

## Renal risk associated with sodium phosphate medication

Sodium phosphate drugs (solutions, tablets or enemas) are used since 1990s as laxatives for bowel cleansing before endoscopy and radiology examination, or occasionally for treatment of severe constipation. Sodium phosphate drugs are low-volume osmotic purgatives, their administration is connected with high load of phosphates and sodium. Originally it was believed that due to the osmotic effect, components of these laxatives are not absorbed from the gut. However, data from the last decades showed evidence of systemic sodium and phosphate absorption. The sodium overload can be easily managed by physiological regulatory mechanisms without any long-term impact, but the massive acute phosphate load may lead to several unfavorable clinical consequences in risky patients.

Contraindications to oral sodium phosphate administration
<ul style="list-style-type: none"> <li>• age &gt;80, &gt;85 or clinically significant debilitation</li> <li>• women with underweight and status, pregnancy or breastfeeding</li> <li>• dehydration or risk for dehydration</li> <li>• decreased renal or cardiac volume (due to congestive heart failure, brachycardia or acute, asymptomatic hypotension)</li> <li>• acute renal failure, kidney disease, previous chronic hypotension, renal insufficiency</li> <li>• underlying conditions with potential failure for electrolytes (e.g., systemic lupus erythematosus)</li> <li>• use of medicines that affect renal perfusion function (diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or non-steroidal anti-inflammatory drugs, especially if in combination)</li> <li>• preexisting hyperphosphatemia of any cause, hypercalcemia, hypocalcemia</li> <li>• cardiovascular disease (heart failure, myocardial infarction, ischemic heart disease, recent myocardial infarction, unstable angina, hypertension, prolonged QT interval, arrhythmias, peripheral vascular disease, cerebrovascular disease)</li> <li>• gastrointestinal disease (obstruction, sigmoiditis, proctitis, ileus, inflammatory bowel disease, acute colitis, toxic colitis and toxic megacolon, gastroenteritis with decreased QT interval including anti-cholinergic medication), gastric bypass or gastric surgery, heart prosthesis, malabsorption syndrome with hyperphosphatemia</li> <li>• diabetes mellitus</li> <li>• nephrolithiasis (kidney stones) or chemical structure which predisposes to nephrolithiasis, e.g., hyperparathyroidism, gout, gouty arthritis, hyperuricemia, hyperoxaluria, and urinary tract infection</li> <li>• systemic metabolic disease affecting sodium/phosphate metabolism (hyperparathyroidism, hyperparathyroidism, hypoparathyroidism, acromegaly, multi-drug resistant hypoparathyroidism, or vitamin D deficiency)</li> <li>• medication that could increase renal failure (antidiuretics, beta-blockers, rifampin, sulfonamides, central agents, ACE-inhibitors, diuretics, anticholinergics, methotrexate, sodium bicarbonate, potassium citrate, and osimertinib)</li> <li>• medication affecting sodium/phosphate metabolism (thiazide, sodium, loop diuretics)</li> <li>• drugs that prolong QT interval (anticholinergics, antiarrhythmics, antibiotics, prokinetics, prostanoids, quinolones, oral, or injectable antibiotics)</li> <li>• drugs that might increase sodium (acetaminophen, phenylephrine, salicylate, or anti-depressants)</li> <li>• vitamin</li> <li>• hyperphosphatemia in the ingredients</li> </ul>

Fig. 1. Contraindications to oral sodium phosphate administration.

Since the mid-1990s, dozens of serious adverse events of the sodium phosphate purgatives have been published and/or reported to the government agencies. These adverse events emerged when used in patients with following risk factors: older age (55 years and above), dehydration, acute or chronic kidney disease, kidney stones, urinary tract infection, heart failure, liver cirrhosis, intestinal diseases, diabetes mellitus, and using medications that affect kidney perfusion or function (such as diuretics, angiotensin-converting-enzyme inhibitors, angiotensin-receptor blockers, non-steroidal anti-inflammatory drugs). Therefore, in that risky situation, sodium phosphate drugs are not recommended. Figure 1 shows contraindications to oral sodium phosphate administration.

Among adverse events connected with the use of sodium phosphate drug has been reported:

1/ mineral imbalances; namely high level of phosphates (hyperphosphatemia) and compensatory low level of calcium (hypocalcemia) in the blood serum. Severe hyperphosphatemia and hypocalcemia with subsequent tetany, hypocalcemic coma or death was documented only in patients with above mentioned risks factors. Well-hydrated adults with normal renal function usually tolerate this amount of phosphate load and rarely develop symptomatic hyperphosphatemia and hypocalcemia.

2/ kidney impairment named “acute phosphate nephropathy”. This is a acute kidney injury characterized by acute and subsequent chronic kidney failure as a result of calcium phosphate precipitation and formation of hydroxyapatite crystals in the tubules. Figure 2 shows typical finding in kidney biopsy: black-stained crystals of calcium phosphate in the tubules.

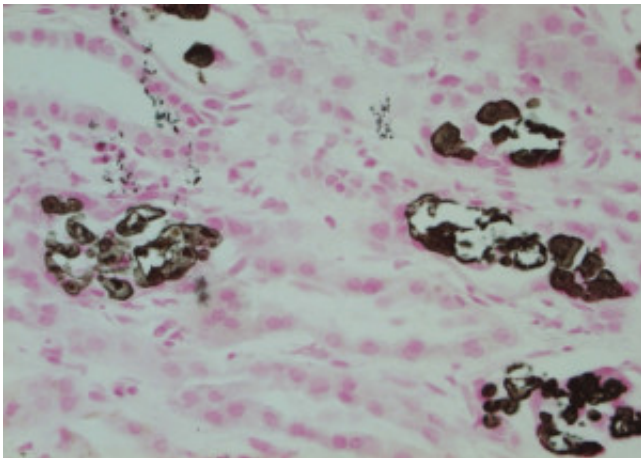


Fig. 2. Renal biopsy showing acute phosphate nephropathy (original magnification 400×). Black stained intraluminal crystals of calcium phosphate in the renal tubules.

Kidney injury varies from mild involvement to progressive disease with irreversible changes. In some cases, chronic kidney failure due to acute phosphate nephropathy requires regular hemodialysis or even renal transplant. Studies evaluating biopsy-confirmed acute phosphate nephropathy and population studies on renal adverse events related to sodium phosphate bowel cleansing found that the incidence of acute phosphate nephropathy is relatively low, possibly up to 1 in 1000 patients who receive sodium phosphate drugs. It seems that renal complications are rare, when millions of people who used sodium phosphate purgatives are taken into account.

Based on available data, sodium phosphate medication seems to be safe when used in adequately hydrated otherwise healthy adults. Thus, there is no need to be limited of using sodium phosphate products in healthy adults with no history of co-morbid conditions.

## Publication

[Renal risk associated with sodium phosphate medication: safe in healthy individuals, potentially dangerous in others.](#)

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