

# Recognizing the clinical contraindications to the use of oral sodium phosphate for colon cleansing: A case study

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Oral sodium phosphate has been demonstrated in numerous clinical trials to be an effective and well-tolerated colonic cleansing agent. However, there exists a potential to induce shifts in intravascular volume. The phosphate load often results in hyperphosphatemia, which may precipitate hypocalcemia. A review at the authors' institution identified four patients with adverse events related to oral sodium phosphate. Three of these cases had pre-existing comorbidities that predisposed them to the adverse event, or had received doses higher than that used or recommended in previous trials. Recommendations for relative and absolute contraindications to the use of oral sodium phosphate are described.

**Key Words:** *Colon cleansing; Colonoscopy; Oral sodium phosphate*

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Oral sodium phosphate (NaP) is a small volume osmotic solution that was first demonstrated to be an effective colon cleansing agent for colonoscopy in 1990 (1). Since that time, numerous trials have confirmed it to be an effective and well-tolerated method for preparing the colon (2-13). However, its osmotic action has the potential to induce shifts that may compromise intravascular volume and the phosphate load results in transient hyperphosphatemia in most patients, thereby potentially risking symptomatic hypocalcemia (14,15). As a result of these concerns, most experts feel this agent is contraindicated in patients who have comorbid conditions that make them vulnerable to the adverse effects of changes in intravascular volume or hypocalcemia.

We have recently reviewed the clinical trials that examined the use of NaP for colon cleansing (16). This review demonstrated that 2496 patients in 26 clinical trials had received NaP and not a single patient experienced a serious adverse event attributable to the use of NaP. However, all patients received the appropriate dose and most investigators excluded patients with comorbid conditions which are thought to put patients at increased risk (16). The review also examined the case reports of toxicity with NaP and found that they were almost entirely due either to improper dosing or to the use of this agent in patients who had recognizable contraindications. At the Hotel Dieu Hospital in Kingston, Ontario, there is over 10 years experience with the use of NaP for colon cleansing

## Reconnaître les contre-indications cliniques du phosphate de sodium oral pour le lavage du côlon : Étude de cas

De nombreux essais cliniques ont démontré que le phosphate de sodium par voie orale est un agent de lavage efficace et bien toléré au niveau des voies digestives. Par contre, il peut induire des modifications du volume intravasculaire. La charge de phosphate entraîne souvent une hyperphosphatémie susceptible de déclencher une hypocalcémie. L'examen des dossiers provenant de l'établissement des auteurs a permis d'identifier quatre patients qui ont présenté des réactions indésirables au phosphate de sodium par voie orale. Trois de ces cas présentaient déjà des comorbidités qui les prédisposaient à cette réaction indésirable ou avaient reçu des doses plus fortes qu'il n'est habituel ou recommandé, selon les essais antérieurs. Le présent article formule des recommandations au sujet des contre-indications relatives et absolues à l'utilisation du phosphate de sodium oral.

and an estimated 15,000 patients received this preparation during this time. In view of our significant experience with this agent, we retrospectively reviewed our cases between 1995 and 2001 and found four patients at our centre who had serious adverse events related to the use of NaP. The present report describes those cases and compares our experience with the reported literature. The findings highlight the potential for toxicity with NaP when used inappropriately and emphasize the comorbidities that should be considered as relative or absolute contraindications.

## CASE PRESENTATIONS

### Case 1

A 49-year-old man was admitted with anemia and melena. He had no significant comorbidities and was on no medications. After an upper endoscopy failed to reveal a bleeding source, a colonoscopy was planned. The patient ingested 45 mL of NaP at both 16:00 and 22:00 the day before the procedure, while on a clear fluid diet. The following morning, the patient experienced perioral paresthesia, which over the next hour advanced to involve his entire face and extremities. Serum calcium was 1.9 mmol/L (normal values 2.15 mmol/L to 2.5 mmol/L), phosphate was 1.78 mmol/L (normal values 0.8 mmol/L to 1.5 mmol/L), potassium was 2.8 mmol/L (normal 3.5 mmol/L to 5.2 mmol/L) and magnesium was 0.69 mmol/L (normal values 0.8 mmol/L to 1 mmol/L) (Table 1). Sodium, chloride

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**TABLE 1**  
**Summary of clinical data**

	Case 1 49-year-old man		Case 2 69-year-old woman		Case 3 54-year-old man		Case 4 38-year-old man	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Calcium (total), mmol/L (normal 2.15–2.5 mmol/L)	N/A	1.9	N/A	1.62	2.36	1.27	1.86	0.9
Phosphate, mmol/L (normal 0.8–1.5 mmol/L)	N/A	1.78	N/A	1.93	0.96	6.3	1.3	5.59
Sodium, mmol/L (normal 135–147 mmol/L)	140	142	140	141	137	151	139	143
Potassium, mmol/L (normal 3.5–5.2 mmol/L)	3.7	2.8	4.4	2.3	4.7	4	3.7	4.3
Creatinine, $\mu\text{mol/L}$ (normal <110 $\mu\text{mol/L}$ )	60	60	77	92	*	*	239	278
QTc interval, ms (normal <440 ms)	395	N/A	458	522	404	604	459	590

\*Patient was receiving dialysis. Pre and post refer to the timing of the laboratory test relative to the ingestion of oral sodium phosphate. N/A Not available

and renal function tests remained within the normal range. Intravenous calcium gluconate and magnesium were administered with complete relief of the patient's symptoms within minutes. He subsequently underwent colonoscopic examination without further difficulty. No cause was found for the anemia.

