Meta-analysis and cost comparison of polyethylene glycol lavage versus sodium phosphate for colonoscopy preparation

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Authors’ objectives
The objectives were to compare patient compliance, efficacy and safety of polyethylene glycol (PEG) lavage solution and sodium phosphate (NaP) laxative using meta-analysis, and to compare the cost of colonoscopy with both methods.

Searching
MEDLINE was searched from 1980 to 1996 for publications in the English language, using the search headings 'polyethylene glycols' and 'phosphates'. The articles were limited to those examining 'diagnostic' and 'therapeutic' uses and 'toxicity'. Additional references were identified by searching the bibliographies of retrieved articles, textbooks and other reviews.

Study selection
Study designs of evaluations included in the review
Double-blind randomised controlled trials (RCTs) comparing NaP and PEG solutions were eligible for inclusion.

Specific interventions included in the review
Studies comparing colonoscopy using either NaP or PEG for bowel preparation were eligible for inclusion. All of the included studies used equivalent doses (not stated). The specific cointerventions that accompanied NaP in two trials were a single dose of bisacodyl and a 'small enema'.

Reference standard test against which the new test was compared
The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis.

Participants included in the review
Studies of adult patients undergoing elective colonoscopy were eligible for inclusion.

Outcomes assessed in the review
The included studies were required to report at least one of the following: the inability to complete the preparation as described; the quality of the preparation of the colon; and adverse effects.

How were decisions on the relevance of primary studies made?
Two independent reviewers decided on the relevance of the primary studies. Any discrepancies were resolved in conference.

Assessment of study quality
The validity of the studies was judged on the following criteria: definition of the study population; baseline equivalence of the treatment groups; adequate and comparable potency of the interventions; definition of the outcome variables; and the blinding status of the endoscopist. The treatment groups were considered equivalent at baseline if none of the baseline variables differed statistically or clinically (by 40% or more); the latter criterion was determined arbitrarily a priori. A quality score was generated by summing the standards. The score ranged potentially from 0 (no standards satisfied) to 5 (all standards satisfied). The two authors independently evaluated the validity of the studies. Any discrepancies were resolved in conference.

Data extraction
The two authors independently extracted descriptive data to determine the clinical comparability of the studies, and
quantitative data on the number of patients in each treatment group and the number of patients with each outcome. Any discrepancies were resolved in conference.

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis. For each outcome, the pooled relative risks (RRs) were calculated using a random-effects model. The summary point estimates of effect were computed using precision-based weighted averages of stratum-specific RRs, with the weights derived primarily from the reciprocals of the variance, and secondarily from a correction factor determined by the degree of statistical heterogeneity. Where the RRs demonstrated a clear benefit for one preparation, the number-needed-to-treat (NNT) was calculated.

How were differences between studies investigated?
Statistical heterogeneity between the studies was tested for using the method of DerSimonian and Laird (see Other Publications of Related Interest no.1).

Results of the review
Eight RCTs (1,315 participants randomised; 1,286 participants analysed) were included in the review.

Failure to complete preparation (favours PEG).
For all studies (8 studies; n=1,286), the RR was 0.23 (95% confidence interval, CI: 0.18, 0.28) and the NNT was 7 (95% CI: 5, 12). When excluding any outliers (7 studies; n=1,214), the RR was 0.20 (95% CI: 0.16, 0.24) and the NNT was 7 (95% CI: 5, 9). The best estimate (5 trials; n=842) RR was 0.25 (95% CI: 0.20, 0.30) and the NNT was 7 (95% CI: 5, 10).

Adequate preparation (favours NaP).
For all studies (8 studies; n=1,286), the RR was 1.19 (95% CI: 1.09, 1.32) and the NNT was 9 (95% CI: 5, 625). When excluding any outliers (5 studies; n=685), the RR was 1.02 (95% CI: 0.99, 1.05); the NNT was not calculated. The best estimate (3 studies; n=313) RR was 1.06 (95% CI: 0.95, 1.19); the NNT was not calculated.

