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# Kalimate (calcium polystyrene sulfonate) and bowel perforation – a cause not to be ignored

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## ABSTRACT

Calcium polystyrene sulfonate (CPS), also known as Kalimate, is a cationexchange resin (CER), commonly used to treat hyperkalemia.

A case of a patient with chronic kidney disease (CKD) who underwent right hemicolectomy for colonic perforation due to intestinal necrosis secondary to oral CPS administration is presented.

The histopathological findings confirmed the colonic ischemia and perforation and showed a luminal deposition of crystals with a fish scale pattern, compatible with CER (Kalimate).

This report aims to present and discuss this unusual case considering the most updated scientific evidence.

**Keywords:** kalimate, cation exchange resin, hyperkalemia, bowel perforation

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## Introduction

Hyperkalemia reflects an electrolyte imbalance commonly seen in patients with CKD, which can be hard to treat and sometimes lead to fatal cardiac arrhytmias [1]. One of the therapeutic options to treat this condition is the use of CER, such as Kayexalate, a sodium polystyrene sulfonate (SPS) and Kalimate, a calcium polystyrene sulfonate (CPS). Kalimate exchanges potassium ions in the intestine for calcium ions of the medicine, prompts potassium excretion and lowers blood level of potassium [2]. It can be administered orally, by rectal enema or via nasogastric tube [3].

A recent study reviewed 135 cases of gastrointestinal adverse events induced by Kayexalate and Kalimate (103 and 32 cases respectively) and concluded that this pathology affects most commonly the colon (76.3%) and has a considerably mortality rate (20.7%) [3]. As mentioned above, the most affected gastrointestinal site is the colon, followed by the small intestine and duodenum, rectum and less frequently the upper gastrointestinal tract (stomach and esophagus) [3]. It may be related with the administration route, with the oral administration explaining the last two mentioned sites [2,4].

There are several predisposing factors to develop the gastrointestinal consequences of CER administration, such us CKD, ESRD (end stage renal disease), hypertension, solid organ transplantation and immunosuppression, which can be in part related with the increased risk of developing hyperkalemia in this group of patients, and therefore the need of CER intake [2,3,5,6].

There is a well-documented, although rare, relation between Kayexalato (SPS) with and without sorbitol and gastrointestinal adverse events [3,7]. In fact, the first evidence emerged in 1973 and was later supported by other studies, which showed a relationship between SPS administered with hypertonic sorbitol (given in order to prevent constipation, considering its cathartic properties) and colonic necrosis [8]. Although it is consensual that sorbitol can be related with intestinal necrosis, some recent studies had reported cases of colonic necrosis in patients receiving SPS or CPS, without sorbitol [9,10].

However, only a few studies focus on the exclusive role of Kalimate (calcium polystyrene sulfonate), instead of Kayexalate, especially without sorbitol, in this context [11].

## Material and methods

An 88-year-old male patient, with multiple comorbidities including stage IIIB CKD due to chronic pyelonephritis and obstructive uropathy, was admitted to the pulmonology service for a respiratory exacerbation of COPD (chronic obstructive pulmonary disease).

Oral CPS/ Kalimate in a dose of 20g, 3 times a day, was introduced at day five and taken for a total of seven days, for hyperkalemia in the context of an AKI (acute kidney injury), related with the introduction of diuretic treatments.

At the eleventh day of admission, he presented with constipation, nausea and vomiting, acute abdominal pain and abdominal distension, without blood loss identified.

On physical examination, the patient was apyretic, hemodynamically instable, with hypotension and tachycardia, but with sustained diuresis. On rectal examination, sphincter was normotonic, ampoule filled with liquid stools, without endoluminal palpable mass, without blood but with liquid fecal content on glove finger.

At this time, blood tests revealed worsened anemia (Hb 7.4g/dL), compared to his baseline, and leukocytosis of 29300 WBC (white blood cells)/uL, with neutrophilia.

However, the arterial blood gas analysis, under oxygen therapy at 2L/min, showed normal values, including normal lactates. The unenhanced abdominal computed tomography (CT) showed moderate intraperitoneal effusion and voluminous pneumoperitoneum (Figure 1), suggesting bowel perforation, although no obvious rupture site could be identified.

A nasogastric tube was introduced, and shortly after fluid therapy and a loading dose of antibiotic therapy (piperacillin plus tazobactam) a surgical approach was decided.

In the operative room, a markedly distended cecum was observed, without any palpable mass or other signs suggesting the presence of a tumor, and also distension of the entire small bowel, probably secondary to an incompetent ileocecal valve. Besides, there was hemoperitoneum (500-700cc) and perforation of the right colon, distal from the distended cecum, with a minimal and contained fecal contamination of the intraperitoneal space. A right hemicolectomy with terminal ileostomy was performed, in context of damage control surgery. Perioperatively, the patient ended up needing blood transfusion and vasopressor support due to hemodynamic instability, which led to the need to his admission in an intensive care unit. There was an unfavorable clinical evolution and the patient died within less than 24 hours.