### Case 2

A 69-year-old woman underwent colonoscopy to investigate chronic iron deficiency anemia. She had previously undergone attempted colonoscopies that were limited because of inadequate colonic cleansing. Due to these previous difficulties, the patient was given two doses of 45 mL of NaP for the two consecutive nights (at 17:00 and 22:00) before the colonoscopy (total dose was 180 mL). The patient had an extensive medical history that included ischemic heart disease, congestive heart failure, type 2 diabetes mellitus, polymyalgia rheumatica, hypothyroidism, cerebrovascular disease and moderate aortic insufficiency. Early in the evening before her colonoscopy (second day of preparation), she developed paresthesias in her extremities and perioral area as well as carpal spasm. She did not seek medical attention until her scheduled colonoscopy time. On examination, her vital signs were normal. Trousseau's sign was positive. Serum calcium was 1.62 mmol/L (normal values 2.15 mmol/L to 2.5 mmol/L), phosphate was 1.93 mmol/L (normal values 0.8 mmol/L to 1.5 mmol/L) and potassium was 2.3 mmol/L (normal values 3.5 mmol/L to 5.2 mmol/L) (Table 1). Her remaining electrolytes and renal function were normal. Electrocardiogram displayed a lengthened QT interval (QTc 522 ms, previous 458 ms). Her symptoms and prolonged QT resolved with the administration of calcium chloride.

### Case 3

A 54-year-old man was scheduled to undergo colonoscopy for polyp surveillance. His medical history included renal failure requiring hemodialysis for five years, hyperparathyroidism with parathyroidectomy and mild chronic obstructive pulmonary disease. He ingested two 45 mL bottles of NaP the evening before the colonoscopy, with 2 h between doses rather than the recommended 5 h. The patient felt lightheaded upon awakening the following day. On arrival at the endoscopy suite, he complained of perioral and fingertip paresthesias. He was hypotensive (blood pressure 70/50 mmHg). Electrocardiogram revealed a prolonged QT interval (QTc 604 ms, previous 404 ms). Serum total calcium was 1.27 mmol/L (normal values 2.15 mmol/L to 2.5 mmol/L), ionized calcium was 0.5 mmol/L (normal values 1.19 mmol/L to 1.31 mmol/L), and phosphate was 6.3 mmol/L (normal values 0.8 mmol/L to 1.5 mmol/L)

(Table 1). The remaining electrolytes were within normal range. The patient was administered intravenous calcium gluconate and admitted to hospital. He underwent dialysis that day. The next day the paresthesias had resolved and the QT interval normalized.

### Case 4

A 38-year-old man was admitted to hospital for multiple abdominal abscesses and suspected entero-enteric fistulae. His medical history included rhabdomyolysis-induced renal failure requiring temporary dialysis. His renal function had partially improved (creatinine 239  $\mu\text{mol/L}$ , [normal values 60  $\mu\text{mol/L}$  to 110  $\mu\text{mol/L}$ ]), allowing dialysis to be stopped. Inflammatory bowel disease was suspected and a colonoscopy arranged. He was given 45 mL of oral NaP at 16:00 and 20:00 the day before the colonoscopy. In addition, due to a lack of bowel movements, he was administered a sodium phosphate rectal enema at 05:00 the day of the procedure. Approximately 12 h after the procedure, the patient was noted to have poor urine output. He complained of clenched fists and perioral paresthesias. On examination, vital signs were normal. The patient was noted to have carpal spasm and a positive Chvostek's sign. Electrocardiogram displayed inferolateral ST elevation. The QT interval had increased (QTc 590 ms, previous 459 ms). Cardiac enzymes and echocardiogram confirmed myocardial infarction. Sodium, potassium and chloride remained in the normal range. However, the patient's creatinine increased (278  $\mu\text{mol/L}$ , previous 239  $\mu\text{mol/L}$ ), and ionized calcium was 0.55 mmol/L (normal values 1.19 mmol/L to 1.31 mmol/L). Phosphate was markedly elevated at 5.59 mmol/L (normal values 0.8 mmol/L to 1.5 mmol/L) (Table 1). Intravenous calcium gluconate was administered in a bolus fashion initially. However, the patient's symptoms recurred and a continuous infusion was initiated. After 48 h, his symptoms had resolved and the infusion was discontinued.

