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REVIEW

Paediatrics: how to manage viral gastroenteritis

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Abstract

Background: Viral gastroenteritis is the most common diarrhoeal disorder seen in general practice and emergency departments. This article aims to provide a narrative updated review on the evaluation and management of viral gastroenteritis in children.

Methods: A PubMed search was performed with Clinical Queries using the key term ‘viral gastroenteritis’. The search strategy included clinical trials, meta-analyses, randomized controlled trials, observational studies and reviews. The search was restricted to the English literature and the paediatric population.

Results: Acute viral gastroenteritis is usually self-limiting. However, it can lead to dehydration and electrolyte imbalance if not properly treated. Adequate fluids containing physiological concentrations of glucose and electrolytes should be provided to compensate for gastrointestinal losses and cover maintenance needs. Oral rehydration therapy is as effective as intravenous (IV) fluid therapy for rehydration for children with mild-to-moderate dehydration. Measurements of serum electrolytes, creatinine and glucose are usually not necessary and should only be considered in a subset of children with severe dehydration who require hospitalization and IV therapy. Judicious use of ondansetron can increase the success rate of oral rehydration therapy and minimize the need for IV therapy and hospitalization.

Conclusion: Acute viral gastroenteritis is associated with substantial morbidity in developed countries and significant mortality in developing countries. Physicians should educate caregivers on proper personal hygiene and handwashing to prevent faecal to oral transmission of the pathogen as well as the importance of rotavirus vaccine in the prevention of rotavirus gastroenteritis. Several norovirus vaccines are currently undergoing clinical trials with promising results. It is hoped that development of an effective norovirus vaccine will further reduce the incidence of viral gastroenteritis.

Keywords: dehydration, diarrhoea, gastroenteritis, ondansetron, oral rehydration, viral, vomiting.

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Introduction

Viral gastroenteritis is one of the most common causes of morbidity and mortality worldwide, especially in young children in developing countries.1–5 Dehydration, which may be associated with electrolyte imbalance and metabolic acidosis, is the most frequent and dangerous complication.6

Methods

This article provides a narrative updated review on the evaluation, diagnosis and management of viral gastroenteritis in children. A PubMed search was performed in November 2020 with Clinical Queries using the key term ‘viral gastroenteritis’. The search strategy included clinical trials, meta-analyses, randomized controlled trials, observational studies and reviews published within the past 10 years. The search was restricted to the English literature and children. The information retrieved from the above mentioned search was used in the compilation of the present article.

Aetiology

Worldwide, viruses account for approximately 75–90% of childhood acute gastroenteritis.7 The most common viral pathogens are norovirus and rotavirus, followed by sapovirus,
Epidemiology

Acute viral gastroenteritis is most common in children 5 years of age and younger. The sex ratio is approximately equal. The average child younger than 5 years of age experiences 2.2 diarrhoeal episodes per year in industrialized countries, with this rate being significantly higher in developing countries. Worldwide, acute viral gastroenteritis accounts for over 200,000 child deaths per year, primarily in developing countries. Outbreaks of acute viral gastroenteritis occur most frequently during the winter. The majority of viral pathogens are transmitted via the faecal–oral route through person-to-person contact and contaminated food and water. Airborne transmission of norovirus, rotavirus and SARS-coronavirus has been suggested in some outbreaks.

Pathophysiology

The pathophysiology of viral gastroenteritis has been extensively studied with rotavirus. Rotavirus preferentially infects enterocytes in the mature small intestine, leading to the destruction of these cells with impaired capacity for absorption of intestinal fluid and secondary disaccharidase deficiency. The disaccharidase deficiency results in malabsorption of carbohydrates with resulting osmotic diarrhoea. Villous tips receive the most extensive damage with sparing of the crypts. Excessive secretion from the intestine may be secondary to the loss of villous tips and the filling of crypts with rapidly multiplying cells, leading to an imbalance between absorption and secretion and resulting in a net secretion (villous cells are largely absorptive and crypt cells are secretory). In addition, the rotavirus non-structural protein 4 (NSP4) functions as an enterotoxin, which can lead to hypersecretion of intestinal fluid.

