

## CASE REPORT

# Severe hyperphosphataemia and metabolic acidosis after administration of phosphate-containing enema in a 10-year-old girl – case report and review of literature

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## ABSTRACT

Constipation is among the most common complaints in GPs' offices, affecting over 10% of children reporting to the doctor [1]. Due to the COVID-19 pandemic, access to specialist care has become difficult, which has led to neglect of diagnosis and managing chronic diseases. We present a case of a 10-year-old girl admitted to the emergency department (ED) with symptoms of severe constipation and abdominal pain and a history of ongoing constipation and faecal soiling for 6 months. In the ED she was given a sodium-phosphate enema twice. After a few hours she developed life-threatening hyperphosphataemia, hypocalcaemia, and metabolic acidosis. The presented patient presents an example of severe, chronic, and improperly treated constipation with an extremely rare side effect of a sodium-phosphate enema. It is important to underline that monitoring after the procedure and quick and proper treatment, if the mentioned effect occurs, can save the patient's life.

## KEY WORDS:

**children, telemedicine, constipation, hyperphosphataemia, enema.**

## INTRODUCTION

Constipation is one of 10 most common problems encountered by general paediatricians [2]. There are many factors predisposing to constipation. Among the most frequent are low socioeconomic status, insufficient daily fibre and fluid intake, immobility, and fear of painful defecation manifested as deliberate withholding of stool masses. The genetic background can also be the root of the problem, for example in Hirschsprung's disease [3, 4]. The main symptoms are infrequent bowel evacuation, large stools, and difficult or painful defecation, although soiling may also be observed. The incontinence

of the stool is frequently mistaken for diarrhoea. Parental concern is often high. In prevention of chronic constipation, the non-pharmacological treatment can be launched, including a high-fibre diet, increased fluid intake, education of parents and child, toilet training, regular physical activity, biofeedback, and psychological consultation [5, 6]. In long-term conditions clinicians examine paediatric patients, searching for abnormalities in gastrointestinal, metabolic, endocrine, or nervous systems, and if there is no pathology, they diagnose them with functional constipation according to the ROME IV criteria [7].

The pharmacological approach is based on various substances administered orally or rectally and on main-

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tenance therapy [8]. Both oral laxatives, such as mineral oils, high-molecular-weight macrogols (PEG 3350, PEG 4000), lactulose, and lactitol, and rectal treatments including glycerol, bisacodyl suppositories, phosphate, saline, or mineral oil enemas have been shown to be effective and are considered safe. Conversely, soap and water or magnesium enemas should be avoided, and there have been several fatal hypermagnesaemia cases reported in the medical literature [2, 9]. Although the efficiency of oral laxatives and enemas has been proven to be equal, rectal laxatives are preferred due to quick relief of symptoms [10].

Phosphate enema (commercially known as Rectanal®, Enema® in Poland, and Fleet®, Travad®, Fletcher's® in Western countries) contains osmotically active substances: sodium acid phosphate and sodium phosphate. It prevents water reabsorption in the intestine lumen, increasing the volume of the stool, which stimulates rectal motility. Rectal sodium phosphate is extemporaneously prescribed in constipation, before endoscopic examination, surgery, or labour. There are numerous contraindications such as bowel obstruction or perforation, acute kidney failure, appendicitis, hypertension, and congestive heart failure. According to the manufacturer's advice, it should not be used in young children (< 3 years) and dehydrated patients [11].

Here we present a case of a 10-year-old patient who developed a life threatening hyperphosphataemia as an adverse effect to sodium-phosphate enema administration, and we summarise the findings on other similar cases in the medical literature.

## CASE REPORT

A 10-year-old girl was admitted to the emergency department (ED) with symptoms of severe constipation and abdominal pain. She complained of loss of appetite, nausea, and vomiting for the last couple of days. She reported passing a large stool with effort and pain every 3 weeks. On admission she was alert and awake. Her vital signs were as follows: heart rate 113 beats per minute; respiratory rate 18 per minute; oxygen saturation 97%; and blood pressure 119/80 mm Hg. Clinical examination revealed abdominal rigidity, muscle guarding, and palpa-

ble resistance caused by faecal masses. Her mucous membranes were dry and aphthae were present. Laboratory tests (electrolytes and blood gas analysis) made shortly after admission did not reveal any abnormalities.

