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Effects of the Addition of High-Dose Vitamin C to Polyethylene Glycol Solution for Colonic Cleansing: A Pilot Study in Healthy Volunteers

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ABSTRACT

Background: Polyethylene glycol (PEG) solutions, with or without osmotic agents, are used to empty the large intestine before procedures such as colonoscopy or colonic surgery. Data concerning the effectiveness of vitamin C as an ingredient in colonic preparations are scant.

Objective: The aim of this article was to assess the effectiveness, acceptability, and tolerability of 6 preparations of a standard PEG electrolyte solution containing different doses of PEG, vitamin C (as an osmotic agent), and sodium sulfate in colonic cleansing.

Methods: This double-blind, randomized, 2-period crossover study was conducted at the Lariboisière Hospital, Paris, France. Healthy adult volunteers were randomly assigned to receive 2 of 6 colonic cleansing preparations, each containing different doses of PEG (100 or 125 g/L), vitamin C (0, 5, or 10 g/L, in the form of sodium ascorbate, ascorbic acid, or a mixture of both), and sodium sulfate (5 or 7.5 g/L), diluted in water to a volume of 2 L. Study drug administration was separated by a washout period of 7 to 15 days, after which the volunteers received an alternate preparation. Stools were collected for 10 hours after the start of solution ingestion. The primary efficacy end point was stool volume. Secondary end points included acceptability of taste, assessed using a 100-mm visual analog scale (VAS) (0 = excellent to 100 = execrable), taste criteria (saltiness, acidity, and sweetness, assessed on a 4-point Likert-type scale [0 = very pleasant to 3 = intolerable]) and tolerability (clinical effects [changes in body weight, blood pressure, heart rate, and nausea and vomiting] and biologic effects [changes in serum electrolytes, creatinine, hematocrit, and ascorbic acid]).

Results: Thirty volunteers (15 men, 15 women; mean [SD] age, 29.8 [8.2] years [range, 20–45 years]) were enrolled and completed the study. Mean (SD) stool volume obtained with preparations containing 10 g/L of vitamin C did not differ

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significantly from the volume obtained without vitamin C (2.54 [0.54] L vs 1.93 [0.62] L; 95% CI, –0.13 to 1.47). Mean (SD) VAS scores for acceptability of taste ranged from 54.4 (25.0) (preparation E) to 74.4 (20.1) (preparation C) (P = 0.03 preparation E vs all other preparations). The only significant difference in taste criteria was in acidity, with preparation A being the least acidic according to patients' ratings on the VAS (1.4 [0.7] vs 1.8 [0.4] [mean of the other 5 preparations combined]; P = 0.04 preparation A vs all other preparations). Mild dehydration occurred in 6 subjects (1 for each preparation). No clinical or biological adverse effects were found.

Conclusions: In this study of 6 colonic cleansing preparations in healthy volunteers, the use of high-dose vitamin C as an osmotic agent in addition to PEG did not significantly increase stool output. All 6 preparations were well tolerated. (*Curr Ther Res Clin Exp.* 2005;66:486–500)

Key words: vitamin C, stool output, acceptability, taste, polyethylene glycol solution, colonic preparation, ascorbate, ascorbic acid.

INTRODUCTION

The diagnostic value of colonoscopy is dependent on the ability to achieve adequate colon preparation, characterized by the absence of fecal residue in the large intestine, to maximize visibility for the endoscopist.[1] For >20 years, iso-osmotic polyethylene glycol (PEG) solutions have been used for colon cleansing before colonoscopy, double-contrast barium enema, or colon surgery.[2–8] Despite the well-established effectiveness and tolerability of these preparations, some patients are unable to drink the large volume required (≥4 L) over a short period of time (up to 1 L/h), as well as when a 2-step procedure is used.[4,6] Some patients also find the taste of the solutions unpleasant.[4–6] Several attempts have been made to reduce the required volume by adding stimulant laxatives, such as senna,[5] bisacodyl,[7] or other osmotic agents (eg, mannitol, magnesium, sodium salts), with variable results in terms of acceptability of taste.[4–8]

