Bowel Preparation for CT Colonography: Blinded Comparison of Magnesium Citrate and Sodium Phosphate for Catharsis[1]

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Purpose: To compare colonic cleansing and fluid retention of double-dose magnesium citrate with those of single-dose sodium phosphate in patients undergoing computed tomographic (CT) colonography.

Materials and Methods: This retrospective HIPAA-compliant clinical study had institutional review board approval; informed consent was waived. The study included 118 consecutive patients given single-dose sodium phosphate for bowel catharsis and 115 consecutive patients at risk for phosphate nephropathy, who were instead given double-dose magnesium citrate. The bowel preparation regimen was otherwise identical. Four-point scales were used to assess residual stool and fluid in the six colonic segments, and attenuation of residual fluid was measured. An a priori power analysis was performed, and unpaired *t* tests with Welch correction were used to compare the two groups on stool and fluid scores and fluid attenuation.

Results: Both cathartic regimens offered excellent colon cleansing, with no significant difference for residual stool in any of the six segments. Stool scores of 1 or 2 (ie, no residual stool or residual stool <5 mm) were recorded in 88.6% (627 of 708) of colonic segments in the sodium phosphate group and in 88.1% (608 of 690) in the magnesium citrate group. No clinically important differences were seen in residual fluid scores in any of the six segments, with the only significant difference seen in the sigmoid colon (2.17 for sodium phosphate vs 2.44 for magnesium citrate; $P < 0.01$). Fluid attenuation was significantly different between magnesium citrate and sodium phosphate groups (790 HU ± 216 vs 978 HU ± 160; $P < .001$).

Conclusion: Both sodium phosphate and magnesium citrate provided excellent colon cleansing for CT colonography. Residual stool and fluid were similar in both groups, and fluid attenuation values were closer to optimal in the magnesium citrate group. Since bowel preparation provided by both cathartics was comparable, magnesium citrate should be considered for CT colonography, particularly in patients at risk for phosphate nephropathy.

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Computed tomographic (CT) colonography has been shown to be a feasible and cost-effective alternative to optical colonoscopy to aid in the detection of colorectal neoplasia (1–3). CT colonography provides a promising and clinically relevant means of decreasing the current colorectal cancer mortality rate of 52 000 per year (4). Despite the benefits of current screening methods, an estimated 41.8 million adults in the United States who are in the average-risk screening population do not undergo any form of screening, thus leaving a large candidate pool that could potentially be reached with CT colonography. The addition of CT colonography as a screening option by an institution has demonstrated evidence of improved colorectal cancer screening compliance by increasing overall numbers of individuals enrolled within both colonoscopy and CT colonography programs (5–7).

With current methods, it is necessary to undertake adequate colonic cleansing to achieve acceptable CT colonographic sensitivity and specificity. This is especially important with primary three-dimensional reading techniques or with same-day polypectomy protocols where excess stool creates pseudopolyps on CT colonographic images and obscures true soft-tissue polyp visualization (Fig 1) (8). Protocols adhering to either a single-dose or a double-dose sodium phosphate regimen have been shown to be effective in colon cleansing (9). This low-volume regimen is reported to be superior to the use of a polyethylene glycol electrolyte solution as regards residual fluid retention, colon cleansing, and patient preference and compliance (10–12). Still, sodium phosphate poses additional risks in patients with cardiac and renal disease, owing to hyperphosphatemic and hypocalcemic effects such as acute phosphate nephropathy (13). An alternative cathartic agent, such as magnesium citrate, is advantageous in these patients, owing to decreased electrolyte disturbances and an improved therapeutic index (14).

The purpose of this study was to compare the efficacy of double-dose magnesium citrate in colonic cleansing and fluid retention with that of a single-dose sodium phosphate regimen.

Materials and Methods

No industry support was provided to the authors for any portion of this study. One author (P.J.P.) was a consultant for and another (D.H.K.) was on the medical board of C. B. Fleet (Lynchburg, Va). However, neither author participated in the evaluation of the preparation adequacy, and the other authors (none of whom had a reportable relationship with industry) collectively had control of inclusion of any data and information that might represent a conflict of interest for the two authors with such a relationship.