Clinical manifestations

The incubation period is usually 12–72 hours, depending on the causative viral pathogen. The main clinical features of acute viral gastroenteritis include vomiting and diarrhoea, often accompanied by malaise, nausea, abdominal cramps, and fever. It is interesting to note that children with gastroenteritis caused by norovirus or sapovirus may present with isolated vomiting in the absence of diarrhoea. Vomiting is a prominent feature in most cases of rotavirus and norovirus gastroenteritis. Stools are typically loose to watery. Mucous and gross blood are uncommon. In rotavirus gastroenteritis, stools have a distinct odour. The severity of the disease depends on the virulence of the virus, the viral load, the host immune system and comorbidities. Diarrhoea usually lasts less than 7 days, most often improving after 1–3 days, and does not last longer than 14 days. Diarrhoea that lasts longer than 14 days is considered chronic and therefore does not fit into the definition of acute gastroenteritis.

Extraintestinal manifestations, such as respiratory symptoms, may occur with rotavirus infection and headache and myalgia may occur with norovirus infection. Extraintestinal manifestations are especially common with gastroenteritis caused by SARS-coronavirus, echovirus, coxsackievirus, influenza virus type B and poliovirus.

Clinical evaluation

A detailed history and a thorough physical examination are essential to establish the diagnosis of acute gastroenteritis and to exclude other causes of vomiting and/or diarrhoea. In viral gastroenteritis, the incubation period is usually longer than 12 hours, vomiting is prominent, fever is usually low grade, stools usually do not contain blood, and the entire illness usually lasts less than 7 days. However, the differentiation of viral gastroenteritis from bacterial gastroenteritis based on clinical manifestations alone is often difficult. Red-flag symptoms and clinical signs suggestive of acute bacterial gastroenteritis include bilious or bloody vomiting, blood or mucus in stool, excessive irritability, inconsolable crying, high fever, toxic appearance, tachypnoea, cyanosis, poor peripheral perfusion, petechial rash, neck stiffness and altered sensorium.

History

The history should focus on the age of the child and the onset, duration, number of episodes and quantity of the diarrhoea and vomiting as well as on the amount and type of fluid intake. The character of vomiting (e.g. projectile, bilious) and diarrhoea (e.g. presence of blood and mucus) should be noted. The child’s weight before onset of the illness, associated symptoms (e.g. such as fever, abdominal cramps, tenesmus), overall activity level, consumption of contaminated foods or fluid, concurrent illness in family members, exposure to individuals with gastroenteritis, outbreak of gastroenteritis in the community, day-care attendance, medical history (e.g. comorbid disease, immunodeficiency), recent travel to a diarrhoea-endemic area, recent infection, recent use of antibiotics, duration of breastfeeding, and immunization status should be noted.

Physical examination

The general condition of the patient, vital signs (temperature, weight, heart rate, respiratory rate, blood pressure), and the...
severity of dehydration should be assessed.\textsuperscript{4,5,28} Although loss in body weight is a useful indicator of dehydration, it should always be corroborated by changes in clinical signs because weight measurement is susceptible to many potential errors (such as the use of different scales or unstandardized measurement techniques).\textsuperscript{4} Additionally, weight may change significantly depending on whether the child has recently eaten, defecated or voided.\textsuperscript{36} A thorough physical examination may help to exclude other causes of vomiting and/or diarrhoea.

### Diagnosis

The diagnosis of acute gastroenteritis is a clinical one based on the presence of diarrhoea (usually no blood in the stools), often accompanied by vomiting, fever and abdominal pain. Acute viral gastroenteritis refers to acute gastroenteritis caused by a viral pathogen. A presumptive diagnosis of acute viral gastroenteritis can be made in the absence of atypical features such as high fever, bilious vomiting, projective vomiting, gross blood or mucus in stool, persistence of diarrhoea more than 7 days without improvement, recent antibiotic use, severe dehydration, focal abdominal tenderness, marked abdominal distension, and absent bowel sounds.\textsuperscript{24}