The most widely used osmotic agent worldwide, sodium phosphate (solution or tablet), exerts its action by drawing water from the body into the large intestine.[2–4,7,8] In several randomized, controlled, investigator-blinded trials enrolling >1300 patients, sodium phosphate was found to be similarly effective and better accepted because of the low volume (2 L vs up to 6 L) required to clean the large intestine compared with standard PEG electrolyte solutions.[3,4,7–9] Moreover, in randomized, single-blind trials in >1300 patients requiring colonoscopy for colon cancer screening, the use of oral sodium phosphate was associated with the lowest rate of need for repeat endoscopy due to inadequate cleansing, together with a low cost per patient, compared with standard PEG solutions (between-group differences, 65% and 10%–15%, respectively).[10–12] Patients' ability to drink the entire preparation, and tolerability, as assessed by the prevalences of clinical and biological adverse effects, have

been compared in sodium phosphate solutions and standard PEG solutions.[4,7,8,13] Of the trials involving >1300 patients, some, but not all, trials found that a significantly larger proportion of patients (up to 75%) were able to drink the required amount of sodium phosphate solutions compared with 40% of patients administered standard PEG solutions ($P < 0.001$).[10–13] Abdominal discomfort was reported in a significantly higher proportion of patients (15%) receiving the PEG solution compared with 7% receiving sodium phosphate solution ($P < 0.005$).[4,8–13] Finally, >90% of patients indicated that they were willing to repeat using the oral sodium phosphate preparations compared with 15% to 30% using the standard PEG solutions.[4,7–13]

However, sodium salts (eg, sodium phosphate, sodium sulfate) have several limitations, including their salty taste and their contraindication in patients with cardiovascular or renal impairment.[4,8,14] Significant changes in volume of body water and serum concentrations of electrolytes, leading to hyperphosphatemia, hypocalcemia, hypokalemia, and/or dehydration with potentially fatal outcomes, and colonic mucosal ulcerations have been described in some patients.[4,8,14]

The ideal colonic cleansing preparation would be tolerable in all populations of patients, including elderly patients and those with cardiovascular or renal impairment. It would be well tolerated and have acceptable required volume and taste. Two liters of solution containing sufficient amounts of osmotic agents to obtain optimal stool volume (usually >3 L) without a laxative (eg, a senna compound) might optimize both colon cleansing and compliance.[15,16]

One possible choice of osmotic agent is ascorbic acid (vitamin C), a 6-carbon, ketolactone, water-soluble vitamin structurally related to glucose and other hexoses.[17] Vitamin C is readily absorbed from the proximal small intestine by 2 saturable, energy- and dose-dependent transporters.[17,18] Because of the hexose structure of vitamin C, the unabsorbed fraction may act as an osmotic agent in the gut lumen, leading to water excretion and an increase in stool volume.[17–21] In 2 open-label studies in 100 healthy volunteers, the administration of an amount of vitamin C larger than physiologically required for supplementation (up to 30 g) was associated with low prevalences of adverse effects (eg, kidney stones, abdominal pain, severe acidosis).[17,19] In a nonlinear, 2-compartment disposition model of the pharmacokinetic properties of vitamin C with saturable, time-constrained intestinal absorption, a single oral dose led to decreased absorption, from 75% with 1 g to 20% with 5 g.[20] After ingestion of 6 g of vitamin C, 1.5 g was absorbed, and the ingestion of 12 g led to the absorption of 1.9 g of vitamin C.[17,20]

We hypothesized that vitamin C could be used in colonic preparations to decrease the volume required for effective cleansing. Based on a literature search using MEDLINE (key terms: *vitamin C, sodium ascorbate*, and *colon cleansing*; years: 1975–2005), data concerning the effectiveness of vitamin C as an ingredient in colonic preparations are scant. However, 1 solution containing 160 g of PEG 3350, 17 g of sodium sulfate, 18 g of ascorbic acid, 7.9 g of sodium chloride, and 2.2 g of potassium chloride, diluted in water to a volume of 3 L,

has been available in Australia for almost 15 years and has been found to be well tolerated (no cases of toxicity have been reported to the manufacturer).[22] Patients have reported that the solution has an acceptable taste despite containing a large amount (>27 g) of salt. Moreover, 3 L of this solution has been found to be sufficient to achieve effective colonic cleansing.[23]

