



BRIEF ANSWERS
TO SPECIFIC
CLINICAL
QUESTIONS

Q: What are the caveats to using sodium phosphate agents for bowel preparation?

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A: Sodium phosphate (NaP) agents were introduced to provide a gentler alternative to polyethylene glycol (PEG) bowel preparations, which require patients to drink up to 4 liters of fluid over a few hours.

However, in May 2006 the US Food and Drug Administration (FDA) issued an alert that NaP products for bowel cleansing may, in some patients, pose a risk of acute phosphate nephropathy, a rare form of acute renal failure.

Although NaP preparations are generally safe and well tolerated, they can cause significant fluid shifts and electrolyte abnormalities. As such, they should not be used in patients with baseline electrolyte imbalances, renal or hepatic dysfunction, or a number of other comorbidities.

■ CURRENT BOWEL-CLEANSING OPTIONS

For many years the standard preparation for bowel cleansing was a 4-liter or a 2-liter PEG electrolyte solution plus a laxative (eg, magnesium citrate, bisacodyl, or senna).¹⁻³ The most frequent complaint heard from patients was that “the preparation is worse than the colonoscopy,” attributable to the taste and volume of the fluid they had to consume. Thus, compliance was often a significant issue with patients presenting for colonoscopy. In fact, inadequate bowel preparation is one of the most common reasons polyps are missed during colonoscopy.

Aqueous and tablet forms of NaP (sometimes with a laxative) have become a widely

used alternative to PEG solutions because they require much less volume and as a result are more palatable, thereby improving compliance.^{4,5}

NaP agents cleanse the colon by osmotically drawing plasma water into the bowel lumen. The patient must drink significant amounts of water or other oral solutions to prevent dehydration.

NaP-based bowel-cleansing agents are available in two forms: aqueous solution and tablet. Aqueous NaP (such as Fleet Phosphosoda) is a low-volume hyperosmotic solution containing 48 g of monobasic NaP and 18 g of dibasic NaP per 100 mL.⁶ An oral tablet form (such as Visicol and OsmoPrep) was developed to improve patient tolerance.⁷ Each 2-g tablet of Visicol contains 1,500 mg of active ingredients (monobasic and dibasic NaP) and 460 mg of microcrystalline cellulose, an inert polymer. Each OsmoPrep tablet contains 1,500 mg of the same active ingredients as Visicol, but the inert ingredients include PEG and magnesium stearate.

At first, the regimen was 40 tablets such as Visicol to be taken with water and bisacodyl. Subsequent regimens such as OsmoPrep with fewer tablets have been shown to be as effective and better tolerated.⁸ Microcrystalline cellulose in the tablet can produce a residue that may obscure the bowel mucosa. Newer preparations contain lower amounts of this inert ingredient, allowing for improved visualization of the colonic mucosa during colonoscopy.⁹

■ ADVANTAGES OF SODIUM PHOSPHATE BOWEL CLEANSERS

In a recent review article, Burke and Church¹⁰ noted that NaP cleansing regimens

Poor compliance is often a problem with PEG regimens because of the volume and taste of the fluid to be consumed

have been shown to be superior to PEG-electrolyte lavage solution with respect to tolerability and acceptance by patients, improved quality of bowel preparation, better mucosal visualization, and more efficient endoscopic examination. In addition, the volume of the preparation may also help decrease the risk of aspiration in some patients.^{2,3}

■ DISADVANTAGES OF SODIUM PHOSPHATE AGENTS

Despite their comparable or better efficacy and their better tolerability, NaP agents have certain disadvantages.

Effects on the colonic mucosa

In rare cases NaP agents have been shown to alter the microscopic and macroscopic features of the colonic mucosa, and they can induce aphthoid erosions that may mimic those seen in inflammatory bowel disease and enteropathy or colopathy associated with nonsteroidal anti-inflammatory drugs (NSAIDs).^{11–13} Therefore, NaP agents should not be used prior to the initial endoscopic evaluation of patients with suspected inflammatory bowel disease, microscopic colitis, or NSAID-induced colonopathy.

