

## Polyethylene glycol and bisacodyl for colonoscopy: has the time arrived?

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Colonoscopy is the current standard method for evaluating the colon. Recent surveys have shown that the proportion of individuals aged 50 years or older who have undergone colonoscopy within the last 10 years is growing and currently ranges from 6-25% in various European countries and to 62% in the United States [1,2]. Bowel preparation for colonoscopy is a complex undertaking, involving diet modifications and laxative choice according to patients' needs. An adequate level of cleansing is critical for the efficacy of colonoscopy. Two key quality indicators of colonoscopy, cecal intubation rate and polyp detection rate, are inversely associated with the quality of bowel cleansing [3,4]. An inadequate level of bowel cleansing also results in further costs as the examination has to be re-scheduled or alternative investigations have to be organized [5]. Furthermore, discomfort and inconvenience of taking bowel preparation (BP) may affect the acceptability and uptake of colonoscopy in screening programs [6].

Polyethylene glycol (PEG) is an isosmotic solution that passes through the bowel without absorption or secretion. PEG-based preparation for colonoscopy has been shown to be safe in patients with serum electrolyte imbalances, advanced hepatic dysfunction, acute and chronic renal failure and congestive heart failure [7]. However, PEG is usually administered as a 4 L solution in order to achieve an adequate cathartic effect. Such a high volume has been shown to reduce tolerability and compliance to bowel preparation [7].

To overcome this limitation, a low-volume preparation that combines 2 L PEG with bisacodyl has been proposed [7,8]. In the meta-analysis published in this issue of *Annals of Gastroenterology*, Clark *et al* compared the benefit and burden of this regimen with those of a 4 L PEG preparation. The authors collected information from six studies including over 1,500 patients. They demonstrated an apparent equivalence in the efficacy of the two regimens, whilst the low-volume+bisacodyl preparation seemed to be better tolerated in terms of nausea, vomiting and bloating.

Does this mean that we should be ready to implement 2 L PEG with bisacodyl for elective outpatient colonoscopy? Despite the fact that the findings of the meta-analysis are substantiated by a relatively large population, there are some drawbacks that generate residual uncertainty. First of all, there was a very high degree of heterogeneity in the main outcome of the analysis, i.e. the quality of the bowel preparation. This was due to the fact that, albeit non-significant, 3 of the 5 studies used for this endpoint showed some superiority for the 4 L PEG compared with the low-volume regimen. Therefore, there is residual uncertainty about the real equivalence between the two regimens, and further studies are needed to elucidate this fact. When considering that colonoscopy preparation is prescribed to thousands of patients every year, this uncertainty is critical. For instance, there is much more homogeneity in the comparisons between 4 L PEG and 2 L PEG+ascorbate than between 4 L PEG and 2 L+bisacodyl [7]. Second, there is residual uncertainty over the safety of this preparation. As outlined by the authors, bisacodyl may cause ischemic colitis [9]. Despite the fact that the relative risk may be very rare, the absolute number of episodes may still be significant, when considering the multitude of subjects undergoing bowel preparation. Thirdly, in order to reduce such a risk of ischemic colitis, the FDA requested substantial reduction in the dose of bisacodyl. As admitted by the authors, such a low dose has not been tested in the studies included in their meta-analysis [8]. Recent studies including low-dose bisacodyl showed only controversial results [10-12]. Fourthly, it should never be marginalized that 4 L PEG has been tested in several studies including hundreds of thousands of patients, whilst 2 L+bisacodyl has only been tested in a few relatively small studies with conflicting evidence [13-18]. Fifthly, there are now several competitors in the field of low- or very low-bowel preparations, and it is unclear whether the proposed regimen may be the actual winner [7].

In conclusion, the meta-analysis by Clark *et al* represents a major step in the clinical implementation of 2 L+bisacodyl in practice. However, further data on the generalizability and reproducibility of these findings with low doses of bisacodyl are still needed.

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