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Safety Issues Regarding Colonic Cleansing for Diagnostic and Surgical Procedures

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Abstract

There are various methods available to cleanse the colon in preparation for diagnostic and surgical procedures. The popular options are diet and cathartic regimens, gut lavage and phosphate preparations. Each method has its own unique characteristics and safety profile. Diet and cathartic regimens are based on traditional methods of colonoscopy preparation and remain an acceptable and safe alternative for patients unwilling or unable to tolerate other bowel preparations. Gut lavage methods involve ingestion of 2–4L of osmotically balanced solutions containing polyethylene glycol, which have been shown to be safe and effective for colon cleansing, including for special patient populations with cardiac, renal or hepatic dysfunction. Phosphate preparations have also been shown to be safe and effective for colon cleansing and are generally better tolerated than counterpart gut lavage solutions. However, this method has safety concerns for some patients with cardiac, renal and hepatic dysfunctions.

Optimal cleansing of the colon for diagnostic and surgical procedures should be obtained by a preparation regimen that cleanses the colon with reasonable levels of patient tolerance and safety. Currently, the three popular choices for cleansing include regimens that use dietary modifications and cathartic laxatives, gut lavage or phosphate preparations. However, recently the US FDA has raised concerns regarding the safety profiles of bowel cleansing preparations. Even clinicians who do not regularly have to prepare their patients for diagnostic or surgical procedures should be aware of the unique characteristics of each method.

The aim of this review is to provide an overview of the methods available for colonic cleansing, with a focus on the unique characteristics, efficacy and safety profile of each preparation.

A Medline search was conducted from 1966 through January 2003 using the keywords and subjects 'colonoscopy', 'sodium phosphate', 'polyethylene glycol', 'adverse events' and 'safety'. Further related articles were found using the reference citations from articles identified in the Medline search.

1. Diet and Cathartics

Traditional preparations for colonoscopy cleansing consisted of clear liquid diets for 48–72 hours combined with laxatives and cathartics.[1] Dietary restrictions ranged from 1 to 4 days resulting in poor patient compliance, patient intolerance and safety concerns about malnutrition. Elderly patients, in particular, had difficulties adhering to strict dietary regulations, which could lead to significant protein and calorie malnutrition.[2,3] DiPalma et al.[4] studied the effects of various diets in combination with laxatives and enemas. This study showed that 1–3 days of a diet designed to leave a minimal colonic faecal residue was as good as, or better than, diets that only allowed clear liquids for 3 days. Furthermore, patients preferred the minimum-residue diet regimens. The diet was designed to leave a minimal colonic faecal residue with suggested foods for breakfast such as scrambled eggs, white toast with jelly, apple juice, water, tea or coffee. For lunch, bouillion soup and a white meat chicken or turkey sandwich was allowed. For dinner, bouillion, non-citrus juice, jello-type dessert, water, coffee or tea was suggested. No butter, mayonnaise, lettuce or cream was allowed.

Table I. Popular colonic cleansing regimens

Cleansing method	Description
Diet and cathartics	
Diet	Clear liquids for 72 hours or 1–3 days of a diet designed to result in a minimal colonic faecal residue
Cathartic	Magnesium citrate or X-Prep®[a] liquid (extract of senna fruit)
Additional cathartic	Bisacodyl tablets and/or suppositories
Enema	Tap water enemas
Gut lavage	
PEG-ELS	GoLYTELY® Colyte®
SF-ELS	NuLYTELY® Half Lytely® (reduced-volume NuLYTELY® with bisacodyl)
Phosphates	
Oral phosphosoda	Fleet® Phospho-soda®
Phosphate tablets	Visicol®

a The use of trade names is for product identification purposes only and does not imply endorsement.

PEG-ELS = polyethylene glycol electrolyte lavage solution; **SF-ELS** = sulphate-free polyethylene glycol electrolyte lavage solution.

