Gastroenterology 2015;149:79–88

Split-Dose Preparations Are Superior to Day-Before Bowel Cleansing Regimens: A Meta-analysis

Myriam Martel,[1,2] Alan N. Barkun,[1,3] Charles Menard,[4] Sophie Restellini,[5] Omar Kherad,[6] and Alain Vanasse[2]

[1]Division of Gastroenterology, [3]Epidemiology and Biostatistics and Occupational Health, McGill University Health Center, McGill University, Montreal, Canada; [2]Département de Médecine de Famille et de Médecine d'Urgence, [4]Medicine, University of Sherbrooke, Sherbrooke, Canada; [5]Department of specialties of Internal Medicine, Division of Gastroenterology, Geneva University Hospital, and [6]Internal Medicine, La Tour Hospital, University of Geneva, Geneva, Switzerland

This article has an accompanying continuing medical education activity on page e14. Learning Objective: Upon completion of this test, successful learners will be able to discuss the appropriate timing of administration of bowel preparation in split-dose bowel preparations, review the efficacy of different bowel preparation products when they are administered as a split preparations, and identify the efficacy of split-dose bowel preparation versus day-before bowel preparation for the same bowel preparation product.

BACKGROUND & AIMS: There are different regimens of preparing the colon for colonoscopy, including polyethylene glycol (PEG), sodium phosphate, picosulfate, or oral sulfate solutions. We performed a meta-analysis to determine the efficacy of split-dose vs other colon preparation regimens, the optimal products for use, and the most effective preparation volumes. **METHODS:** We performed systematic searches of MEDLINE, EMBASE, Scopus, CENTRAL, and ISI Web of knowledge databases, from January 1980 to March 2014, for published results from randomized trials that assessed split-dose regimens vs day-before colonoscopy preparation. We excluded studies that included pediatric or hospitalized patients, or patients with inflammatory bowel disease. The primary outcome was efficacy of bowel cleansing. Secondary outcomes included side effects or complications, outcomes of procedures, patients' willingness to repeat the procedure, and the amount of time required for patients to resume daily activities. **RESULTS:** We identified 47 trials that fulfilled our inclusion criteria (n = 13,487 patients). Split-dose preparations provided significantly better colon cleansing than day-before preparations (odds ratio [OR], 2.51; 95% confidence interval, 1.86–3.39), as well as day-before preparations with PEG (OR, 2.60; 95% confidence interval, 1.46–4.63), sodium phosphate (OR, 9.34; 95% confidence interval, 2.12–41.11), or picosulfate (OR, 3.54; 95% confidence interval, 1.95–6.45). PEG split-dose preparations of 3 L or more yielded greater bowel cleanliness than lower-volume split-dose regimens (OR, 1.89; 95% confidence interval, 1.01–3.46), but only in intention-to-treat analysis. A higher proportion of patients were willing to repeat split-dose vs day-before cleansing (OR, 1.90; 95% confidence interval, 1.05–3.46), and low-volume split-dose preparations vs high-volume split-dose preparation (OR, 4.95; 95% confidence interval, 2.21–11.10). There were no differences between preparations in other secondary outcome measures. However, there was variation among studies in definitions and main and secondary outcomes. **CONCLUSIONS:** Based on meta-analysis, split-dose regimens increase the quality of colon cleansing and are preferred by patients compared with day-before preparations. Additional research is required to evaluate oral sulfate solution–based and PEG low-volume regimens further.

Keywords: Meta-analyses; Bowel Preparation; Split-Dose; Bowel Cleansings.

High-quality colonoscopy increasingly is being associated with favorable patient outcomes in colorectal cancer screening initiatives[1,2]; adequacy of the preparation is one of its most important predictors,[3] with the need for repeat procedures because of poor preparation carrying significant costs.[4] The recent move toward split-dose and low-volume preparations coupled with the release of newer products in the United States have outdated most previous pertinent meta-analyses, justifying more contemporary systematic reviews. As part of many summary analyses informing recent recommendations by the Multi-Society Task Force (MSTF),[5] we performed targeted meta-analyses determining the efficacies of day-before preparations vs split-dose regimens using contemporary used products, including polyethylene glycol (PEG), sodium phosphate (NaP), picosulfate (PICO), and oral sodium sulfate (OSS).

Materials and Methods

Search Strategy

Systematic searches were performed (January 1980 to March 2014) using MEDLINE, EMBASE, Scopus, CENTRAL, and ISI Web of knowledge. Citation selection used a highly sensitive search strategy identifying randomized trials[6] with MeSH headings relating to the following: (1) colonoscopy, (2) gastrointestinal agents, (3) bowel preparation, and (4) generic and brand names (Appendix 1). Recursive searches, cross-referencing, and subsequent hand-searches were completed.

Abbreviations used in this paper: **ITT, intention-to-treat; MSTF, Multi-Society Task Force; NaP, sodium phosphate; OR, odds ratio; OSS, oral sodium sulfate; PEG, polyethylene glycol; PICO, picosulfate; PP, per-protocol; WMD, weighted mean difference.**

© 2015 by the AGA Institute
0016-5085/$36.00
http://dx.doi.org/10.1053/j.gastro.2015.04.004

Trial Selection and Patient Population

All fully published randomized trials in French or English with at least 1 arm administering split-dose PEG, NaP, PICO, or OSS were included. Trials comprising only pediatric patients, in-patients, or inflammatory bowel disease patients were excluded.