### Differential diagnosis

Acute viral gastroenteritis should be differentiated from bacterial causes of acute gastroenteritis (e.g. \textit{Salmonella}, \textit{Shigella}, diarrhoeagenic \textit{Escherichia coli}, \textit{Campylobacter jejuni}, \textit{Clostridium difficile}), parasitic causes of acute gastroenteritis (e.g. \textit{Giardia intestinalis}, \textit{Entamoeba histolytica}, \textit{Cryptosporidium} species), food poisoning, antibiotic-associated diarrhoea, acrodermatitis enteropathica, parenteral diarrhoea (e.g. ostitis media, urinary tract infection), haemolytic uremic syndrome, malabsorption syndromes (e.g. celiac disease, cystic fibrosis, disaccharidase deficiency) and inflammatory bowel disease (e.g. Crohn’s disease, ulcerative colitis).\textsuperscript{24} Gross blood or mucus in the stool are unusual in viral gastroenteritis, the presence of which should prompt consideration of other aetiologies.

### Laboratory evaluation

Measurements of serum electrolytes, creatinine and glucose are usually not necessary in most immune-competent children with typical findings of acute viral gastroenteritis as the results do not change the management.\textsuperscript{33,37} These tests should only be considered in a subset of children with severe dehydration who require hospitalization and intravenous (IV) therapy.\textsuperscript{34,38} Routine aetiologic testing of viral pathogens is typically not necessary but may be employed during outbreaks for epidemiological purposes. Faecal leukocytes and stool cultures should be considered in children with bloody diarrhoea, high fever and severe abdominal cramps as these symptoms are not consistent with uncomplicated viral gastroenteritis.\textsuperscript{27,33}

Complete blood cell count and appropriate cultures should be considered when sepsis is suspected.

### Complications

Dehydration and electrolyte imbalance are the most common complications. If the dehydration is severe enough, it can lead to shock, coma and even death. Children with poor nutrition status are at increased risk.\textsuperscript{6} Shock and acute renal failure may result from severe dehydration.\textsuperscript{39} Other complications include irritant diaper dermatitis, hypoglycaemia, carbohydrate intolerance, renal tubular damage, renal stone, hyperuricaemia, impaired liver functions and seizures.\textsuperscript{50–47} Gastroenteritis is associated with enormous costs either directly through medical expenses or indirectly through loss of working hours by parents of sick children because of the frequency of the disease.\textsuperscript{48,49}

### Management

#### Rehydration therapy

The goal of treatment is to maintain adequate hydration of the child with gastroenteritis.\textsuperscript{50,51} Adequate fluids should be provided to compensate for gastrointestinal losses and cover maintenance needs.\textsuperscript{4} Children weighing <10 kg should receive 60–120 mL of an oral rehydration solution (ORS) per episode of vomiting or diarrhoeal stool whilst those weighing >10 kg should receive 120–240 mL of ORS per episode of vomiting or diarrhoeal stool in addition to their normal daily requirements.\textsuperscript{24} The daily fluid maintenance requirement is 100 mL/kg for the first 10 kg, 50 mL/kg for the next 10 kg, and 20 mL/kg for each subsequent kilogram over 20 kg.\textsuperscript{4}

It has been shown that oral rehydration therapy (ORT) is as effective as, if not better than, IV fluid therapy for rehydration for children with mild-to-moderate dehydration.\textsuperscript{52–55} Compared with IV therapy, ORT is less traumatic, easier to administer, cheaper and can be administered in a variety of settings, including the home.\textsuperscript{2,50,53,54}