Excellent preparation (favours NaP).
For all studies (7 studies; n=1,068), the RR was 1.28 (95% CI: 1.11, 1.48) and the NNT was 10 (95% CI: 5, 53). When excluding any outliers (5 trials; n=644), the RR was 1.24 (95% CI: 1.02, 1.52) and the NNT was 11 (95% CI: 7, 26). The best estimate (3 trials; n=272) RR was 1.72 (95% CI: 1.16, 2.53) and the NNT was 5 (95% CI: 4, 7).

Patient tolerance and side-effects.
There were no consistent, clinically important differences in symptom side-effects. However, because of variation in the extent, detail and method of measuring the side-effects, a clinically meaningful direct quantitative comparison was not possible. In one study, orthostasis was more common among patients using PEG. There were also consistent, transient increases in serum phosphorous and sodium, and in two studies a transient decrease in calcium, although no clinical adverse side-effects accompanied these changes.

Cost information
The direct costs of diagnostic colonoscopy using NaP were $465, compared with $503 for PEG. A sensitivity analysis of the cost variables within the specified ranges revealed no change in the qualitative result; colonoscopy with NaP remained less expensive. A sensitivity analysis of the need to repeat colonoscopy, because of a poor preparation,
revealed that the absolute difference in the percentage of repeat procedures would have to exceed 4% for NaP before the costs would favour using PEG. In the base-case, the difference was -5% in favour of NaP (3% for NaP and 8% for PEG).

For the cost comparisons, it was assumed that the quality of the preparation for colonoscopy could be satisfactory or unsatisfactory with either method, and if unsatisfactory, the colonoscopy was repeated using the same preparation. The quality of all repeat preparations was assumed to be satisfactory. Point estimates for the proportions of repeat procedures were derived from published data (see Other Publications of Related Interest no.2). The direct costs were computed from the accounting and billing departments of a university-affiliated county medical centre, and were based on 1995 Medicare payment amounts (relative value units for physician costs) and diagnosis-related groups. The costs of preparations were the average wholesale prices obtained from the 1995 Red Book (see Other Publications of Related Interest no.3). The base-case estimates and ranges for all the variables were reported.

For a full discussion of the economic aspects of this study see NHS EED record 21998001391.

Authors' conclusions
The results suggested that NaP is as effective as PEG, but less costly and with a more easily completed preparation. It is the preferred method of preparation for colonoscopy for certain patient subgroups.

CRD commentary
This was a well-designed review, with clearly presented objectives, methods and results. The authors provided details of the literature sources searched and the search terms used, which enables other researchers to repeat their search. However, relevant information might have been missed as only one database was searched and there was little attempt to specifically identify unpublished work. Limiting the search to only English language articles might also have excluded relevant studies.

The study inclusion criteria were quite specific and only one dose regimen was considered. Therefore, it would seem appropriate for the authors to include the data in a meta-analysis. The authors found a significant level of heterogeneity between the studies and the data presented takes this into account. Not all of the study participants who were randomised were included in the analyses; it would have been useful to have analysed the results on an intention-to-treat basis. Assessments of study quality and heterogeneity were included.

Overall, the results appear to support the authors' conclusions. However, the review only included generally healthy study populations, which may limit its generalisability. Indeed, the authors highlighted in their discussion that NaP may not be appropriate for patients with cardiac problems, renal conditions, or suspected or known inflammatory bowel disease. The findings should therefore be interpreted with caution when considering patients and dose regimens outside of those specifically outlined in the inclusion criteria.

Implications of the review for practice and research
Practice: The authors stated 'this analysis cannot determine the better preparation for an individual patient. That decision requires clinician judgements and informed patient preference'.

Research: The authors did not state any implications for further research.

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Bibliographic details
Other publications of related interest

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Subject indexing assigned by NLM

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