

An Effective 2 L Polyethylene Glycol (PEG) Electrolyte Lavage Solution for Bowel Cleansing

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ABSTRACT

Purpose: A new 2 L PEG electrolyte lavage solution containing ascorbic acid (9.4 g) and sodium ascorbate (11.8 g) (MoviPrep[®]) has been developed for bowel cleansing. Ascorbic acid and sodium ascorbate enhance the flavor and osmotic effect of PEG. This study evaluated the efficacy of the new 2 L PEG vs a 4 L PEG electrolyte lavage solution (Klean-Prep[®]) using a 4-point Visual Analog Scale (VAS) that was used in clinical trials with NaP tablets.

Methods: In a German multicenter, investigator-blinded study, 359 pts received 2 L or 4 L PEG solution in two equally split doses for bowel cleansing prior to colonoscopy. The first dose was taken the afternoon or evening before colonoscopy, and the second dose the morning of colonoscopy. Each 1 L regimen of the 2 L PEG prep was followed by 500 mL of additional clear liquid. A 4-level scoring system, which divided the colon into 5 segments (rectum, sigmoid, descending, transverse, and ascending), was used to assess overall quality of colon cleansing (A = all colon segments clean; B = at least 1 segment with residual amounts of brown liquid/semisolid stool, which can be easily removed or displaced; C = at least 1 segment with only partially removable stool, preventing complete visualization; D = at least 1 segment which cannot be examined due to the presence of solid stool). A random sample of 100 colonoscopy videos (50 per treatment arm) from the German study was reviewed by a blinded investigator (DK). Overall colon cleansing was graded with the scoring system used in US NaP trials (excellent: >90% mucosa seen, mostly liquid stool, minimal suctioning for adequate visualization; good: >90% mucosa seen, w/ significant suctioning needed; fair: >90% mucosa seen w/ mixture of liquid/semisolid stool, could be suctioned and/or washed; inadequate: <90% mucosa seen, contents could not be suctioned or washed).

Results: Overall colon cleansing was rated excellent or good for 88% and 96% of patients receiving 2 L and 4 L PEG, respectively. These results are similar to those found in the German study where overall colon cleansing was rated A or B for 88.9% and 94.8% of patients receiving 2 L and 4 L PEG, respectively.

Conclusion: Use of an established grading system for colon cleansing confirms the efficacy of a new 2 L PEG solution containing ascorbic acid and sodium ascorbate. These results are nearly identical to those from a large, multicenter, investigator-blinded study demonstrating that the new 2 L PEG is comparable to 4 L PEG solution.

INTRODUCTION

- A new 2 L polyethylene glycol electrolyte lavage solution (PEG) (MoviPrep[®]; Salix Pharmaceuticals, Inc, Morrisville, NC) was approved by the US Food and Drug Administration in August 2006
 - Indicated for colon cleansing in preparation for colonoscopy in patients ≥18 years of age
 - Components
 - PEG-3350 (200 g)
 - Ascorbic acid (9.4 g) and sodium ascorbate (11.8 g)
 - Sodium sulfate (15 g), sodium chloride (5.4 g), potassium chloride (2.0 g)
 - Excipients
 - Two dosing options approved
 - Split dose:** 1 L PEG over 1 h (8 oz q 15 min), then drink 0.5 L (~16 oz) of clear liquid the evening before; 1 L PEG over 1 h (8 oz q 15 min), then drink 0.5 L (~16 oz) of clear liquid in the morning (complete at least 1 h before colonoscopy)
 - Evening only:** starting ~6 PM the evening before colonoscopy, drink 1 L PEG over 1 h (8 oz q 15 min); about 1.5 h later, drink 1 L PEG over 1 h (8 oz q 15 min). In addition, consume 1 L (~32 oz) of clear liquid
- New 2 L PEG has several advantages
 - Low volume
 - Does not require irritant laxatives
 - No interruption of prior workday to administer bisacodyl
 - Pleasant lemon flavor

OBJECTIVE

- To compare the colon-cleansing efficacy of a new 2 L PEG versus 4 L PEG using a 4-point, validated, US scoring system from sodium phosphate tablet clinical trials¹⁻³

METHODS

- German, phase 3, randomized, investigator-blinded, multicenter, noninferiority study conducted in hospitalized patients undergoing elective colonoscopy (N=369)
- Treatment (no solid food permitted starting at noon on day before colonoscopy)
 - 2 L PEG split dosing: 1 L PEG over 1 h followed by at least 500 mL clear fluid the evening before (completed by 10 PM) and 1 L PEG over 1 h followed by at least 500 mL clear fluid in the morning (completed at least 1 h before procedure) or
 - 4 L PEG split dosing: 2 L PEG the evening before (completed by 10 PM) and 2 L PEG in the morning (completed at least 1 h before procedure)
- Original study assessments
 - All procedures videotaped for review by expert blinded to treatment
 - Each of 5 predefined colonic segments (rectum, sigmoid colon, descending colon, transverse colon, and ascending colon) individually rated using 5-point scale, and each score applied to classify overall colon cleansing using grade of A to D (Table)
 - Primary endpoint: overall colon-cleansing grade of A or B (responders) in per-protocol population (n=308)*
- Post hoc sampling
 - Randomized sampling of 100 videos (50 per treatment arm) with reviewer blinded to treatment
 - Physician questionnaire completed during video review applying a 4-point, validated, US colon-cleansing scale (Table)¹⁻³
 - Primary endpoint: overall colon-cleansing score of excellent or good (responders)
 - Secondary endpoint: ascending colon-cleansing score of excellent or good (responders)
 - Statistics not performed, given that only a subset (n=100) of full patient population assessed and therefore, sample size insufficient to establish noninferiority

