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PERINATAL/NEONATAL CASE PRESENTATION

Necrotizing enterocolitis in a 850 gram infant receiving sorbitol-free sodium polystyrene sulfonate (Kayexalate): clinical and histopathologic findings

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We report a 27-week, 850 g infant with severe *Streptococcus* group B sepsis and life-threatening hyperkalemia due to progressive anuria. On the fourth day of life, after he failed treatment with diuretics, salbutamol, insulin, calcium gluconate and sodium bicarbonate, he was treated with sorbitol-free Kayexalate enemas. Potassium level slowly decreased from 9.2 mmol/l to normal level along with a recovery of normal urine output. On the 11th day of life, clinical and radiological signs of a perforated necrotizing enterocolitis (NEC) occurred and the patient required surgical intestinal resection. Histologic examination of the ileum specimen revealed areas of necrosis with fibrosis and giant cell reaction to a nonpolarizable material consistent with sodium polystyrene sulfonate. Usually, Kayexalate is suspended in hyperosmolar sorbitol solutions and the elevated osmolarity seems to be responsible for hemorrhagic colitis, transmural necrosis and definitely NEC. Our case report shows that Kayexalate *per se*, and not necessarily suspended in sorbitol, can lead to gastrointestinal tract complications and NEC in preterm infants.
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Introduction

Necrotizing enterocolitis (NEC) is a severe gastrointestinal disease that can be lethal for preterm infants. The causes of NEC are not well defined and many have been suggested (e.g. infection, local ischemia, poor host protective mechanisms).[1] Sodium polystyrene sulfonate (SPS) (Kayexalate) is a sodium-potassium cation-exchange resin that can be administered in hyperkalemia, both orally and rectally.[2] Rectal SPS is commonly suspended in 20 to 25% sorbitol to prevent intestinal obstruction. However, this concentration maybe harmful to the intestinal mucosa of very low-birth-weight infants and, as a matter of fact, some cases of NEC secondary to sorbitol-suspended SPS enemas have been reported.[3–6] In some case series, it has been suggested that SPS prepared in water or normal saline may be safe for preterm infants.[4] We report a case of a preterm infant who developed NEC following sorbitol-free SPS enemas for severe hyperkalemia.

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Case report

This male infant was born at 27 weeks of gestation with cesarean section due to twin pregnancy and maternal fever. Birth weight was 850 g and APGAR scores were 7 and 9 at 1 and 5 min of life, respectively. After birth, he was intubated and received surfactant. On the third day of life, a severe *Streptococcus* group B sepsis was documented and the patient developed progressive renal failure (maximum serum creatinine level of 2.85 mg/dl and maximum serum blood urea nitrogen level of 79.9 mg/dl), anuria and severe hyperkalemia with maximum central arterial serum potassium level of 9.2 mmol/l. He failed treatment with salbutamol, furosemide, insulin, sodium bicarbonate and calcium gluconate and, over 24 h, he started to show severe bradycardia, peaked T-waves and widened QRS complexes on the electrocardiogram, and pheripheral SpO_2 <50%. Therefore, after having considered the risk-benefit ratio, treatment with sorbitol-free Kayexalate enemas was started on the fourth day of life. SPS was suspended in water and was given every 2 h rectally via a five french nasogastric tube inserted 1–2 cm into the rectum and injected slowly via syringe, with the buttocks together, at a dose of 1 g/kg (0.85 g), for a total of 6.8 g over 24 h. We kept treatment with insulin, calcium gluconate and furosemide as well. After 8 doses of SPS, hyperkalemia and anuria resolved, and urine output, creatinine and blood urea nitrogen levels reached normal levels. Although the infant was not fed since birth, a bluish, firm distended abdomen was noted in the following days. At 8 days of life, clinical and radiological signs of perforated NEC occurred and a local drainage was inserted. At 12 days of life, he underwent a surgical resection of 3 cm of the ileum and an ileostomy was created. The histological examination of the ileum specimen showed multiple areas of

trans-mural necrosis, whereas the lumen showed basophilic and Zihel–Neelsen stain positive angulated crystals surrounded by fibrinoid and giant cells exudates (Figure 1). These findings were consistent with SPS crystals. In the following weeks, the patient improved gradually and was weaned completely from the mechanical ventilation. He started enteral feeds a week after surgery, and re-anastomosis was performed at 2 months of age. The infant was discharged at the age of 4 months.

Discussion

We have presented a case of NEC in a preterm infant affected by severe hyperkalemia and treated with SPS not suspended in sorbitol.

SPS is a cation-exchange resin, which may be administered either orally or rectally. In very-low-birth-weight infants, it is commonly used as a rectal enema for treatment of hyperkalemia.[7]

In the early use of SPS, the resin was suspended in water. As some patients suffered from colonic impaction and constipation,[8–11] the resin was then suspended in hypertonic sorbitol to promote an osmotic diarrhoea. However, following cases of colonic perforation associated to SPS suspended in sorbitol have been documented[3,4,12] and clinicians started to warn on its use when suspended in a hypertonic solution. Moreover, in 1987, Lillemoe *et al*.[13] administered isovolemic enemas of normal saline, SPS alone, sorbitol alone and SPS suspended in sorbitol to groups of rats. The rats showed no colonic pathology in the control, normal saline, SPS alone groups, whereas more than 60% of rats showed colonic necrosis in the SPS plus sorbitol, and sorbitol alone group. In 1995, Milley *et al*.[4] published a retrospective study on the association of hematochezia with the use of hypertonic SPS enemas in premature infants. They found no association between the magnitude or number of SPS doses and the onset of bleeding. Also, there was no association between the concentration of sorbitol in the suspension and the bleedings. Ohlsson and Hosking[10] reviewed

