Original Article

Oral Rehydration Solution Protects against Intravascular Volume Contraction during Colonic Cleansing with Orally Administered Sodium Phosphate (NaP) in Rajavithi Hospital

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ABSTRACT

Background: Colonic cleansing with sodium phosphate causes intravascular volume contraction in some patients. This study tested the hypothesis that oral rehydration solution protects against intravascular volume contraction during colonic cleansing with orally administered NaP.

Methods: Adult outpatients were randomized to ingest the regular clear fluid or an oral rehydration solution (ORS) during pre-colonoscopy purgation by ingestion of aqueous sodium phosphate. Clinical hemodynamic measurements and biochemical tests were obtained at baseline and after bowel preparation. Tolerability and colonoscopy visualization were assessed with questionnaires.

Results: One hundred sixty patients completed the study. There were 80 patients receiving regular clear fluid (control group) and 80 patients receiving ORS (treatment group). By comparison with control, the treatment group resulted in significantly less intravascular volume contraction. The changes in orthostatic pulse (p <0.045), BUN/Cr ratio (p <0.002), urine specific gravity (p <0.000) were significantly greater in control than treatment group. The changes in biochemical parameters after purgation also suggested a greater degree of volume contraction in control than treatment group. Tolerability of the preparations was similar in both groups (p = 0.809).

Conclusions: Oral rehydration solution protects against intravascular volume contraction during preparation for colonoscopy by ingestion of sodium phosphate. This approach is well tolerated by patients.

Key words : colonic cleansing, ORS, sodium phosphate

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INTRODUCTION

Colonoscopy has become an essential procedure for the detection and treatment of colonic lesions; therefore, cleansing the bowel for adequate visualization of the colonic mucosa during colonoscopic examination is very important. Currently, there are many regimens of bowel preparation for patients who undergo colonoscopy, such as polyethylene glycol (PEG), sodium phosphate, sodium picosulphate, bisacodyl, etc. Although PEG provided safe and effective bowel cleansing, the patient was required to take 3-4 L of a salty tasting solution within a short period of time[1-6]. As reported, 5-15% of patients were unable to finish the prescribed dosage[1,7], potentially resulting in a

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poorly cleansed colon and inadequate colonoscopic assessment[2,4].

Oral sodium phosphate (NaP) is a highly osmotic cathartic containing monobasic and dibasic sodium phosphate. The mechanism of NaP is through the osmotic effect of phosphate. This draws large amounts of water into the bowel, creating a flushing action and a laxative effect within 30 min after ingestion and lasting an average of 2-3 hours[4,8,15]. A comprehensive systematic review showed that PEG and NaP were the most frequently investigated bowel preparations. There was no significant difference between the two agents, but NaP was better tolerated [8-10]. Randomized controlled trials have demonstrated equivalent efficacy and superior tolerability of NaP compared with PEG-electrolyte formulations[2,4]. Consequently, NaP has become widely used and is increasingly considered the agent of choice for colonic purgation[11]. Although NaP is safe for most patients, its osmotic action has raised a concern about intravascular volume contraction[12].

Studies in which hemodynamic variables were measured during oral NaP-based colonic preparation have found evidence of plasma hypovolemia in 7% to 30% of patients[4]. Because carbohydrate-electrolyte rehydration by means of the oral route has been shown to counteract the intravascular volume contraction associated with acute infectious diarrhea[13], it was hypothesized that this would similarly attenuate the iatrogenic hypovolemia induced by NaP.

Thus, this prospective, randomized open label study compared the effects of a balanced oral rehydration solution (ORS) protects against intravascular volume contraction during colonic cleansing with orally administered NaP at Rajavithi Hospital.

Patients and Methods

The study was prospective, single-centered, randomized, controlled study. All patients, who underwent elective colonoscopy from various indications, were obtained from the Rajavithi Hospital from March 2009 to December 2009.

Exclusion criteria were bowel ileus, chronic diarrhea, congestive heart failure, renal insufficiency (creatinine >1.5 mg/dl), suspected bowel obstruction, used of diuretics, previous history of colorectal surgery and history of hypersensivity to NaP. Data of 160 patients who underwent elective colonoscopy were collected. Patients gave informed written consent before enrollment and the study was approved by the human ethics committee of the Rajavithi Hospital.

