroxytryptamine3, 5-HT3) receptor antagonists were widely employed in the vomiting child.

The concerns regarding antiemetic use described above, combined with the knowledge that vomiting in acute gastroenteritis is self-limited in nature and improves with correction of dehydration, led to the belief among many pediatric emergency medicine experts that antiemetics should not be used in children with acute gastroenteritis (9,35). However, more recently, two authors have published results revealing that antiemetic use is common in children with gastroenteritis and that the rate of side effects may be less than previously reported (67,68). Kwon et al. performed a cross-sectional survey randomly sent to physicians board certified in the specialties of emergency medicine, pediatrics, and pediatric emergency medicine (67). The majority (361, 60.9%) of responders reported using antiemetics for acute gastroenteritis in the last year. A $>$ 50% utilization rate of antiemetics was reported for all three specialty groups. Emergency physicians had the highest administration of antiemetics (79%). The most commonly used antiemetic was promethazine, followed by trimethobenzamide. Adverse reactions were noted by 73 (20.2%) survey responders. The most common adverse reactions were extrapyramidal. The medications most commonly reported as causing adverse reactions were prochlorperazine (42%) and promethazine (40%). The authors concluded that use of antiemetics was common in children with acute gastroenteritis. They cautioned that an antiemetic should be chosen with an understanding of its adverse reactions. Li et al. performed a retrospective review of 20,222 children, ages 1 month to 18 years, presenting with acute gastroenteritis (68). Nine percent were given a prescription for an antiemetic. The majority (90%) of these children were prescribed promethazine. The adverse reaction rate was 0.39%. Subgroup analysis performed in children $<$ 5 years of age failed to demonstrate a statistically significant difference in the prescription rate or the number of adverse reactions that occurred.

Serotonin type-3 receptor antagonists, such as ondansetron, are effective antiemetics. They have been shown to have superior antiemetic effects in children receiving cancer chemotherapy when compared with phenothiazine-type antiemetics, droperidol, or metoclopramide (69). Serotonin type-3 receptor antagonists also have been shown to be effective antiemetics in postsurgical-induced emesis in children (70–72). All of these studies also noted a lack of major side effects, including extra-

Table 6. Potential Indications for Admission Criteria

Dehydration $>$ 5% and unable to tolerate oral fluids
Serious underlying diagnosis such as:
  Sepsis
  Urinary tract infection
  Inborn error of metabolism
  Intra-abdominal catastrophe
  Diabetic ketoacidosis
Intractable or bilious emesis
Significant electrolyte disturbances
Poor social situation such as:
  Parental noncompliance or inability to follow prescribed therapy
  Suspected neglect

pyramidal reactions. Several authors have looked at the efficacy and safety of ondansetron in patients with acute gastroenteritis.

Cubeddu et al. evaluated children aged 6 months to 8 years who had vomited twice within 1 h (73). Thirty-six children were enrolled: 12 receiving placebo, 12 receiving metoclopramide 0.3 mg/kg, and 12 receiving ondansetron 0.3 mg/kg. All patients were hospitalized for 24 h with oral hydration attempted. The mean and the median number of emetic episodes over a 24-h time course were 5 and 3, respectively, for the placebo group; 5 and 6, respectively, in the metoclopramide group; and 2 and 0, respectively, among the ondansetron group. Emesis was observed in 10 (83%) children receiving placebo, 8 (67%) in the metoclopramide group, and 5 (42%) children receiving ondansetron. The authors found a statistical difference between ondansetron and placebo ($p = 0.039$), in ondansetron's favor. Conversely, they did not determine a significant difference between metoclopramide and placebo. Patients in the investigation received similar amounts of hydration fluid, but there were more episodes of diarrhea in both the metoclopramide and the ondansetron groups.

Ramsook et al. performed a randomized double-blind placebo-controlled trial of oral ondansetron in 145 children aged 6 months to 12 years with acute gastroenteritis (74). The patients also received oral hydration at 5 cc/min. For patients able to be discharged from the ED, five additional doses were administered at home. Ondansetron was effective in decreasing the episodes of emesis during oral hydration, as well as the hospital admission rate. The frequency of emesis during ED observation ranged in the placebo group from 0 to 7 and from 0 to 2 in the ondansetron group. The rank sum of emesis episodes was lower in the ondansetron group ($p = 0.001$). The proportion of patients who were emesis-free after study enrollment was greater for the ondansetron group then it was for the placebo group ($p = 0.004$) during the ED stay. However, those who were discharged in the ondansetron group were more likely to revisit the ED than those in the discharged saline group. There was also an increase in the rate of diarrhea in those who received ondansetron.

Reeves et al. performed a randomized, double-blind, placebo-controlled trial of 107 children (54 to intravenous ondansetron, 53 to placebo) with gastroenteritis (75). This investigation compared 0.15 mg/kg of i.v. ondansetron to placebo (saline) in children from 1 month to 22 years of age. Ondansetron was associated with a decrease in the number of episodes of emesis. After drug administration, 38 (70%) of the ondansetron group had a complete cessation of emesis, compared to 27 (51%) of the placebo group. The authors were unable to demonstrate a decrease in the rate of overall hospitalization in the entire ondansetron-treated group vs. the placebo-treated group. However, ondansetron was shown to decrease hospitalization in first-time treated children with a measured serum carbon dioxide level > 15 mEq/L. Of note, the ondansetron group, compared to the placebo group, had a greater proportion of children with a measured serum carbon dioxide (CO_2) < 15 (20% and 4%, respectively). At the author's institution, patients with a $CO_2 < 15$ were routinely admitted and the authors therefore expected an admission bias against the ondansetron group. Ondansetron was found to be cost-effective compared to saline hydration alone in their setting.