She reported constipation and faecal soiling for about 6 months before being admitted to the hospital. During that time, she was treated by her GP (using telemedicine technology because of the COVID-19 pandemic). In the course of her previous visits encopresis and faecal soiling (resulting from chronic constipation) were misdiagnosed as diarrhoea, and she was treated with antidiarrhoeals. There was one episode of lower gastrointestinal bleeding. Her last bowel movement was 3 weeks before the admission. Her past medical history included asthma, regularly treated with  $\beta$ -2 adrenergic receptor agonists inhalers. The child's development was normal, and in her medical records no potential underlying cause of constipation could be found.

One hour later, because of faecal masses in her abdomen, she was given sodium-phosphate enemas twice (in doses of 100 ml and 150 ml) – both with poor effect. During administration of laxatives she gave a large amount of loose stool and vomited. Shortly after that she became lethargic, weak, and confused. Tetany, dehydration, anisocoria, and tachycardia (130 BPM) appeared. Laboratory results showed severe electrolyte abnormalities. She developed hyperphosphataemia (9.35 mmol/l), hypocalcaemia (1.41 mmol/l), hyperkalaemia (6.1 mmol/l), and hypernatraemia (156 mmol/l). Moreover, blood gas analysis revealed decompensated metabolic acidosis with pH – 7.16,  $pCO_2$  – 38 mm Hg,  $pO_2$  – 148 mm Hg, and BE – (–) 14.4 mmol/l. Of note were the levels of magnesium (0.92 mmol/l) and glucose (147 mg/dl). The total calcium level was 1.18 mmol/l. Table 1 and Table 2 shows laboratory results of hyperphosphatemia and metabolic acidosis as they were developing. Levels of serum creatinine (0.68 mg/dl) were correct. Inflammatory markers were within the normal range at admission but started to rise after a few hours, with peak CRP (120.48 mg/l) and PCT (24.8 ng/ml) on the second day of hospitalisation.

In the ED intravenous fluid therapy was started with 650 ml of multi-electrolyte fluid and 10 ml of calcium chloride in 100 ml of 0.9% sodium chloride. Other drugs

TABLE 1. Follow-up of serum electrolytes after enema administration. (“–” – electrolyte level not determined)

mmol/l	Ref. range	Day 1 20:00	Day 1 23:00	Day 2 05:00	Day 2 13:00	Day 3 0:00	Day 3 6:21	Day 3 17:11
Sodium	135–145	156	148	145	145	132	134	140
Potassium	3.5–4.5	6.1	4.27	3.8	4.38	5.2	5.64	3.79
Calcium	2.19–2.69	1.41	1.24	–	1.49	1.74	2.28	2.01
Ionised calcium	1.12–1.32	0.29	0.45	0.61	0.72	1.06	1.35	1.26
Phosphate	1.05–1.70	–	9.35	5.93	1.88	1.33	1.1	0.63
Magnesium	0.7–0.86	0.92	0.85	1.12	0.93	0.88	0.8	0.69

Source: Patient's medical record

**TABLE 2.** Follow-up of blood gas parameters after enema administration

	Ref. range	Day 1 20:00	Day 1 23:00	Day 2 5:00	Day 2 13:00
pH	7.35–7.45	7.16	7.22	7.35	7.416
pCO <sub>2</sub> (mm Hg)	35–45	38	38.7	35	35.4
pO <sub>2</sub> (mm Hg)	80–100	64	64.1	164	77.4
SO <sub>2</sub> (%)	94–98	85	83.4	99	95.7
HCO <sub>3</sub> <sup>-</sup> (mmol/l)	21–26	13.5	15.6	19.3	22.2
BE (B) (mmol/l)	-3–3	-14.4	-11.3	-5.6	-1.7

Source: patient's medical record

included drotaverine and 500 ml of 10% glucose and 12 units of insulin R-100 ml/h i.v., due to high levels of potassium (Table 1). Later on, during her hospital stay, she underwent computed tomography of the head, which did not show any abnormalities.

