

The Effect of Polyethylene Glycol Gavage on Plasma Volume¹

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Submitted for publication June 21, 1993

This study examines the hypothesis that whole gut irrigation with polyethylene glycol-electrolyte gavage solution (PEG-ELS) increases intravascular volume. Seventeen patients drank 6 to 8 liters of PEG-ELS in preparation for elective colonoscopy. The patients were weighed and serum electrolytes, albumin, hematocrit, blood urea nitrogen, and creatinine were obtained prior to the gavage and 8 hr following gavage. Plasma volume was measured before and after gavage using an isotope dilution technique involving ¹²⁵I-human serum albumin. No patients developed symptoms of intravascular volume excess or depletion following gavage. There was no significant change in body weight, serum sodium, chloride, potassium, bicarbonate, blood urea nitrogen, or creatinine following gavage with PEG-ELS. When measured by the isotope dilution technique, the mean plasma volume increased from 3174 ± 117 ml before gavage to 3365 ± 160 ml following gavage (*P* = 0.03). This represented a mean percentage change in plasma volume of 5.88 ± 2.4%. The percentage change in plasma volume associated with gavage ranged from -9.8 to +29.8%. This data supports the hypothesis that gavage with polyethylene glycol-electrolyte solution is associated with an increase in plasma volume. Although in most patients the increase in plasma volume is minimal, there is significant variability in this response, with some patients experiencing substantial increases in plasma volume. © 1994 Academic Press, Inc.

INTRODUCTION

Whole gut gavage with polyethylene glycol-electrolyte solutions (PEG-ELS) (Colyte, Read & Carnick, Jersey City, NJ, or GoLYTELY, Braintree Lab., Inc., Braintree, MA) is a popular means of mechanically cleansing the colon prior to diagnostic and therapeutic procedures. Many studies have demonstrated this solution to be well tolerated and efficacious [1-4]. Although early electrolyte gavage solutions were associated with intravascular volume expansion and serum electrolyte

disorders [5-8], the addition of polyethylene glycol and sodium sulfate to the basic electrolyte solution reduced fluid and electrolyte fluxes. Early studies employing rectal effluent volume, hematocrit, serum albumin, and body weight as indices of plasma volume suggest that plasma volume is unchanged by gavage with PEG-ELS. [1, 4, 5, 9-11] Despite these studies, there remains much confusion regarding the effect of PEG-ELS solution on plasma volume. Many clinicians administer intravenous fluids to patients undergoing gavage to compensate for potential intravascular volume depletion. Others administer parenteral diuretics to prevent intravascular volume excess.

Since clinical parameters such as those employed by previous studies are relatively insensitive to small changes in plasma volume [12-16], we postulated that a more sensitive means of measuring plasma volume would more accurately document plasma volume changes following gavage. This study examines the hypothesis that gavage with 6 to 8 liters of PEG-ELS significantly increases plasma volume. In order to test this hypothesis intravascular volume was measured using an ¹²⁵I-human serum albumin dilution technique. This methodology provides an accurate measure of acute changes in intravascular volume [16-18].

METHODS

Patients who were to undergo PEG-ELS gavage in preparation for elective colonoscopy were considered for inclusion in this study. Exclusion criteria included active bleeding, parenteral fluid administration, symptoms of bowel obstruction, inflammatory bowel disease, diarrhea, and enterocolitis. The goal of these exclusion criteria was to produce a cohort of patients who had no factors which might alter plasma volume (e.g., bleeding or intravenous fluid administration) or the absorptive or secretive function of the gut (e.g., prior gastrointestinal resections, inflammatory bowel disease, colitis, or diarrhea). Twenty patients met these criteria and were enrolled in this study. Three patients were excluded from the study: 2 were unable to tolerate the gavage and 1 patient had subcutaneous extravasation of the isotope

¹ Presented at the Annual Symposium of the Association of Veterans Administration Surgeons, Augusta, GA, April 28-May 1, 1993.

during intravenous injection. Thus 17 patients form the cohort studied.