A pilot study[24] conducted in 6 healthy adult male volunteers at the Unit of Therapeutic Research, Department of Internal Medicine, Lariboisière Hospital, Paris, France, found that 10 g of vitamin C added to a standard iso-osmotic PEG solution increased the stool volume by 35% compared with the standard solution alone (2.2 [0.4] L vs 1.4 [0.2] L; $P < 0.01$). The addition of a third osmotic agent (sodium sulfate, 11.1 g) to the vitamin-C–containing solution was associated with an almost 2-fold increase from baseline in stool volume (1.4 [0.1] L vs 2.7 [0.2] L; $P < 0.001$). Thus, the combination of PEG, vitamin C, and sodium sulfate diluted in water to a volume of 2 L might increase fecal output.

The aim of this study was to assess the effects of 6 colonic cleansing preparations containing different doses of PEG (100 or 125 g/L), vitamin C (0, 5, or 10 g/L, in the form of sodium ascorbate, ascorbic acid, or a mixture of both), and sodium sulfate (5 or 7.5 g/L), diluted in water to a volume of 2 L, before colonoscopy or colon surgery.

SUBJECTS AND METHODS

This double-blind, randomized, crossover study was conducted at Lariboisière Hospital, Paris, France, between April and June 2000. Healthy volunteers aged 20 to 45 years were recruited from a pool of medical students and staff at the hospital. The study protocol was approved by the local ethics committee. Due to ethical limitations, we were not authorized by the committee to perform colonoscopy to directly assess the efficacy of the tested preparations. Subjects provided written informed consent to participate and were compensated for their participation.

Study Design

Diet was standardized 2 days before and during the study to avoid alteration of gastrointestinal transit time. Each volunteer was randomized to receive 2 of the 6 preparations (A to F, with A being the control preparation because it did not contain vitamin C) (**Table I**), 1 during each of 2 study periods separated by a 7- to 15-day washout period. Subjects were asked to ingest the entire preparation within 2 hours (two 1.25-L glasses every 15 minutes). Compliance with the regimen was visually monitored by one of the study investigators (G.S.) using a timer.

Assessments

Efficacy

Stool volume was measured for 10 hours after the start of solution ingestion. Total fecal output at the end of the 10-hour follow-up period was the primary end point.

Table I. Concentrations (g/L) of the ingredients of 6 colonic cleansing preparations.

Ingredient	Preparation A (Control)	Preparation B	Preparation C	Preparation D	Preparation E	Preparation F
PEG	100	100	100	100	100	125
Sodium sulfate	7.5	7.5	7.5	7.5	5	7.5
Ascorbic acid	0	5	5	10	5	5
Sodium ascorbate	0	0	5	0	5	5

PEG = polyethylene glycol.

Acceptability

The taste of each preparation was assessed as a secondary end point, using a 100-mm visual analog scale (VAS) (0 = excellent to 100 = execrable). Taste criteria (saltiness, acidity, and sweetness) were assessed on a 4-point Likert-type scale (0 = very pleasant to 3 = intolerable).

Tolerability

Tolerability was assessed using measurements of body weight, blood pressure, heart rate, urinary output, volume of excess fluid ingested, and the prevalence of nausea or vomiting during ingestion of the colonic preparation and over the 10-hour follow-up period. Two blood samples were drawn—1 just before the beginning of preparation ingestion and 1 at the end of the follow-up period—to assess changes in serum sodium, potassium, bicarbonate, creatinine, ascorbic acid concentrations (ascorbemia), and hematocrit.

Statistical Analysis

Because it would not have been feasible to give all 6 preparations to each volunteer, statistical analysis was designed to obtain 5 balanced blocks of 6 treatments. A difference in stool volume of at least 0.8 L between preparations with and without vitamin C at a level of significance of 0.05 for 2-sided comparisons between 6 preparations (with an expected residual SD of 0.4 L) was the primary end point, based on the pilot study conducted in 6 healthy volunteers, with 85% statistical power. Hence, 10 observations were needed per preparation, with 2 preparations per subject (block size, k = 2). Thus, 30 subjects needed to be enrolled in this crossover study. Results were analyzed according to the intent-to-treat principle. Comparisons of primary and secondary end points were performed using analysis of variance (ANOVA), followed by the Scheffe test adjusted for multiple comparisons when an overall significance was detected on ANOVA. Statistical comparisons were performed using StatView ver-

sion 5.01 (SAS Institute, Cary, North Carolina). Results are expressed as mean (SD) and range, where applicable.