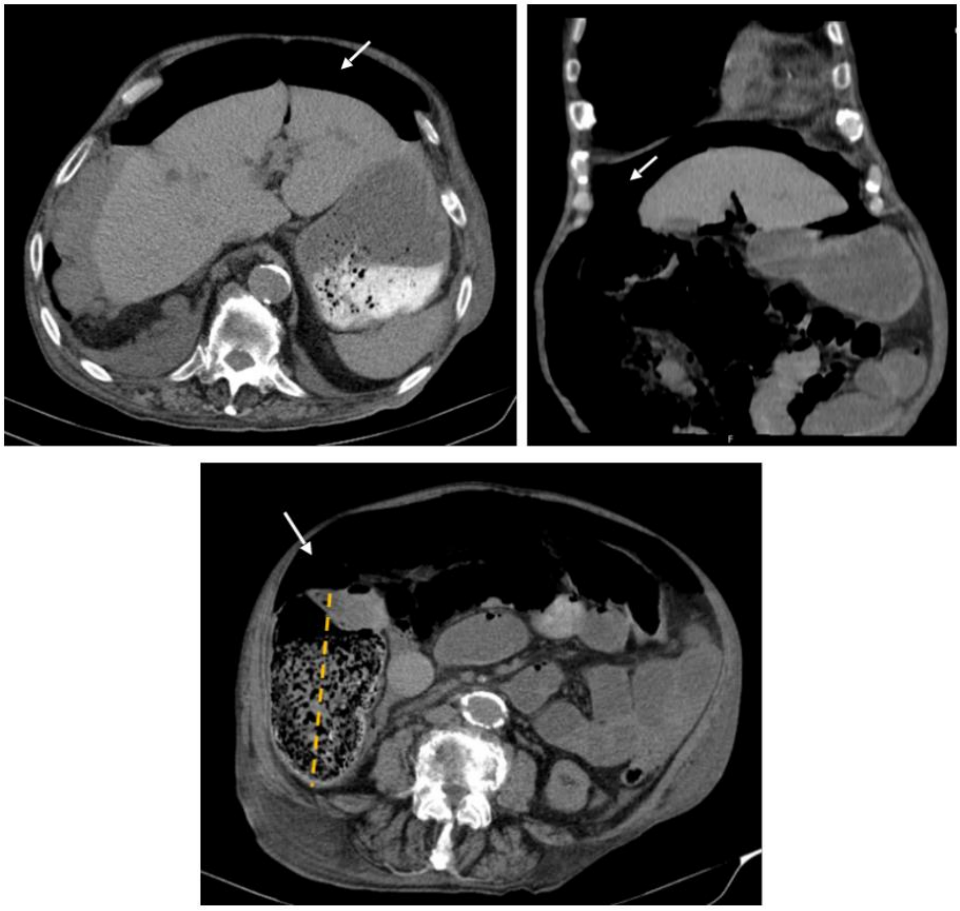

**Figure 1.** The patient realized an unenhanced abdominal CT on the 12th day since admission (2 days after the symptoms began), which showed moderate intraperitoneal effusion and voluminous pneumoperitoneum suggesting bowel perforation, without no obvious rupture site seen. The white arrow points the voluminous pneumoperitoneum from different CT planes and the yellow dashed line shows the distended cecum, with a maximum diameter of 13cm. (CT: computed tomography)

