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Case Report

Severe Gastrointestinal Hemorrhage in a Child after Taking an Improper Oral Rehydration Solution

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Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Oral rehydration solution (ORS) is safe and effective for the prevention and treatment of dehydration in children. It has been commercially available as a small packaging unit that needs to be taken with a specified amount of water. Intake of incorrectly formulated ORS results in side effects, such as electrolyte imbalance and upper gastrointestinal (GI) disturbance. We experienced a case of severe GI hemorrhage from gastric and duodenal ulcers in a previously healthy child following intake of incorrectly formulated ORS. GI hemorrhage in children is often life threatening and reaching a diagnosis may be challenging. Commercially manufactured packets of powdered oral rehydration salts have been widely used and GI hemorrhage associated with an improperly diluted ORS has been rarely reported. Caution and education for proper preparation of ORS are imperative.

Keywords: World Health Organization oral rehydration solution; Gastrointestinal hemorrhage

INTRODUCTION

Oral rehydration solution (ORS) is a type of fluid therapy used to prevent and treat dehydration, which is usually administered to mitigate the effects of diarrhea. Oral rehydration therapy (ORT) has been commonly used because it is less invasive than intravenous (IV) rehydration especially in situations of management in primary care units, lack of skilled staff, or difficulty of access to veins [1].

ORS consists of modest amounts of salts. Since the World Health Organization (WHO) adopted ORS in 1978 as its primary tool to fight diarrhea, WHO recommends an ORS composition as follows: 245 mOsm/L of osmolarity with 75 mmoL/L of sodium, 65 mmoL/L of chloride, 75 mmoL/L of glucose, 20 mmoL/L of potassium, and 10 mmoL/L of citrate solution. Adding sugar to oral rehydration salts can enhance the absorption of fluid because transportation of sodium and glucose in the small intestine are coupled; glucose promotes absorption of sodium ions and water [2]. Even though the standard WHO-ORS composition could not be optimized to reduce the volume of stool and the duration of diarrhea taking into account the relatively high levels of sodium in well-nourished children, ORT has been

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considered as a safe and effective therapeutic tool globally and is widely used even at home to prevent and treat mild to moderate dehydration [3-5]. Common beverages such as juices, soda, and sports drinks are not appropriate for use as ORS, because these are relatively low in sodium concentration and high in osmolarity. Hypotonic fluid intake such as water, tea or diet sodas should also be limited in dehydrated patients. Commercially prepackaged ORS varies in osmolarity and sodium concentration, but it is generally manufactured with a composition in accordance to WHO recommendations and it needs to be dissolved in a specified amount of clean water [6].

ORT is usually safe but paralytic ileus was found to be more common in children receiving ORT than in children receiving IV rehydration [7]. Additionally, when the prepackaged salts are dissolved in a smaller amount of water than the recommended amount, severe complications may occur. High osmolarity or high salt concentrations may induce electrolyte imbalance, diarrhea or upper gastrointestinal (GI) disturbances [8,9]. However, acute GI bleeding associated with an improperly diluted ORS has been rarely reported. We experienced a case of severe GI bleeding from gastroduodenal ulcers after ingestion of improperly diluted ORS in a previously healthy child.

The case report was reviewed and approved by the Institutional Review Board of the Gyeongsang National University Hospital (GNUH 2019-12-012).

CASE REPORT

A previously healthy 5-year-old boy was transferred to our hospital because of melena and hematemesis. The child complained of periumbilical pain and vomiting four days before initial visit to our hospital, and a histamine 2 receptor (H_2) antagonist and an antispasmodic agent were administered under the impression of acute enteritis. Powdered oral rehydration salts was also prescribed at a private clinic because of mild dehydration one day before the visit. Abdominal cramps and hematemesis occurred in two hours after taking ORS at home and the child was admitted at a private hospital. The medical history was unremarkable except that *Helicobacter pylori* infection was diagnosed in the mother of the child a few months ago. The vital signs at the first hospital were relatively stable and the hemoglobin level was 11.5 g/dL. However, the child was transferred to our hospital because of recurrent hematemesis, development of melena, and dizziness. Initial vital signs in our hospital were as follows: blood pressure, 104/66 mmHg; heart rate, 133/minutes; respiratory rate, 22/minutes; and body temperature, 36.8°C. The child looked acutely ill and dehydrated. Anemic conjunctivae and pale, dried lips were also noted. Chest auscultation revealed clear breath sounds and tachycardia. Abdominal examination revealed epigastric tenderness and rigidity. There was no hepatomegaly or splenomegaly. Pale skin without purpura or rash was noted. Mental status was alert. Abdominal X-ray was unremarkable, but abdominal computed tomography (CT), performed because of abdominal rigidity, showed duodenal and gastric wall thickening. Complete blood cell counts were, hemoglobin, 6.9 g/dL; white blood cell count, 12,970/mm^3; and platelet count, 384,000/mm^3. Among the blood coagulation tests, prothrombin time, activated partial thrombin time, and international normalized ratio were 15.4 (reference range: 11.9–14.3) s, 31.1 (29.1–43.5) s, and 1.20, respectively. Biochemical laboratory analyses were performed and the results were as follows: sodium, 130.0 mmoL/L (135–145); potassium, 4.4 mmoL/L (3.3–5.1); chloride, 93 mmoL/L; serum osmolarity, 272 mOsm/L (276–300); aspartate aminotransferase, 17 U/L (15–50), and alanine aminotransferase, 6 U/L(5–45). Urinary blood

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and red blood cells were negative. Stool wet smear and culture were unremarkable but occult blood in stool was positive (432.5 ng/mL, 0–12.0).