Study Design

This retrospective clinical study was conducted according to an institutional review board–approved protocol. The need for informed consent was waived, and the study was compliant with the Health Insurance Portability and Accountability Act of 1996. CT colonographic data in 118 consecutive patients who received sodium phosphate (October 18, 2007 to December 18, 2007) and in 115 consecutive patients (subset of patients at risk for phosphate nephropathy) who received magnesium citrate (November 21, 2005 through December 4, 2007) for colon cleansing were assessed for adequacy of preparation. The patient population was identified from a database of patients at our institution who underwent CT colonography for colon cancer screening. The database included information regarding CT colonographic findings, follow-up findings, and any associated complications. At our institution, the standard bowel preparation regimen has been single-dose sodium phosphate. However, in patients known to have or suspected of having renal or cardiac insufficiency or in patients older than 70 years of age with hypertension (especially if taking angiotensin-converting enzyme inhibitors), we use double-dose magnesium citrate. As a result, the mean age of the magnesium citrate group (64.5 years ± 10.5) was significantly higher than that of the sodium phosphate group (55.8 years ± 5.2) ($P < .001$).

CT Colonography Protocol

Bowel preparation was identical between the two groups, with the exception of the primary cathartic agent being used. Starting the day before the scheduled CT examination, patients were restricted to a clear liquid diet and received two 5-mg bisacodyl tablets, which were taken before 11:00 AM. The patients were instructed to ingest the cathartic agent—a single dose of 45 mL of sodium

Advances in Knowledge

- The results of this study confirm that both magnesium citrate and sodium phosphate provide excellent bowel cleansing for CT colonography.
- Magnesium citrate bowel preparation was associated with a more optimal residual fluid attenuation (790 HU) than was sodium phosphate (978 HU).

Implication for Patient Care

- Given the concern for acute phosphate nephropathy associated with sodium phosphate and the equal or possibly superior bowel preparation provided by magnesium citrate, magnesium citrate should be considered a front-line laxative for bowel preparation for CT colonography in population screening.

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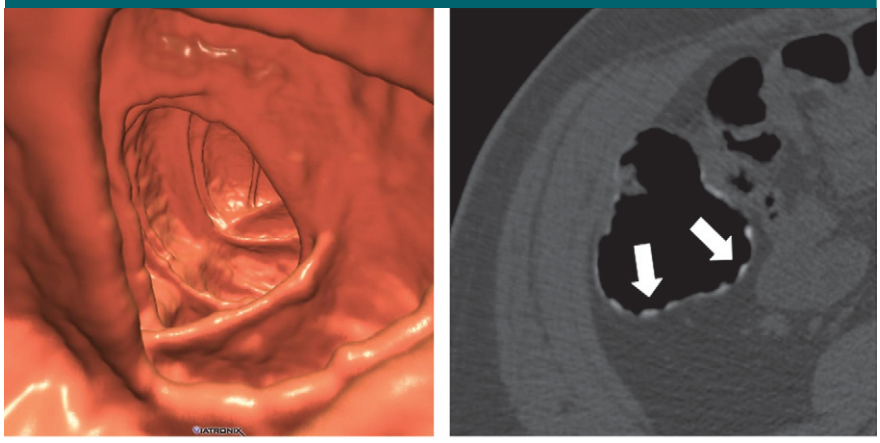
Guarantors of integrity of entire study, Z.B., J.L.H.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, P.J.P., D.J.A., J.L.H.; clinical studies, P.J.P., D.A., J.L.H.; statistical analysis, J.L.H.; and manuscript editing, P.J.P., D.K., J.L.H.

See Materials and Methods for pertinent disclosures.

