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Complications following oral administration of exchange resins in extremely low-birth-weight infants

A. Ohlsson and M. Hosking

University of Toronto Perinatal Complex, Regional Perinatal Unit, Women's College Hospital, 76 Grenville Street, Toronto, Ontario M5S 1B2, Canada

Abstract. Complications of the oral use of sodium polystyrene sulfonate and calcium polystyrene sulfonate are reported in five extremely low-birth-weight infants in which exchange resins were used to treat hyperkalemia. Radio opaque masses outlining the stomach were seen in all infants and could be palpated in the left upper quadrant of the abdomen. In two infants, at autopsy the palpable mass could be identified as a solid chalk-like concretion outlining the stomach. X-ray diffraction studies identified the material as Brushite. Administration of exchange resins by the gastric route should be avoided in the treatment of hyperkalemia in critically sick, extremely low-birth-weight infants.

Key words: Chelating agents – Hyperkalemia – Neonate – Complications

Introduction

The incidence of hyperkalemia causing cardiac arrhythmias in extremely low-birth-weight infants is not known. In our own unit between 1980–1984 12.4% (11 of 89) of all early neonatal deaths in infants with a birth weight less than 1000 g were associated with cardiac arrhythmias and hyperkalemia. Sodium polystyrene sulfonate (SPS) (Kayexalate™) or calcium polystyrene sulfonate (CPS) dissolved in water, 10% dextrose in water or sorbitol currently are recommended in the treatment of hyperkalemia (serum potassium > 7.0 mmol/l) either by the oral or the rectal route [1–6].

Following oral administration, sodium is released from the resin in exchange for hydrogen ions in the acid environment of the stomach. As the resin passes through the intestines, hydrogen cations exchange with those cations that are in greater concentrations and the cationically modified resin is excreted in the feces. Because of the relatively high concentration of potassium present in the large intestine, conversion of the resin to the potassium form occurs principally at this site [6]. SPS has successfully been used orally in the treatment of a term infant with hyperkalemia without any reported side effects [8]. Aspiration of this material as a terminal event has occurred in an infant, who suffered neonatal asphyxia and meconium aspiration [7]. Sherman et al. [10] reported two cases of neonatal bowel opacification on abdominal radiographs secondary to oral and rectal administration of SPS. Apart from those reports, we were not able to locate any studies regarding the beneficial or adverse effects of the use of exchange resins in neonates in the current literature. We recently recognized, during a period of less than a week, serious complications from the oral use of exchange resins in the treatment of hyperkalemia in five critically sick neonates. This prompted us to review the charts of all neonates who had received exchange resins by the oral route during the preceding 6 months, and to present the following report.

Offprint requests to: A. Ohlsson

Abbreviations: SPS = sodium polystyrene sulphonate; CPS = calcium polystyrene sulphonate

Case reports

During a 6-month period eight neonates received multiple oral doses of SPS or CPS at 1 g/kg per dose as a suspension in water. Five infants developed complications and three did not. Two neonates received the same dose twice rectally without complications. Table 1 summarizes the pertinent clinical findings of those five infants with complications following the use of exchange resin (Group A), those three without (Group B) as well as two previously reported cases (Group C) [10]. Table 2 shows laboratory and electrocardiographic findings in Groups A and B. All infants were ventilated, those in group A often requiring dopamine and/or tolazoline infusion and increased mean air way pressure to maintain adequate perfusion and gas exchange. Radiographs of the abdomen showed similar dense opacifications in the stomach and decreased amount of air in the intestinal system in all five patients in group A (Fig. 1). The roentgenograms in group B were normal. All infants weighed less than 1000 g and were of ≤ 26 weeks gestation.