Patients received a clear liquid diet the day of the gavage. The patients drank 6 to 8 liters of PEG-ELS over a 4- to 6-hr period the evening prior to colonoscopy. The patients were then maintained NPO until completion of the colonoscopy. The chemical composition of the PEG-ELS gavage solution (Colyte, Read & Carnick) is as follows: 60 g/liter polyethylene glycol 3350, 1.46 g/liter sodium chloride, 0.745 g/liter potassium chloride, 1.68 g/liter sodium bicarbonate, and 5.68 g/liter sodium sulfate (anhydrous). The patients were weighed before and the morning after gavage. Blood was drawn for determination of plasma volume, serum electrolytes, serum albumin, hematocrit, blood urea nitrogen (BUN), and creatinine immediately prior to the gavage and at 8:00 AM the morning following gavage (8 hr following completion of the gavage).

Plasma volume was measured using a dilution technique with ^{125}I -labeled human serum albumin (Mallinckrodt, St. Louis, MO) as described previously [16-18]. This measurement is based on the relationship expressed in the equation

$$A_1 V_1 = A_2 V_2,$$

where V_1 and V_2 are the volumes of a sample of radioactive substance before and after dilution by an unknown volume and A_1 and A_2 are the activities per volume before and after dilution. Thus if V_1 represents the patient's plasma volume and a known volume V_2 of a radiolabeled substance with a known activity A_2 is injected intravenously, the plasma volume may be calculated if the radioactivity of the sample A_1 is known. This is expressed by rearranging of the above equation into

$$V_1 = \frac{V_2 A_2}{A_1}$$

or

$$\text{plasma volume} = \frac{\text{injected volume} \times \text{injected activity}}{\text{plasma activity}}.$$

The technique was as follows: 10 μCi of ^{125}I -albumin was injected into a peripheral vein. Five, 10, and 15 min following the injection, 10 ml of blood was withdrawn into heparinized tubes from a second venopuncture. The blood was centrifuged and an aliquot of plasma was placed into a counting vial. The standard and plasma sample was then counted for 10 min. Background radiation in the plasma was counted and subtracted from the plasma counts. The net counts per minute (cpm) of the three plasma samples was plotted on semilog paper and extrapolated to 0 circulation time to obtain the net cpm of the plasma at the time of injection. Plasma volume

TABLE 1

Patient Demographics, Indications for Colonoscopy, and Associated Illnesses

	<i>N</i> (mean \pm SEM)
Population	17
Age (mean \pm SE)	62.9 \pm 3 years
Indications	
Heme + stool	9
Polyps	5
Other	3
Volume consumed	
6 liters	4
8 liters	13
Serum creatinine	
<1.5 mg %	12 (1.03 \pm 0.03 mg %)
\geq 1.5 mg %	5 (2.58 \pm 0.88 mg %)
Diuretics (<i>N</i>)	
None	7
Thiazide	3
Furosemide	
20 mg	3
>20 mg	4

was then calculated using the equation as listed above. All patients received five drops of Lugol's solution the day prior to injection of the isotope to prevent uptake of the isotope by the thyroid gland.

This study was approved by the Human Research Advisory Committee at the Ann Arbor Veterans Administration Hospital. All subjects gave informed consent at the time of entry into the study.

Statistics

Continuous data are expressed as means \pm SEM. A paired two-tailed Student's *t* test was used to assess differences between pre- and postgavage measurements in individual patients. Differences were considered significant if $P < 0.05$.

RESULTS

Patient Demographics, Associated Diagnoses, and Indications for Colonoscopy (Table 1)

The seventeen patients studied tolerated the PEG-ELS gavage well. All patients were able to drink the solution and no one required the placement of a nasogastric or nasoduodenal tube.

In most cases the indication for colonoscopy was the evaluation of occult gastrointestinal bleeding and the retrieval of polyps identified by barium enema. Three patients had other indications including the evaluation of a change in bowel habits and recurrent complex fistula *in ano*.