ORSs containing physiological concentrations of glucose and electrolytes should be used.\textsuperscript{36,37,56} Fluids containing non-physiological concentrations of glucose and electrolytes, such as carbonated drinks and sweetened fruit juices, are discouraged because these drinks have a high carbohydrate content, very low electrolyte content, and high osmolality.\textsuperscript{6,36} The administration of such hyperosmolar solutions in large amounts may produce osmotic diarrhoea. On the other hand, plain water should not be used for rehydration as intake of large amounts of plain water may lead to hypoglycaemia and hyponatraemia.\textsuperscript{36} For infants who are breastfed, breastfeeding should be continued.\textsuperscript{7,57} It is not necessary to dilute formula or to give lactose-free formula in refeeding non-breastfed infants.\textsuperscript{34}
Children with mild-to-moderate dehydration can be managed as outpatients with ORT as mainstay of treatment.2,7,58 For children refusing ORS, the key is to give small amounts of ORS at frequent intervals and the volume should be gradually increased until the child can drink as desired.59 Using a dropper or syringe for very small infants and spoon for older infants and young children can significantly increase the success rate.2,36 In a child who refuses to drink, squinting the ORS into the mouth with a syringe may help.36 Flavoured ORS or ORS popsicles, which may be more acceptable to some children, may also be tried. If children refuse to drink by any of the above measures, nasogastric gavage should be considered before IV hydration is attempted.60 Nasogastric rehydration provides the physiological benefits of enteral rehydration and avoids the potential complications of IV therapy.61

For children with severe dehydration, Ringer’s lactate or normal saline (20 mL/kg) should be given intravenously over 1 hour.37,62,63 Vital signs should be monitored and the patient reassessed on a regular basis. Boluses of IV fluid may have to be given until pulse, perfusion and mental status return to normal.34 IV rehydration should also be considered in children with protracted vomiting despite small and frequent feedings and on those undergoing antiemetic treatment or with impaired consciousness, paralytic ileus, and severe acidosis.34,37 Hypotonic saline solutions are inappropriate for IV rehydration as administration of large volume of hypotonic solution might lead to dilutional hyponatraemia.4 ORT should be started when the child’s condition is stable.61

Early refeeding

Early refeeding with an age-appropriate diet has been shown to induce digestive enzymes, promote the recovery of disaccharidases, improve the absorption of nutrients, enhance enterocyte regeneration, decrease the intestinal permeability changes induced by infection, reduce the duration of diarrhoea, improve nutritional outcomes and maintain growth.54,65 Foods high in complex carbohydrates (e.g. rice, cereals, bread, wheat and potatoes), fruits and vegetables, and lean meat are better tolerated than foods containing high levels of simple sugar and fats.57 Foods high in simple sugars should be avoided as they may cause osmotic diarrhoea.57 With the exception of a subset of children with transient secondary disaccharidase deficiency, most children with acute gastroenteritis are able to tolerate milk and lactose-containing diets.

Antiemetic medications

Judicious use of ondansetron can increase the success rate of ORT and decrease the need for IV therapy and hospitalization.58,64,66–68 In a meta-analysis of 24 randomized clinical trials comparing the antiemetic effects of ondansetron, dimenhydrinate, domperidone, granisetron, metoclopramide and dexamethasone, ondansetron was the only intervention that revealed an effect on the cessation of vomiting.69 Compared to placebo, ondansetron increased the proportion of children with cessation of vomiting (OR 0.28; 95% CI 0.16–0.46; high quality of evidence) and decreased the proportion of children with the need for hospitalization (OR 0.93; 95% CI 1.69–6.18; moderate quality of evidence).69 The recommended IV dose of ondansetron is 0.1–0.5 mg/kg, with a maximum of 4 mg.4 The recommended oral dose is 2 mg for children weighing 8–15 kg, 4 mg for children weighing >15 kg to ≤30 kg, and 8 mg for children >30 kg.70–72 A single dose of oral ondansetron is usually sufficient for the treatment of gastroenteritis-related vomiting.64,66,71 The dose may be repeated if the child vomits within 15 minutes after taking the medication.7 However, the use of ondansetron is associated with increased risk of diarrhoea.54,73 Ondansetron should be avoided in children who are at risk for malignant hyperthermia and those with prolonged QT interval.57,74 Other antiemetics such as dimenhydrinate, promethazine, metoclopramide, droperidol, domperidone, prochlorperazine, trimethobenzamide, and dexamethasone are not recommended for use in children either because of lack of efficacy data or because of the significant adverse events associated with their use.2,57