At the time of treatment with exchange resins the serum levels of potassium, urea and creatinine, and the frequency and type of arrhythmias were similar between the groups (Table 2). Gastric fluid was below pH 5 in infants of both groups. Group B demonstrated no evidence of intestinal hypomotility as indicated by early and regular meconium passage. Neonates in both groups had passed meconium by 48 h, however, neonates in group A passed meconium later and less frequently than neonates in group B, who passed meconium at least every 8 h. SPS and CPS exchange resins were given for a serum potassium level of greater than 7.0 mmol/l, as we have noted arrhythmias occurring at that level. A dose of 1 g/kg in 3 ml water by nasogastric tube or per rectum was used. Abdominal masses were first noted by palpation in patients 1 and 3, by radiographs in patients 2 and 4 and by the inability to re-

Table 1. Case reports. HMD = Hyaline membrane disease; PFC = Persistent fetal circulation; IVH = Intraventricular hemorrhage; NG = Nasogastric tube; PIE = Pulmonary interstitial emphysema; PH = pulmonary hypoplasia; MIO = Multiple intestinal obstruction; PR = Per rectum; PDA = Patent ductus arteriosus

Case no.	Sex	BWT (g)	Gest. age (week)	Diagnosis	Urine output (ml/kg/h)		Age meco-nium passed	Resin				Complication and time of X-ray findings	Outcome
					0–12 h	12–24 h		Type	Total no.	Doses NG	Via PR		
Group A													
1	M	980	26⅘	HMD PFC	0.5	1.5	40	SPS	2	2	0	Abdominal mass + distention (60 h)	Alive. Normal
2	F	760	25	HMD PIE PFC	0	0.8	35	CPS	2	2	0	Abdominal mass (30 h)	Died at 35 h (HMD)
3	M	680	25	HMD	0	1.0	42	CPS	2	1	1	Abdominal mass (23 h)	Died at 53 h (Grade IV IVH)
4	M	910	25	PH HMD	0.5	1.5	32	SPS	6	3	3	Perforation with intra-abdominal resin (64 h)	Died at 6 months (BPD, MIO)
5	F	590	25	HMD PH PIE	0.2	1.7	40	SPS CPS	3 5	7	1	NG imbedded in gastric mass (48 h)	Alive. Normal
Group B													
6	F	630	25	Sepsis	2	2	22	SPS	6	6	0	None	Alive. Normal
7	M	730	26	Mild HMD	2	2	24	SPS	4	3	1	Heavily coated NG tube	Alive. Normal
8	F	990	25	Mild HMD	2	2	26	SPS	6	4	2	None	Alive. Normal
Group C [9]													
9	F	652	24	HMD	?	?	24 h	SPS		1 g/ q 4 h	1 g	Concretion in stomach (4 days)	Died at 11 days Cardiac arrest
10	F	630	?	Hypothermia, shock, PDA	?	?	?	SPS		0.6 g/ q 6 h		Opacification of stomach and bowel (2 days)	Died at 33 days cardiorespiratory insult

Table 2. Case reports. Laboratory and electrocardiography findings at the age when exchange resin was first given. VT = Ventricular tachycardia; JR = junctional rhythm with aberrant conduction

	Age (h)	Serum K^+ (mmol/l)	Urea (mmol/l)	Creatinine (mmol/l)	Electrocardiogram
Group A					
1	53	7.4	13.3	159	Normal
2	13	8.3	8.8	158	Peaked T waves
3	14	9.2	7.8	106	VT
4	20	10.8	7.5	115	VT
5	11	8.9	20.5	191	VT/JR
Group B					
6	20	8.6	9.0	115	VT
7	18	7.8	12.0	120	Peaked T waves
8	22	8.6	8.0	110	Peaked T waves

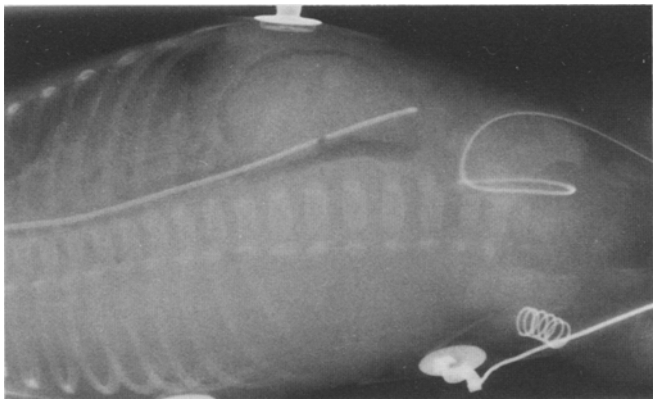

Fig. 1. Case 5. Radiograph, with air as a contrast medium, showing a large radio opaque mass in the stomach with the nasogastric tube embedded inside it