We were particularly interested in comparing the effects of ascorbic acid 5 g versus no ascorbic acid (preparation B vs A), sodium ascorbate 5 g + ascorbic acid 5 g versus ascorbic acid 5 g (preparation C vs B), sodium ascorbate 5 g + ascorbic acid 5 g versus ascorbic acid 10 g (preparation C vs D), and sodium sulfate 7.5 g versus sodium sulfate 5 g (preparation C vs E) (**Table I**). The relationship between stool output and pretreatment body weight was described using the Spearman rank correlation coefficient (r_s). Changes in serum electrolyte concentrations and hematocrit at the end of preparation ingestion were compared using ANOVA followed by the Scheffe test when an overall significance was detected.

RESULTS

Demographic Data

Thirty volunteers (15 men, 15 women) were enrolled and completed the study. The mean (SD) age of the study population was 29.8 (8.2) years (range, 20–45 years), and the mean (SD) weight and height were 70.5 (13.1) kg (range, 46–100 kg) and 173.2 (9.8) cm (range, 155–195 cm), respectively. No significant between-group differences in baseline characteristics, including weight before ingestion of the preparations, were found (**Table II**).

Twenty-nine volunteers ingested the entire 2-L preparation within 2 hours (mean [SD] ingestion time, 115.7 [12.3] minutes [range, 90–145 minutes]); 1 subject ingested only 1.8 L of preparation B during period 1 but completed the study and was therefore included in the intent-to-treat analysis. Ingestion time was not correlated with mean stool output (r_s, –0.125; $P = 0.35$).

Efficacy

Stool output ranged between 0.65 L (preparation A) and 3.50 L (preparation F) and was not correlated with pretreatment body weight (r_s, 0.007) (**Table III**). The between-group differences in mean stool volume were not statistically significant. Although preparation F contained 125 g/L of PEG and preparation C contained 100 g/L of PEG, we did not find any significant differences in stool volume between these 2 formulations. Neither period effect nor treatment–period interactions were found in this crossover study.

Acceptability

As shown in **Table IV**, all 6 preparations were given a relatively high mean VAS score (≥68.9) except preparation E, which contained 5 g/L of sodium sulfate and had the lowest mean (SD) VAS score (54.4 [25.0]; $P = 0.03$ vs all other preparations). Likewise, no significant between-preparation differences in VAS scores for saltiness or sweetness were found. However, the mean (SD) VAS score for acidity was significantly lower for preparation A (1.4 [0.7]), which contained no

Table II. Body weight before and after solution ingestion in volunteers receiving colonic preparation solutions.*

Parameter	Preparation A (Control) (n = 10)	Preparation B (n = 10)	Preparation C (n = 10)	Preparation D (n = 10)	Preparation E (n = 10)	Preparation F (n = 10)
Weight before ingestion, kg						
Mean (SD)	69 (13)	70 (13)	71 (16)	73 (14)	69 (13)	72 (10)
Range	44–89	48–92	46–100	56–100	46–93	57–85
Weight after ingestion, kg						
Mean (SD)	69 (13)	70 (13)	70 (16)	72 (13)	68 (12)	71 (10)
Range	42–89	48–92	46–100	54–98	46–93	57–85

*No significant between-group differences were found.

Table III. Mean (SD) stool volume (liters) after ingestion of colonic preparations containing polyethelene glycol and low-dose (5-g/L) or high-dose (10-g/L) vitamin C with or without high-dose (7.5-g/L) sodium sulfate.*

Stool Volume	No Vitamin C (Preparation A)	Low-Dose Vitamin C (Preparation B)	Vitamin C and Sodium Sulfate (Preparations C, D, and F)	Vitamin C and Low-Dose Sodium Sulfate (Preparation E)	Preparations C, D, E, and F
Mean (SD)	1.93 (0.60)	2.25 (0.44)	2.59 (0.58)	2.40 (0.37)	2.54 (0.54)
Range	0.65–2.62	1.58–2.84	1.17–3.50	1.49–2.60	1.17–3.50

*No significant between-group differences were found.

