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## What is the best strategy for successful bowel preparation under special conditions?

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such as those with chronic kidney disease, who are taking drugs that affect renal function, or who suffer from heart failure. Other special conditions that may affect an individual's tolerance of the cathartic agent or ability to complete the administration routine include stroke, severe constipation, hematochezia, suspicious lower gastrointestinal bleeding, and mental disorders such as dementia. All ingestible bowel preparation solutions can be instilled into the stomach and duodenum through nasogastric tube or esophagogastroduodenoscopy with the aid of a water irrigation pump for patients with difficulties swallowing or ingesting the large volumes of fluid required. In addition, dietary regimens based on clear liquids and low-residue foods for 1-4 d prior to the colonoscopy may be supplemental bowel preparation strategies. Achieving an effective and safe cleansing of the bowel is important for successful colonoscopy in all patients, so full knowledge of the individual's condition and capabilities is necessary to select the most appropriate colonic cleansing agent and delivery regimen.

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**Key words:** Colonoscopy; Preparation; Polyethylene glycols; Special conditions; Cathartic agent

### Abstract

Adequate bowel preparation is important for successful colonoscopic examination. Several effective colonic cleansing agents are available and routinely prescribed, but each carries its own limitations and benefits from particular dosing regimens. The most frequently prescribed colonic cleansing agent, the polyethylene glycol (PEG) cathartic solution, suffers from low patient compliance in general, due to its unpalatable taste and smell coupled with the large ingested volumes required. However, PEG is preferred over other cathartics for use in individuals of advanced age, sufferers of chronic kidney disease, heart failure and inflammatory bowel disease, and women who are pregnant or lactating. The laxative agents sodium phosphate (NaP) and sodium picosulfate plus magnesium citrate have been applied and have improved patient compliance and tolerance. NaP, however, should be avoided in individuals with impaired renal function or plasma clearance,

**Core tip:** Adequate bowel preparation is important for successful colonoscopic examination. A patient's general health condition or concurrent medications may impair their ability to tolerate a certain cathartic agent, and mental or physical disabilities may preclude their ability to complete the ingestion regimen. While impaired health increases the risk of agent-related complications, failure to comply with bowel preparation instructions in general limits adequate cleansing of the bowel. Unremoved fecal matter occludes the colonoscopic view, necessitating repeat examination. This review discusses the special conditions encountered most frequently in the endoscopic clinic so that effective and safe bowel

preparation agents/regimens can be chosen.

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## INTRODUCTION

Bowel preparation for colonoscopy was designed as a means to improve the diagnostic and therapeutic accuracy and safety of this semi-invasive visualization procedure. The most common method of bowel preparation involves oral ingestion of a large volume of a cathartic agent with laxative properties over a defined period of time. The most commonly prescribed cathartic regimen is 4 L of polyethylene glycol (PEG; an osmotically balanced electrolyte lavage solution). Unfortunately, the regimen suffers from poor compliance rates, for which patients have cited the unpalatable taste and smell of the PEG solution, as well as difficulty of consuming such a large volume. Complimenting the PEG regimen with other laxative agents, such as sodium phosphate (NaP) and sodium picosulfate plus magnesium citrate, has proven useful in helping to improve the compliance<sup>[1-5]</sup>.

A patient's age (*i.e.*, the elderly and pediatric populations), general health condition [*i.e.*, pregnancy or lactation, renal or cardiac insufficiency or failure, severe constipation, and hematochezia or suspicious lower gastrointestinal (GI) bleeding] or concurrent medications (*i.e.*, drugs that impair renal function) may lower their tolerance to a certain cathartic agent, and mental or physical disabilities (*i.e.*, dementia or stroke) may preclude their ability to complete the ingestion regimen. While impaired health increases the risk of agent-related complications, failure to comply with bowel preparation instructions in general limits adequate cleansing of the bowel. Unremoved fecal matter occludes the colonoscopic view, resulting in missed lesions, cancelled procedures, increased procedural time, and a potential increase in procedure-related complications, such as perforation, hemorrhaging and infection. Repeated colonoscopy may be unavoidable. This review discusses the special conditions encountered most frequently in the endoscopic clinic so that effective and safe bowel preparation agents/regimens can be chosen.