## DISCUSSION

The use of NaP for colon cleansing before colonoscopy has rapidly expanded over the past decade because of its relative effectiveness and patient tolerability compared with other available agents. Although clinical trials have shown this agent to be very safe, our review of reported adverse events and recent advisories regarding potential adverse events with NaP (17,18) prompted a review of the experience at our centre. Four patients under the care of other physicians were identified with clinical manifestations suggesting an adverse event related to the use of NaP. We acknowledge that this was a retrospective review and the potential exists for missing other less serious

**TABLE 2**  
**Summary of predisposing factors to toxicity with oral sodium phosphate (NaP)**

	Inappropriate dose or interval	Chronic renal failure	Pre-existing electrolyte abnormality	Dehydration	Enteric fistula	Other	No predisposing factor identified
Previously published cases (n=29)*	20	6	2	4	0	2 <sup>†</sup>	4
Current case series (n=4)	2	2	0	0	1	1 <sup>‡</sup>	1

\*n=13 cases received NaP for colonoscopy, 16 cases received NaP for other reasons; <sup>†</sup>Jejunioleal bypass, obstructing colon cancer; <sup>‡</sup>Parathyroidectomy. Adapted and reprinted with permission from reference 16

adverse events outside of a prospective evaluation. Nonetheless, these cases, together with those reported in the literature, highlight that serious toxicities can be predicted based on inappropriate dosing or patient selection (Table 2). There may also be a very small group of patients who experience mild symptoms of transient hypocalcemia without any predictable precipitant.

In this case series three of these adverse events were predictable. In cases 2 and 3, the dose administered exceeded that recommended. In addition, case 3 had chronic renal failure requiring hemodialysis and had undergone a previous parathyroidectomy, rendering him more susceptible to hypocalcemia. Case 4 also had multiple predisposing factors. He had renal failure although he no longer required hemodialysis. More importantly, he was suspected of having an enteroenteric fistula with microperforation, and therefore he was at risk to accumulate NaP in an extraluminal space. This almost certainly occurred given his markedly prolonged hypocalcemia following the ingestion of the NaP.

One patient (case 1), however, experienced mild hypocalcemia, hyperphosphatemia, hypokalemia and hypomagnesemia without any known predisposing factor. Our recent review of the literature also identified several patients with symptoms of hypocalcemia who also did not appear to have an identifiable predisposing factor (16). Although these symptoms are not life threatening in these individuals, endoscopists need to be aware of this potential.

The potential for toxicity with NaP must be balanced against that of alternative agents, in addition to its enhanced effectiveness and greater tolerability for patients. Currently, there are no available agents that have been shown to be without risk. The most commonly used alternatives to NaP are the large volume polyethylene glycol solutions. Between 1997 and August 2002, the American Food and Drug Administration received 100 reports of adverse events involving polyethylene glycol solution, 30 of which were considered serious (life threatening, and/or requiring hospitalization, and/or resulting in disability or death) (FDA, Freedom of Information Report). The frequency of these reports does not differ from those received for NaP (16). In addition, Ayus et al (19) recently reported three cases of PEG-associated dysnatremia, two of which resulted in death. Of particular concern is that two of these patients had renal failure requiring hemodialysis, a setting where PEG is commonly used in place of NaP.

In summary, NaP can be administered safely if appropriate dosages and intervals (at least 5 h [1,15,16]) are used and patients with comorbid conditions that may predispose them to adverse events are identified. There is growing evidence based on the literature and our own experience that absolute and relative contraindications to NaP can be identified (Table 3) (16). There are little safety data available concerning the use of oral NaP in children, but one report suggests there may be

**TABLE 3**  
**Contraindications to the use of oral sodium phosphate**

Absolute	Renal insufficiency	
	Inability to maintain adequate fluid intake	
	Pre-existing electrolyte disturbances	
	Ascites	
	Symptomatic congestive heart failure	
	Recent (< 6 months) symptomatic ischemic heart disease (unstable angina or myocardial infarction)	
	Enteric fistulas	
	Bowel obstruction	
	Relative	Extremes of age
		Active inflammatory bowel disease
Parathyroidectomy		
Delayed bowel transit		

greater effects on phosphate levels than seen in adults (20). We recommend careful screening of patients before colonoscopy and appropriate testing of serum electrolytes and renal function in patients susceptible to age-related reduced renal function (50 years of age or older) (21) and those with comorbidities. The safety profile of oral NaP can also be enhanced by the addition of oral carbohydrate electrolyte solution (Gatorade, USA) during the day of preparation. A recent controlled trial has shown that patients ingesting the sports drink experienced significantly less volume contraction than those assigned to ingestion of the usual clear fluids and had better cleansing of the colon (22).

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