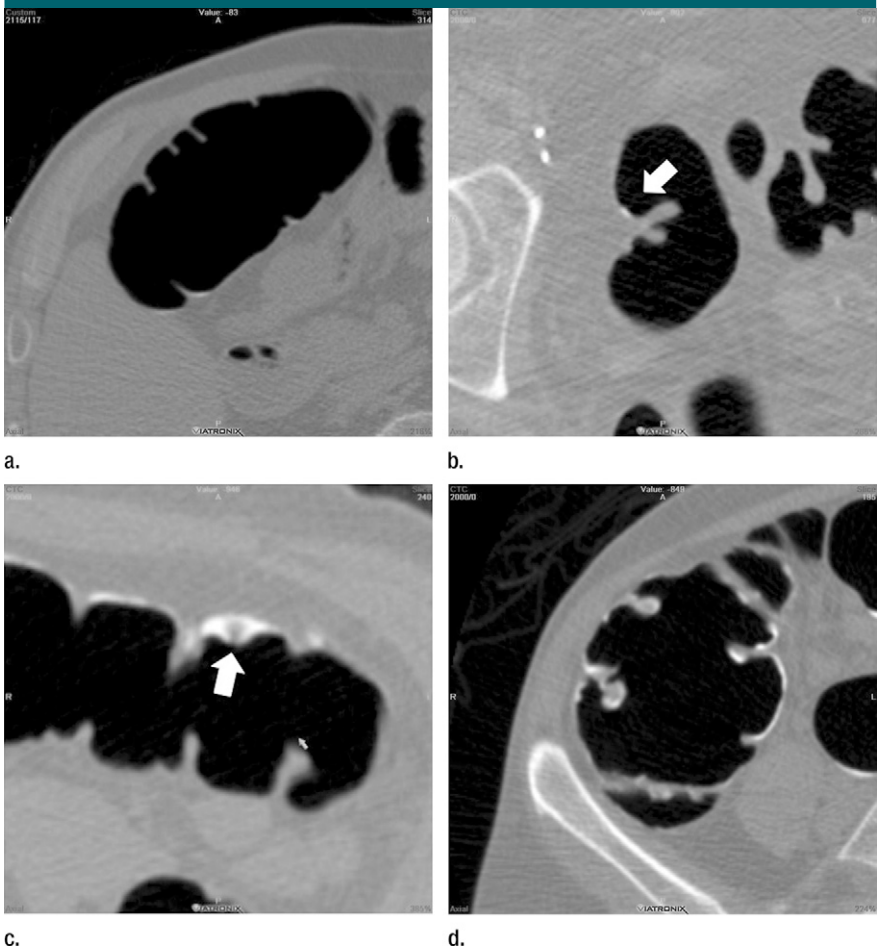
Figure 1



a. b.

Figure 1: (a) Three-dimensional endoluminal view of ascending colon and cecum in a patient with substantial retained stool. Residual stool has the appearance of pseudopolyps, which makes evaluation of both three- and two-dimensional images more challenging and can obscure abnormalities. **(b)** Two-dimensional axial image in same patient shows the strongly tagged stool (arrows), which appears as pseudopolyps on a three-dimensional image.

Figure 2



a. b.

c. d.

Figure 2: Axial two-dimensional CT colonographic images show stool scoring system. **(a)** Stool score of 1: no residual stool. **(b)** Stool score of 2: one stool particle smaller than 5 mm in diameter. Arrow = small well-tagged stool particle. **(c)** Stool score of 3: one to three stool particles smaller than 5 mm in diameter. Large arrow = large partially tagged residual stool particle, small arrow = viewing direction in three-dimensional field of view. **(d)** Stool score of 4: stool particle larger than 5 mm in diameter or more than three particles of any size. In this case, there is extensive tagged stool lining the cecum.

phosphate solution (Phospho-soda; Fleet Laboratories) or a double dose of 296 mL of magnesium citrate solution (Sun-Mark, San Francisco, Calif) divided into two discrete doses separated by 3 hours, with the first dose taken 3–6 hours after the bisacodyl tablets. Both patient groups were also given 250 mL of 2% wt/vol barium sulfate (Readi-cat 2; E-Z-Em, Lake Success, NY) and one bottle (60 mL) of sodium diatrizoate/diatrizoate meglumine (MD-Gastroview; Mallinckrodt, Hazelwood, Mo), which was taken 2–3 hours after the barium sulfate.