Fluid and electrolyte shifts

Because NaP acts by drawing plasma water into the bowel lumen, significant volume and electrolyte shifts may occur.^{14,15} These can cause hypokalemia, hyperphosphatemia, hypocalcemia, hyponatremia or hypernatremia, hypomagnesemia, elevated blood urea nitrogen levels, decreased exercise capacity, increased plasma osmolarity,^{15–17} seizures,¹⁸ and acute renal failure with or without nephrocalcinosis.^{17,19–21}

Thus, patients with significant comorbidities—such as a recent history of myocardial infarction, renal or hepatic insufficiency, or malnutrition—should not use NaP agents.²²

Pivotal study of adverse events

In May 2006, the FDA issued an alert outlining the concerns of using oral NaP in specific patient populations. Of note were documented cases of acute phosphate nephropathy in 21 patients who used aqueous NaP (Fleet

Phospho-Soda or Fleet Accu-Prep), and in 1 patient who used NaP tablets (Visicol).²³ Acute renal injury was not limited to patients with preexisting renal insufficiency. It is uncertain whether this means that otherwise healthy people suffered renal injury or had risk factors besides renal insufficiency, since the data cited by the FDA report do not elucidate the possible risk factors for the development of nephropathy in patients with no preexisting renal insufficiency. So far, no cases of acute phosphate nephropathy or acute renal failure have been reported with OsmoPrep, a NaP tablet bowel preparation recently approved by the FDA.²⁴ The long-term safety of OsmoPrep needs further evaluation.

■ PROCEED WITH CAUTION

Certain situations such as advanced age and cardiac, renal, and hepatic dysfunction call for extreme caution in the use of NaP bowel preparation agents. Therefore, it is recommended that patients with the following conditions should avoid using NaP agents for colon preparation:

- Hepatic or renal insufficiency (there are no data as to the degree of hepatic or renal insufficiency)
- Congestive heart failure
- Over age 65
- Dehydration or hypercalcemia
- Chronic use of drugs that affect renal perfusion, such as NSAIDs, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, or diuretics for hypertension.

Patients who take diuretics should not take them while they are using NaP for bowel preparation because of the risk of electrolyte abnormalities such as hypokalemia. In patients who have no alternative but to proceed with NaP preparation, our recommendation would be that the patient hold off taking diuretics, ACE inhibitors, and angiotensin receptor blockers while using the NaP prep. Given the importance of these medications in controlling diseases such as hypertension, the physician and the patient should jointly determine whether the benefits of using an NaP agent justify holding these drugs. We

Taking a diuretic while taking the NaP agent may lead to hypokalemia

TABLE 1

Comparison of polyethylene glycol and sodium phosphate agents for colon preparation

AGENTS	ADVANTAGES AND DISADVANTAGES
Polyethylene glycol solutions	Cause minimal volume shift or electrolyte abnormalities Some solutions come with a choice of flavor The large volume needed is difficult for some patients, and this can affect compliance Risk of aspiration in some patients
Sodium phosphate agents	Small volume or quantity results in better tolerance and compliance Volume shift and electrolyte abnormalities Risk of adverse effects in patients with volume depletion and comorbidities In rare cases, may alter microscopic and macroscopic features of the colonic mucosa

believe that patients taking these drugs should try using a PEG solution before considering NaP.

TASK FORCE GUIDELINES

Guidelines for using NaP bowel preparation agents, published by a task force of the American Society of Colon and Rectal Surgeons, the American Society for Gastrointestinal Endoscopy, and the Society of American Gastrointestinal and Endoscopic Surgeons,²⁵ include the following caveats:

- Aqueous and tablet NaP colonic preparations are an alternative to PEG solutions, except in pediatric populations, patients over age 65, and those with bowel obstruction or other structural intestinal disorder, gut dysmotility, renal or hepatic insufficiency, congestive heart failure, or seizure disorder.
- Dosing should be 45 mL in divided doses, 10 to 12 hours apart, with at least one dose taken on the morning of the procedure.²⁵
- The significant volume contraction and

resulting dehydration seen in some patients using NaP preparations may be lessened by encouraging patients to drink fluids liberally during the days leading up to their procedure, and especially during NaP bowel preparation.²⁶

- NaP tablets should be dosed as 32 to 40 tablets. On the evening before the procedure the patient should take 20 tablets and then 12 to 20 tablets approximately 3 to 5 hours before undergoing endoscopy. The tablets should be taken four at a time every 15 minutes with approximately 8 oz of clear liquid.²⁵

To maximize the efficacy and safety of colonoscopy, it is paramount that the colon be adequately prepared. Agents for bowel cleansing should be inexpensive, effective, safe, palatable, and easy to take. The most commonly used regimens are based on either PEG or NaP, and each has advantages and disadvantages (TABLE 1). The decision whether to use PEG or NaP for bowel cleansing should be individualized and should take into consideration the pros and cons of the agents and the patient's general health. ■

Select an agent the patient is most likely to use properly

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