Non-laxative CT colonography with barium-based faecal tagging: is additional phosphate enema beneficial and well tolerated?

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Objective: The purpose of this study was to investigate the efficacy and tolerance of an additional phosphate enema prior to non-laxative CT colonography (CTC).

Methods: 71 patients (mean age 80 years, 28 male, 43 female) underwent non-laxative CTC following 4 oral doses of diluted 2% w/w barium sulphate. Patients were invited to self-administer a phosphate enema 2 h before CTC. An experienced observer graded the volume of retained stool (1 (nil) to 4 (>75% bowel circumference coated)), retained fluid ((1 (nil) to 4 (>50% circumference obscured)), retained stool tagging quality (1 (untagged) to 5 (≥75% to 100%) tagged) and confidence a polyp ≥6 mm could be excluded (yes/no) for each of six colonic segments. Tolerance of the enema was assessed via questionnaire. Data were analysed between those using and not using the enema by Mann–Whitney and Fisher's exact test. 18/71 patients declined the enema.

Results: There was no reduction in residual stool volume with enema use compared with non-use either overall (mean score 2.6 vs 2.7, $p=0.76$) or in the left colon (mean 2.3 vs 2.4, $p=0.47$). Overall tagging quality was no different (mean score 4.4 vs 4.3, $p=0.43$). There was significantly more retained left colonic fluid post enema (mean score 1.9 vs 1.1, $p<0.0001$), and diagnostic confidence in excluding polyps was significantly reduced (exclusion not possible in 35% segments vs 21% without enema, $p=0.006$). Of 53 patients, 30 (56%) found the enema straightforward to use, but 4 (8%) found it unpleasant.

Conclusion: Phosphate enema use prior to non-laxative CTC leads to greater retained fluid, reducing diagnostic confidence, and is not recommended.

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Meta-analysis data suggest that the diagnostic accuracy of CT colonography (CTC) for significant colorectal pathology is high [1–3], and the technique has become increasingly popular for the assessment of the large bowel in those presenting with lower gastrointestinal symptoms [4].

Conventional CTC protocols employ full osmotic laxative cleansing, which, as well as being unpleasant for patients [5–8], may potentially have detrimental adverse effects. In addition, although rare, serious complications can occur, including acute disturbances in calcium and electrolyte homeostasis (especially in the elderly and those with pre-existing renal or cardiac disease) and chronic renal failure [9].

One of the major advantages of CTC over colonoscopy is that high diagnostic accuracy may potentially be maintained after significantly reducing or even eliminating laxatives [10–12]. Such reduced laxative regimes use oral contrast agents (such as barium and/or iodinated contrast) to label or “tag” the residual colonic contents to

a higher attenuation, facilitating the detection of true neoplasia in the stool-laden colon [10, 13, 14]. It is unlikely, however, that non-laxative CTC will reliably match the diagnostic accuracy of full cathartic examinations. Notably, in our own clinical experience of non-laxative CTC and also within the existing literature [13, 14], tagging quality may be suboptimal in the left colon, presumably because of slow intestinal transit of tagging agents in some patients. The majority of colorectal cancers arise in the rectum and distal colon, with approximately 50% arising from the rectum and recto-sigmoid area, with a further 25% arising from the sigmoid colon [15]. It is known that self-administered phosphate enema prior to flexible sigmoidoscopy is effective, well tolerated and more acceptable than full bowel cleansing regimes such as sodium picosulphate [16, 17].

We therefore hypothesised that self-administered phosphate enema could be a safe, well-tolerated and effective method of overcoming the problem of sub-optimal faecal tagging and improve visualisation of the left colon in non-laxative faecal-tagging CTC. The purpose of the study was to retrospectively compare colonic preparation quality in patients undergoing non-laxative CTC with and without additional phosphate enema, and to assess patient tolerance of the enema.

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Methods and material

Local ethics approval was obtained for this retrospective study.

Patient selection

As part of routine clinical practice at a single secondary referral centre, all patients aged over 70 years (and younger patients with significant medical comorbidity) referred for CTC automatically underwent a non-laxative protocol with barium faecal tagging. A change in clinical protocol was instigated in January 2007 when an additional self-administered phosphate enema (118 ml sodium dihydrogen phosphate dihydrate (18.1% w/v) and disodium phosphate dodecahydrate (8.0% w/v); Fleet Enema, C.B. Fleet Company Inc., Lynchburg, VA) was introduced to the standard non-laxative CTC protocol. The study cohort consisted of 71 consecutive patients (43 female and 28 males, mean age 80 years) undergoing CTC. Of the 71 patients, 44 (62%) had a change in bowel habit, 7 (10%) had rectal bleeding, 21 (30%) had abdominal pain, 9 (12%), had low haemoglobin, 16 (23%) had weight loss, 2 (3%) had a positive family history and 1 (1%) had a positive faecal occult blood test.

