

# ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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## Oral Preparations for Colonoscopy

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**G&H** With all the recent advances in oral preparations for colonoscopy, can any of them be considered “easy” to use?

**WT** Bowel preparations are never easy; they are the most difficult part of a colonoscopy for most patients. The one advantage that some of the preparations have is a reduced volume. The easiest preparation is one that is most palatable and causes little abdominal discomfort or nausea. They all result in a catharsis and cleansing of the bowel (which is obviously a bit unpleasant to deal with), but the critical issues consist of the volume and taste of the preparation, which is what patients complain about the most. The combination of smaller volumes (2 L vs 4 L) of polyethylene glycol (PEG) and bisacodyl has been reported to be better tolerated by patients. The Phosphosoda preparations in pill form are also generally palatable to patients, but have renal safety concerns. The combination of magnesium citrate plus 2 L of PEG also provides the advantage of a small volume, though it still involves nearly 3 L of fluid intake. The emerging sulfate-based regimen has the potential to be the easiest preparation if proven to be safe in future studies.

**G&H** Could you further discuss the emerging sulfate-based regimen and any others that hold promise?

**WT** Generating much interest is a sulfate-based preparation, which was recently compared with a 2-L PEG

ascorbic acid regimen by Di Palma and associates. This new preparation appears to be well tolerated and very efficacious. Its main advantage is its volume; with this preparation, a patient has to drink only 1 L, followed by some water or clear fluids, as opposed to the standard 2- or 4-L PEG-based preparations. The data on this new preparation are very limited at this point, but there are some encouraging early results. It is certainly a potential new regimen that holds promise for patients undergoing colonoscopy, particularly for those who are opposed to using large-volume preparations.

Another emerging colonoscopy preparation, one that is commonly used in clinical practice despite a virtual lack of data, involves the use of an over-the-counter PEG without the balancing electrolytes (PEG 3350) that is approved for constipation, mixed with an oral electrolyte solution such as Gatorade or other sports drinks. Although many clinicians assume that this particular regimen is safe and effective, there are very scant data evaluating it. If this regimen does prove to be efficacious and safe, it will likely be widely used, as it is anticipated that patients will find it more palatable than the currently approved PEG-based regimens with electrolyte solutions (mainly due to the improved taste that results from mixing it with Gatorade or other sports drinks).

**G&H** Could you further discuss the issue of renal toxicity resulting from colonoscopy preparations and any advances that have been made for prophylactic treatment for this concern?

**WT** Some studies have attempted to assess whether hydrating patients with an extensive amount of oral hydration prior to the initiation of bowel preparation prevents renal injury, but emerging data suggest that it does not.

Although clinically significant renal injury appears to be very rare, the actual incidence of long-term renal insults is not clear. This is one of the reasons that the US Food and Drug Administration placed a black box warning on prescription Phospho-soda preparations and urged people to avoid using over-the-counter Phospho-soda, which has subsequently been withdrawn from the market. Several animal- and physiology-based studies suggest some degree of renal impairment, particularly when using two doses of Phospho-soda. The second dose appears to be the critical issue promoting calcium and phosphate deposits in the kidney that can lead to renal impairment up to 1 year later.

### **G&H** What is the effect of the number of preparation doses on efficacy and patient tolerance?

**WT** Examining the effectiveness of a preparation when it is split into multiple doses as opposed to taken in one short time interval the day prior to the procedure is currently one of the most debated issues in this field. The Phospho-soda preparations have historically been a split-dose regimen in which one dose was taken the day prior to the procedure and the other dose was taken the morning of the procedure. This concept led to the idea of evaluating split-dose preparations for PEG-based regimens. Clinical studies suggest that splitting the dose does provide an improved preparation of the colon, particularly in patients who receive their second dose of PEG approximately 4–8 hours prior to the procedure. The issue that is unclear is whether, on a population basis, this will be widely accepted by patients. This is a great regimen for patients who undergo their procedure in the late morning or early afternoon, as the second dose can be timed to be taken very early on the morning of the procedure. However, patients who have their procedure scheduled for the early morning would have to take their second dose around 2 AM, which would be very inconvenient and unlikely to be widely accepted by patients. This inconvenience must be related to the potential benefits of improved quality of the colonoscopy examination with an excellent preparation.