Table I reviews the popular colonic cleansing methods. The diet and cathartic methods use laxatives and enemas. Bisacodyl and castor oil may be useful cathartics. However, patients commonly report cramping as an adverse effect.[5] Lactulose should be avoided as it results in the production of potentially combustible gases that pose a risk during electrocautery. As with all cathartics, adequate hydration is necessary to prevent complications of volume depletion and subsequent electrolyte disturbances.[5] A large, randomised trial studied senna in colonoscopy preparations, prospectively comparing doses of 300mg taken in divided doses with a dose of 150mg on the day prior to the examination.[6] Acceptable preparations were seen in 97.3% of the patients using high-dose senna. Adverse reactions consisted mainly of abdominal pain and nausea in 11% of patients. However, there are no other large trials comparing senna with other popular forms of bowel preparation. Nonetheless, diet and cathartics remain a safe alternative for patients unable to tolerate other bowel preparations.

2. Gut Lavage

Orthograde gut lavage provides for rapid colon cleansing in preparation for colonoscopy, barium enema and colonic surgery.[7-11] These are electrolyte and osmotically balanced solutions, which include polyethylene glycol electrolyte lavage solution (PEG-ELS) and sulphate-free polyethylene glycol electrolyte lavage solution (SF-ELS).

2.1 Polyethylene Glycol Electrolyte Lavage Solution

Davis et al.[12] developed the osmotically balanced solution PEG-ELS for gut lavage. It was

found to be safe and effective. The most common adverse effects associated with its use are volume-related symptoms of abdominal fullness, nausea and bloating[13] (table II). Prior to the use of polyethylene glycol there had been reports of explosions during electrocautery.[14,15] For the most part, these solutions had contained mannitol, which when fermented by colonic bacteria, produced combustible gases such as methane and hydrogen. Polyethylene glycol solutions do not contain mannitol and, thus, do not produce the combustible by-products. Davis et al.[12] reported this lack of measurable combustible gases in PEG-ELS faecal suspensions. In addition, it has been shown that breath hydrogen measurements of the combustible gases methane and hydrogen after administration of PEG-ELS are below explosive concentrations.[4,16] However, there is concern that patient self-administered flavouring additives such as sweeteners may provide a substrate for the bacterial production of methane and hydrogen gas. For this reason, coupled with the knowledge that additives will alter the osmotic balance of polyethylene glycol solutions, patients should be instructed to avoid any self-administered additives. However, PEG-ELS and sulphate-free solutions do contain flavourings for palatability such as cherry, lemon-lime and orange, which have shown no production of combustible gases.[17]

Gut lavage preparations available before the introduction of PEG-ELS used saline or balanced electrolyte solutions, which often required upwards of 7–12L of volume administration.[18] Saline lavage can result in water absorption of up to 819 mL/hour resulting in a net water gain of up to 8L of fluid, whereas PEG-ELS has been shown to cause only minimal fluid shifts.[12] Because of these large volumes, electrolyte imbalances and fluid shifts, an osmotically balanced solution such as PEG-ELS became a safer alternative. Indeed, over a 3- to 4-hour period, standard administration of 3–4L of PEG-ELS was shown to result in only 190–250mL of fluid absorption.[13] Davis et al.[12] also demonstrated that electrolyte shifts are minimal. These results have been confirmed by others, showing that no significant differences could be found when comparing parameters such as electrolytes, BUN (blood urea nitrogen) levels, urine-specific gravity and patient weight between groups taking PEG-ELS and those on a standard regimen of diet and cathartics.[4,19-21]

Table II. Reported adverse effects of bowel preparations

Cleansing method	Adverse effects
Diet and cathartics	Electrolyte disturbances Dehydration
Gut lavage	Aspiration Allergic reactions: angioedema, urticaria, anaphylaxis Bleeding reactivation Volume-related symptoms: bloating, nausea, vomiting Esophageal tears Perforation Pill malabsorption Hypothermia
Oral phosphates	Electrolyte disturbances: hyperphosphataemia, hypocalcaemia, hypokalaemia, hypomagnesaemia Dehydration Renal failure Seizures Colonic aphthous ulcerations