Automated CO_2 delivery was used to achieve colonic distention. After equilibrium intraluminal pressure was achieved, immediate review of distention was conducted on scout views and two-dimensional axial images with the patient in both

supine and prone positions to ensure adequate insufflation of the colon. An eight- or 16-section multidetector CT scanner (Lightspeed series; GE Healthcare, Milwaukee, Wis) was used for all examinations, with a CT technique of 1.25-mm collimation, 120 kVp, and 50–75 mAs. The images were reviewed on a picture archiving and communication system (McKesson PACS; McKesson, San Francisco, Calif) with reconstructed images of 1.25-mm section thickness and 1-mm reconstruction interval.

Image Evaluation

A previously established four-point scoring system was used to evaluate residual stool in each of six colon segments (cecum; ascending, transverse, descending, and sigmoid colon; and rectum) with lower scores corresponding to decreased residual stool (Fig 2) (9). Specifically, a colonic segment with no stool was given a score of 1; a segment with a single residual stool particle smaller than 5 mm in diameter, a score of 2; a segment with one to three particles of stool all smaller than 5 mm in diameter, a score of 3; and a segment with stool particles larger than 5 mm or more numerous than three, a score of 4.

A similar four-point scale was used to assess the six colon segments for residual luminal fluid, with lower scores corresponding to a decreased percentage of the distended colonic segment occupied by residual fluid (Fig 3) (9,12). Specifically, the score reflected the percentage of the colonic lumen filled with fluid. A segment with no fluid was given a score of 1; a segment with less than 25% of the lumen filled, a score of 2; a segment with 25%–50% of the lumen filled, a score of 3; and a segment with more than 50% of the lumen filled, a score of 4.

The scoring was performed by two independent readers (D.J.A., a resident with 1 year of experience evaluating CT colonographic studies; and M.G.L., an abdominal imaging fellow with 2 years of experience evaluating such studies) under the supervision of another author (J.L.H., who is fellowship trained in abdominal imaging and has 5 years of experience reading CT colonographic studies and had read more than 1000 such studies) who trained the readers specifically for this investigation. The readers were blinded to the specific cathartic regimen used for each case and reviewed the images in random order on a picture archiving and communication system workstation. The higher of the two positional scores from each reader was used, and the scores from the two readers were averaged to give an overall stool and fluid score for each segment in each patient.

In addition, the attenuation value of the residual fluid was obtained by placing a single region of interest (ROI) that was approximately 2 cm in diameter (although by necessity, the size would vary depending on the amount of residual fluid) in the largest fluid collection in both the ascending and descending colon on both prone and supine images. The mean of these measurements was calculated to establish a mean fluid attenuation for each case.

Statistical Analysis

An a priori power analysis was performed to determine the appropriate sample size. Since we were attempting to test for a null hypothesis, the acceptable β error was limited to .05. The α error was also limited to .05. Because of the inherent subjectivity of the measurements, we presumed that the standard deviation might be large and therefore used 1.0 for the expected