The patients were randomized into two groups by consecutive method. The control group was assigned to receive 90 mL of NaP in a split regimen of two 45 mL doses separated by 12 h. The treatment group was assigned to receive 90 mL of NaP in a split regimen of two 45 mL plus ORS 4 sachets separated by 12 h prior to the colonoscopy evaluation. Colonoscopy was scheduled after 8:00 a.m. for all patients and patients were asked to present at the endoscopy room by 8:00 a.m. on the day of examination.

ORS using in this study consists of sodium chloride 60 mmol/L, trisodium citrate dehydrate 10 mmol/L, potassium chloride 20 mmol/L and glucose 111 mmol/L that are equal to Na^+ 90 mEq/L, K^+ 20 mEq/L, Cl^- 80 mEq/L, Citrate 10 mEq/L and glucose 111 mEq/L.

Hemodynamic and Biochemical Data

Clinical hemodynamic and biochemical measurements were obtained at enrollment and on the morning of the day during which colonoscopy was performed. Hemodynamic data included weight, orthostatic pulse, and blood pressure. To ensure consistency of recording, single physician obtained all measurements by using standardized methods: pulse and blood pressure with the patient supine for 5 minutes, pulse and blood pressure after the patient was upright for 1 minute.

Hematologic and biochemical data included hematocrit, blood urea nitrogen, creatinine, electrolytes, phosphate, magnesium, calcium and urine specific gravity were measured at 5-7 days before and in the morning on the day of colonoscopy.

Acceptance and Tolerability

On the morning of the day during which colonoscopy was performed and before the procedure, patients completed a multiple-choice questionnaire designed to assess tolerance for the bowel preparation. The questionnaire was similar to that used in previous studies[14]. Patients were asked to estimate the number of ORS sachet consumed during the preparation period.

Endoscopic Evaluation

Quality of colonic cleansing was assessed with a previously validated questionnaire[14] that was com-

pleted in the Outpatient Endoscopy Unit by the gastroenterologist who performed the procedure. Endoscopists rated the quality of visualization as follow: excellent, good, fair, poor.

Statistical Analysis

Published data indicate that approximately 43% of patients who undergo NaP-based colonic purgation for colonoscopy experience orthostatic changes in pulse and arterial blood pressure. Based on this baseline estimate, a sample size of 80 patients in each arm was calculated to detect at least a 65% reduction in the frequency of orthostasis, with 80% power at a standard level of significance $\alpha = 0.05$ (2-tailed).

The primary outcome in this study was the frequency of hypovolemia. Hypovolemia was considered when at least three of the clinical measurements were found as following;

1. Decrease ≥20 mmHg in systolic BP
2. Increase ≥10 mmHg in diastolic BP
3. Increase in pulse rate ≥15 bpm
4. BUN/ Cr ratio ≥20:1
5. Increase Hct ≥3%
6. Urine spgr ≥1.020
7. Lose ≥5% of body weight

Additional continuous variables of secondary clinical interest included hematocrit, serum creatinine, phosphate, calcium, magnesium and urine specific gravity. For all variables, differences before and after purgation were compared with the *t*-test. Categorical variables were compared with Fisher exact test or with chi-square test, as appropriate. All summary statistics are expressed as mean (SD). All statistical computations were executed by using statistical software.

Results

One hundred sixty consecutive outpatients scheduled to undergo preparation for colonoscopy by NaP purgation between March 2009 and December 2009 were randomized to the control or the treatment group. The demographic characteristics of 160 patients were summarized in Table 1. There were no significant differences between two groups with respect to demographic data and comorbid conditions. The most common indication for colonoscopy (approximately two-third of patients) was screening or surveillance for neoplastic polyps.

Table 1. Demographic and baseline clinical data

	Treatment group (n = 80)	Control group (n = 80)	*p*-value
Age (mean ± SD)	54 ± 12	55 ± 13	0.207
Sex M:F	24:56	27:53	0.611
Diabetes mellitus (%)	11 (13.8%)	4 (5%)	0.058
Hypertension (%)	16 (20%)	22 (27.5%)	0.265

Clinical Hemodynamic Data

Changes in clinical hemodynamic variables in treatment group and control group patients after NaP purgation are shown in Table 2.