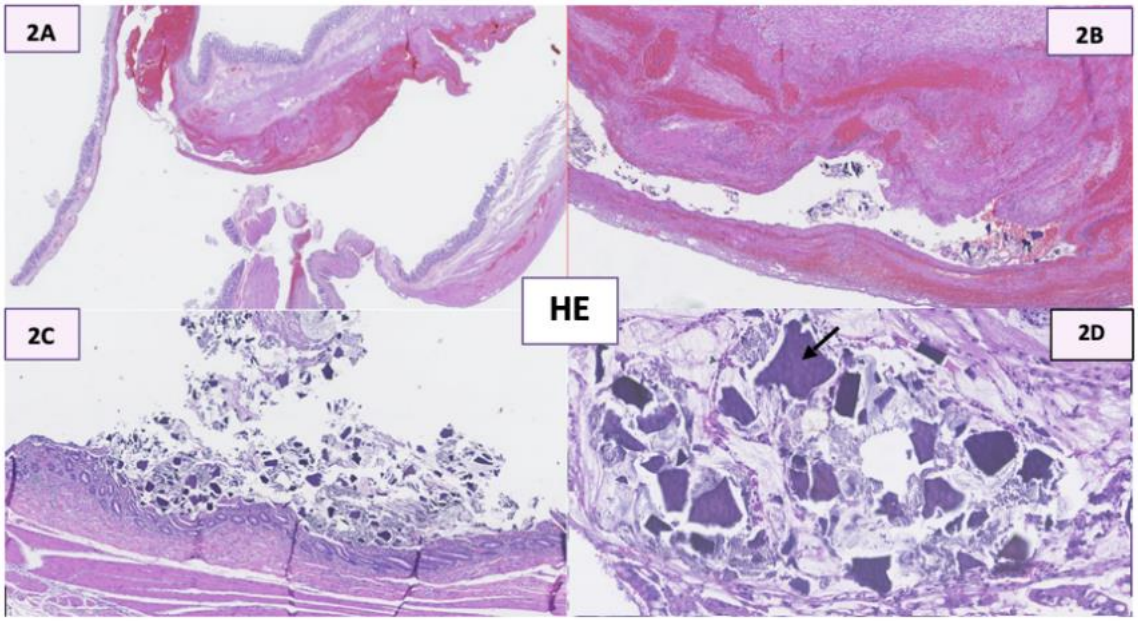


**Figure 2.** Histopathological sections of the resected right colon. 2A: Colic wall with perforation and associated hemorrhage. 2B: Detail of the colic wall with subserosa hemorrhage, with CER/ Kalimate resins inside. 2C: Mucosa of the colic wall in relation with resin particles. 2D: Luminal material that includes multiple particles of Kalimate resin, following a fish scale pattern. The black arrow shows a Kalimate resin crystal.(HE: hematoxylin and eosin staining; CER: cation exchange resin)

The histopathological examination showed ischemic and ulcerative lesions of the colonic mucosa with wall perforation (Figure 2A), associated with the presence of rhomboid and triangular basophilic crystals, following a fish scale pattern, compatible with CER (Kalimate/Kayexalato) (Figure 2D). Three colonic tubular adenomas with lowgrade dysplasia were additionally identified.

## Discussion

The most common histopathological findings associated with CER use are intestinal wall ulcerations, necrosis and, less frequently, perforation [3]. Several theories tried to explain the pathogenesis of CERs associated gastrointestinal effects and accordingly to a recent in vitro study, the presence of these crystals can decrease the metabolic activity in situ, which is associated with a neutrophil and monocyte infiltrate, leading to mucosal necrosis. Its presence can also work as a self-amplifier of a preexisting barrier dysfunction and inflammation [12].

In the present case, the perforation occurred in the colon, as it seems to be the most affected site described in literature for CER in general3. Kalimate, the CPS reported in this article, particularly seems to affect more the sigmoid colon and cecum [11].

The adverse gastrointestinal effects could have an acute presentation (as early as 2 days after exposure) or a chronic evolution, most likely presented in this patient (7 days of use, in a total of 340g, taken in 17 doses) [11]. Obviously, the severity may depend on the dosage and duration of the CER administration, but a recent observational study suggeststhat a dose of 15 g of SPS, during approximately 2 weeks is well-tolerated and may be a secure option to treat hyperkalemia [11,13]. However, it needs validation in other CER, such as Kalimate, which uses calcium,

unlike sodium, as an exchanger.

Also, in this case, the CPS was administered without sorbitol, which is in line with the most recent literature, as discussed before.9,10 This supports the latter evidence, that intestinal necrosis may be related to the resin itself, in this case Kalimate, without the simultaneous intake of sorbitol. However, several unanswered questions remain, such as whether sorbitol could exacerbate the effects of CER, since both seem to be related with intestinal necrosis.

Although histopathological identification of this crystals is pathognomonic for the diagnosis of this condition, a recent study showed that its identification was only reported in approximately 21% of the patients [3,10]. This can possibly be explained by the absence of histopathological examination in some cases or the lack of identification or interpretation of the crystals at samples examination, since it is a rare condition.

## Conclusion

Although the adverse gastrointestinal effects such as ischemia, necrosis and bowel perforation can be considered a rare complication of CER (CPS/SPS) administration, due to its considerably high mortality rate, its importance must be highlighted.

The identification of CER, including Kalimate, crystals in histopathological examination can be crucial to identify the cause of some adverse intestinal events in patients underneath its use, especially in those with CKD. However, since the natural evolution can often be rapid and fulminant, the importance of a detailed clinical history, with correct identification of the patient's medication and comorbidities is even more imperative to avoid a detrimental evolution such as the herein reported.

Physicians should be aware of this condition, especially the nephrologists, since they are the major prescribers of these drugs. The patient's intestinal motility, previous surgeries, medical history and other comorbidities should be carefully assessed before the prescription of CER for hyperkalemia management. This is especially true for the ESRD patients, who must be closely monitored, and the surgeon must be involved early if there are clinical signs of constipation, gastrointestinal bleeding, pain and bloating.

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