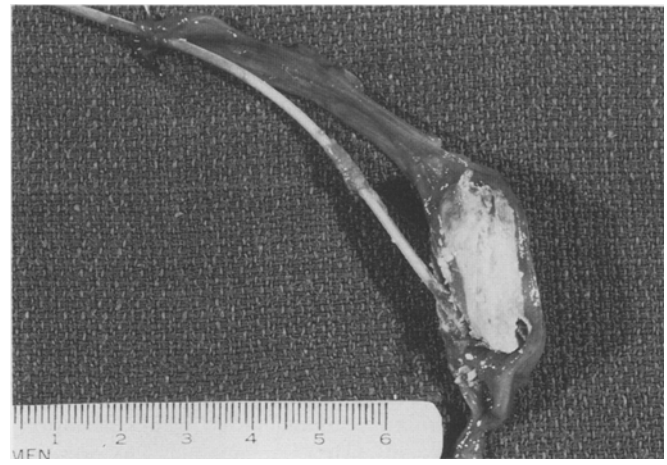

Fig. 2. Case 2. Chalk-like mass outlining the whole stomach after opening of the stomach at autopsy

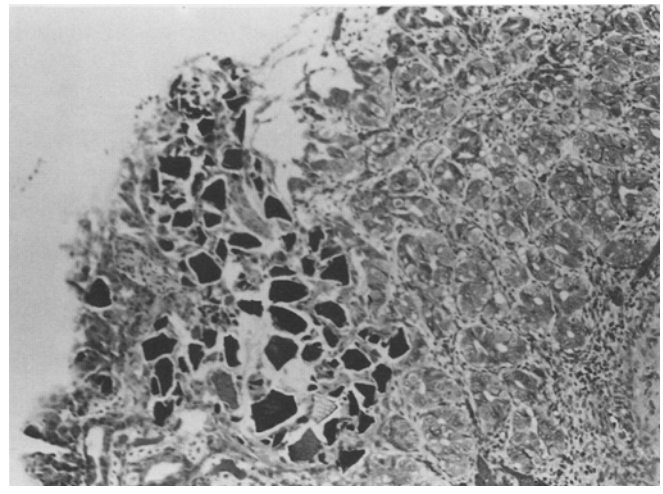

Fig. 3. Collection of crystalline material embedded in folds of the gastric mucosa (55×)

move the nasogastric tube associated with a palpable left upper quadrant mass in patient 5. Transient gastric obstruction occurred only in patient 1. The overall clinical outcome seemed not to be affected adversely by the presence of the resin concretions. In patient 4, who developed necrotizing enterocolitis and bowel perforation, the degree to which the presence of exchange resin influenced these complications is uncertain. Those infants (patient 4 and 5), who developed the largest bezoars and patient 5, who had the nasogastric tube embedded in the bezoar, had their nasogastric tubes left untouched without lavage or removal for 16 h at a stretch. Though heavy coating of the nasogastric tube was seen in both groups, the nasogasatric tubes of group B had been lavaged or changed at least every 12 h.

In patient 5 it was possible to remove the nasogastric tube after sliding the tubing of a De Lee trap over the nasogastric tube to anchor the gastric mass. The mass subsequently broke into several pieces which were then readily dissolved by saline lavage.

Autopsy results in patients 2 and 3 correlated well with the clinical and radiographic findings. In both neonates, 1×1.5 cm gastric masses were found that were encased in mucus membranes (Figs. 2, 3). After disruption of the membrane, pieces of the bezoars dissolved readily in water, normal saline, sodium bicarbonate and in an acid, pH 4.8.

Microscopic examination of the gastric mucosa in cases 2 and 3 demonstrated collections of crystalline material embedded in folds of gastric mucosa and the bezoars consisted of the same material intermingled with strands of mucin. The microscopic appearance of resins was identical to one earlier report [7]. X-ray diffraction studies revealed rings with d-spacings characteristic of $CaHPO_4 \cdot 2H_2O$ (Brushite); the absence of potassium indicating that no exchange had occurred.

To determine if concretions develop in vitro, we added suspensions of CPS and SPS in water, normal saline and methyl cellulose to water, normal saline, and solutions with pH of 7.0 and 4.8. After 24 h the resins had sedimented but not formed concretions in any of the solutions and could easily be shaken into a suspension again. CPS and SPS suspended in methyl cellulose remained the most pliable sediments.