Weight reduction from baseline in the control group (3.05 kg) was greater than in treatment group (2.77 kg) without statistic significant ($p = 0.467$). Both control group and treatment group experienced modest changes in orthostatic pulse and blood pressure, these were more pronounced in control group compared with treatment group patients. A decrease in SBP in treatment group (1.78 mmHg) was higher in control group (1.2 mmHg) ($p = 0.137$). DBP was increased in control group (6.35 mmHg) more than in treatment group (3.91 mmHg) ($p = 0.163$) without statistic significant.

The orthostatic increase in pulse was greater in control group than the treatment group patients significantly [12.22 vs 8.92 ($p = 0.045$)]; moreover, increase urine specific gravity (Urine spgr) in the control group was greater than in treatment [0.81 vs 0.47 ($p = 0.000$)]. A significantly greater proportion of BUN/

Table 2. Clinical hemodynamic data

	Treatment group (n = 80)	Control group (n = 80)	*p*-value
ΔWeight[#] (kg)	2.77 (±2.36)	3.05 (±2.53)	0.467
ΔSBP[†] (mm Hg)	-1.78 (±13.0)	1.20 (±12.1)	0.137
ΔDBP[†] (mm Hg)	3.91 (±8.81)	6.35 (±12.7)	0.163
ΔHR[†] (bpm)	8.92 (±9.81)	12.22 (±10.85)	0.045*
BUN/Cr ratio[#]	12.07 (±4.61)	14.70 (±5.96)	0.002*
ΔHct[#]	0.33 (±4.15)	0.14 (±3.14)	0.754
Urine spgr[#]	0.48 (±0.50)	0.81 (±0.39)	0.000*

Data are expressed as mean (SD) ; Δ, Difference; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; Cr, creatinine; Hct, hematocrit; Urine spgr, urine specific gravity. [#]Change from baseline, [†]Orthostatic change

Table 3. Biochemical data

	Treatment group (n = 80)	Control group (n = 80)	*p*-value
ΔSerum BUN[#] (μmol/L)	-3.30 (±4.01)	-1.03 (±5.50)	0.003*
ΔSerum Cr[#] (μmol/L)	-0.01 (±0.14)	0.005 (±0.15)	0.360
ΔSerum $Na^{+\#}$ (mmol/L)	1.53 (±3.78)	0.56 (±3.05)	0.076
ΔSerum $K^{+\#}$ (mmol/L)	-0.18 (±0.49)	-0.21 (±0.55)	0.757
ΔUrine SG[#]	0.002 (±0.008)	0.007 (±0.008)	0.000*
ΔSerum $Ca^{2+\#}$ (mmol/L)	-0.31 (±0.73)	-0.33 (±1.15)	0.922
ΔSerum $Mg^{2+\#}$ (mmol/L)	0.002 (±0.26)	0.09 (±0.25)	0.020*
ΔSerum $PO_4^{\#}$ (mmol/L)	1.44 (±1.20)	1.74 (±1.06)	0.094

Data expressed as mean (SD). Δ, Difference; Cr, serum creatinine; urine SG, urine-specific gravity; Ca^{2+}, serum calcium; PO_4, serum phosphate. [#]Change from baseline: value in colonoscope day - value in baseline

Cr ratio experienced in control group (14.70) than treatment group (12.07) ($p = 0.002$).

Biochemical Data

Changes in hemodynamic relevant biochemical variables after NaP purgation (Table 3) also suggested a greater degree of plasma volume contraction in the control group than the treatment group.

Urine-specific gravity increased significantly in the control group compared with the treatment group ($p = 0.000$). Similarly, relative changes in BUN suggested a greater degree of hypovolemia in control group patients compared with treatment group.

There were no significant differences between groups with respect to changes in serum calcium and phosphate levels after purgation. Although the decrease in calcium (-0.33 vs -0.31) was similar in both groups, There were no significant differences observed in hematocrit, serum sodium, potassium and creatinine. Blood urea nitrogen decreased in both groups, presumably because of decrease in available nitrogen resulting from purgation and possibly an increase in urea excretion.

Frequency of Hypovolemia

Frequency of hypovolemia was showed in table 4. Hypovolemia were less commonly found in treatment group than control group with statistical significant (11.2% vs 33.8%, $p = 0.001$).

Symptoms/tolerability

Symptom profiles during the preparation period were similar for patients in both groups (Table 5). Overall tolerability of the two preparation protocols was similar, with approximately 80% of both control patients and treatment patients finding the respective preparation easy or only slightly difficult to tolerate.