There appear to be no toxicities associated with the oral ingestion of PEG-ELS.[22] A study showed that patients ingesting PEG-ELS had no changes in urinary polyethylene glycol or sulphate levels, suggesting little if any absorption.[23] After direct parenteral administration of PEG-ELS into animal models at doses of up to 90 mg/kg for 2–12 months, no adverse effects were seen and no abnormalities noted on either gross or microscopic examination of cranial, thoracic or abdominal organs.[24]

Contraindications for PEG-ELS administration include cases of gastric outlet obstruction, high-grade small bowel obstruction, significant colonic obstruction, perforation, diverticulitis and haemodynamic instability.[13] In cases of suspected incomplete obstruction a 1L trial of lavage can be administered under observation to ensure tolerance.[1] Gastroparesis should also be considered a relative contraindication for gut lavage preparation but a 1L trial may also be attempted. Allergies to polyethylene glycol compounds are a contraindication to PEG-ELS and SF-ELS. There have also been case reports of systemic allergic and urticarial reactions to polyethylene glycol solutions.[25-29]

Mallory-Weiss tears and bleeding reactivation have been reported with the use of gut lavage preparations.[13] However, studies support the safety and

efficacy of PEG-ELS administration in acute lower gastrointestinal bleeding.[30-32] In cases of severe haematochezia, appropriate cleansing can be safely achieved with as little as 500mL of polyethylene glycol solution.[22] Among patients with inflammatory bowel disease (IBD) and bleeding, PEG-ELS administration has also been found to be safe. Despite active disease, IBD patients given PEG-ELS solution showed no significant polyethylene glycol absorption.[23]

Further adverse events include rare cases of reported hypothermia and lavage-induced pill malabsorption[13] (table II). However, most pills that were recovered in these cases were found to only contain the waxy outer coating of the pill instead of the active medication itself.[33,34]

2.2 Sulphate-Free Polyethylene Glycol Electrolyte Lavage Solution

Due to the common complaint of a disagreeable taste associated with PEG-ELS preparations, SF-ELS was developed, which eliminated the 'rotten egg' smell and salty taste caused by sodium sulphate.[35] SF-ELS was found to be both safe and effective when used as a preparation for colonoscopy, barium enemas and elective bowel surgery.[36-40] It has a different mechanism of action than PEG-ELS. SF-ELS results in less net movement of water or electrolytes than PEG-ELS. PEG-ELS relies upon the cleansing action of its osmotic gradient generated from its molecular weight and the electrochemical gradient generated by sodium sulphate.[5] In contrast, SF-ELS largely relies upon the osmotic potential of polyethylene glycol for its cleansing actions.

In a prospective trial, SF-ELS was similar to PEG-ELS with respect to safety, efficacy and patient tolerance.[37] This study included a high-risk subset of patients with prior histories of cardiac, renal, diabetic or hypertensive disease. Only clinically insignificant changes in a few laboratory parameters were noted when comparing SF-ELS and PEG-ELS. Patients who showed a taste preference favoured SF-ELS.

2.3 Reduced-Volume Method

Gut lavage administration requires large volumes of liquid and volume-associated adverse effects are common. Efforts have been made to develop an effective colonic preparation with a reduced volume lavage by the use of adjunct agents.[41] Enemas have been shown to provide no additional benefit at the expense of increasing rectal trauma.[42] The prokinetic agents metoclopramide and cisapride were found to confer no benefits in reducing lavage amounts or the symptoms associated with its ingestion.[43-45] Trials with bisacodyl and magnesium citrate as pre-treatment agents have been promising. Sharma et al.[46,47] demonstrated similar efficacy of a reduced-volume (2L) lavage coupled with magnesium citrate as pre-treatment compared with a standard 4L PEG-ELS administration. Bisacodyl was also found to have similar success to magnesium citrate at reducing lavage volume.[48]

DiPalma et al. studied results of colonic preparation using a standard 4L of SF-ELS compared with a regimen consisting of 2L of SF-ELS and bisacodyl 20mg.[49] The prospective study of 200 patients showed similar efficacies of colonic preparation between the two groups. From a safety perspective, no clinically significant differences could be detected between the two groups in comparisons of weight, haematological and biochemical changes. The reduced-volume group experienced significantly less volume-related symptoms of fullness, nausea, vomiting and overall discomfort.