Table. Comparison of Scoring System From Original Study and US Scoring System

European scoring system		US scoring system ¹⁻³	
Grade*	Description	Grade*	Description
A	All 5 segments clean; each with minor amount of fluid or small amount of liquid stool; easily removed by suctioning	Excellent	>90% of mucosa observed, mostly liquid stool, minimal suctioning required
B	At least 1 segment with residual amounts of brown liquid/semisolid stool that could be easily removed/displaced	Good	>90% of mucosa observed, mostly liquid stool, substantial suctioning required
C	At least 1 segment with only partially removable stool preventing complete visualization of mucosa	Fair	>90% of mucosa observed, liquid/semisolid stool mixture, could be suctioned and/or washed
D	At least 1 segment that could not be examined due to presence of remaining solid stool	Inadequate	<90% of mucosa observed, semisolid/solid stool mixture, could not be suctioned or washed

*Score of A or B (original study) or excellent or good (sampling) considered responders.

RESULTS

- High overall colon-cleansing responder rate was observed for both 2 L PEG and 4 L PEG (88% and 96%, respectively; Figure 1)
 - Similar to results observed for entire phase 3 patient population when applying European definition of responders
 - 89% of 153 patients who received 2 L PEG and 95% of 155 patients who received 4 L PEG (97.5% confidence interval; -12.0, ∞)

*Per-protocol population defined as patients who satisfied all inclusion and exclusion criteria with no major protocol violations and consumed ≥75% of scheduled total dose of assigned bowel preparation (did not take into account volume of clear liquid consumed with 2 L).

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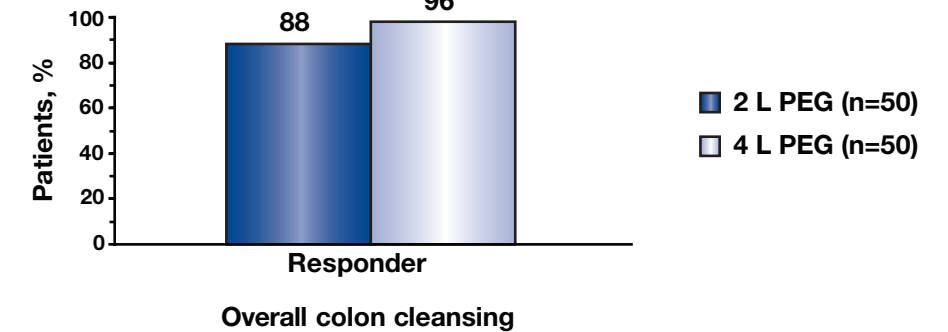


Figure 1. Percentage of responders (excellent or good score) for overall colon cleansing. PEG = polyethylene glycol electrolyte lavage solution.

- In addition, a high responder rate for ascending colon cleansing was observed for both 2 L PEG and 4 L PEG (91% and 94%, respectively; Figure 2)

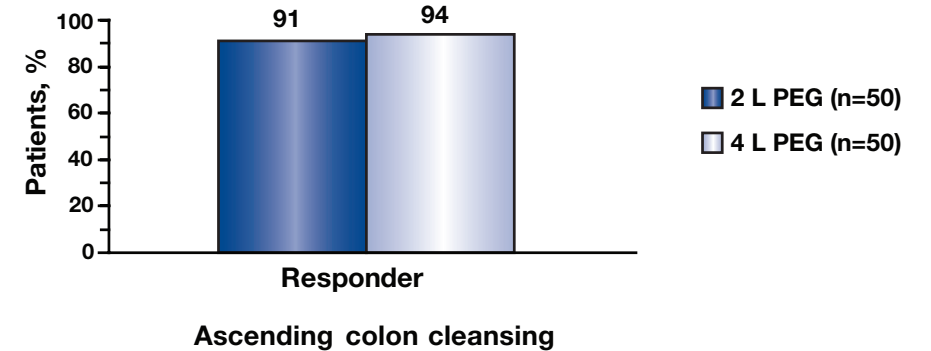


Figure 2. Percentage of responders (excellent or good score) for ascending colon cleansing. PEG = polyethylene glycol electrolyte lavage solution.

- Lower incidence of superficial mucosal aphthous ulcerations with 2 L PEG (2% for 2 L PEG vs 10% for 4 L PEG)
- Comparable number of endoscopic interventions in both groups (70%-72%)

CONCLUSIONS

- A new 2 L PEG purgative (MoviPrep), recently approved by the FDA, is effective for colon cleansing
 - Similar high rate of overall and ascending colon cleansing with 2 L PEG and 4 L PEG
- Current results from 100-patient assessment similar to full dataset from large, randomized, multicenter trial that demonstrated 2 L PEG (MoviPrep) was as effective as 4 L PEG

DISCUSSION

- Smaller volume requirement with 2 L PEG may enhance patient acceptance of colonoscopy and compliance with colon cancer screening recommendation by improving tolerability
- MoviPrep combines low volume and efficacy, and this represents an advance in bowel purgatives
- MoviPrep does not disrupt the workday prior to colonoscopy; the impact of colon purgation on productivity should be an important consideration when selecting a purgative