Rectal ulcer due to Kayexalate deposition – an unusual case

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SUMMARY
Sodium polystyrene sulfonate (PSP) or Kayexalate is a cation-exchange resin, widely used in the management of hyperkalaemia due to renal disease. A rare, yet potentially dangerous, adverse event related to sodium polystyrene sulfonate use is intestinal mucosal injury, especially in the colon. The injury to the gastrointestinal mucosa can range from mild and superficial to wall necrosis and bowel perforation. The mechanism that leads to mucosal damage remains unclear. However, it is believed that sorbitol, commonly given to counteract PSP’s tendency to cause constipation, may play an important role in the development of gastrointestinal injury. Other potential risk factors are ureaemia or end-stage renal disease, hemodynamic instability, solid organ transplantation, postoperative status and concomitant opioid administration. The authors present a case of diarrhoea and haematochezia after the administration of PSP without sorbitol, in a patient with hyperkalaemia due to acute kidney injury, in the absence of other risk factors. A colonoscopy was performed and revealed a rectal ulcer which histological findings were suggestive of mucosal injury due to Kayexalate deposition. This case supports the concept that this widely used drug can itself, without sorbitol, cause injury to the gastrointestinal wall. Even though this is a rare adverse effect, the widespread use of this medication may put a large population at risk.


INTRODUCTION
Sodium polystyrene sulfonate (PSP) or Kayexalate is an ion exchange resin, composed of an insoluble structure that acts by binding to potassium ions along the digestive tract, by exchange with sodium ions, promoting its elimination. The first studies on the use of these drugs in the treatment of hyperkalaemia date back to the 1950s and are currently widely used in the treatment of hyperkalaemia secondary to renal failure1-4. The oral route is the preferred form of administration, and rectal administration is still possible when oral administration is not available. Although it is primarily used in the treatment of hyperkalaemia secondary to chronic renal disease, its relatively fast onset (2-12 hours) allows its use in acute situations, in association with other hypocalcaemia drugs5. Gastrointestinal side effects, such as nausea and constipation, are relatively frequent, and colic ulceration and/or colic necrosis is a rare but well documented complication of this therapy5-7. Concomitant administration of PSP and sor-
bitol to counterbalance the obstipation effect of PSP is a common practice, with the majority of reported cases of kayexalate crystal colitis occurring after the administration of this treatment combination. The mechanism by which PSP damages the intestinal mucosa is not fully understood and until recently it was thought that sorbitol was responsible for the lesion, possibly through hemodynamic phenomena of vasospasm and stimulation of prostaglandin production. Lillemeo et al. reported for the first time in 1987 five cases of colic necrosis following the administration of PSP and sorbitol, as an enema, in uremic patients. In the same work, the authors compared the effects of PSP alone, PSP and sorbitol, and sorbitol alone in rats, verifying that only rats exposed to sorbitol (with or without PSP) developed pathological gastrointestinal histological alterations with an impact on morbidity. For this reason, the use of PSP with sorbitol has been discouraged.

However, a recent systematic review of a total of 58 published cases has identified 17 cases of PSP gastrointestinal injury without sorbitol, demonstrating that intestinal necrosis may also occur when the resin is not associated with sorbitol. Previously, Haupt and Hutchins had already demonstrated how inoculation of PSP into the airway of rats led to the development of inflammation after only 24 hours. Thus, it is currently accepted that PSP itself causes tissue damage.