Table 4. Symptom of hypovolemia

	Hypovolemia	
	No (%)	Yes (%)
Treatment group (n = 80)	71 (88.8%)	9 (11.2%)
Control group (n = 80)	53 (66.2%)	27 (33.8%)

*$p = 0.001$

Quality of Bowel Preparation

There was no significant difference in the quality of the bowel preparation between groups ($p = 0.809$) at colonoscopy. Most patients were considered "good" preparation by endoscopists (58% treatment patients; 51% control patients). (Fig. 1)

Discussion

With the growing demand for colonoscopy, the importance of optimizing the safety of this procedure becomes increasingly relevant. This study compiled the largest collection of hemodynamic data for patients undergoing preparation for colonoscopy by oral ingestion of NaP. The major finding is that the intravascular volume contraction resulting from colonic cleansing with NaP can be mitigated by the ingestion of a readily available, inexpensive oral rehydration solution. Although the clinical hemodynamic changes resulting from ingestion of NaP were associated with few reported symptoms of hypovolemia, larger changes in

Table 5. Symptom profiles for patients in treatment and control groups

Symptoms	None	Mild	Moderate	Severe	*p*-value
Bloating	56/55	20/21	4/2	0/1	0.638
Dizziness	50/51	25/24	4/4	1/1	0.999
Nausea	39/37	39/37	2/6	0/0	0.340
Vomiting	59/59	19/18	2/3	0/0	0.893

Values in each cell denote numbers of treatment/control patients

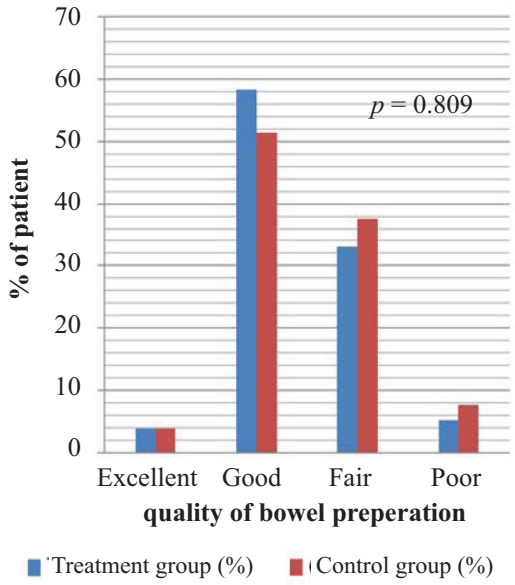

Figure 1. Quality of colonic preparation in patients in the treatment group (blue bars) and control groups (red bars).

orthostatic vital signs compatible with significant volume contraction were noted in several patients. Furthermore, the hemodynamic changes induced by NaP are similar in magnitude to those observed in other acute hypovolemic states. Even in the absence of symptoms, acute hypovolemia could increase the risk of syncope and end-organ hypoperfusional injuries such as acute tubular necrosis and myocardial ischemia, especially in patients with additional risk factors for such conditions.

A relatively large volume (2-4 L) of supplemental fluid was selected for this study in an attempt to maximize the effects of oral rehydration solution on plasma volume restoration. Although a greater proportion of patients in the treatment group felt that the prescribed fluid volume was too large, overall tolerance of the bowel preparation was similar between the groups.

The therapeutic value of an oral rehydration solution that contains carbohydrates and electrolytes is well established. Glucose enhances sodium absorption by stimulating the cotransporter present in the brush border of intestinal epithelium, leading to passive uptake of water. The fact that both groups of patients in the present study ingested comparable volumes of fluid during the preparation period suggests that the composition of the oral rehydration solution was more important than the actual fluid volume in mediating the beneficial effects on plasma volume.

Although oral rehydrate solution lessened the degree of intravascular volume contraction, it did not abolish it and it had no demonstrable effect on the hyperphosphatemia resulting from NaP ingestion. In some patients there was a corresponding decrease in serum calcium level, but the decrease was not significantly different between the groups.

In summary, this study demonstrated that carbohydrate-electrolyte rehydration with oral dehydration solution significantly decreased intravascular volume contraction induced by ingestion of NaP, resulting presumably in a safer procedure for patients. Furthermore, it resulted in an overall improvement in the degree of colonic cleansing and was well tolerated by patients.

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