Bowel preparation

The basic tagging regimen consisted of a light diet 4 days before the CTC. A comprehensive guide to low-residue foods was sent to the patient. Examples of low-residue foods allowed included white bread and rice, minced or well-cooked meat, and fish. Bran, brown toast and potatoes with skins were not permitted. Tagging was achieved using two 250 ml containers of 2% w/v barium sulphate (E-Z Cat, EZEM, Bracco UK Ltd, Woodburn Green, UK). Patients were asked to dilute each 250 ml barium sulphate suspension with 250 ml of water and then split the resulting volume into two; 250 ml of this diluted barium suspension was then ingested with each of the four meals prior to CTC, commencing with the evening meal 2 days before the appointment. On the actual day of the CTC, patients were asked to drink clear fluid only.

In addition, patients were also invited to self-administer a phosphate enema at home 2 h before the study. Specifically, patients were asked to self-administer the enema 1 h before they left home for the CTC, holding on to the enema as long as possible and ideally for 15 min. They were then asked to empty their bowels on at least two separate occasions before leaving home and then again just prior to the CTC examination.

To increase compliance with this bowel preparation regimen, all patients were given a prior appointment with a member of the nursing staff, when the preparation was explained and the barium products and phosphate enema were supplied, together with full written instructions. In addition, patients were given a questionnaire (Appendix 1) pertaining to their experience of the phosphate enema, which they were asked to complete and hand in at the time of their CTC appointment.

Final study cohort

Of the 71 patients, 53 used the phosphate enema, whereas 18 declined, complying only with the basic barium-based tagging regimen.

CT colonography protocol

All patients underwent a standard CTC protocol. All patients received 40 mg of buscopan prior to colonic insufflation. Colonic distension was achieved using automated carbon dioxide insufflation (Protocol, EZEM, Westbury, NY) and patients were scanned in the prone and supine position on a 16-slice CT scanner (GE Light Speed 16 CT scanner, General Electric, OR) using the following parameters: 120 kV, 250 mA, pitch 0.938–1, 1.25 mm slices reconstructed on a 1 mm increment and 100 ml of intravenous contrast unless contraindicated (Visipaque, GE Healthcare, Chalfont St Giles, UK).

Grading of bowel preparation

A single radiologist, experienced in over 150 CTC examinations and blinded to the study purpose and use of phosphate enema, graded the quality of the bowel preparation using a system adapted from Taylor et al [5].

The large bowel was divided into six segments from the rectum to the caecum for analysis according to the original definitions. The axial slice with the greatest residual stool in each segment was used to assign a score for that particular segment, based on the percentage of the mucosal circumference coated. Scores were as follows: 1, no residual stool; 2, coating of <25% or thin circumferential film less than 2 mm in depth; 3, coating $\geq$ 25% to 50%; 4, coating >50%.

Residual fluid was graded according to the maximum axial anteroposterior (AP) diameter submerged by fluid, again using the slice with the most residual fluid for each segment. Scores were as follows: 1, no fluid; 2, <25% AP diameter; 3, $\geq$ 25% to 50% AP diameter; 4, >50% AP diameter.

The quality of the stool tagging was scored using a system adapted from Lefere et al [18]. First, the stool was divided into two groups that measured $\leq$ 5 mm and $\geq$ 6 mm (based on two-dimensional measurement using electronic callipers).

The percentage of overall stool burden which was satisfactorily graded for each size was then graded for each segment of bowel as follows: 1, all residual untagged; 2, 1% to <25% tagged; 3, $\geq$ 25% to 50% volume tagged; 4, $\geq$ 50% to 75% tagged; 5, $\geq$ 75% to 100% tagged. See Figures 1–4 for examples of the grading system.

Finally, the observer assessed each segment to see whether, in their opinion, the quality of preparation was sufficient such that a polyp $\geq$ 6 mm could be excluded in day-to-day clinical reporting practice.

Statistical analysis

Data were visualised using normal plots to assess distribution. All collated data (residual fluid, stool and tagging

Figure 1. Axial slice through the rectosigmoid. Fleet enema had been used. Residual stool was graded as four and residual fluid graded as four.

quality) were found to be highly skewed in distribution and thus non-parametric methods were applied.

Residual stool, fluid and tagging quality scores were compared between those patients who did and those who did not receive a phosphate enema using the Mann-Whitney *u*-test for all segments combined. Given the presumed local effect of the enema, the analysis was repeated after dividing into the left colon (rectum, sigmoid and descending) and right colon (transverse, ascending and caecum). Confidence in excluding a polyp ≥ 6 mm on a colonic segmental basis was compared between the two patient cohorts using Fisher's exact test. Significance was assigned at the $p < 0.05$ level.

