

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Split Dosing for Bowel Preparation



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G&H What have studies reported regarding the efficacy of split dosing versus evening-before dosing for bowel preparation?

DKR Thus far, I am aware of 12 trials that have directly compared split dosing with evening-before dosing for bowel preparation, and all but 1 of these trials found that split dosing was superior with regard to efficacy. None of the trials found evening-before dosing to be superior. In these studies, the benefits of split dosing were particularly evident in the ascending, or right, colon. The magnitude of the effect of split dosing was quite impressive; in some of these studies, the number of patients who had an excellent or adequate preparation increased by 30–40% with split dosing, compared to evening-before dosing of the same preparation. Differences of this magnitude have not been seen when comparing different bowel preparations. Thus, splitting a bowel preparation is a more effective way of attaining an excellent or adequate bowel preparation than switching to a different preparation.

G&H Why is split dosing more effective than evening-before dosing?

DKR Administering a bowel preparation either the day before a colonoscopy or in a split-dose fashion, with the second dose on the same day as the colonoscopy, is effective for clearing fecal material out of the colon. However, after the fecal material has been cleared, more material—including intestinal secretions, chyme, and mucus—start to come out of the small intestine. These materials can stick quite tenaciously to the colon, especially in the

cecum and ascending colon. Thus, even though the bowel preparation cleared out the stool, the preparation starts to deteriorate, especially in the cecum and right colon, because of these materials, as time passes from the administration of the bowel preparation.

G&H What split-dose bowel preparations are currently available, and how do they compare?

DKR Two split-dose bowel preparations have been approved by the US Food and Drug Administration: Suprep (Braintree Laboratories), which is an oral sodium sulfate preparation that can be used only in a split-dose manner, and Moviprep (Salix), a polyethylene glycol (PEG) preparation that can be used in either an evening-before or split-dose manner. However, any bowel preparation currently being used—including any type of 4-L or 2-L PEG preparation—can be split by administering half of it the evening before a colonoscopy and the other half the morning of a colonoscopy.

There have not been many head-to-head comparisons between split-dose preparations. Studies usually compare a preparation given in split doses with a different preparation given entirely the evening before a colonoscopy. In these studies, the split-dose preparation is invariably superior. In the few head-to-head studies that have been conducted comparing different preparations both given in split doses, preparations have generally been found to be equivalent. In my opinion, however, there is a dose-response effect with PEG preparations, so the failure rate with 2-L PEG electrolyte lavage solution preparations is higher than that for 4-L preparations. It should not be an

unexpected result that 4-L preparations are more effective than 2-L preparations.

G&H Can split dosing be used in all patients undergoing a colonoscopy?

DKR I believe that split dosing can be given to all patients. There has been some concern regarding the use of split doses in patients who have known delayed gastric emptying, are diabetic, or take opioids or tricyclic antidepressants (which might slow gastric emptying). However, the studies that have been conducted thus far have not identified any evidence that split dosing poses a greater risk in these patients. Therefore, in my opinion, and in my practice, any patient can be given a split-dose bowel preparation.

G&H Are there any safety concerns regarding the use of split dosing for bowel preparation?

DKR One of the main safety concerns is that split dosing may lead to an increased risk of aspiration pneumonia. It has been speculated that patients may have more liquid in their stomach after undergoing split dosing and may be more likely to reflux and aspirate when they are sedated. The research conducted thus far in patients who stop taking clear liquids 2 hours or longer prior to sedation indicates that the volume of residual gastric fluid appears to be independent of when liquid intake was stopped. In other words, there is no difference in the volume of residual gastric fluid among patients who stopped taking liquids 12 hours, 8 hours, or 2 hours before colonoscopy. Nevertheless, the amount of residual gastric fluid is variable in patients, even those who have been nil per os for more than 8 hours. Endoscopists are well aware of this from their performance of routine upper endoscopy in patients who have been nil per os since the night before. The mean volume of residual gastric fluid in these patients is approximately 20 cc; however, some patients have up to 120 cc of fluid, with or without split dosing.

Thus, it is important to be vigilant about the possibility of reflux when patients undergo deep sedation because they may not be able to protect their airway if they experience reflux. In my experience, reflux and aspiration tend to occur when patients develop hiccups or have diaphragmatic spasms. In addition, patients often heave or retch slightly prior to experiencing reflux. Therefore, when these symptoms appear, doctors should have patients turn on their side and should be ready to suction patients' mouths to try to prevent aspiration. When aspiration does occur in the setting of deep sedation—independently of split dosing—the aspiration tends to be just small amounts of liquid, usually resulting in a period of coughing and perhaps bronchospasm but usually not pulmonary infection.

Split dosing may actually be safer than evening-before dosing, particularly with regard to electrolyte imbalance, because the patient takes only part of the preparation and then has time to recover, from an electrolyte standpoint, before drinking the rest of the preparation. Electrolyte abnormalities that are induced by the preparation are probably more severe when the entire preparation is taken over a short period of time. However, this issue has not yet been studied.