Transfusion of packed red blood cells, octreotide and a proton pump inhibitor were promptly initiated after exclusion of surgical abdomen. Gastroduodenofibroscopy was performed to identify the cause of melena and hematemesis, which revealed linear ulcers and scattered submucosal hemorrhages in the prepyloric area of stomach, and large circular ulcers in the first and second portions of the duodenum. The duodenal ulcers were along the folds. The mucosal margin of the ulcers was distinct and easily friable (**Fig. 1**). Pathologic examination showed ulcer debris, gastritis, and active duodenitis (**Fig. 2**). Serologic test for *H. pylori* immunoglobulin G and M, and rapid urease test were negative. *H. pylori* was also not detected on pathologic examination using Giemsa stain (**Fig. 2**). Additionally, there was no evidence of vasculitis on pathologic examination (**Fig. 2**). Serum gastrin level was 28.5 pg/mL (13–115). After the results were reported, the mother recalled that a packet of ORS was reconstituted with a lesser amount of water (≈50 mL) than the instructed amount on the manual (200 mL) when the aggravation of abdominal pain and hematemesis occurred. The ORS reconstituted in 50 ml of water had higher osmolarity (992 msom/kg) and higher concentrations of sodium (176.5 mEq/L), potassium (81.8 mEq/L), glucose (9,451 mg/dL), and citrate (122.6 mEq/L) compared with the ORS reconstituted in 200 mL of water (**Table 1**). The abdominal pain was resolved promptly and melena disappeared in two days after treatment was initiated. The

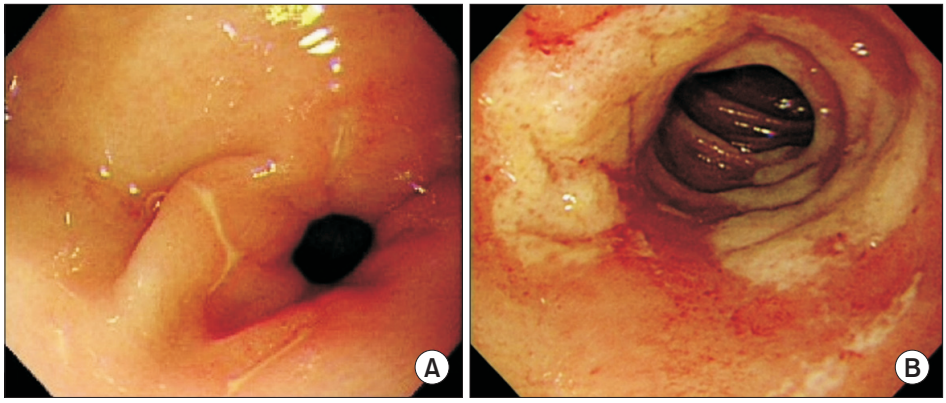

Fig. 1. Endoscopic examination showed (A) linear ulcers in the gastric pre-pyloric area and (B) circular ulcers with distinct margins and mucosal friability in the first and second portions of the duodenum. No active bleeding or exposed vessels were observed.

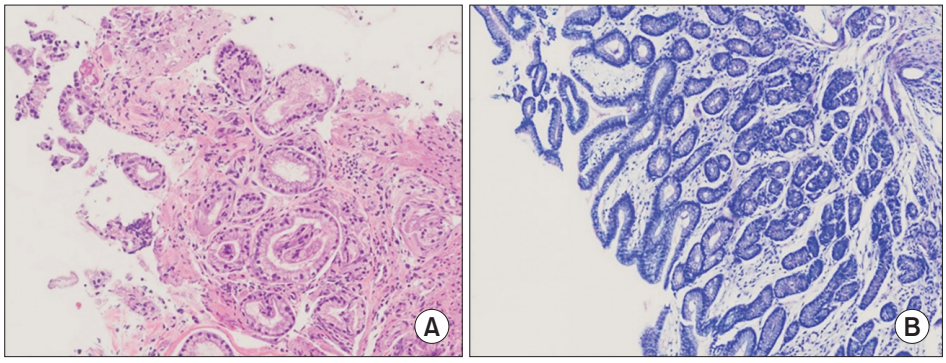

Fig. 2. Pathologic examination showed (A) ulcer debris and chronic active duodenitis (hematoxylin and eosin stain, ×400) and (B) no evidence of *Helicobacter pylori* infection (Giemsa stain, ×400).