Table IV. Acceptability scores of the 6 colonic preparations, as evaluated by the subjects.

Parameter	Preparation A (Control)	Preparation B	Preparation C	Preparation D	Preparation E	Preparation F
Taste						
No. of patients	10	10	10	10	10	10
Score*						
Mean (SD)	71.8 (20.6)	73.6 (27.2)	74.4 (20.1)	68.9 (18.9)	54.4 (25.0)†	73.9 (10.7)
Range	35–98	20–100	38–100	35–98	21–93	58–95
Saltiness						
No. of patients	9	8	9	9	7	8
Score‡						
Mean (SD)	2.6 (0.5)	2.6 (0.5)	2.4 (0.5)	2.1 (0.6)	2.0 (0.6)	2.1 (0.4)
Range	2–3	2–3	2–3	1–3	1–3	2–3
Acidity						
No. of patients	8	9	8	7	5	6
Score‡						
Mean (SD)	1.4 (0.7)§	2.0 (0.5)	1.6 (0.5)	1.9 (0.7)	1.8 (0.4)	1.8 (0.4)
Range	0–2	1–3	1–2	1–3	1–2	1–2
Sweetness						
No. of patients	10	8	8	9	7	8
Score‡						
Mean (SD)	2.1 (0.6)	2.1 (0.4)	2.1 (0.6)	2.3 (0.7)	2.0 (0)	2.1 (0.6)
Range	1–3	2–3	1–3	1–3	2–2	1–3

*Assessed using a 100-mm visual analog scale (0 = excellent to 100 = execrable).
†$P = 0.03$ preparation E versus all other preparations.
‡Assessed using a 4-point Likert-type scale (0 = very pleasant to 3 = intolerable).
§$P = 0.04$ preparation A versus all other preparations.

vitamin C and thus was the least acidic, compared with the other preparations (≥1.6; all, $P = 0.04$).

Tolerability

Fourteen mild adverse events were reported during the study. As shown in **Table II**, the mean body weight at the end of the 10-hour follow-up period did not differ significantly between the 6 preparations or from baseline body weight in any group. Body weight loss ranged from 0.25 kg (preparation B) to 1.1 kg (preparation D) over the study period. Conversely, mean urinary output decreased by 50% from baseline (330 [155] vs 610 [340] mL, respectively; 95% CI, 100–880; $P = 0.002$) at the end of the follow-up period but did not differ significantly between preparations. Overall, the volume of extra fluid ingested by the study subjects ranged from 350 (90) to 510 (120) mL and did not differ significantly between preparations. Six subjects (1 for each preparation) indicated thirst and asked to drink a large amount (≥500 mL) of water after they ingested the second liter of preparation. Other adverse events included abdominal pain, noted in 1 subject each with preparations B, C, D, and E; nausea and vomiting, in 1 subject each with preparations B and F; and headache, in 1 subject each with preparations E and F. Overall, no adverse events were noted with preparation A, 1 with preparations C and D, and 2 with preparations B, E, and F. Due to the number of adverse events reported in the current study, statistical comparison between the 6 preparations could not be performed. These adverse events were transient and did not appear to be related to vitamin C intake. No moderate or severe adverse events occurred in any of the treatment groups.

Blood pressure, heart rate, and weight remained stable in each subject throughout the study in each treatment group. Mean (SD) systolic blood pressure was 123 (12) mm Hg before and 123 (16) mm Hg after treatment. Mean (SD) diastolic blood pressure was 73 (9) mm Hg before and 73 (7) mm Hg after treatment. Mean (SD) heart rate was 71 (9) bpm before and 69 (10) bpm after treatment. Mean (SD) patient weight was 70.5 (13.1) kg before and 70.1 (15.5) kg after treatment.