G&H How do split dosing and evening-before dosing compare in terms of patient tolerability?

DKR A recent meta-analysis and several separate randomized controlled trials have shown that split-dose preparations are better tolerated by patients compared to evening-before preparations. I am not aware of any studies showing that split-dose preparations are tolerated more poorly by patients.

G&H How receptive have patients been to the idea of split dosing?

DKR My colleagues and I conducted a survey to examine this issue. We found that if patients are given an explanation for why split dosing is important, they are typically quite willing to use it. The patients who are most inconvenienced by split dosing are those who schedule early morning colonoscopies (at 7:00–9:00 AM). These early morning appointments are usually coveted by patients because the colonoscopy unit is less likely to be running behind schedule. Our experience has been that even patients with these early appointments are quite willing to get up during the middle of the night to take the second dose of preparation once they understand why it is important to do so. Patients who are not willing to get up during the night can either schedule later appointments or take the second dose of the preparation very late on the night before the colonoscopy. In the latter case, patients will still have a relatively good preparation because the preparation does not deteriorate all of a sudden; it deteriorates gradually as the number of hours since taking the preparation increases.

G&H Have doctors also been receptive to adopting split-dose bowel preparation?

DKR Doctors have been increasingly receptive to split dosing for bowel preparation; once they try it, they tend to like it because colonoscopy is much more effective and efficient, and less time is spent cleaning the colon. However, there is often initial resistance to trying split dosing, often due to the mistaken belief that patients are unwill-

ing to get up during the night to take the second dose of the preparation. In my experience, patients are quite serious about colonoscopy because they understand the value of giving their doctor the best possible opportunity to prevent colon cancer.

Occasionally, doctors are also concerned that patients will have to stop on the way to the colonoscopy suite to go to the bathroom. This issue has been examined several times; the number of patients who have to stop to go to the bathroom does increase with split dosing, but the difference is not statistically significant, and the overwhelming majority of patients do not need to stop.

G&H When using a split-dose bowel preparation, what is the ideal time interval between the last dose and the colonoscopy?

DKR We do not know the answer to this question with certainty. In my opinion, it is probably best to start taking the second dose of the preparation approximately 4–5 hours before the scheduled time for the colonoscopy. At my center, we instruct patients to finish drinking the preparation 3 hours before the scheduled time of the colonoscopy, and the smallest time interval in which we are comfortable sedating patients is 2 hours. This adheres to the American Society of Anesthesiology's policy on fasting prior to sedation and anesthesia, which allows patients to take clear liquids up until 2 hours before sedation. As previously discussed, bowel preparation deteriorates slowly over time. Having 6–8 hours between the last dose and the colonoscopy yields a fairly good-quality preparation; however, with each additional hour, the quality of the preparation decreases.

G&H What are the next steps in research in this area?

DKR A recent area of interest has involved a variation of split dosing called same-day dosing, in which the patient takes the entire bowel preparation on the day of the colonoscopy. This dosing strategy appears to achieve

the same benefits as split dosing with regard to efficacy. However, it is still unclear whether this dosing strategy is well tolerated by patients, though it does appear to interfere less with their activities the day before the colonoscopy, compared to split dosing.

Another area of future research involves the amounts of preparation to be given in the split doses. Splitting the dose usually means taking half of the preparation the night before and the other half the morning of the colonoscopy, but the split does not necessarily have to be equal. There has been some research on taking three fourths of the bowel preparation the night before and one fourth of the preparation the morning of the colonoscopy; however, more investigation is needed on this issue.

More research is also needed regarding whether the time interval between the bowel preparation and the colonoscopy has any influence on the appearance of polyps, particularly serrated polyps and hyperplastic polyps in the proximal colon. These polyps are detected by endoscopic signs such as the mucus cap and the polyp's debris field. It would be beneficial if doctors could time the preparation to optimize the quality of the mucus cap or debris field, thus increasing the chance that an important polyp could be detected.

Suggested Reading

Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM; American College of Gastroenterology. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol*. 2009;104:739-750.

Di Palma JA, Rodriguez R, McGowan J, Cleveland MB. A randomized clinical study evaluating the safety and efficacy of a new, reduced-volume, oral sulfate colon-cleansing preparation for colonoscopy. *Am J Gastroenterol*. 2009;104:2275-2284.

Huffman M, Unger RZ, Thatikonda C, Amstutz S, Rex DK. Split-dose bowel preparation for colonoscopy and residual gastric fluid volume: an observational study. *Gastrointest Endosc*. 2010;72:516-522.

Unger RZ, Amstutz SP, Seo da H, Huffman M, Rex DK. Willingness to undergo split-dose bowel preparation for colonoscopy and compliance with split-dose instructions. *Dig Dis Sci*. 2010;55:2030-2034.

Aoun E, Abdul-Baki H, Azar C, et al. A randomized single-blind trial of split-dose PEG-electrolyte solution without dietary restriction compared with whole dose PEG-electrolyte solution with dietary restriction for colonoscopy preparation. *Gastrointest Endosc*. 2005;62:213-218.