A randomized, controlled, double-blind trial of the adjunct use of tegaserod in whole-dose or split-dose polyethylene glycol electrolyte solution for colonoscopy preparation CME

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Background: Problems of compliance, quality, and safety of colon preparation regimens have prompted continued investigation with alternative forms of cleansing.

Objective: To evaluate the efficacy of tegaserod as an adjunct to a polyethylene glycol electrolyte solution (PEG-E), given as a whole dose or split dose, in colonoscopy preparation.

Design: Randomized, placebo-controlled, double-blind trial.

Setting: A single university-based hospital.

Patients: Patients who were undergoing elective colonoscopy.

Interventions: A 4-arm randomization scheme that compared tegaserod with a placebo, each with whole-dose or split-dose PEG-E preparation.

Main Outcome Measurements: Efficacy of colon cleansing was the primary outcome. Secondary outcomes included adherence, tolerability, adverse effects, and patient perceptions of their preparation quality.

Results: A total of 382 patients completed the trial. Patients who received the split-dose preparation had significantly better colon cleansing than those who received the whole-dose preparation (88.9% vs 42.6%, $P < .001$). The addition of tegaserod did not significantly improve the overall colonoscopy preparation quality compared with a placebo. However, there were fewer poor preparations in the whole-dose PEG-E group (12.4% vs 1.1%, $P = .002$, Bonferroni correction removes significance) and more excellent preparations in the split-dose group (53.3% vs 38.3%, $P = .035$, Bonferroni correction removes significance) in favor of tegaserod. Interobserver and intraobserver variability analysis showed substantial agreement among endoscopists. Adherence was significantly lower in the whole-dose group versus the split-dose PEG-E group (68.8% vs 91%, $P < .001$), independent of the use of tegaserod. Adverse effects were not different between study groups.

Limitations: A 4-arm randomization and the single-center nature of the study.

Conclusions: Tegaserod has a marginal effect on the quality of colonoscopy preparation when used as an adjuvant to PEG-E. The split-dose PEG-E was superior to the whole-dose PEG-E and resulted in better colon cleansing, adherence, and tolerance. (Gastrointest Endosc 2008;68:294-300.)

A colonoscopy is the preferred procedure for investigating large-bowel and terminal ileal disease in adults and children. The diagnostic accuracy of a colonoscopy depends on the quality of the bowel preparation.[1] Polyethylene glycol electrolyte solutions (PEG-E) are the most commonly used laxatives for colonic cleansing. However, the unpleasant taste and the large volume of PEG-E lead to poor compliance with recommended regimens and result in patient dissatisfaction and the often-voiced complaint that ''the preparation is worse than the test.'' The use of reduced-volume PEG-E with bisacodyl or split-volume PEG-E has been shown to reduce adverse effects and lead to improved adherence, tolerance, and colon preparation. The adjuvant use of prokinetics (eg,

Abbreviations: 5-HT, 5-hydroxytryptamine; Cmax, peak plasma concentrations; NaP, sodium phosphate; NS, not significant; PEG-E, polyethylene glycol electrolyte solution.

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cisapride) or stimulant laxatives (eg, bisacodyl or senna) with PEG-E may improve colon cleansing but has been associated, in some cases, with greater adverse effects.[2-7] A small volume of oral sodium phosphate (NaP) solution, taken as a split dose with water or a carbonated beverage remains an effective alternative option for bowel cleansing. However, comparative studies of NaP and PEG-E showed conflicting results regarding the quality of bowel preparation, with some studies showing unsatisfactory preparation with NaP.[4,5,7] Moreover, oral NaP solutions are rarely associated with acute nephrocalcinosis and kidney failure, and are contraindicated in patients with renal insufficiency, congestive heart failure, or cirrhosis, hence limiting the use of this solution in an open-access system.[8-12]