Minor changes in serum but not urinary electrolyte concentrations were observed after treatment completion with all preparations tested (**Table V**). However, the values reported remained within normal limits, and no significant intergroup or intragroup differences were found. Mean (SD) hematocrit ranged from 40.5% (3.9%) (preparation E) to 42.1% (4.4%) (preparation D) and remained stable in all patients throughout the study period. Mean (SD) serum sodium and potassium concentrations ranged from 140 (1.2) mmol/L (preparation B) to 145.4 (2.2) mmol/L (preparation F), and from 4.0 (0.2) mmol/L (preparation B) to 4.6 (0.2) mmol/L (preparation D), respectively, and did not change significantly during the study period. Mean (SD) serum bicarbonate concentrations ranged from 26.3 (3.2) mmol/L (preparation F) to 28.9 (2) mmol/L (preparation D) and from 25.5 (1.8) mmol/L (preparation D) to 26.7 (1.5) mmol/L (preparation A) before and after treatment, respectively. Mean (SD) serum creatinine concentration ranged from 73.5 (13) μmol/L (preparation F) to

Table V. Changes in hematocrit and serum electrolyte concentrations from before ingestion of the 6 colonic preparations to the end of the 10-hour follow-up period. Values are mean (SD).

Concentration	Preparation A (n = 10)	Preparation B (n = 10)	Preparation C (n = 10)	Preparation D (n = 10)	Preparation E (n = 10)	Preparation F (n = 10)
Hematocrit, %	0.77 (0.45)	–0.04 (0.45)	1.35 (0.75)	1.47 (0.52)	0.88 (0.66)	0.89 (0.54)
Sodium, mmol/L	2.50 (0.79)	2.10 (0.89)	3.22 (0.66)	1.90 (0.59)	2.89 (1.09)	4.50 (0.78)
Bicarbonate, mmol/L	–0.20 (0.80)	–2.10 (0.82)	–1.78 (0.60)	–3.40 (0.60)	–1.89 (0.72)	–0.70 (0.75)
Potassium, mmol/L	0.08 (0.09)	0.41 (0.11)	0.51 (0.10)	0.61 (0.13)	0.19 (0.14)	0.43 (0.07)

81.4 (12) μmol/L (preparation D) and did not vary significantly throughout the study. Overall, the changes observed in serum electrolyte concentrations and hematocrit did not differ significantly between the 6 colonic cleansing preparations.

The mean (SD) serum vitamin C concentrations were 67.5 (97.4) mmol/L with preparation A (no vitamin C), 141 (75) mmol/L with preparation B (5 g/L ascorbic acid), and 189.7 (52.6) mmol/L with preparation E (5 g/L ascorbic acid and 5 g/L sodium ascorbate).

DISCUSSION

The tolerability and volume of a cleansing preparation might limit its acceptability and, therefore, efficacy of colonic cleansing.[25–27] A preparation volume of 2 L was chosen based on previous reports establishing that at least 3 L of stool was required to achieve effective colonic cleansing.[15,16] The combinations of osmotic agents used in the 6 preparations tested in the present study were chosen to achieve this outcome.

The effects of vitamin C, in the form of ascorbic acid, sodium ascorbate, or a mixture of both, on stool volume was assessed because its hexose structure, tolerability, and saturable absorption led us to assume that this vitamin can be administered at high doses and act as an osmotic agent in the gut lumen, thereby increasing stool volume.[17–21] The differences in serum vitamin C concentration were not linear with the dose of vitamin C, and were variable, which agrees with the previously described nonlinear, saturable pharmacokinetic properties of vitamin C in humans.[20] The prevalence of ascorbemia (141 [75] mmol/L with preparation C vs 154.4 [46] mmol/L with preparation D) was not correlated with the use of preparations in which half of the ascorbic acid was replaced with sodium ascorbate, suggesting that both formulations share the same absorptive capacity across the human small intestine. Acidity as reported by the volunteers was not related to ascorbemia (data not shown). Based on the literature search, this is the first report of the effect of vitamin C on fecal output in humans. Although stool output obtained with the combinations providing the highest stool output (preparations C, D, and F; **Table II**) did not achieve the outcome of 3 L of stool, the use of 20 g of vitamin C with a standard 2-L volume of solution containing PEG 200 g and sodium sulfate 15 g increased stool volume by up to 1500 mL in some subjects compared with control.