Discussion

Extremely low-birth-weight, profound immaturity (< 26 weeks gestation), and hyperkalemia with arrhythmia were

conditions shared by all neonates in both the complicated and uncomplicated group, but bowel hypomotility occurred only in the complicated group. Hyperkalemia was probably secondary to several factors, including bruising from delivery, immature renal function and cell injury from perinatal asphyxia. As modes of therapy, hemodialysis or peritoneal dialysis are impractical for technical reasons, but Setzer et al. [9] have reported on the effectiveness of exchange transfusion using washed red blood cells for the treatment of severe hyperkalemia. Intravenous therapy with calcium, bicarbonate or a combination of insulin and glucose results in a transient shift of potassium into the cells. The only currently available pharmacological method of removing potassium from the body is oral or rectal use of exchange resin.

In extremely premature infants (<26 weeks gestation) hyperkalemia can present early as arrhythmia. The presence of arrhythmia is a poor prognostic sign, with many infants succumbing within the next 24–36 h despite treatment. Because of this we aggressively treat a rising serum potassium level (>7.0 mmol/l) already present in the first 24 h of life, especially when associated with oliguria as in group A. Administration of rectal exchange resin appears to retard the rate of serum potassium rise. However, it is the improved clinical and physiological state that ultimately leads to the resolution of hyperkalemia.

We postulate that inspissation occurs only in critically ill, extremely premature infants with a functional ileus, who are treated for hyperkalemia with exchange resins by the oral route. Gastric stasis allows a mucous membrane to form around the bezoar. The membrane protects the bezoar from the gastric contents and the exchange of ions is prevented. X-ray diffraction studies in two of our patients indicated that no exchange had occurred in the stomach. Sherman et al. [10] reported on complications from SPS in two extremely low-birthweight infants (Table 1). They speculated that since an infant on a respirator is hypoactive, this hypoactivity combined with bowel immaturity and hypomotility contributes to the precipitation of SPS in the stomach. They did not perform autopsies. Our findings confirm this hypothesis as all infants forming concretions had a functional ileus and passed meconium much later compared to the three infants that did not develop concretions. Even if gastric motility returns, the concretion is protected from the gastric contents by the mucous membrane. In vitro no mucous membrane was formed, and the resin that had sedimented could easily be shaken into a suspension again. Inspissation occurred equally with both SPS and CPS and neither resin appeared directly to diminish bowel mobility. The total number of oral doses was not a primary determinant of inspissation, as the number of oral doses per patient was higher in group B. Our choice of water as a solvant may have added to the risk of inspissation, however, the hypertonicity of sorbitol precluded its use as a suspension medium, as is recommended for older patients. As the conditions of the infants improved, gastric intestinal motility increased allowing for the mass finally to break up, with larger remaining pellets possibly causing a transient gastric outlet obstruction, as in case 1.

Oral exchange resins have a place in the treatment of hyperkalemia in more mature neonates, who have normal gastrointestinal motility. Our less sick, extremely low-birthweight, neonates demonstrated that oral administration of resin is not contraindicated, as long as they have bowel movements every 12 h. If oral exchange resins are used in more mature neonates frequent manual palpation will allow early detection of any bezoar formation. Although not proven, using a smaller dose (i.e. 0.5 g/kg) at more frequent intervals may be beneficial. Prophylactic laxative therapy is recommended with the use of exchange resin [6], but is unlikely to be applicable in the very immature infants. An in vitro suspension of SPS or CPS in methylcellulose remained more formable than the others, and possibly could prevent the formation of a solid mass. It remains to be proven if this combination is effective in decreasing the level of serum potassium. Even if concretions do develop, with clinical improvement and presumed associated improved gastric motility, the gastric bezoars seem to disintegrate. Any gastric outlet obstruction from fragments should be treated with lavage and intermittent nasogastric suction with an expectation of complete resolution.

As the major location for exchange by these resins is the large intestine, oral administration of resin to critically ill, extremely immature neonates (<26 weeks gestation) with a proven or suspected functional ileus should be avoided. Hyperkalemia in these neonates should be treated with either rectal exchange resins and/or exchange transfusion with washed red cells [9].

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