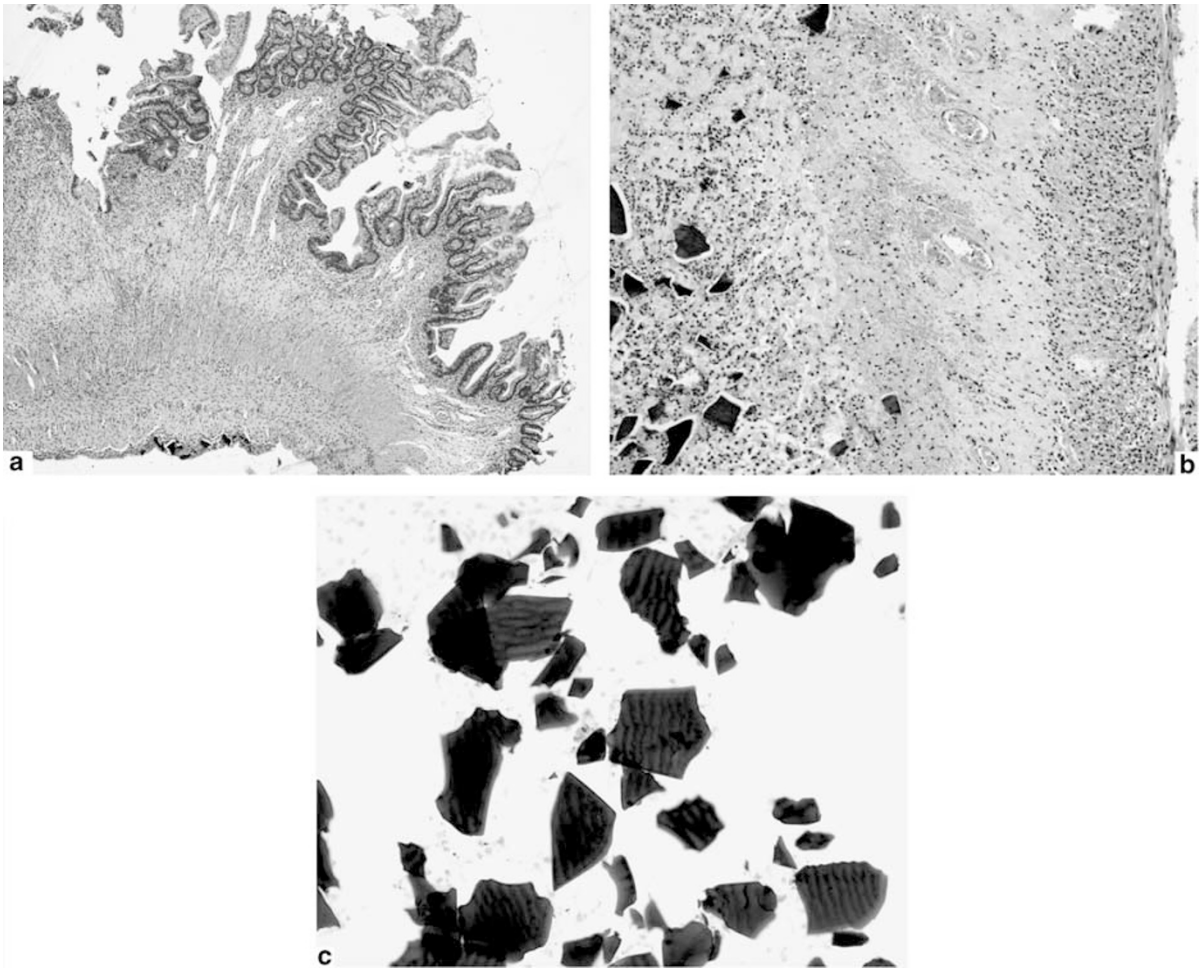

Figure 1 Kayexalate crystals in histologic sections. (**a**) Section of the intestine wall: basophilic Kayexalate crystals are present under the sierosa (hematoxylin–eosin stain). (**b**) Numerous Kayexalate crystals within mucosal and submucosal necrosis of the intestine wall specimen (hematoxylin–eosin stain). (**c**) Classic mosaic pattern of Kayexalate crystals (Zihel–Neelsen stain).

the use of SPS given orally, rectally, suspended in water or in sorbitol in 10 infants weighing less than 1000 g. In this study, it seemed that SPS suspended in water could be safely used, as none of the patients who received rectal SPS suspended in water were noted to have hematochezia. Same findings are available in adults, where sorbitol seems to be the causing agent of the necrosis of the gastrointestinal tract.[14] Besides bleeding, hypernatremia has been also associated with the use of SPS in extremely low-birth-weight infants.[15]

Although our patient received rectal SPS suspended in water and not in hypertonic sorbitol, Kayexalate crystals within mucosal and submucosal necrosis of the intestine wall specimen were demonstrated. No evidence of colonic bezoar was shown in the histologic specimen, ruling out the possibility that a colonic impaction could be the trigger for the following necrosis and perforation of the intestinal wall. In our patient, the severe *Streptococcus* group B sepsis could have injured his immature gut, jeopardizing its mucosal and submucosal integrity. However, we caution against the use of SPS *per se*, not necessarily suspended in hypertonic solution, and we suspect that this issue may not have been reported in earlier small studies. Studies with higher number of patients could be useful to address this issue.

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