Figure 3

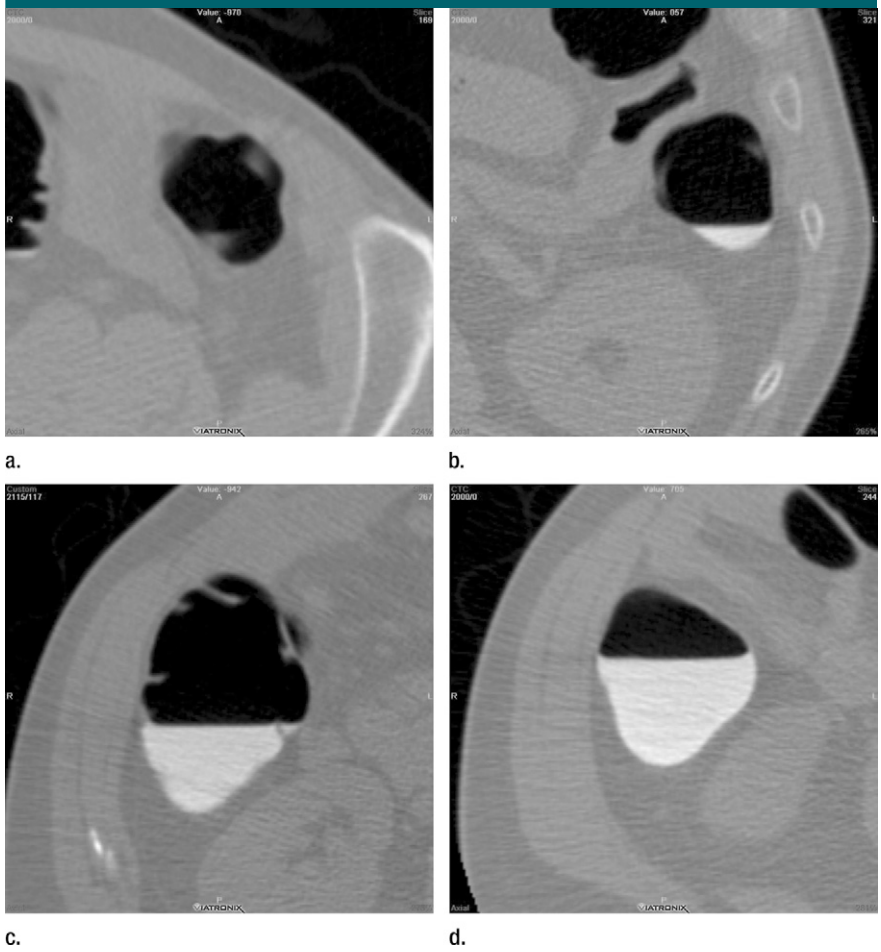


Figure 3: Axial two-dimensional CT colonographic images show stool scoring system. **(a)** Fluid score of 1: no residual fluid. **(b)** Fluid score of 2: less than 25% of the lumen filled with fluid. **(c)** Fluid score of 3: 25%–50% of the lumen filled with fluid. **(d)** Fluid score of 4: more than 50% of the lumen filled with fluid.

Stool and Fluid Scoring according to Cathartic and Colonic Segment

Segment	Sodium Phosphate*	Magnesium Citrate*	*P* Value
Stool			
Cecum	1.72 (0.67)	1.57 (0.64)	.1
Ascending	1.62 (0.72)	1.76 (0.78)	.2
Transverse	1.43 (0.72)	1.45 (0.71)	.8
Descending	1.30 (0.63)	1.28 (0.56)	.8
Sigmoid	1.47 (0.69)	1.39 (0.68)	.4
Rectum	1.34 (0.64)	1.38 (0.61)	.6
Total	1.48 (0.68)	1.47 (0.66)	.8
Fluid			
Cecum	2.03 (0.32)	2.01 (0.33)	.6
Ascending	2.79 (0.74)	2.81 (0.76)	.8
Transverse	2.30 (0.61)	2.26 (0.61)	.6
Descending	2.67 (0.78)	2.64 (0.84)	.8
Sigmoid	2.17 (0.72)	2.44 (0.91)	.01
Rectum	1.87 (0.54)	1.92 (0.74)	.6
Total	2.31 (0.62)	2.35 (0.70)	.3

Note.—Scoring was performed on a scale of 1–4, with lower scores indicating less residual stool or fluid.

* Data are mean scores, with standard deviation in parentheses.

standard deviation. A difference of 0.5 on the grading scale was thought to reflect a clinically significant difference between the two study populations. By using these data, the required sample size was 104 patients to achieve 95% power. We chose to increase the sample size by approximately 10% to ensure the validity of our findings. Continuous data were expressed as means with standard deviations. Unpaired *t* tests with the Welch correction were used to compare the stool and fluid scores, as well as the fluid attenuation, between the two study groups by using software (Instat, version 3.0a; GraphPad, San Diego, Calif). A *P* value of less than .05 indicated a statistically significant difference.

Results

No complications were encountered with either bowel preparation.