All 6 preparations in this study were well tolerated. Abdominal pain was reported in 4 subjects, while nausea and vomiting occurred in 2 subjects. Fermentation of ascorbate mediated by colonic bacteria, such as *Escherichia coli*, has been previously reported.[28] Ascorbate might be fermented in the large bowel, producing hydrogen, carbon dioxide, short-chain fatty acids, and protons, which are readily absorbed but are also likely to produce abdominal discomfort. A large degree of variability is introduced by the residence time of the ascorbate solutions in the colon. Consequently, fecal output

might be decreased: as more gas and short-chain fatty acids are produced, less osmolite remains in the colon.[28]

To predict the efficacy and tolerability of vitamin C in colonic cleansing preparations, future studies might assess the amount of hydrogen produced using a breath test and the amount of ascorbate excreted in stool to anticipate stool volume recovery.

In the present study, the minor changes in electrolyte concentrations observed remained within normal limits and were not likely to have been related to the presence of vitamin C but rather to that of oral sodium sulfate: similar electrolyte changes have been described with this osmotic agent.[4,8,14,29] Despite a statistically nonsignificant decrease in mean serum bicarbonate concentrations with all 6 preparations (**Table V**), especially with preparation D, which contained 10 g/L of ascorbic acid, the serum bicarbonate concentration and blood pH remained within normal ranges. This base deficit appeared to be due to the presence of ascorbic acid and to be dose dependent, although the latter hypothesis could not be confirmed in the present study.

Because the taste of sodium ascorbate was less acidic compared with that of ascorbic acid based on responses on the Likert scale, combinations of ascorbic acid and sodium ascorbate or ascorbic acid alone were tested in the current study, resulting in improved acceptance of the preparations that contained sodium ascorbate (C, E, and F). Moreover, a slight but statistically nonsignificant decrease in the serum bicarbonate concentration did not differ significantly between preparations (**Table V**). Therefore, preparation C, which was found to have efficacy similar to those of preparations D and F, would be expected to have a more acceptable taste.

A few subjects, regardless of preparation ingested, reported thirst and asked to drink a large amount (≥500 mL) of water after they ingested the second liter of preparation. Dehydration might explain this thirst, and might have been evidenced by the observed mean weight loss of up to 1.1 kg (especially with preparation D) and the low mean urinary output (330 mL over the 10-hour follow-up period vs 610 mL during ingestion), together with a decrease in the serum potassium concentration and an increase in the serum sodium concentration. However, we hypothesized that when a smaller volume of colonic preparation is required, patients might be able to self-monitor their thirst and increase the volume of water on an individual basis, thus increasing the acceptability of a preparation.

A limitation of this study was the lack of a colonoscopy performed to directly assess the quality of colonic cleansing after the ingestion of each preparation. However, based on the assumption that a stool volume of ≥3 L might be predictive of adequate colonic cleansing,[16] the results of the present study suggest that adding high-dose vitamin C (10 g/L) and sodium sulfate (7.5 g/L) in a 100-g/L PEG solution did not adequately increase stool output and therefore might be inadequate for colonic cleansing before colonoscopy or colonic surgery. Further studies testing alternative combinations of osmotic agents with higher doses of vitamin C compared with those in the preparations used

in the present study are warranted, with or without colonoscopy, depending on the study population and design.

Future pilot studies enrolling specific patient populations, such as elderly patients or those with cardiac or renal dysfunction whose salts or stimulant laxatives might be restricted, are needed.[29–31] Such studies should test preparations containing a combination of sodium ascorbate with ascorbic acid rather than ascorbic acid alone because the decrease in serum bicarbonate concentration might become clinically significant if higher doses of ascorbic acid are used alone, based on the results of the current pilot study. Finally, the acceptability of future combinations might be optimized by self-monitored ingestion of water, preventing the risk for dehydration.

CONCLUSIONS

In this study of 6 colonic cleansing preparations in healthy volunteers, the use of high-dose vitamin C as an osmotic agent in addition to PEG did not significantly increase stool output. All 6 preparations were well tolerated.

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