**CLINICAL CASE**

We present the case of an 83-year-old female patient with a personal history of major depressive disorder and hypertension. The patient went to the emergency department for a clinical diagnosis, after two weeks of evolution, of asthenia, anorexia and weight loss. According to the patient’s family, she also had bizarre behaviour, urging her children to feed her, refusing to eat alone, emotional lability and isolation. She also mentioned that the onset of this condition coincided with the diagnosis of neoplasia in her husband. The objective examination performed at the emergency department revealed only signs of dehydration, without hypotension or signs of peripheral hypoperfusion. From the analytical evaluation, a new alteration of renal function was observed, with creatinine of 2.2 mg/dL and urea of 177 mg/dL (Acute Kidney Injury Network stage 2 rating) and severe hyperkalaemia (9 mEq/dL). Renal ultrasound did not show any changes. In view of the two-week dietary refusal, acute renal injury was considered secondary to hypovolemia due to dehydration. Serum therapy and ion-exchange resin (PSP without sorbitol) were prescribed for the treatment of severe hyperkalaemia, and the patient was admitted to the medical ward. Observation was requested by psychiatry, who considered that the patient presented a probable Histrionic Personality Disorder, proceeding to the adjustment of the psychiatric therapy. On the second day of hospitalization, there was noticeable improvement in renal function and normalization of the calemia, and resin therapy was suspended. The next day, about 48 hours after the first PSP, the patient started complaints of colicky abdominal pain and liquid diarrhoea without blood, mucus, or pus. Simultaneously, an increase in inflammatory parameters was observed, and microbiological examinations were carried out, such as uroculture, coproculture, parasitological examination, and C. difficile toxin investigation in faeces. Once the diagnosis of infectious diarrhoea was excluded, the elevation of inflammatory parameters was attributed to a urinary tract infection after isolation of Proteus mirabilis in uroculture. It was prescribed targeted antibiotic therapy and optimization of therapy and diet was performed. Due to the maintenance of diarrhoea, abdominal pain and the appearance of haematocrits, colonoscopy and abdominal and pelvic tomography (CT) were proposed, which the patient refused. Only after three weeks of hospitalization, with maintenance of the symptoms, the patient agreed to these tests. A colonoscopy was performed and, despite poor intestinal preparation, which allowed only the visualization of the rectum, a depressed area in the lower rectum, partially ulcerated, without apparent necrosis was found and biopsied (Figure 1). Abdominal and pelvic CT revealed a diffuse parietal thickening of the sigmoid loops and rectal ampulla, more evident in the right anterior slope of the rectosigmoid transition, which may correspond to the inflammatory process. Finally, rectal ulcer biopsy revealed the presence of basophilic structures with mosaic pattern, similar to fish scales, surrounded by an intense active chronic inflammatory infiltrate, aspects compatible with lesion caused by ion exchange resin deposition (kayexalate crystals) (Figure 2). There was a slow and gradual symptomatic improvement, and no endoscopic or CT reassessment was performed at the option of the patient.
DISCUSSION

PSP crystals deposition colitis appears to occur in about 1% of patients receiving PSP and sorbitol treatment\(^14,15\). The lower number of reported cases suggests that the incidence in patients exposed to PSP alone is lower, which makes this case even more uncommon\(^6\). Several risk factors for colic injury by kayexalate crystals have been identified in the literature. In most reports, at least one of the following conditions would be present: uraemia or end-stage renal disease, hemodynamic instability, postoperative, post-renal transplantation, and concomitant administration of opioids\(^6,9,14,16-18\). Furthermore, as already mentioned, the administration of sorbitol seems to increase the risk of development of this entity. As in the case presented, a retrospective American study identified some cases of intestinal involvement in stable patients and without chronic kidney disease, however, all had been submitted to combined sorbitol and PSP therapy\(^8\).

It can be argued that the presence of hypovolemia due to dehydration may have contributed to the development of colic injury, despite the absence of hemodynamic instability. Nonetheless, this case demonstrates that even in the absence of many known risk factors, short-term exposure (about 24 hours) to PSP without sorbitol may cause gastrointestinal damage.

Regarding the clinical presentation, the case is in agreement with the described one, since the most common symptoms are abdominal pain, low digestive haemorrhage and diarrhea\(^5,6,8\). As observed in this case, on average the symptoms appear two days after the beginning of exposure to the resin\(^6\).

It was impossible to assess the extent of the disease since the patient refused to undergo a new colonoscopy. However, although only ulcerated rectal lesion without necrosis has been documented, the presence of more extensive and severe disease is suggested by
O polistireno sulfonato de sódio (PSP) ou kayexalato é uma resina de troca iônica, amplamente usada no tratamento da hipercalemia associada à doença renal. Um efeito adverso raro, mas potencialmente grave, dessa terapêutica é a agressão à parede do trato gastrointestinal, principalmente ao nível do cólon, que pode levar a efeitos obstrutivos que podem se complicar com necrose e perforação intestinal. O mecanismo pelo qual o PSP lesa a mucosa intestinal não é totalmente conhecido. Contudo, pensa-se que o sorbitol, frequentemente administrado em simultâneo para contrabalançar o efeito obstrutante do PSP, possa ter um papel preponderante no desenvolvimento de lesão gastrointestinal. Outros potenciais fatores de risco são a presença de uremia ou doença renal secundária a lesão renal aguda, sem outros fatores de risco que, na ausência de sorbitol, pode levar a um aumento do uso de PSP na prática clínica. A investigação etiológica com colonoscopia revelou a presença de uma úlcera retal, cujo estudo histológico foi compatível com lesão por deposição de cristais de kayexalato. Este relato incomum reforça o conceito de que este fármaco de uso frequente, mesmo na ausência de sorbitol, pode ser lesivo para a mucosa intestinal. Assim, e apesar de este ser um efeito adverso raro, a utilização difundida do PSP coloca uma vasta população em risco.


REFERENCES