Stool Score

In the sodium phosphate group, a stool score of 1 or 2, indicating no stool or only minimal residual stool smaller than 5 mm, was seen in 88.6% (627 of 708) of colonic segments. Additionally, a score of 3 was seen in 9.0% (64 of 708), and a score of 4 was seen in 2.4% (17 of 708). For the magnesium citrate group, a score of 1 or 2 was seen in 88.1% (608 of 690) of segments. Scores of 3 and 4 were seen in 10.7% (74 of 690) and 1.2% (eight of 690) of segments, respectively. Cathartic agent did not show a significant association with residual stool for the cecum ($P = .08$), ascending colon ($P = .2$), transverse colon ($P = .8$), descending colon ($P = .8$), sigmoid colon ($P = .4$), or rectum ($P = .6$). Overall mean score for all segments was 1.47 for magnesium citrate and 1.48 for sodium phosphate ($P = .8$), which, once again, was not significantly different.

Fluid Score

In the sodium phosphate group, a residual fluid score of 1 or 2, indicating that less than 25% of the lumen was filled with residual fluid, was seen in 63.7% (451of 708) of colonic segments. A score of 3 was seen in 26.0% (184 of 708), and a score of 4 was seen in 10.3% (73 of 708). For the magnesium citrate group, a score of 1 or 2 was seen in 61.0% (421 of 690) of segments. Scores of 3 and 4 were seen in 22.9% (158 of 690) and 16.1% (111 of 690) of segments, respectively. There was no significant association between cathartic agent and fluid retention for the cecum ($P = .6$), ascending colon ($P = .8$), transverse colon ($P = .6$), descending colon ($P = .8$), or rectum ($P = .6$). A significant association was identified for the sigmoid colon ($P = .01$), with the magnesium citrate group significantly more likely to have retained more fluid in the sigmoid colon (score of 3 or 4). However, the actual numeric difference between the two groups was only 0.27 point (2.44 vs 2.17). There was no significant difference between the total fluid score for the cathartic agents (2.31 for sodium phosphate, 2.35 for magnesium citrate, $P = .3$).

The scoring for all segments is summarized in the Table. Please note that all parameters for all segments were within the limits set for our a priori power analysis, indicating a power of greater than 95% for all comparisons.

Residual fluid attenuation was significantly different between the two groups, with a mean of 978 HU ± 160 (range, 120–1250 HU) for sodium phosphate versus 790 HU ± 216 (range 170–1130) for magnesium citrate ($P < .001$).

Discussion

Sufficient colon cleansing is paramount for sensitive and specific CT colonographic results. The presence of residual stool and fluid increases the difficulty and time required to identify colonic polyps. Additionally, untagged residual stool can be misidentified as a colon polyp, resulting in a false-positive CT colonographic finding and an unnecessary optical colonoscopy. This is especially pertinent for stool particles larger than 5 mm in size, since polyps smaller than this (ie, diminutive polyps) are currently not reported at most institutions and are not likely to be clinically relevant. Historically, sodium phosphate has been favored owing to a perceived advantage for colonic cleansing and was initially used in nearly 90% of cases in our program (8). In addition, 94% of patients prefer low-dose sodium phosphate rather than polyethylene glycol (PEG), the use of sodium phosphate has been shown to increase compliance from 19% to 97% for completion of the cathartic regimen (15).

Although we have not encountered complications with either bowel preparation, sodium phosphate has been shown to result in rare adverse effects including hyperphosphatemia, hypocalcemia, and acute phosphate nephropathy (13,16,17). The true incidence of these adverse effects is not known but is thought to be approximately one in 1000 (13). However, it is also likely that these entities are underdiagnosed, and even when they are identified, the relationship with sodium phosphate may not be appreciated. Decreased renal function after oral sodium phosphate solution usage, as measured with decreased glomerular filtration rate, showed particular concordance with patients taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers or those with a clinical diagnosis of diabetes, particularly in the elderly (18). Additionally, sodium phosphate has been shown to decrease blood pressure as the increased stool volume is derived from intravascular pools. Previous work has shown that a single dose of sodium phosphate is just as effective as a double dose at colonic cleansing for CT colonography and that this dose reduction decreases the risk of these adverse effects (9). However, the risk remains, especially in patients with renal or cardiac insufficiency. Therefore, an alternative without the effects of electrolyte imbalances and nephropathy would be advantageous. Magnesium citrate offers a low-volume alternative to PEG solution but without the potential risks associated with sodium phosphate. Previous research indicates that 75% of patients prefer magnesium citrate to PEG, which would likely lead to patient compliance similar to that for sodium phosphate (11).