Results

Of the 53 patients using the phosphate enema, the mean age was 79 years (range 75–90 years), 25 were male and 28 female whereas of the 18 declining the enema the

Figure 2. Axial slice through the rectum. Fleet enema had been used. Residual stool was graded two and residual fluid graded three.

Figure 3. Axial slice through the rectum. Fleet enema has not been used. Residual stool graded one and residual fluid graded one.

mean age was 82 years (range 64–90 years), 4 were male and 14 female. There was a significant difference in the age and sex distribution between the two cohorts ($p = 0.03$).

Bowel preparation

Average scores for residual stool and fluid together with comparative statistics are shown in Table 1, and split into left and right colon in Table 2.

There was overall significantly more retained fluid in those who took the phosphate enema than in those who

Figure 4. Axial slice through the rectum. Fleet enema has not been used. Residual stool graded four and residual fluid graded one.

Table 1. Scores for retained stool, fluid and tagging quality according to patient cohort (all colonic segments combined)

	<i>n</i>	Mean score for residual stool (SD)	Mean score for residual fluid (SD)	Mean score for tagging quality (SD)	
				≤5 mm	≥6 mm
No fleet enema	18	2.6 (0.8)	1.2 (0.6)	4.2 (1.3)	4.4 (1.2)
Fleet enema	53	2.7 (1.0)	1.7 (1.2)	4.4 (1.2)	4.3 (1.3)
<i>p</i> -Value ^a		0.76	<0.0001	0.48	0.43

SD, standard deviation.

^aMann–Whitney *u*-test, no fleet enema vs fleet enema.

did not. Specifically, this difference was limited to left colonic segments, there being no difference in the right colon.

There was no significant difference in the volume of residual stool or tagging quality, either overall or between the left and right colons.

Diagnostic confidence

In those receiving the phosphate enema, segmental preparation quality was sufficient such that a polyp ≥6 mm could be confidently excluded in 206/318 segments (65%; 95% confidence interval (CI) 60–70%). In the non-phosphate enema group, however, there was a significantly higher rate of adequate segments in terms of polyp exclusion: 85/108 segments (79%; 95% CI 71–86%), *p*=0.006.

Patient experience

All patients who used the phosphate enema returned the questionnaire.

Of the 53 patients who used the phosphate enema, 30 (56%) found the enema very straightforward to use, 19 (36%) reported that the enema was “uncomfortable but okay to use” (phrase included on the questionnaire) and 4 (8%) found the enema very unpleasant, but the enema worked. No patients reported the enema intolerable to use or very unpleasant with no result.

A total of 16 (30%) patients had a completely empty bottle after use, 24 (45%) patients had a nearly empty bottle, 12 (23%) patients used only approximately half the enema, whereas 1 (2%) patient had a bottle that was mostly full after the enema.

The amount of time that the patients estimated that they were able to retain the fluid was variable: 6 (11%)

were unable to retain the fluid for long, whereas 9 (17%) were able to retain the enema for 15 min.

Discussion

CTC is being increasingly implemented as a test with high reported sensitivity for significant colorectal neoplasia in symptomatic patients. One major advantage over both colonoscopy and barium enema is that laxative burden can be eliminated while apparently maintaining diagnostic performance [10, 12]. Although the diagnostic performance of non-laxative CTC with faecal tagging may approach that of conventional CTC, it is almost certain that overall accuracy will be higher in those patients in whom colonic preparation is optimised by full purgation. In particular, the tagging quality in the left colon is often inferior to that on the right. We hypothesised that one potentially simple and safe way to improve left-sided colonic preparation in non-laxative CTC was to administer a phosphate enema just prior to the examination. It is known from the endoscopic literature, for example, that phosphate enema is effective and well tolerated prior to flexible sigmoidoscopy [16, 17].

We found, however, that, rather than improving colonic preparation, visualisation of the left colon deteriorated. This was due to an increase in retained colonic fluid obscuring mucosal visualisation and significantly reducing the diagnostic confidence for excluding larger lesions.

Although an increase in colonic fluid was to be expected following the enema (the laxative has an osmotic effect drawing water into the lumen of the gut, producing distension and promoting peristalsis and bowel evacuation), patients were instructed to empty their bowel on at least three more occasions before the CTC. Clearly, however, this was insufficient to remove

Table 2. Scores for retained stool and fluid according to patient cohort (left and right colon)

	<i>n</i>	Mean score for residual stool (SD)		Mean score for residual fluid (SD)		Mean score for tagging quality (SD)			
		Left colon	Right colon	Left colon	Right colon	≤5 mm left	≤5 mm right	≥6 mm left	≥6 mm right
No fleet enema	18	2.4 (0.8)	2.8 (0.8)	1.1 (0.4)	1.3 (0.7)	4.1 (1.5)	4.3 (1.1)	4.4 (1.2)	4.4 (1.2)
Fleet enema	53	2.3 (1.1)	3.0 (0.9)	1.9 (1.1)	1.5 (1.3)	4.0 (1.5)	4.6 (0.8)	4.0 (1.5)	4.5 (1.0)
<i>p</i> -Value ^a		0.47	0.40	<0.0001	0.40	0.81	0.41	0.12	0.46

SD, standard deviation.