The degree of renal impairment in the population studied was mild. Five patients had serum creatinine lev-

TABLE 2
Changes in Laboratory Values and Weight Before and After PEG Gavage

	Weight (kg)	HCT (%)	P. volume (ml)	Albumin (g/dl)	Serum Na (meq/liter)	Serum K (meq/liter)
<i>N</i>	12	11	17	9	10	12
PrePEG	82.7 ± 3.7	38.0 ± 1.8	3174 ± 117	3.9 ± 0.2	138.2 ± 1.1	3.88 ± 0.1
PostPEG	81.9 ± 3.8	37.9 ± 1.7	3365 ± 160	3.7 ± 0.2	140.5 ± 1.3	3.94 ± 0.1
% change	-0.71	-0.18	5.8*	-0.17	1.67	-0.72

* $P = 0.03$, paired Student's *t* test.

els greater than 1.5 mg/dl (range 1.5 to 6.1 mg/dl) and only one had a serum level greater than 2.0 mg/dl. No patients required dialysis.

Six patients had a history of heart disease. This was manifested by episodic angina pectoris and a remote history of myocardial infarction in three patients and a history of congestive heart failure in three others. All of these patients were asymptomatic at the time of this study and appeared to be medically optimized. One patient had advanced liver disease with ascites and a slightly elevated serum bilirubin.

Ten patients were receiving diuretics at the time of the study. The indication for the diuretic was the treatment of hypertension in three patients, heart disease in six patients, hepatic and renal disease in one each. Five patients were receiving vasoactive agents such as calcium channel antagonists or beta receptor antagonists at the time of this study.

Hematologic, Clinical, and Chemical Changes (Table 2)

No patient suffered a complication related to the gavage or developed symptoms of intravascular volume excess or contraction. No patient suffered an exacerbation of prior medical problems following the gavage. Serum albumin, hematocrit, BUN, serum creatinine, and body weight did not significantly change following gavage with PEG-ELS. Similarly gavage did not significantly affect serum sodium or potassium concentrations.

Plasma Volume Determination (Fig. 1)

The mean plasma volume of these patients prior to gavage was 3174 ± 117 ml. This increased significantly to 3365 ± 160 ml following gavage ($P = 0.03$). This represented a mean percentage change in plasma volume of 5.88 ± 2.4%. Of greater importance than the mean change in plasma volume was the variability of the plasma volume changes experienced by this heterogeneous population of patients. The percentage change in plasma volume ranged from -9.8 to +29.8%. Thus the impact of gavage on plasma volume ranged from the loss of 542 ml to the addition of 1103 ml of fluid to the intravascular space.

There was no difference in plasma volume changes in those patients who drank 6 liters (8.25 ± 1.4%) when

compared to those that drank 8 liters of PEG-ELS (5.65 ± 3.1%). The difference between those patients receiving 6 liters and those receiving 8 liters of PEG-ELS was solely the volume of solution required to render the rectal effluent consistently clear or tea colored.

DISCUSSION

There is little debate that PEG-ELS provides an efficacious, well-tolerated, and safe method of preparing the colon for colonoscopy, barium enema, and operative procedures. The 3- to 4-day preparation of cathartics, dietary restrictions, and enemas has been supplanted by the ingestion of 4 to 8 liters of PEG-ELS the night prior to the procedure.

Early work with balanced electrolyte solutions without poorly absorbed osmotically active agents was associated with water, sodium, and chloride absorption [5-8]. Davis *et al.* [9] formulated a polyethylene glycol-electrolyte solution with no resultant net water and electrolyte absorption or secretion in five normal pa-

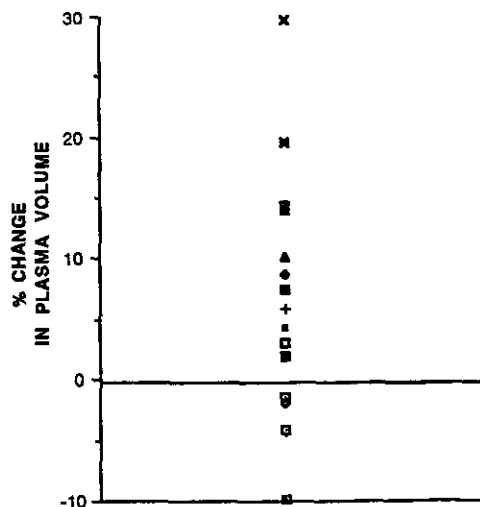


FIG. 1. Percentage change in plasma volume for all patients. Note the significant degree of variability of plasma volume changes following gavage with PEG-ELS. The mean percentage change in plasma volume was 5.88 ± 2.4% with a range from -9.8 to +29.8%.

tients. Polyethylene glycol became the osmotic agent of choice when explosive complications were associated with colonoscopic electrocautery use following gavage with mannitol-containing solutions [19].