## SPECIAL CONDITIONS AFFECTING BOWEL PREPARATION FOR COLONOSCOPY

### Elderly patients

Elderly patients ( $\geq 80$ -year-old) show higher rates of inadequate colon cleansing for colonoscopy by the common preparation strategies<sup>[6]</sup>. Application of the NaP-

PEG combination (or NaP as an alternative single agent) is generally not recommended in elderly patients, due to the decrease in renal function that accompanies advanced age and represents an increases risk of agent-related toxic side effects<sup>[7]</sup>. However, when Seinela *et al*<sup>[8]</sup> performed a comparative analysis of the efficacy and safety profiles of NaP and PEG solution in elderly patients no differences were detected; the study's small sample size and in-patient character limit the generalizability of these findings, and the fact that confounding variables (such as education level of the treating healthcare team and occurrences of hypovolemia and electrolyte imbalance) were not evaluated limits the statistical strength of the findings.

Recent investigations have provided insights into the effects of age-related renal failure on oral NaP and aimed to design safe dosing regimens or effective alternatives<sup>[9-16]</sup>. Since NaP use in the elderly has been reported to induce serious electrolyte abnormalities, assessing and monitoring the levels of serum electrolytes, phosphorus, potassium, and calcium is recommended when the agent is considered superior to all other potential agents/regimens for a particular patient. Practice of a dietary regimen including clear liquids and low-residue foods over the course of 1-4 d prior to the main preparation procedure or colonoscopy is helpful in the difficult bowel preparation. While comparative analyses of efficacy and tolerability of split-dose and single-dose regimens have yielded inconsistent findings, consumption of the PEG solution less than at least 5 h before the procedure has shown superior bowel cleansing, particularly for the right colon.

### Pediatric patients

No standardized guidelines for bowel cleansing prior to colonoscopy have been established for the pediatric patient population. The most widely reported regimen in children is 1.25 mg/kg PEG administered over a 4 d period with a liquid diet given on the fourth day<sup>[9]</sup>. The lack of evidence from systematic investigations leaves the possibility open for a shorter and simpler regimen, such as that used in adults of PEG only over a 6-8 h period prior to the colonoscopy<sup>[9,10,17]</sup>. In pediatric cases, delivery of the PEG solution through a nasogastric tube is commonly used when the patient cannot tolerate the oral ingestion method. The common dosage for nasogastric administration is 20-30 mL/min delivered over a 1.2-1.8 h period<sup>[16]</sup>; however, as with adult patients, it is important to modulate the speed of administration *via* nasogastric tube according to subject's situation. Enemas have also been reported as alternative bowel cleansing strategies in pediatric patients, but their effect is limited to the distal colon.

### Pregnant and lactating/breastfeeding women

PEG and NaP solutions are Pregnancy Category C drugs, as designated by the Food and Drug Administration according to their potential benefit to the gravida and inconclusive risk to the fetus<sup>[10]</sup>. Although the need

**Table 1** Bowel preparation under special conditions

Special condition	Considerations for appropriate bowel preparation
Elderly	Avoid NaP to reduce risk of electrolyte imbalance and phosphate accumulation
Childhood	1.25 mg/kg PEG for 4 d with liquid diet on the fourth day
Pregnancy	PEG may be preferable to NaP
Breastfeeding	Interrupt breastfeeding during and after bowel preparation
Severe/chronic constipation	Extend the liquid diet requirement Alternate the bowel preparation agent (PEG or NaP) Provide adjunctive laxative agents (magnesium citrate, bisacodyl, or senna) Apply a combined bowel preparation agent (both PEG and NaP) or double the dosage of PEG solution
Stroke, dementia	If patients have difficulty swallowing, provide the bowel preparation agent <i>via</i> endoscopic irrigation pump or nasogastric tube
IBD	NaP and sodium picosulfate plus magnesium citrate should be avoided because of mucosal damage and irritation
Diabetes	Appropriate dose and proper tempo of fluid intake is important because of delayed colonic transit time NaP should be avoided due to possible risk of hyperphosphatemia, metabolic acidosis, and renal failure
Hypertension	NaP should be cautiously applied in patients taking a drug that affects renal function (diuretics, ARB, ACEi)
Chronic kidney disease	NaP preparation is not recommended because of increased risk of renal dysfunction
Congestive heart failure	PEG solution should be cautiously applied because of an association with increased intravascular volume NaP preparation is not recommended because of electrolyte imbalance and volume loss
Lower GI bleeding	PEG solution may be more effective than enema If a rectal bleeding focus is suspected or severe bleeding is present, enema can be useful