^aMann–Whitney *u*-test, no fleet enema vs fleet enema.

the excess fluid. It is known that "wet" preparations favoured by endoscopists are unsuitable for CTC, which requires a drier colon [19, 20], and thus addition of the enema became detrimental. While some radiologists now prefer a "wetter" preparation based on tagging with iodinated contrast [11, 12], the important difference is that the additional residual fluid is tagged. Our protocol instituted the enema after the completion of the oral barium-tagging regimen, and thus retained fluid was always going to be untagged. One intriguing possibility would be to add a tagging agent to the enema or indeed administer a small volume of dilute gastrograffin *per rectum* prior to CTC. Of course, such a manoeuvre would have to be proved efficacious given its invasiveness and the additional level of complexity.

It was perhaps surprising that the volume of stool (tagged or otherwise) was not reduced by the enema. Self-reported compliance was apparently high, suggesting that most patients used the enema correctly. Furthermore, all were given face-to-face instructions in the department by a nurse who explained how to use the barium-tagging mixture as well as the phosphate enema. We therefore can conclude that the use of a phosphate enema held no clear advantage, even in reducing retained stool volumes.

It is reassuring, however, that the quality of tagging produced by the dilute barium regimens was high, with the mean tagging score being >4 . Although consensus may be moving towards iodine base-tagging agents, we have shown that simple barium-based protocols are effective.

We did find that, in general, patients did tolerate the enema well and found it easy to use. Although this is reassuring, given the lack of positive benefit on examination quality there seems no indication to continue use of the enema in routine clinical practice; indeed, this has now changed. Given that non-laxative CTC benefits from being very well tolerated in terms of bowel preparation, the only justification to increase invasiveness by administering an enema would have been a very clear advantage in terms of colonic visualisation. This was certainly not the case.

Our study does have weaknesses. It was a non-randomised, retrospective audit following a change of clinical practice and, as such, we cannot be sure that the two groups were comparable in terms of demographics. Indeed, those patients choosing not to use the enema were more likely to be female and were significantly older than those using it. We cannot be sure that there are no patient-specific confounding factors influencing our data. However, the only difference we found was in the volume of retained fluid, which is intuitively what would be expected given the nature of the enema. There was no difference in tagging quality of residual stool between the two groups. Furthermore, the difference was limited to the left colon only, again supporting the effect being a result of the enema rather than any intrinsic difference between the patient cohorts. The choice of contemporary controls (as opposed to collating a retrospective cohort for comparison) was done for pragmatic reasons. At the time of the study, our hospital did not have a picture archiving and communications systems/radiology information systems (PACS/RIS) database and identification of controls prior to 2007 would have involved a labour-intensive manual search of paper records.

We used only a single observer to grade the bowel preparation. However, this observer was fully blinded to the purpose of the study and patient selection. Thus, any individualisation of grading scores would have been evenly distributed throughout both groups. The choice of a polyp cut-off size of ≥ 6 mm is arguably a little small for this older symptomatic patient cohort. However, given the fact that colonic preparation actually deteriorated after the enema, there cannot be any justification for its use even if this were not to have an impact on excluding a larger sized lesion. Finally, although our patient number is relatively small, the fact that such a highly significant result ensued is testament to the magnitude of the effect encountered.

Conclusion

Although well tolerated, use of a phosphate enema prior to non-laxative CTC leads to greater retained fluid reducing diagnostic confidence and is therefore not recommended.

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Appendix A

Fleet enema/faecal-tagging CT colonography preparation.

Questionnaire

Did you use the Fleet enema preparation?

Yes ◇yes
No ◇no

How easy did you find it to use the Fleet enema?

Very straightforward ◇5
A bit uncomfortable but OK ◇4
Very unpleasant but I think it worked ◇3
Very unpleasant and probably did not work ◇2
Intolerable ◇1

If you did use the Fleet enema, how much fluid was left in the bottle after its use?

The bottle was empty ◇1
The bottle was nearly empty ◇2
The bottle was still half full ◇3
The bottle was mostly full ◇4

If you did use the Fleet enema, how long did you retain the enema for?

15 min ◇5
10 min ◇4
5 min ◇3
2 min ◇2
No time at all ◇1