Because the administration of enemas was unsuccessful, after consulting with the surgeon she was qualified for urgent manual evacuation of stool. After the procedure she was transferred to the paediatric intensive care unit. On admission to the intensive care unit (ICU), the girl's general condition was severe. She was under general anaesthesia and ventilated with a transport respirator with a gastric tube and Foley's catheter applied. Her skin was pale, and the oral mucosa was dry. Her pupils were dilated with slow reaction to light. She had a soft abdomen and vigorous peristalsis. Sat. 98%, HR 140/min, RR 130/80 mm Hg. In the ICU she was analgo-sedated, given anti-oedema drugs (mannitol 3 × 30 ml i.v., dexamethasone 4 mg i.v.), and intravenous fluid therapy (500 ml of 5% glucose + 20 ml 15% KCl + 10 ml CaCl<sub>2</sub> and 500 ml of NaCl) was applied. Other drugs included furosemide 3 × 5 mg i.v. for forced diuresis and ondansetron 4 mg i.v. to prevent nausea after the surgical procedure. The following morning, she was stable and successfully extubated. Correction of the patient's electrolyte and metabolic parameters was noticed; therefore, she was discharged from the paediatric ICU (Table 2).

## DISCUSSION

Rectal laxatives treat constipation and promote bowel evacuation before diagnostic and surgical procedures [12]. A sodium phosphate enema is widely used in paediatric and adult patients and is generally regarded as safe. The study analysing water-electrolyte complications after application of a sodium-phosphate enema before sigmoidoscopy showed a tendency towards increased concentration of phosphorus serum level, but within normal range [13]. It was confirmed in the trial that mild hyperphosphataemia after sodium phosphates enemas usually correlates

with retention time – not with dose [14]. Temporary electrolyte disturbances after enema administration in most cases are asymptomatic, and the development of hyperphosphataemic acidosis is not expected. Adverse effects occur usually only in particular circumstances. Sudden fluid loss due to the excretion of water into the intestinal lumen or vomiting combined with the intake of sodium and phosphorus can cause hypertonic dehydration and hyperphosphataemia. Following these changes, hypocalcaemia develops as a result of calcium binding [15]. Moreover, phosphorus, which is mainly absorbed in the duodenum and jejunum, may be absorbed in the colon [13]. The general cause of intoxication is associated with either increased uptake or decreased elimination of sodium and phosphorus from the patient's system.

A systematic review of 29 paediatric cases has shown that nausea, abdominal pain and distention, water-electrolyte imbalance (dehydration due to osmotic activity of the drug, hyperphosphataemia, hypocalcaemia, hypernatraemia, hypokalaemia, and metabolic acidosis), tetany, neurological manifestation, QT prolongation, bone mineralisation abnormalities, acute renal or respiratory failure, and intravascular haemolysis are in the spectrum of adverse effects of sodium-phosphate enemas. The mortality rate in the mentioned group was 13.8%, with reported higher risk of death in patients with comorbidities [16].

It is reported that a small group of patients is predisposed to phosphate enema side effects. Those at higher risk include patients with cardiac disease and reduced glomerular filtration rate (chronic or acute kidney diseases) [14]. A literature review showed that complications after enemas are also more common in children with gastroenterological conditions; for example, Hirschsprung's disease [17]. Yet, most of the reported severe adverse events were because of overdose, simultaneous admission of oral and rectal laxatives, or other contraindications [18]. Our patient presents an extremely rare case of developing typical side effects with no coexisting conditions. The diagnostic process excluded endocrinological and metabolic abnormalities. Moreover, 2 months after discharging the patient, anorectal manometry was conducted to rule out Hirschsprung's disease.

Núñez Sánchez reported a case of a generally healthy girl aged 2 years and 7 months, who had been given sodium-phosphate enema twice due to constipation. After 2 hours she presented painful hypertonia of the upper and lower extremities, and her laboratory tests showed hyperphosphataemia, hypocalcaemia, and metabolic acidosis [17].

Wason described the reaction of a 5-month-old female who was given by her mother the entire contents of Adult Fleet®. The girl suffered from neurological disturbances as well as metabolic complications. She was lethargic during admission to the hospital, and then unresponsive to pain [19]. According to up-to-date guidelines and manufacturer's advice, sodium-phosphate enemas should not be used

under the age of 3 years [11]. This information is worth sharing among clinicians worldwide in order to prevent life-threatening complications in the youngest patients.

Rectal laxatives should only be prescribed extemporaneously. Becknell described a 4-year-old male with a medical history of anorectoplasty for imperforate anus and constipation, who received sodium-phosphate enemas twice a day, 3 times a week for 8 months. On the day of admission, he presented similar symptoms to our patient. He became “weak” and unresponsive. Fifteen minutes after his regular enema administration he developed hyperphosphataemia, hypocalcaemia, and metabolic acidosis. Standard fluid resuscitation did not have the desired effect, and haemodialysis was performed [12].