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Table 1. Chemical analysis of oral rehydration salts reconstituted with water

Composition of salts	Amount of water used for reconstitution (mL)	
	50	200
pH	6.8	7
Osmolarity (mOsm/kg)	992	244
Na (mEq/L)	176.5	42.5
K (mEq/L)	81.8	18.6
Cl (mEq/L)	134.3	27.6
Glucose (mg/dL)	9,451	2,533
Citric acid (mEq/L)	122.6	28.5

Chemical analysis was performed using the Cobas 8000 c702 Chemistry Autoanalyzer (Roche Diagnostics System, Basel, Switzerland).

child was discharged with good general condition after eight days of hospital stay. He has been in good general condition during the last six months.

DISCUSSION

Inflammation of the gastric and duodenal mucosa in children generally occur in association with a systemic condition such as head trauma, overwhelming sepsis, or as a sequelae to intake of drugs, such as non-steroidal anti-inflammatory agents. Gastroduodenal ulcer may also occur in specific conditions, such as Zollinger-Ellison syndrome, Crohn's disease, Henoch-Schonlein purpura, and *H. pylori* infection [10]. In our case, severe GI bleeding occurred due to gastroduodenal ulcers and we investigated the cause of bleeding. Initially, *H. pylori* infection was suspected as a cause of ulcers because of family history. However, there was no evidence of *H. pylori* infection based on the results of several non-invasive and invasive tests. Next, Henoch-Schonlein purpura was considered as a possible cause of abdominal cramps and GI bleeding at this age. However, there was no history of skin lesions, arthralgia, and urinary abnormality or pathologic evidence of vasculitis.

The patient was previously healthy and the drugs prescribed at the first hospital were an H_2 antagonist and an antispasmodic agent. However, these drugs are generally not known to be associated with GI hemorrhage. Intact esophageal mucosa, several erosions and blood clots in gastric pre-pyloric area, and circular ulcers in duodenum were revealed by endoscopic examination. The appearances led to a suspicion of ingested chemical injury [11]. Therefore, we measured and compared the concentrations and osmolarity of ORS according to the amount of water used for reconstitution. A packet of oral rehydration salts was dissolved in 50 mL of water as the child's mother did and another packet was dissolved in 200 mL of water as per instruction on the ORS packet. We analyzed pH, osmolarity, and concentrations of Na, K, Cl, glucose, and citric acid in both samples of ORS. The osmolarity and citric acid concentration of the ORS reconstituted in 50 mL of water were approximately four times higher than the ORS reconstituted in 200 mL of water (**Table 1**).

The osmolarity of commercially distributed citrus juice was 327–1,174, soft drink 26–817 (Pepsi 716 [Pepsi Co. Inc., Purchase, NY, USA], Coca-Cola 695 [Coca-Cola Co., Atlanta, GA, USA]), and regular milk 282 mOsm/kg [12,13]. Hence, GI bleeding in this case could not be explained by the high osmolarity of the solution alone, even though high osmolarity could irritate the intestinal mucosa. Sodium citrate and citric acid may cause abdominal or epigastric soreness or pain, nausea, vomiting, diarrhea, black stools, and sometimes bloody vomiting [9]. Previously, esophageal variceal bleeding in patients with portal hypertension

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has been reported in citric acid intoxication [14] and oral administration of potassium citrate has been recommended with caution in a patient with upper GI wall disease because potassium citrate aggravated ulcer and gastritis [15]. It is unclear how citric acid triggers severe GI bleeding, but salivary response to stimulation with citric acid has been suspected to increase histamine-stimulated gastric acid secretion [16]. In the present case, the child's mother prepared the solution with a higher concentration than recommended. Hence, the higher concentration of citric acid may be attributed for the GI hemorrhage in this case.

ORT has been widely used to prevent or treat mild-to-moderate dehydration, even at home because ORS has often been proclaimed as an important therapeutic advance, and has been demonstrated to be safe and efficacious in adults and young children with enterotoxin-mediated diarrhea, such as enterotoxigenic *Escherichia coli* diarrhea, and cholera [4,17]. Nevertheless, side effects of ORS has rarely been reported except paralytic ileus [7]. Two cases of hypernatremia caused by inadequate dilution of prepackaged salts have been reported in India. The previous cases occurred because of confusion arising from varying prepackaged doses of oral rehydration salts [8]. However, GI bleeding associated with ORT in children has been rarely reported. To the best of our knowledge, till date this is the first case of severe GI bleeding related to improperly diluted ORT in a child.

Thus, it is important that prepackaged powdered ORS is diluted with the instructed amount of water. Improperly diluted ORS with abnormally high concentration has high osmolarity and high concentration of salts, and it may lead to electrolyte imbalance and intestinal mucosal injury causing GI bleeding as in our case. Proper and intensive education, when ORT is initiated at home, is necessary. Therefore, pediatricians and pharmacists are expected to explain proper method of reconstitution of ORS and the side effects of ORT to patients receiving the same.

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