NaP: Sodium phosphate; PEG: Polyethylene glycol; ARB: Angiotensin receptor blockers; ACEi: Angiotensin converting enzyme inhibitors; IBD: Inflammatory bowel disease; GI: Gastrointestinal.

for colonoscopy is rare during pregnancy and no well-controlled studies of pregnant women have been reported, PEG is generally preferred over NaP because small amounts of PEG safely control constipation in pregnancy<sup>110</sup>. In addition, no study in the publicly available literature has yet reported the safety profiles of the various bowel preparation agents/regimens in lactating patients. Interrupting breastfeeding during and after bowel preparation with cathartic agents or application of a tap water enema for sigmoidoscopy have been suggested as cautionary options<sup>9</sup>.

### Severe constipation

Delayed colon transit time from severe or chronic constipation resistant to laxatives can cause inadequate bowel cleansing. Several approaches have been recommended to help overcome this challenge. First, a longer period of liquid diet has shown promising results. Second, consecutive application of alternating bowel preparations (*i.e.*, switching from PEG to NaP or *vice versa*) has been reported as a good option if the cleansing regimen will be completed within 48 h. Third, use of an adjunctive laxative, such as magnesium citrate, bisacodyl or senna, may help to improve the efficacy of the main full-dose regimen. The PEG-NaP combination preparation showed reasonable efficacy but may not be repeated within 24 h because of NaP-related toxicity<sup>110</sup>. Fourth, a double-dose of PEG solution has provided successful bowel preparations.

### Stroke and dementia

Patients who have suffered stroke may have physical difficulties swallowing, and patients with dementia may also be physically incapable of completing the preparation regimen, especially of ingesting the large amounts of fluid required. In such cases, it is preferable to instill

the bowel preparation solution directly into the stomach or duodenum through an esophagogastroduodenoscope with the aid of a water irrigation pump or nasogastric tube<sup>9,10</sup>. Dietary regimens including clear liquids and low-residue foods 1-4 d before colonoscopy and enema can sometimes be helpful in these patients as well.

### Inflammatory bowel disease

NaP and sodium picosulfate plus magnesium citrate may cause mucosal abnormalities that manifest symptoms mimicking colitis<sup>118</sup>; thus, when an initial colonoscopic evaluation is ordered for suspicious inflammatory bowel disease, especially Crohn's disease or colitis, NaP and sodium picosulfate plus magnesium citrate regimens should be avoided. NaP, in particular, can cause aphthoid lesions, erosions, or ulcers. The mucosal lesions caused by both NaP and sodium picosulfate plus magnesium citrate often occur as multiples and are predominantly located in the rectum and distal sigmoid colon<sup>110,118</sup> (Table 1).