The majority of presented patients suffering from adverse effects of enema were primarily dehydrated. We believe that the mucous examination and capillary refill time in hydration assessment should not be omitted while deciding on enema administration in children or in adults.

It is worth noting that some patients, including the presented 10-year-old girl, develop severe water-electrolyte disturbances in occasional treatment, while others who receive rectal laxatives repeatedly never show the symptoms. This fact raises the question of whether there are any genetic predispositions that indicate higher risk of complications associated with treatment. In fact, animal studies have shown correlation between phosphate regulation disorders and genetic changes [20]. The Ladenhauf report could be considered as to the hypothesis’ advantage because a similar pathological reaction to sodium-phosphate enema was observed in previously healthy siblings aged 5 and 2.5 for 6 months’ duration [15].

Because the adverse effects can be fatal in some cases, it is crucial to assess the hydration level of the patient before enema admission. In some cases, especially with visible dehydration, performing an ionogram should be considered. In addition, since kidney disease is one of the contraindications to the administration of enema, it is worth considering whether the level of creatinine (eGFR) should be examined before the administration. It is necessary to monitor the patient’s vital signs and condition for at least 1 hour after the supply (because the intoxication symptoms can develop rapidly) in order to quickly detect any abnormalities, establish diagnosis, and implement proper treatment. For this purpose, when disturbing symptoms appear, electrolytes, blood gas analysis, and creatinine (eGFR) should be re-examined.

The typical treatment for sodium phosphate toxicity is intravenous fluid resuscitation and administration of diuretics to increase diuresis and renal clearance of phosphate. If such therapy does not bring the expected results – a decrease in phosphorus levels and an increase in calcium levels – haemodialysis is advised. Our patient reacted to the standard treatment (in combination with manual stool evacuation), and therefore no haemodialysis

was performed. It is also worth noting that haemodialysis is a typical treatment of hyperphosphataemia in patients with chronic kidney disease [12].

Sodium-phosphate enemas are thought to be prescribed in nearly half of paediatric patients visiting an ED with symptoms of constipation. They have a proven efficiency and give early relief of symptoms [10]. Therefore, supposedly, there is no need to restrict its use – provided a few suggestions are taken into consideration before administration.

An alternative management in severe constipation is the prescription of oral laxatives, because it is less invasive and more acceptable for children. The most common oral laxative is PEG (PEG 4000, PEG 3350 +/- electrolytes) [21]. The major disadvantage of the method is delayed symptoms relief; however, it is proven to be equally effective and PEG 4000 is not associated with relevant electrolyte disturbances. In fact, in many countries high-molecular-weight macrogols represent a first-choice therapy in chronic constipation [22, 23].

It is important to acknowledge that the presented girl developed severe constipation during the pandemic of COVID-19. Many of the health centres established a phone consultation as a compromise between giving medical advice and minimising the risk of contact between mildly sick and potentially seriously ill patients [24, 25]. Conversely, giving medical advice indirectly can lead to miscommunication between the patient and doctor. The message given by the parents may not be correct; they may misinterpret the symptoms and condition of their child. On the other hand, the doctor may have a problem with receiving the message and interpret it incorrectly. This could have happened in the presented case. Our patient’s parents reported soiling to the GP who did not have a chance to examine the patient in person, which led to misdiagnosis and prescription of loperamide – an intestinal  $\mu$ -opioid receptor agonist [26] that possess anti-secretory properties and blocks intestinal sodium channels [27]. Undoubtedly, the epidemiological situation in the country delayed transferring the patient to a paediatric gastroenterologist.

## CONCLUSIONS

Sodium-phosphate enema is a standard treatment in chronic constipation, with proven efficiency. However, its adverse effects in children can result in life-threatening metabolic complications. Doctors must take into consideration examining patients before prescribing laxatives. It is obligatory to monitor the patient’s vital signs and laboratory results in search of hyperphosphataemia symptoms, and to launch fluid resuscitation or renal replacement therapy if needed. This complication is extremely rare but was repeatedly reported in the medical literature; therefore, it should be acknowledged by doctors worldwide.

## DISCLOSURE

The authors declare no conflict of interest.

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