Antidiarrhoeal medications

Racecadotril, an antisecretory drug, exerts its antidiarrhoeal effects by inhibiting intestinal endopeptidase (also known as enkephalinase), which helps to prevent the breakdown of enkephalins in the gastrointestinal tract and reduce the secretion of electrolytes and water into the gastrointestinal tract without affecting its motility.75,76 A 2007 systematic review of three randomized controlled studies (238 children in the treatment group; 233 children in the control group) showed a reduction in the stool output and duration of diarrhoea in treated children with acute gastroenteritis.76 In a 2018 systematic review and meta-analysis of 24 randomized controlled trials, racecadotril reduced the time to cessation of diarrhoea from 106.2 hours to 78.2 hours (mean reduction 28.0 hours; p<0.0001).77 More studies are needed before the routine use of racecadotril in the treatment of acute gastroenteritis can be recommended.

Smetectile/diosmectite, an adsorbent, has been used for the treatment of diarrhoea in many European countries.57 A 2018 Cochrane systematic review of 18 randomized and quasi-randomized trials (n=2616 children) showed that smectite reduced the duration of diarrhoea by approximately 24 hours (mean difference =24.38 hours; 95% CI –30.91 to –17.85; 2,209 children, 14 studies; low-certainty evidence), increased clinical resolution at day 3 (RR 2.01; 95% CI 1.30–3.39; 312 children, 5 trials; low-certainty evidence) and reduced the output of stools (mean difference =11.37; 95% CI –21.94 to 0.79; 634 children, 3 studies; low-certainty evidence).78,79 Based on the above low-certainty evidence, smectite might have a role in the treatment of diarrhoea in children with acute viral
Antimicrobial agents

Generally, antimicrobial agents are not indicated in the treatment of viral gastroenteritis. Nitazoxanide, a broad-spectrum antiparasitic and antiviral agent, has been shown to reduce the duration of diarrhoea in children with viral gastroenteritis in several studies. Well-designed, large-scale, randomized, double-blind and placebo-controlled studies are necessary to confirm the efficacy of nitazoxanide in order to make formal recommendations regarding their use in the management of viral gastroenteritis in children.

Probiotics

Probiotics such as Lactobacilli reuteri, Lactobacilli rhamnosus GG, Saccharomyces boulardii, Bifidobactium bifidum and Streptococcus thermophilus have been used in the treatment of viral gastroenteritis with varying success. Presumably, probiotics work by improving the barrier function of the intestine, competing for nutrients necessary for the survival of pathogens, competitive blockage of receptor sites, enhancement of the immune response and the production of substances that inactivate viral particles. A 2020 systematic review and meta-analysis showed that, in patients with acute viral gastroenteritis, probiotics can shorten the duration of diarrhoea (mean difference 0.7 day; 95% CI 0.31–1.09 days; n=740, 10 trials) and the duration of hospitalization (mean difference 0.76 day; 95% CI 0.61–0.92 day; n=329, 4 trials). Well-designed, large-scale, randomized, double-blind and placebo-controlled studies are necessary to determine the specific strains and optimal dosages of probiotics that are most helpful.

Zinc supplementation

Zinc supplementation in children with diarrhoea in developing countries leads to reduced duration and severity of diarrhoea. One way of administering zinc during acute diarrhoea is to mix it with ORS. The recommended dose is 20 mg zinc supplements per day for 10–14 days for children with acute diarrhoea (10 mg per day for infants younger than 6 months of age). In a recent study conducted in India and Tanzania, 4500 children aged 6–59 months with acute diarrhoea were randomized to receive 5 mg, 10 mg and 20 mg of zinc sulphate orally for 14 days. The mean number of diarrhoeal stool was 10.7, 10.9 and 10.8 in the 20-mg, 10-mg and 5-mg groups, respectively. The authors concluded that lower doses of zinc have non-inferiority efficacy for the treatment of children with acute diarrhoea and have less vomiting than the standard 20-mg dose. A 2016 Cochrane review found that zinc supplementation may be of benefit in the treatment of diarrhoea in children aged 6 months and older in areas where the prevalence of zinc deficiency or malnutrition is high. The current evidence does not support the routine use of zinc supplementation in children less than 6 months of age, in well-nourished children and children in areas at low risk of zinc deficiency. Given the effectiveness of traditional ORS and the increased cost of zinc supplementation, zinc supplementation is not routinely recommended in developed countries.