2.4 Nasogastric Administration

The administration of gut lavage through nasogastric tubes is an alternative reserved for patients unable to tolerate the standard oral administration. Because the majority of these patients are elderly with diminished mental states, decreased insight into their medical conditions or multiple other medical problems, there exists an increased risk of lavage aspiration with this route of administration. Patients needing nasogastric tube administration are often not closely monitored during lavage administration and they lack the necessary skills to notify staff of problems when they arise. A nasogastric tube has also been known to rupture the seal of the normal esophageal gastric junction,[50] promoting gastroesophageal reflux.

Of the six case reports of PEG-ELS aspiration complications, the common feature is the nasogastric tube administration.[51-54] Two of these cases

involved administration in children whereas the rest were represented by adults unable to tolerate their solutions by conventional oral means. The aspiration resulted in adult respiratory distress syndrome and non-cardiac pulmonary oedema. In this series three patient deaths were reported.

The use of nasogastric tubes for administration should only be used under close monitoring. Tube placement in proper position should be verified and full aspiration precautions employed, including head of bed elevation during and after preparation administration.

2.5 Elderly Patients

In a study addressing age, 557 patients were stratified into two groups, >60 years and ≤60 years of age, all of whom received either PEG-ELS or a diet and cathartics preparation for colonoscopy, barium enema or elective colon surgery.[55] Common symptoms of nausea, vomiting, cramps, abdominal fullness and overall discomfort were analysed. Those patients in the older age group reported significantly fewer cramps ($p < 0.05$) and no differences in overall discomfort than their younger PEG-ELS counterparts. Most patients reported minimal discomfort with either preparation across age groups. Older patients preferred the PEG-ELS method of bowel preparation by 81% compared with prior preparations. No differences were found in the adequacy of colon cleansing between the age groups.

A second study evaluated senior patients >75 years of age randomised to a laxative preparation or standard PEG-ELS lavage.[56] The older patients showed greater tolerance for the laxative preparation with essentially no difference in efficacy.

2.6 Paediatric Patients

Traditionally, children have been prepared for colonoscopy using clear liquids for 48–72 hours, with laxatives and enemas the day before and morning of the procedure.[57] Lavage with PEG-ELS has been shown to be safe and efficacious in the paediatric population.[21,58,59] However, difficulties arise in patient compliance for the ingestion of large amounts of lavage solution. Oral sodium phosphates were compared with PEG-ELS in this population, showing a greater degree of patient acceptance for the sodium phosphate preparations, though at the cost of greater degrees of hyperphosphataemia than the adult population.[60] Dahshan et al.[59] studied three preparations consisting of magnesium citrate with senna and clear liquid diet for 2 days, bisacodyl and phosphosoda enema without dietary restrictions and the standard 4L of PEG-ELS with a clear liquid diet for 1 day. PEG-ELS provided the best cleansing. However, the magnesium citrate regimen with senna was better tolerated with adequate cleansing.

3. Oral Sodium Phosphate

After the initial report of oral sodium phosphate for colonic cleansing by Vanner et al.[61] in 1990, phosphates have become an attractive alternative to gut lavage for colonoscopy preparation. This acceptance is largely due to the smaller amounts of solution required for ingestion, with a recommended dose of 45mL of oral sodium phosphate solution diluted with water and given at two intervals, 12 hours apart. The small volume is possible because of the high osmotic effects and hypertonicity of the solution, which contains 48g (400 mmol/L) of monobasic sodium phosphate and 18g (130 mmol/L) of dibasic sodium phosphate per 100mL.[62] Numerous studies have supported oral sodium phosphate with respect to patient acceptance and efficacy equivalent to or exceeding that of large-volume PEG-ELS.[61,63-70] In addition, oral sodium phosphate tablets have recently been introduced with clinical trials supporting their efficacy and patient acceptance.[65,71,72] The recommended tablet dose is 40 pills taken with ten glasses of water.