Freedman et al. performed a double-blind trial in 215 children with gastroenteritis aged 6 months through 10 years (76). Enrolled patients were randomized to an oral dose of ondansetron or placebo. Ondansetron was administered as an oral disintegrating tablet in a weight-based fashion (children 8–15 kg received 2 mg, 15–30 kg received 4 mg, and over 30 kg were administered 8 mg). Fifteen minutes after medication administration, a 1-h period of intense oral rehydration was initiated that was continued until the point of disposition. The authors determined that children who received ondansetron were less likely to vomit, vomited less often, had greater oral intake, and were less likely to be treated by intravenous rehydration than those who received placebo. Mean length of stay in the ED was reduced by 12% in the ondansetron group. Rates of hospitalization and return visits to the ED did not significantly differ between the placebo and ondansetron group. They concluded that a single dose of oral ondansetron in children with acute gastroenteritis decreases vomiting and facilitates oral rehydration.

Stork et al. compared ondansetron with dexamethasone and placebo in a randomized double-blind trial in patients aged 6 months to 12 years presenting to a pediatric ED with acute gastritis and receiving intravenous hydration (77). Ondansetron was associated with a decrease in the rate of hospitalization (4% vs. 20 % for placebo). The number needed to treat with ondansetron to prevent one hospitalization compared with placebo (i.v. hydration alone) was 6. There was also a higher rate of patients who tolerated oral hydration at 2 h in the ondansetron group. The authors concluded that in children presenting with dehydration secondary to vomiting from acute viral gastritis, ondansetron with intravenous rehydration improved tolerance of oral fluids and decreased the hospitalization rate when compared with intravenous rehydration with or without dexamethasone. Based on this investigation, administration of dexamethasone for dehydration secondary to acute gastroenteritis does not seem to improve tolerance of oral fluids or decrease hospital admission rates. As such, dexametha-

sone cannot be recommended at this time for routine use in the vomiting child with acute gastroenteritis.

Overall, the above-mentioned investigations are favorable in regards to administration of ondansetron for vomiting secondary to AGE, but it should be noted that they are of limited power to detect important but uncommon side effects.

An argument that has been made against the use of ondansetron in gastroenteritis, which is a self-limited disease, is its relatively high cost. However, as noted in the above studies, the use of ondansetron can be associated with a decrease in need for hospitalization and therefore may be cost-effective (35,67–69). Cost-effectiveness studies comparing ondansetron with metoclopramide in oncology patients have shown that ondansetron administered three times a day is at least as cost-effective as metoclopramide, whereas twice-a-day regimens of ondansetron are more cost-effective (78). The doses and route of administration of ondansetron in the above-mentioned investigations can be seen in Table 7.

CONCLUSIONS

In the ED, dehydration is evaluated by synthesizing the various historical, physical examination, and laboratory data points in select patients. These signs and symptoms, when combined into a score, may be helpful in predicting degree of dehydration. However, no one single finding has adequate specificity or sensitivity to predict the degree of dehydration. A subset of four factors (capillary refill $>$ 2 s, absent tears, dry mucous membranes, and ill general appearance) have been demonstrated to predict dehydration as well as the entire set. Similarly, no single laboratory study has been found to be clinically useful in predicting degree of dehydration. Measurement of serum electrolytes may provide useful information regarding other abnormalities such as hypoglycemia, hypokalemia, and sodium abnormalities in children who are dehydrated and are undergoing intravenous rehydration. However, the routine measurement of serum electrolytes in the majority of children presenting to the ED with dehydration due to acute gastroenteritis is not recommended.

The available evidence supports the assertion that the majority of children with gastroenteritis and mild to moderate dehydration can be treated successfully with oral rehydration therapy. ORT is highly effective, safe, and inexpensive. ORT can be initiated more quickly than intravenous therapy, and the rates of successful rehydration at 2 h and 4 h after initiation of therapy are similar. This mode of therapy leads to high degrees of parental satisfaction as well. With the exception of children with severe dehydration requiring resuscitation and children suspected of having paralytic ileus, ORT should be the initial therapy for dehydrated children presenting to the ED. It should also be initiated as early as possible in the treatment of those receiving intravenous rehydration for severe dehydration due to gastroenteritis.

Traditionally, use of antiemetics has been discouraged in the pediatric population with acute gastroenteritis secondary to adverse reactions and the possibility of masking a more sinister illness. The exact rate of side effects such as sedation and extrapyramidal effects is unclear. However, there is ample evidence that the use of ondansetron is associated with a much lower rate of these side effects than the more traditional antiemetics such as promethazine and prochloperazine. Furthermore, the AAP recommendation not to administer an antiemetic was made over a decade ago (1996), before 5-HT3 receptor antagonists were widely utilized. There is accumulating evidence that ondansetron (oral or intravenously) may be effective in decreasing the rate of vomiting, improving the success rate of oral hydration, preventing the need for i.v. hydration, and preventing the need for hospital admission in those receiving i.v. hydration.

Table 7. Doses and Route of Administration of Ondansetron

Investigation	Dose	Route
Ramsook et al. (74)	0.3 mg/kg	i.v.
Reeves et al. (75)	0.15 mg/kg (maximum 8 mg)	i.v.
Stork et al. (77)	0.15 mg/kg	i.v.
Ramsook et al. (74)	6 months to 1 year: 1.6 mg 1 to 3 years: 3.2 mg 4 to 12 years: 4 mg	p.o.

i.v. = intravenous; p.o. = per oral.

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