Tegaserod, a selective serotonin (5-hydroxytryptamine [5-HT]) 5-HT4 receptor partial agonist, was shown to be effective in women patients with irritable bowel syndrome and who had abdominal pain or discomfort and constipation as their predominant symptoms.[13] Tegaserod increases the gastric emptying rate, shortens small-intestinal transit, and accelerates orocecal and colonic transit and filling.[14] These properties make it, in theory, a useful adjunct to standard colonoscopy preparations in that the addition of tegaserod may reduce common adverse effects of large-volume PEG-E (such as nausea, bloating, and fullness), improve patient adherence to the prescribed volume, and consequently improve the quality of bowel preparation.[15] Based on the above, we decided to evaluate, in a prospective, randomized, double-blinded trial, the efficacy of tegaserod as an adjuvant to the PEG-E solution in bowel cleaning for a colonoscopy. The adjunct use of tegaserod was compared with a placebo in either whole-dose or split-dose PEG-E by using a 4-way randomization design.

Capsule Summary

What is already known on this topic

- Polyethylene glycol electrolyte solutions (PEG-E) are the most commonly used agents for colonoscopy preparation, but their taste and large volume lead to poor compliance.

What this study adds to our knowledge

- In a 4-arm randomized, placebo-controlled, double-blinded trial of 382 patients, tegaserod had a marginal effect on the quality of colon preparation when used as an adjuvant to PEG-E.
- Split-dose PEG-E was superior to whole-dose PEG-E, resulting in better cleansing, adherence, and tolerance.

PATIENTS AND METHODS

Patients

Patients seen in the ambulatory outpatient clinics of the American University of Beirut Medical Center and who required elective colonoscopies were enrolled in this study. Exclusion criteria included patients under 18 years of age, the presence of severe renal impairment, moderate or severe hepatic impairment, a history of bowel obstruction, known allergies to PEG or tegaserod, or refusal to consent to the study. The study was conducted at the American University of Beirut Medical Center between February 1, 2005, and July 30, 2006. After informed consent, the patients were provided written instructions, for any of 4 bowel preparations, in a closed opaque envelope by their respective endoscopist who was blinded to the content of the envelope. The envelopes were randomized (by using a computer-generated random numbers table) by an independent investigator who kept the randomization key under lock until the inclusion of the last patient. Colonoscopies were performed with the patients under conscious sedation by 1 of 4 staff endoscopists blinded to the preparation regimen. All colonoscopies were done between 10:00 AM and 4:00 PM. The study protocol was reviewed and approved by the institutional review board of the American University of Beirut.

Preparation instructions

Groups A and B were assigned to the whole-dose PEG-E preparation as described by the following instructions. The patients were instructed to adhere to a liquid diet the day before their colonoscopy, with the last meal being at 6:00 PM, after which they are only allowed water until the procedure time. Group A received 4 packets of PEG-E (Fortrans; Beaufour Ipsen Pharma, France); each contained 64 g Macrogol 4000, 5.7 g anhydrous sodium sulfate, 1.68 g sodium bicarbonate, 1.46 g sodium chloride, and 0.75 g potassium chloride. These 4 packets were to be dissolved in 4 L of water and consumed the evening before the day of the colonoscopy (between 7:00 PM and 9:30 PM). Patients were also provided with 2 tablets of a placebo (that matched the tegaserod pills and were provided in a double-blinded fashion), which were to be taken as follows: 1 tablet at 6:30 PM the evening before the procedure, and 1 tablet 2.5 hours before the colonoscopy. Group B patients were asked to follow the same preparation instructions as group A but were provided with 2 pills of tegaserod (6 mg each) instead of a placebo.

Groups C and D were assigned to a split dose of PEG-E as follows. Patients were allowed a regular diet the day before their colonoscopy, with the last meal being a light meal at 6:00 PM, after which they were only allowed water until the procedure time. Group C patients received 2 packets of PEG-E to dissolve in 2 L of water and consume the evening before the day of the colonoscopy (between 7:00 PM and 9:30 PM). Then, the morning of the procedure, they were to dissolve another 2 packets of PEG-E in 2 L of water and drink this preparation over 1.5 to 2 hours, to be