### Diabetes

The level of colon cleansing achieved by the common cathartic drug-based regimens was shown to be less efficient in diabetics than their non-diabetic counterparts in a prospective study<sup>119</sup>. Specifically, up to 40% of the endoscopic visualization field was occluded by unretrieved fecal matter in the diabetics (*vs* 97% in the non-diabetics) and approximately 10% of the diabetic patients examined were characterized as having "very poor" bowel preparation. The inadequate cleaning in diabetic patients has been attributed to delayed colonic transit time and constipation<sup>120</sup>. This diabetes-related delay in GI transit time is also associated with more rapid and severe manifestation of nausea and vomiting in response to the ingested PEG<sup>121</sup>; therefore, diabetics may benefit from a more flexible dose and timing regimen of the cathartic

agent(s). Diabetic patients have also been reported to be at higher risk of developing acute renal failure following the oral NaP bowel preparation regimen<sup>[22]</sup>; thus, it is recommended that NaP be avoided in diabetics to reduce the potential risk of hyperphosphatemia and metabolic acidosis related to effects on kidney function (Table 1).

### Hypertension

Many of the hypertension drugs are known to affect renal function; these include diuretics, angiotensin receptor blockers, and angiotensin converting enzyme inhibitors<sup>[9]</sup>. Therefore, the medication history and current medications of patients with hypertension should be carefully considered when choosing a bowel preparation strategy. In particular, NaP should be avoided to decrease the risk of complications due to renal insufficiency.

### Chronic kidney disease

The renal insufficiency that accompanies chronic kidney disease is a significant risk factor for acute phosphate nephropathy<sup>[23]</sup>, such as may be induced upon impaired clearance of the NaP bowel cleansing agent<sup>[24,25]</sup>. The higher risk of NaP for aggravating renal dysfunction in patients with preexisting renal disease, compared to PEG, is well established<sup>[25]</sup>. Thus, it is recommended to measure a patient's creatinine clearance by the estimated glomerular filtration rate (eGFR) prior to prescribing NaP in order to avoid its use in patients with renal disease. The specific contraindication for NaP bowel preparation is an eGFR of < 60 mL/min/1.73 m<sup>2</sup> (corresponding to stage 3-5 chronic kidney disease)<sup>[25]</sup>.

### Congestive heart failure

PEG solution cannot be absorbed into the colon mucosa. Yet, a case of a 73-year-old heart failure patient who experienced aggravated respiratory symptoms after administration of PEG solution was reported<sup>[26]</sup>, and a subsequent study comparing plasma volumes before and after administration of the PEG bowel preparation using an isotope dilution technique showed that mean plasma volume was increased after PEG bowel preparation, supporting the theory that PEG solution may be capable of aggravating heart failure *via* absorption<sup>[27]</sup>. Although only two cases of worsened heart failure following administration of PEG solutions have been reported, careful use is advocated in these patients. The alternative cathartic NaP, another non-absorbable osmotic laxative, can also induce volume loss and electrolyte imbalance, and is generally not recommended for use in heart failure patients.

### Hematochezia or lower GI bleeding

Although the role of emergency colonoscopy in lower gastrointestinal bleeding remains controversial, urgent colonoscopy within 12-24 h of admission can improve diagnostic yields and reduce the rates of both rebleeding and surgery<sup>[9]</sup>. Adequate bowel preparation is considered beneficial for identification of the bleeding focus of hematochezia, but a standardized method for emergency

conditions has not yet been established. Lim *et al.*<sup>[28]</sup> performed a comparative analysis of the clinical effectiveness of enema and PEG bowel preparation methods in hematochezia patients and demonstrated that the latter yielded a higher diagnostic rate and a lower rate of repeat colonoscopy. Similarly, Saito *et al.*<sup>[29]</sup> showed that PEG solution was associated with better outcome of acute lower intestinal bleeding. In general, when the amount of bleeding is presumed to be small, bowel preparation using PEG solution may be effective in hematochezia patients; in contrast, if the bleeding focus is suspected to involve the rectal area or if the amount of bleeding is severe, an enema may be more useful and convenient.

## CONCLUSION

Adequate bowel preparation is important for effective colonoscopy but can be limited by an individual's particular physical- and health-related conditions, such as age, pregnancy and comorbidities, or even mental states that inhibit the ability to comply with bowel preparation instructions. Therefore, it is necessary for the endoscopic healthcare team to identify a patient's specific conditions and select an appropriate bowel preparation agent and method in order to maximize the efficacy and safety of both the preparation procedure and the subsequent colonoscopy.

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