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

Lawrence C Hookey MD, Stephen Vanner MD

Oral sodium phosphate (NaP) is a small volume osmotic solution that was first demonstrated to be an effective and well-tolerated colon cleansing agent in 1990 (1). Since that time, numerous trials have confirmed its effectiveness and tolerability. However, there is potential for adverse shifts to 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

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 values 3.5 mmol/L to 5.2 mmol/L) and magnesium was 0.69 mmol/L (normal values 0.8 mmol/L to 1.0 mmol/L). The patient's hand is illustrated in Figure 1. Although he had no significant comorbidities, the patient experienced paresthesia which resolved after cessation of phosphate. The patient had no history of renal impairments, and no prior episodes of abnormal phosphate levels. The patient had no significant comorbidities but had admitted to excessive alcohol consumption. The patient had a history of alcohol abuse which was noted to be significant. The patient had no significant comorbidities but had admitted to excessive alcohol consumption. The patient had no significant comorbidities but had admitted to excessive alcohol consumption.
TABLE 1
Summary of clinical data

<table>
<thead>
<tr>
<th>Case 1 49-year-old man</th>
<th>Case 2 69-year-old woman</th>
<th>Case 3 54-year-old man</th>
<th>Case 4 38-year-old man</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (total), mmol/L (normal 2.15–2.5 mmol/L)</td>
<td>N/A 1.9</td>
<td>N/A 1.62</td>
<td>2.36 1.27</td>
</tr>
<tr>
<td>Phosphate, mmol/L (normal 0.8–1.5 mmol/L)</td>
<td>N/A 1.78</td>
<td>N/A 1.93</td>
<td>0.96 6.3</td>
</tr>
<tr>
<td>Sodium, mmol/L (normal 135–147 mmol/L)</td>
<td>140 142</td>
<td>140 141</td>
<td>137 151</td>
</tr>
<tr>
<td>Potassium, mmol/L (normal 3.5–5.2 mmol/L)</td>
<td>3.7 2.8</td>
<td>4.4 2.3</td>
<td>4.7 4</td>
</tr>
<tr>
<td>Creatinine, µmol/L (normal &lt;110 µmol/L)</td>
<td>60 60</td>
<td>77 92</td>
<td>* *</td>
</tr>
<tr>
<td>Phosphate, mmol/L (normal &lt;0.8 µmol/L)</td>
<td>N/A 1.78</td>
<td>N/A 1.93</td>
<td>0.96 6.3</td>
</tr>
<tr>
<td>QTc interval, ms (normal &lt;440 ms)</td>
<td>395 N/A</td>
<td>458 522</td>
<td>404 604</td>
</tr>
</tbody>
</table>

*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 she 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 µmol/L, normal values 60 µmol/L to 110 µmol/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 µmol/L, previous 239 µmol/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)

<table>
<thead>
<tr>
<th>Previously published cases (n=29)*</th>
<th>20</th>
<th>6</th>
<th>2</th>
<th>4</th>
<th>0</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current case series (n=4)</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

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

Contraindications to oral sodium phosphate

| TABLE 3

Contraindications to the use of oral sodium phosphate

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Renal insufficiency</th>
<th>Inability to maintain adequate fluid intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-existing electrolyte disturbances</td>
<td>Ascites</td>
<td>Symptomatic congestive heart failure</td>
</tr>
<tr>
<td>Enteric fistulas</td>
<td>Recent (&lt; 6 months) symptomatic ischemic heart disease (unstable angina or myocardial infarction)</td>
<td>Enteric fistula</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>Relative</td>
<td>Extremes of age</td>
</tr>
<tr>
<td>Active inflammatory bowel disease</td>
<td>Parathyroidectomy</td>
<td>Delayed bowel transit</td>
</tr>
</tbody>
</table>

REFERENCES


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