Because of the small hypertonic volume of solution, concern exists for the safety profile of oral sodium phosphate. Hypovolaemia and electrolyte disturbances largely consisting of hyperphosphataemia and subsequent hypocalcaemia occur. Studies comparing orthostatic changes in volume between oral sodium phosphate and PEG-ELS showed essentially no differences,[61,70,73] and urine and serum osmolality have shown only minor intravascular contraction.[61,73]

Several studies have reported on the rise in serum phosphorus levels as a result of oral sodium phosphate ingestion, with subsequent falls in serum calcium levels.[61,65,68,70,73,74] In these studies the

lowest serum ionised calcium change was of 1.07 mmol/L.[73] None of the patients in this reported series experienced clinical symptoms from hypocalcaemia or hyperphosphataemia and the authors suggest that such transient electrolyte abnormalities have little clinical relevance.[73] However, it should be noted that the studies excluded patient populations with co-morbidities such as heart failure, renal failure, recent myocardial infarction and known electrolyte abnormalities.

Hyperphosphataemia may exhibit its effects by elevating the calcium-phosphorous solubility product (normally at 40) thereby causing soft tissue calcifications in various organs.[75] DiPalma et al.[74] found the mean peak solubility product to be elevated at 60.9 in a study of seven patients. In this study, significant rises in phosphorus and falls in calcium were seen and one study subject developed nephrolithiasis and renal colic.

Mechanisms for such hyperphosphataemia may include increased absorption from ileus or prolonged impaction, impaired renal excretion or excessive dosages of sodium phosphate.[76] Of the 13 case reports of adverse events from oral sodium phosphate colonoscopy preparation, seven were associated with improper dose administration.[77-81] Two of these seven cases resulted in fatal hyperphosphataemia or hypocalcaemia and renal failure, while the others were noted to have symptomatic electrolyte disturbances. Of the six reported fatal cases of oral sodium phosphate ingestion, all were associated with improper dose administration.[76,80,82,83]

There is less safety experience with the use of oral sodium phosphate tablets. The FDA has reported four cases of hyponatraemia and subsequent seizures associated with the tablet use.[84]

Given the potential for complications and the lack of studies on selected patient populations with pre-existing co-morbidities, phosphates are poor choices for colonoscopy preparation in patients with cardiopulmonary, renal and hepatic diseases as well as in patients with pre-existing known electrolyte imbalances. A FDA safety review suggests obtaining baseline and post-treatment chemistry panel evaluations for patients taking oral sodium phosphate, particularly if the recommended dose is exceeded.[84] Despite these warnings, a study of Canadian colonoscopists showed many to be unaware of these select high-risk patient groups and their potential complications as a result of oral sodium phosphate ingestion.[85]

4. Conclusion

Effective colon cleansing is essential for a proper colonoscopic exam and several available preparations yield acceptable cleansing results. Diet and cathartics, phosphates and orthograde gut lavage have all been shown to provide effective cleansing with good overall safety profiles. Practitioners must be aware of select patient populations such as those with cardiac, renal and hepatic dysfunction, as well as those patients with pre-existing electrolyte abnormalities, in order to avoid potential complications from phosphate solutions. In addition, cases of possible bowel obstruction should be recognised prior to the administration of any regimen. All of the recognised bowel preparations should be given only as per the manufacturer's guidelines because of the potential complications of additives and inappropriate dose administration. Further research is needed in the field to provide a more palatable and better tolerated formula than existing preparations with similar high levels of safety. The choice of preparation must be made on an individual basis taking into account patient preference, compliance and co-morbidities to effectively cleanse the colon in the safest possible way.

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