Choice of Outcomes

The primary outcome measure was bowel cleanliness, defined as the proportion of patients with an adequate preparation. Anticipating heterogeneity in bowel cleanliness nomenclature across studies, preplanned dichotomization grouped excellent or good, as well as successful, optimal, and satisfactory, vs fair, poor, or insufficient bowel preparation cleanliness or mucosal visualization. We defined a *product* as PEG, NaP, PICO, or OSS alone, with or without an adjuvant such as senna, magnesium citrate, magnesium sulfate, magnesium oxide, mannitol, enema, olive oil, castor oil, bisacodyl, cisapride, domperidone, ascorbic acid, alverine citrate, lubiprostone, simethicone, probiotic, metrocopramide, mosapride, simethicone, or sodium ascorbate. Split-dose was defined as administration of product in 2 separate doses: the first dose was the day before and the second dose was the day of the colonoscopy, to minimize the duration of the interval between completion of the bowel preparation and the colonoscopy.[7]

Day-before regimens referred to no dosage of the product given on the day of the colonoscopy. We excluded trial arms that assessed co-administration of 2 different products (combinations of PEG, NaP, OSS, and PICO).

The following comparisons were analyzed: split-dose vs day-before, and split-dose vs another split-dose. These analyses were performed in turn for all products combined, for a given product, or when comparing 2 different products.

Secondary outcomes included patient willingness-to-repeat the preparation, polyp or adenoma detection, side effects, or complications, empirically grouped according to hierarchal symptoms for clarity as follows: nausea or vomiting or nausea/vomiting; abdominal cramps or pain or spasm and discomfort or distress or bloating; insomnia or sleep disturbance; weakness or fatigue; fainting or dizziness; headache; chills; perianal irritation; and additional time required to resume daily activities.

Validity Assessment

Two investigators assessed citation eligibility with discrepancies resolved by an independent reviewer; consequent κ statistics were generated. The quality of trials was graded using the Cochrane risk bias tool and Jadad score[8] (with 1 extra point for reported a priori sample size calculations). All data abstraction and entries were validated independently by 2 authors.

Sources of Possible Heterogeneity: Clinical and Statistical

Possible sources of clinical heterogeneity were noted across trials in keeping with preplanned sensitivity or subgroup analyses. Identification and handling of statistical heterogeneity is described later.

Statistical Methods and Sensitivity Analyses

For each outcome and in every comparison, effect size was calculated as odds ratios (ORs) for categoric variables and weighted mean differences (WMDs) for continuous variables. The Mantel–Haenszel method for fixed-effect models determined corresponding overall effect sizes with confidence intervals, except when statistical heterogeneity was noted, in which case a random-effects model was used according to the DerSimonian and Laird method.[9] WMDs were manipulated using the inverse variance approach. Statistical heterogeneity across studies was defined using a chi-square test of homogeneity with a 0.10 significance level. The Higgins I^2 statistic was calculated to quantify the proportion of variation in treatment effects attributable to between-study heterogeneity.[10]

Values for intention-to-treat (ITT) were preferred to per-protocol (PP) when both were presented. We included non-compliant patients or withdrawals in the ITT analysis to minimize bias.[11]

Preplanned sensitivity analyses assessing bowel cleanliness examined PEG split-dose of varying volumes vs a nonsplit dose. Additional dichotomization criteria were the use of a validated preparation cleanliness scale (Ottawa,[12] Boston,[13,14] Harefield[15] Cleansing Scale, and Aronchick scores[16]), a publication date within the past 10 years, the inclusion of sole PP data, the geographic continent of study, and the type of diet (most dense diet for normal, liquid, low residue, or fasting) if similar in all arms on the precolonoscopy day. Finally, "good" bowel cleanliness may not be sufficient to detect lesions such as flat and sessile serrated adenomas and proximal polyps, an additional analysis with dichotomization for "excellent" or "optimal" bowel cleanliness was assessed. Only results including more than 3 trials were reported in sensitivity analyses.

As a final characterization of possible heterogeneity, we performed meta-regression using mixed-effects models and as successive dependent variables we used the following: year of publication, continent, and the diet followed for the preparation.

Publication bias was evaluated using the Begg adjusted rank correlation test[17] and the Egger regression asymmetry test.[18]

All percentages of outcomes reported in the trials were converted to absolute numbers and no attempt at determining extractable values from graphics or figures was performed to avoid possible subjectivity.

To ensure zero event trials did not significantly affect the heterogeneity or P value, a continuity correction was added to each trial with zero events using the reciprocal of the opposite treatment arm size.[19,20] All statistical analyses were completed using the Meta package in R version 2.13.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Included Studies

Overall, 2523 citations were retrieved; 2181 were rejected based on titles and abstracts, and 342 articles were fully reviewed (Figure 1). Nine trials[21–29] were rejected from initial selection because 1 arm included both split and nonsplit dose regimens depending on the time of procedure,

Download English Version:

https://daneshyari.com/en/article/3292255

Download Persian Version:

https://daneshyari.com/article/3292255

Daneshyari.com