Meta-analysis: the relative efficacy of oral bowel preparations for colonoscopy 1985-2010

CRD summary
The review found no compelling evidence that favoured either of the commonly used bowel preparation regimens for bowel clearance (for providing visualisation in colonoscopy), but polyethylene glycol-based regimens appeared the most effective. Very limited reporting of trial details and the occurrence of unexplained variation across studies means the reliability of the authors' conclusions is unclear.

Authors' objectives
To determine the relative efficacy of bowel preparations for bowel clearance, for providing visualisation in colonoscopy.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to July 2010 for fully published, peer-reviewed studies; search terms were reported. Reference lists of identified papers were also searched and the previous 20 years' editions of six relevant journals were handsearched. The authors stated that no studies were excluded based on language. This was an update of a previous systematic review (see other publications of related interest field).

Study selection
Randomised controlled trials (RCTs) were eligible if they included two or more treatment arms and used different oral bowel preparation regimens. Patients could be undergoing diagnostic, screening or therapeutic colonoscopy. Treatment efficacy had to be reported using an explicit categorical measure.

Few study details were presented. The most frequently studied treatments were polyethylene glycol and sodium phosphate; other studied treatments (sometimes in combination) included sodium picosulphate, senna, prokinetic agents, mannitol, mixed oral sulphates, magnesium citrate and bisacodyl. The single outcome of interest was endoscopist assessment of the adequacy of the bowel preparation.

The authors did not state how many reviewers selected studies.

Assessment of study quality
Study quality was appraised using the Cochrane Collaboration Risk of Bias Tool with the following criteria being rated as satisfactory, unsatisfactory or unclear: randomisation sequence generation, allocation concealment, blinding of participants and outcome assessors, completeness of outcome data, selective outcome reporting or other sources of bias.

Two reviewers assessed study quality, with disagreements resolved by a third reviewer.

Data extraction
Data were extracted on endoscopist's categorical assessment of the adequacy of preparation (satisfactory or unsatisfactory), and were used to calculate odds ratios (OR) with 95% confidence intervals (CI).

Methods of synthesis
When studies were deemed to be sufficiently similar, meta-analyses were performed to calculate pooled odds ratios with 95% confidence intervals, using a random-effects model. Heterogeneity was assessed using $I^2$. For the primary analyses of studies using sodium phosphate only, studies using current dosage recommendations (maximum 90mL in two doses separated by at least 10 hours) were included. A sensitivity analysis was used to examine the effect of this exclusion. Several pre-specified subgroup or sensitivity analyses were also reported. Where meta-analysis was not appropriate, a narrative synthesis was presented.

Results of the review
There were 104 eligible RCTs; 54 were included in the meta-analyses. The total sample size was unclear. The authors
reported low overall study quality; details for individual studies were not presented. It was noted that little or no information was available on randomisation and allocation concealment methods. There were generally few drop-outs and endoscopists were blinded in most studies. In most studies there was no blinding of patients or caregivers.

There was no significant difference for endoscopist assessment in a meta-analysis that compared sodium phosphate (90ml) with polyethylene glycol (24 comparisons); the analysis was subject to statistically significant heterogeneity. However, in studies with previous day dosing in both study arms there was a significant advantage favouring polyethylene glycol (OR 1.78, 95% CI 1.13 to 2.81; five RCTs; I²=14%), but there was no difference between treatments in studies using split-overnight dosage in both arms (four RCTs; I²=0%).

Pooled results from studies that focused on results in the ascending colon significantly favoured polyethylene glycol over sodium phosphate (OR 2.36, 95% CI 1.16 to 4.77; five comparisons; I²=78%). Polyethylene glycol was also significantly more effective than non-sodium phosphate bowel preparation regimens (OR 2.02, 95% CI 1.08 to 3.78; 14 comparisons; I²=80%). In both these analyses the heterogeneity was statistically significant.

Other comparisons were reported which showed no significant difference between regimens.

Authors’ conclusions
Although there was no compelling evidence favouring either of the two most commonly used bowel preparation regimens, this may have reflected shortcomings in study design. Where studies had ensured comparable dosage, or the clinically relevant outcome of proximal bowel clearance was considered, polyethylene glycol-based regimens offered the most effective option.

CRD commentary
The review addressed a clear question and was supported by reproducible eligibility criteria. Several relevant databases were searched and journals were handsearched, but limiting the review to studies published in peer-reviewed journals may have led to the exclusion of some relevant studies; publication bias may have affected the review results. Suitable methods were employed to reduce the risks of reviewer error and bias when assessing study quality, but the authors did not report on whether such methods were used for the data extraction and study selection processes. Appropriate methods were used to pool data and to assess and investigate heterogeneity, but individual study details were not reported which made it difficult to interpret the pooled results. The reporting limitations extended to the quality assessment results. One of the authors was an employee of Norgine Pharmaceuticals, who also funded the review, so there was a potential conflict of interests.

The very limited reporting of trial details, coupled with the frequency of occurrence of unexplained heterogeneity, means the reliability of the authors’ conclusions is unclear.

Implications of the review for practice and research
Practice: The authors state that the finding that polyethylene glycol has been found to give superior cleansing to sodium phosphate in the proximal colon was of importance for bowel cancer screening programmes.

Research: The authors stated that future studies should be targeted at answering specific questions, such as the impact of dose-volume on the efficacy of polyethylene glycol, the role of patient clinical characteristics on treatment outcome, or the benefit of differing levels of dietary restriction. Furthermore, new study endpoints such as the caecal intubation rate or the polyp detection rate should be taken into consideration, as these may more adequately mirror the quality of colonoscopy, rather than subjective endoscopist assessment. Specific attention also should be given to improving the quality of studies in the field, including attention to randomisation and blinding methods, ensuring the equivalence of treatment protocols, use of validated assessment tools and third-party validation of results.

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