Although little research has been conducted on magnesium citrate as the sole cathartic agent for CT colonography, Berkelhammer et al (11) reported that magnesium citrate is more effective in colon cleansing than sodium phosphate and reduces the incidence of rectosigmoid aphthous ulcers in patients undergoing optical colonoscopy. Our study corroborated this finding for CT colonography and also demonstrated that the residual fluid was of lower attenuation in the group receiving magnesium citrate. The lower attenuation of fluid facilitates polyp conspicuity on CT colonographic images. Both sodium phosphate and magnesium citrate regimens resulted in excellent cleansing of stool, with 88.6% and 88.1% of the respective groups having no residual stool or residual stool under the 6-mm threshold for CT colonography reporting. This is pertinent, since stool larger than 5 mm must be analyzed with two-dimensional analysis. This results in increased difficulty and time of review. Additionally, no significant difference in retained stool was found between the different cathartic agents and the six colonic segments.

Residual fluid levels within five of six colonic segments were not significantly associated with the cathartic agent. It is uncertain why the sigmoid colon demonstrated increased residual fluid in the magnesium citrate group as compared with that in the sodium phosphate group. However, this is unlikely to be clinically important because the difference was isolated to the sigmoid colon and was a relatively small increase in fluid volume (mean score: 2.17 vs 2.44). Also, this increase in the magnesium citrate group remained under 50% luminal filling on average and is thus likely negated by the shifting of fluid between prone and supine positions. Use of both sets of images by readers ensures that polyps will be visible in one position for three-dimensional image interpretation and should also be visible within the fluid for two-dimensional image interpretation.

The lower fluid attenuation seen in the magnesium citrate group may in fact have a clinical impact because fluid attenuation has been shown to have a significant effect on polyp conspicuity. In fact, previous research has suggested that optimal viewing conditions in the two-dimensional format are met with fluid attenuation values of approximately 700 HU, due to high conspicuity of all polyps at this level (19). With a mean attenuation of 790 HU, magnesium citrate was closer to this optimal level than sodium phosphate, which has a mean attenuation of 978 HU. The higher attenuation of the fluid in the patients who received sodium phosphate may result in more associated artifacts and likely reduces polyp conspicuity. Such an increase in polyp conspicuity with magnesium citrate could lead to increased sensitivity and specificity of CT colonography.

There were several limitations to our study. The primary limitation was that although we compared the bowel preparation outcome obtained with these two bowel preparation regimens, we did not assess the diagnostic performance possible with them. Because we found no important differences between the bowel cleansing regimens, we would not expect a difference in diagnostic performance, but this was not specifically evaluated. In addition, there was a selection bias in our study. We have since changed our standard bowel regimen to magnesium citrate, but at the time of the study sodium phosphate was our bowel regimen of choice. As a result, the patients in this group were low-risk patients from our screening population. On the other hand, the magnesium citrate group comprised patients thought to be at risk for phosphate nephropathy (older patients, patients with renal or cardiac disease). If anything, this might be expected to affect the bowel preparation with magnesium citrate adversely, but we did not find that to be the case. One other limitation was that we only evaluated two bowel preparation regimens—specifically double-dose magnesium citrate and single-dose sodium phosphate—and there are numerous other options for both catharsis and tagging, as well as ongoing research into "prepless" CT colonography. Further research will be required to continue to refine the bowel preparation prior to CT colonography.

Given the similarity in colon cleansing, the improvement in fluid attenuation values, and the increased therapeutic index, magnesium citrate is an excellent alternative for colon cleansing, especially in an at-risk population.

In conclusion, both sodium phosphate and magnesium citrate provided excellent colon cleansing for CT

colonography. Residual stool and fluid were comparable in both groups, and fluid attenuation values were closer to optimal with magnesium citrate. Given the similarity in colon cleansing, the more advantageous fluid attenuation values, and the increased therapeutic index, magnesium citrate is an excellent alternative for colon cleansing.

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