Human immunoglobulin

A preliminary study showed that oral administration of human serum immunoglobulin to hospitalized immunocompromised children with acute diarrhoea reduced stool output by 50%. Well-designed, large-scale, randomized controlled trials are needed to support the routine use of oral human serum immunoglobulin in hospitalized immunocompromised children with acute diarrhoea.

Prevention

Good personal hygiene is of utmost importance to prevent the spread of pathogens. This includes frequent handwashing with soap, careful diaper disposal, and proper preparation and storage of food and drinking water. Contaminated objects and surfaces should be properly disinfected.

Breastfeeding is recommended for the first year of life with exclusive breastfeeding for the first 6 months. Human milk may reduce the incidence of gastroenteritis and shorten the duration of diarrhoea.

Studies have shown that rotavirus vaccination is both efficacious and effective in the prevention of rotavirus-related diarrhoea and rotavirus-related hospitalizations as well as in the reduction of diarrhoea-associated healthcare utilization and costs. The rotavirus vaccination was licensed in 2006; 10 years after vaccine licensure, a systematic review of 57 articles from 27 countries showed that emergency department visits and hospitalizations due to rotavirus gastroenteritis were reduced by a median of 67% overall and 60%, 59% and 71% in countries with high, medium and low child mortality, respectively. Universal immunization of infants as early as 6 weeks of age and completion of the schedule by 8 months of age with rotavirus vaccine is recommended and will substantially reduce the incidence of rotavirus gastroenteritis and associated morbidity and mortality. A novel multiepitope subunit vaccine is under development for the prevention of norovirus gastroenteritis and the outlook is promising. The vaccine still requires
validation to ensure its safety and effectiveness against norovirus gastroenteritis. Several norovirus vaccines are currently undergoing clinical trials with promising results. It is hoped that development of an effective norovirus vaccine will further reduce the incidence of viral gastroenteritis.

**Conclusion**

Acute viral gastroenteritis is associated with substantial morbidity in developed countries and has a significant mortality in developing countries. Norovirus has surpassed rotavirus as the most common aetiologic agent in regions where rotavirus vaccination is included in the routine childhood immunization programmes. Physicians should educate caregivers on proper personal hygiene and handwashing to prevent the faecal–oral transmission of the pathogen as well as the importance of rotavirus vaccine in the prevention of rotavirus gastroenteritis.

**Key practice points**

- The main clinical features of acute viral gastroenteritis include vomiting and diarrhoea, often accompanied by malaise, nausea, abdominal cramps, and fever.
- Diarrhoea usually lasts <7 days, improving after 1–3 days, and does not last >14 days; diarrhoea that lasts >14 days is considered chronic.
- Respiratory symptoms may occur with rotavirus infection; headache and myalgia may occur with norovirus infection.
- Rehydration therapy with fluids containing physiological concentrations of glucose and electrolytes is required to compensate for gastrointestinal losses and cover maintenance needs.
- Oral rehydration therapy is as effective as intravenous (IV) fluid therapy for rehydration for children with mild-to-moderate dehydration.
- Measurements of serum electrolytes, creatinine and glucose should only be considered in children with severe dehydration who require hospitalization and IV therapy.
- Antiemetic medications such as ondansetron can increase the success rate of oral rehydration therapy and minimize the need for IV therapy and hospitalization.
- The recommended IV dose of ondansetron is 0.1–0.5 mg/kg, with a maximum of 4 mg. The recommended oral dose of ondansetron is 2 mg for children weighing 8–15 kg, 4 mg for children weighing >15 to ≤30 kg, and 8 mg for children >30 kg. A single dose is usually sufficient but may be repeated if the child vomits within 15 minutes after administration.
- Antidiarrhoeal medications are not currently recommended in children.
- The antimicrobial nitazoxanide requires further study to be recommended for use in children.
- Proper personal hygiene and handwashing to prevent faecal to oral transmission of the pathogen is required.
- Norovirus is currently the most common cause of viral gastroenteritis in children; an effective norovirus vaccine should further reduce the incidence of viral gastroenteritis.

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