### **G&H** How helpful is the use of laxatives or other treatment aids with oral preparations?

**WT** There are some older data that suggest that magnesium citrate can improve a preparation, particularly with PEG-based regimens. In fact, magnesium preparations with a smaller volume of PEG (2 L) appear to be as efficacious, or slightly more efficacious, relative to 4 L of PEG. In addition, there is a regimen currently on the market that uses 2 L of PEG followed by a 10-mg dose of

bisacodyl, which is a stimulant laxative. This combination appears to result in an equivalent bowel preparation to the 4-L regimen. There are even older data that suggest that adding simethicone may improve mucosal visualization when taking 4 L of PEG.

### **G&H** How do the various bowel preparations compare in terms of cost?

**WT** This is an important issue; practitioners should be aware of the great variation in cost of the preparations, as some are extraordinarily expensive. The pill form preparations tend to be the most expensive and can cost approximately \$150 for the entire preparation. The newer, smaller-volume PEG-based regimens are also quite expensive, in the range of \$50. One of the advantages of the old over-the-counter Phospho-soda preparations was that they were very inexpensive. The standard PEG-based 4-L regimens generally cost approximately \$20–25. Insurance coverage varies significantly by carrier.

### **G&H** How are bowel preparations graded in terms of adequacy?

**WT** It is difficult to compare most of the studies that have been conducted because they have used different scales and different grading systems to determine the adequacy of the bowel preparation. Recently, there has been some work looking at standardizing the bowel preparation nomenclature and determining whether there is a great deal of interobserver consistency. An example of one of these scales is the Boston Bowel Preparation Scale, which a recent study by Calderwood suggested was reproducible and has near perfect intraobserver consistency and excellent interobserver agreement. When comparing different studies, clinicians need to keep in mind that there is a greater deal of heterogeneity because of the differences in bowel preparation and what is considered acceptable and unacceptable. A common system of reliably grading bowel preparation and a minimum threshold of what provides for an acceptable examination of the colon is greatly needed.

### **G&H** Does performing a digital rectal examination prior to colonoscopy help predict the effectiveness of the preparation?

**WT** A digital rectal examination is not very sensitive, but it is fairly specific. In other words, when the digital rectal examination reveals solid stool, the preparation is not likely to be acceptable. However, a normal rectal examination with no material in the rectum does not in any way guarantee an acceptable preparation.

## G&H Are there any contraindications to the use of bowel preparations?

**WT** There are several contraindications to bowel preparations. If a patient has a bowel obstruction, they should not use an oral-based preparation. If a patient has a risk of aspiration or vomiting, they should not be given a large-volume preparation in which they have to drink 4 L. Other contraindications include patients who have allergic reactions to any of the preparation components.

Certainly, the Phospho-soda preparations are contraindicated for people with renal disease, those taking angiotensin-converting enzyme inhibitors or blockers, and anyone susceptible to sodium overload, including patients with congestive heart failure and advanced liver disease.

There is also a concern that patients should not use lactulose or other nonabsorbable carbohydrates, which are available as laxatives, because of the concern for the production of combustible gases in the colon by residual bacteria. There is a small but not minimal risk of explosion within the colon when cautery is used in the presence of combustible gases.

## G&H What are the next steps in future research?

**WT** As mentioned above, the safety and efficacy of using PEG 3350 plus Gatorade or other sports drinks needs to be clarified. A study of a large private practice was presented at this past year's Digestive Disease Week that found that adding bisacodyl to a combination of PEG 3350 plus magnesium citrate resulted in an increased incidence of ischemic mucosal injury at the time of colonoscopy. When the bisacodyl was removed, that mucosal injury no longer appeared to be present. There are many combinations that should be examined in terms of efficacy and safety, and all of those permutations are open for future study.

The issue of patient acceptability and optimal timing of split-dose regimens, also mentioned earlier, should be examined further.

Studies should also be conducted to evaluate the different bowel preparation regimens and their impact on the adenoma detection rate, which is one of the surrogate clinical markers used to determine the effectiveness of colonoscopy at preventing colon cancer.

Additional data are also required for the new sulfate-based regimen mentioned that has the potential to present a change in colon preparation if further studies show success and safety, as this low-volume palatable preparation will be very attractive to patients. The critical issue here, and with all regimens, is for practitioners to know what has been studied and what has not been studied and to avoid using tailored regimens outside the realm of a clinical study; if a regimen has not been well studied and proven to be effective, particularly proven to be safe, it should be avoided on a large scale.

## Suggested Reading

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