DSEN ABSTRACT

A Systematic Review with Network Meta-Analyses of the Comparative Safety of Bowel Cleansers for Routine Colonoscopy

Summary

- Evidence from randomized trials is lacking regarding the risk of ischemic colitis following the use of any bowel cleanser.
- Bowel cleansers containing 15 mg or more of bisacodyl, with a 2 L PEG base were not found to significantly increase the risk of nausea, vomiting, or cramping compared to other bowel cleansers. Risk of bloating was increased compared to sodium picosulfate. Dizziness was significantly decreased compared to either sodium picosulfate or PEG 2 L plus 5–10 mg bisacodyl, and nausea and vomiting were both significantly decreased compared to PEG 4 L.
- Sodium picosulfate ranked as the top bowel cleanser with respect to comparatively lower risk of nausea, vomiting, and cramping, although it ranked relatively poorly with respect to the risk of dizziness.
- Compliance of finishing bowel cleanser products decreased as the volume of the product increased.
- In narrative summaries, the use of sodium phosphate bowel cleansers was associated with increased risk of electrolyte abnormalities, specifically hypocalcemia and hypokalemia.

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What is the issue?

Bowel cleansers are used prior to colonoscopy to clear the intestines of ingesta to allow effective visualization of the gut wall. Bowel cleansers are generally considered safe; however, in 2011, the US Food and Drug Administration (FDA) withdrew a bowel cleanser kit due to concerns of ischemic colitis development, following the use of 5 mg bisacodyl (BIS) used in conjunction with 2 L polyethylene glycol (PEG). A similar PEG-based kit with 15 mg bisacodyl is available in Canada, and bisacodyl can be prescribed at the discretion of the clinician in combination with other bowel cleansers such as sodium picosulfate (PICO). The general safety of the use of bisacodyl as a bowel cleanser prior to colonoscopy is unknown.

What was the aim of the study?

The following review question was addressed:

- What is the comparative safety of PEG- and sodium-based bowel cleansers, with or without any dose of bisacodyl for the purposes of bowel cleansing for colonoscopy in generally healthy patients?

How was the study conducted?

Ovid MEDLINE, including Epub Ahead of Print and In-Process & Other Non-Indexed Citations, Embase Classic+Embase, and the Cochrane Library on Wiley were searched in 2018 for randomized and quasi-randomized controlled trials (RCTs) that had enrolled generally health patients of any age undergoing routine colonoscopy. Non-randomized controlled studies were included if they enrolled at least 500 patients per arm. Studies were included if patients were randomly allocated to receive a PEG-, PICO-, or other-based bowel cleanser (e.g., sodium phosphate (NaP), with or without bisacodyl. We considered 2 L and 4 L PEG products separately, and bisacodyl was categorized by dose (10-BIS = 5–10 mg bisacodyl; 15+BIS = 15 mg or more bisacodyl). Our primary outcome of interest was ischemic colitis, with the following main secondary outcomes: nausea, vomiting, bloating, cramping, dizziness, compliance, dehydration, seizures, bowel perforation, and hospitalization. Where feasible, we conducted separate analyses for each outcome, using Bayesian network meta-analysis (NMA). Network configuration precluded inclusion of t products not marketed in Canada in the analyses (i.e., only studies evaluating at least two PEG- or PICO-based products were included). We accounted for additions of sodium sulfate (SS), osmotics or prokinetics in bowel cleansers, but other adjuncts and the timing of administration (e.g., single day, split dose) could not be taken into consideration in analyses. Pediatric studies were excluded from NMAs. Analyses adjusted for control-group risk were considered. For outcomes for which network meta-analysis were not possible, detailed narrative summaries were prepared.

What did the study find?

- One-hundred-ninety-seven trials assessing bowel cleansers in 135,985 patients were included, published between 1981 and 2018.
- **Ischemic colitis:** No cases of ischemic colitis were identified, although only one RCT specifically evaluated the outcome in patients receiving PEG 4 L + PICO, PEG 2 L + PICO + 20 mg BIS, PICO, or NaP.
- One-hundred-nine trials evaluated PEG- and PICO-based bowel cleansers in 65,338 patients and were considered for NMA, with 68 trials ultimately included in at least one of six NMAs for nausea, vomiting, bloating, cramping, dizziness, and 100% compliance. Most network comparisons were based on only indirect evidence and single studies. For all NMAs, the unadjusted model was considered the most parsimonious and best fitting model. Minor violations in consistency were identified for some outcomes.
- The focal treatment (PEG 2 L 15+BIS SS) ranked moderately against other bowel cleansers with respect to the risk of most outcomes, except for dizziness, for which it ranked best. However, PEG 2 L 10-BIS SS ranked the worst amongst all treatments for dizziness, a discrepancy that can't be explained.

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Logos if appropriate (can be sent separately by email, if needed)

- Significant differences between PEG 2 L 15+BIS SS and other bowel cleansers were few in any NMA, possibly due to a low power to detect significant differences as a result of node splitting to account for BIS dose and the presence of SS. Specifically, PEG 2 L 15+BIS SS demonstrated a significantly increased risk of bloating vs PICO, and significantly decreased risks of nausea and vomiting (both vs PEG 4 L), and dizziness (vs both PICO and PEG 2 L 10-BIS).
- PICO ranked as the top treatment for the nausea, vomiting, and cramping outcomes, and was ranked second for the bloating outcome. PICO ranked relatively poorly against most other bowel cleansers with respect to the occurrence of dizziness.
- Although not a safety outcome, 100% compliance was found to be highest for products with the lowest volume (i.e., PICO) and decreased as product volume increased.
- Serum electrolyte analyses were hindered by variable outcome definitions and cutoffs used in studies. Narrative summary indicated that NaP was significantly more likely to cause hypocalcemia compared to either PEG 4 L SS or PICO. As well, NaP had a significantly higher risk of hypokalemia compared to PICO.

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