The initial investigation into the effects of whole gut irrigation on plasma volume compared rectal effluent volume, osmolality, and electrolyte composition to that of the gavage solution [9]. Other investigators have examined changes in serum albumin concentration, hematocrit, and body weight to detect plasma volume changes following gavage with PEG-ELS. None of these parameters were changed by gavage with PEG-ELS in the present study or in the experience of others. [1-5, 10, 11]

A number of authors have demonstrated the insensitivity of these and other clinical parameters in assessing changes in plasma and blood volume [12-15]. This prompted the use of an isotope dilution technique to detect relatively small changes in plasma volume. This technique is particularly valuable when consecutive measurements are taken in individual patients [16-18].

Recent studies have suggested that some patients may absorb significant quantities of fluid during gavage with PEG-ELS [1]. This has been further supported by the observation of increased urine output during the first 3 hr of PEG-ELS administration [20]. Using radiolabeled dilution techniques, plasma volume was found to be increased by nearly 6% following gavage with PEG-ELS. This relatively small change in plasma volume would be undetected by measurements of body weight, hematocrit, or serum albumin. The mean volume of fluid sequestered in the intravascular space in this study was 191 ml, the weight of which would be well within the error of hospital bedside scales. Similarly the addition of this volume of fluid would only minimally dilute serum albumin or red blood cell mass and would thus go undetected by these tests.

Similar to the experience of others [1], serum electrolyte composition was unchanged by gavage with 6 to 8 liters of PEG-ELS in the present study. Even in patients who experienced significant increases in plasma volume, the electrolyte composition of the intravascular space appeared unaffected. Serum potassium remained unchanged in the five patients who experienced a greater than 10% increase in plasma volume.

The point of greatest significance of this study is the demonstration that some patients experience large changes in plasma volume following gavage with PEG-ELS. This has previously been suggested by DiPalma and Brady [1] but this is the first study documenting such changes. Plasma volume changes ranged from -9.8 to +29.8% in the population studied. This intravascular fluid challenge represented a subclinical phenomenon since no patients developed symptoms of intravascular volume excess or depletion. However, since all of the patients in this study were clinically stable, the impact of intravascular fluid shifts following PEG-ELS gavage in medically compromised patients remains unclear.

Although the design of this study does not allow for analysis of subsets of patients, several trends are quite interesting and deserve investigation in a prospective fashion. Patients who are physiologically unable to compensate for an acute intravascular fluid challenge appear to be most likely to increase their plasma volume following gavage. Patients more than 70 years of age experienced a $12.9 \pm 2.6\%$ increase in their plasma volume following gavage. Similarly the plasma volume increased $17.45 \pm 5\%$ in patients taking more than 20 mg of furosemide per day, whereas those not taking diuretics experienced a $0.81 \pm 1.88\%$ change in plasma volume. Patients with a serum creatinine greater than 1.5 mg % experienced an increase in plasma volume of $8.9 \pm 2.2\%$, whereas those patients with a normal serum creatinine experienced an increase of $1.9 \pm 1.89\%$. The small size of each of these subsets of patients prohibits accurate analysis of interrelated factors; however, this data does provide information from which prospective studies of these subgroups may be initiated.

In conclusion this study supports the hypothesis that gavage with polyethylene glycol-electrolyte solution is associated with an increase in plasma volume. Although in most patients the increase in plasma volume is minimal, there is significant variability in this response with some patients experiencing substantial increases in plasma volume. This study provides preliminary evidence to direct future investigation into the effect of PEG-ELS on plasma volume in selected subsets of patients and suggests that careful monitoring of patients during and following gavage with PEG-ELS is warranted.

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