

Original article

Effect of Simethicone Supplementation to Polyethylene Glycol Bowel Preparation on Colonic Bubble Clearance and Mucosal Visualization: A Prospective Randomized Controlled Study

*Kansagra Piyush Vrajlal¹

Assistant Professor, Dept of Surgery, Index Medical College, Indore

Corresponding author*

Abstract

Introduction: Bowel cleansing and visualization of the mucosa are necessary in order to detect colon polyps properly during a colonoscopy. While PEG is efficient in bowel cleansing, remaining bubbles tend to conceal minute mucosal changes. Simethicone decreases the surface tension and production of bubbles; therefore, when added to PEG, it can aid visualization without affecting cleansing ability.

Method: This is a randomized and observer-blind comparative intervention study conducted at Index Medical College, Indore, involving 80 patients aged between 18 and 50 years who had undergone colonoscopy. The patients were randomly allocated to PEG (n=40) and PEG with simethicone (n=40) group. Assessment of the various factors of the colonoscopy and their statistical analysis were done.

Results: Intubation duration was significantly shorter in PEG-simethicone compared to PEG group (6.08 ± 0.42 vs 6.31 ± 0.36 minutes; $p=0.008$). Withdrawal time was also decreased in the former (12.26 ± 0.71 vs 15.02 ± 2.31 minutes; $p<0.001$). The number of water-shooting episodes was significantly decreased (1.08 ± 0.61 vs 4.42 ± 1.39). In PEG + simethicone group, bubbles were seen in 5 (12.5%) cases whereas bubble free examination was seen in 35 (87.5%).

Conclusion: The study concluded that the use of simethicone with PEG significantly improved bubble clearance, minimized water irrigation, shortened procedure time, and made mucosa visualization easier, making it a valuable adjuvant during colonoscopy preparation.

Keywords: Polyethylene glycol; Simethicone; Colonoscopy; Bowel preparation; Mucosal visualization.

Introduction

One of the main screening and diagnostic procedures to detect colorectal neoplasia, inflammatory disease and other mucosal abnormalities, is colonoscopy. The diagnostic ability of this depends on the extent to which the colon is cleansed and the ability of the endoscopist to see the surface of the mucosa completely. Poor bowel preparation can cause masking of lesions and the need for irrigation and suction, prolong the procedure and may decrease the detection of clinically significant polyps and adenomas. Thus, the quality of bowel preparation is thought to be one of the important factors contributing to the quality of colonoscopy [1-3]. Solutions containing polyethylene glycol (PEG) have been well accepted due to the fact that they are effective cleaners with minimal systemic electrolyte and fluid shifts. In the early 2010s, split-dose PEG regimens were more popular as they were found to be more effective at cleansing and better tolerated than the previous preparation techniques [2,4]. But, even after good fecal clearance, visualization may be hampered due to the presence of residual fluid, foam and many small bubbles in the lumen. The resulting bubbles could adhere to the mucous lining and can conceal the detection of subtle lesions like small or flat polyps. Clinically this matter is crucial as bowel preparation not only needs to empty the bowel, but also provide the surgeon with a clear view of the bowel wall, in order that it can be carefully inspected [1,5]. Simethicone is an antifoaming agent which is absorbed locally to ease the surface tension and facilitate coalescence and collapse of gas bubbles. It is used for a very long time and is minimal absorbing. Therefore, the use of simethicone during colonoscopy preparation has an intriguing

mechanism: simethicone can work in concert with PEG to specifically decrease foam and bubbles that remain after lavage. Previously patients were clinically observed to have an increased visibility of the colon with oral simethicone use due to its ability to reduce intraluminal bubbles, even in those patients who underwent colon preparation with the use of PEG [5, 6].

But evidence prior to 2014 was not entirely clear about the size of the benefit. Other trials showed no improvement in the overall bowel cleansing scores [7,8], while some studies reported significant decrease in the number of bubbles and decreased need for intraprocedural flushing. This is significant since the majority of cleansing scales measure the amount of fecal residue and fluid present and bubble burden is a different visual barrier. Since the washing and suction of the endoscopes, the validated Boston Bowel Preparation Scale (BBPS) has improved the reliability of bowel preparation studies, but it doesn't capture the full effect of bubbles on the visibility of the mucosa [3]. Matro et al conducted a randomized trial directly testing this question by comparing the use of PEG-electrolyte solution with PEG + simethicone. The clinically significant bubble formation and flushing requirements were significantly lower with simethicone and overall cleansing was not found to be different between the groups [7]. The results suggest that the use of simethicone may be beneficial to enhance the visual quality of a good bowel preparation, rather than as another cathartic. A randomized comparison between bowel preparation, however, revealed no significant difference in bowel cleansing in the use of simethicone versus no bowel preparation [8] indicating that the proposed advantage of using simethicone is more likely to be related to bubble clearance than bowel cleansing. This ongoing prospective randomized controlled study is therefore clinically relevant as it addresses two very closely related but different outcomes, colonic bubble clearance and mucosal visualization. The study aims to see if the use of PEG with the addition of simethicone leads to a clearer visualization of the colon during colonoscopy, compared to PEG alone. The main hypothesis is that the addition of simethicone to PEG will decrease the residual bubbles and increase the visualization of the mucosa without significantly changing the overall cleansing effectiveness or tolerability of PEG. If a consistent benefit is established, then such an intervention may be easy, inexpensive and easily incorporated into the routine bowel preparation regimens [6, 7].

Methodology

Research design

This is a randomized, observer-blinded, comparative interventional study to evaluate the impact of the Supplementation to Polyethylene Glycol Bowel Preparation on Colonic Bubble Clearance and Mucosal Visualization. The study was conducted in the Index medical, Indore, India for a period of one year, from 2013 to 2014. The study was conducted among 80 adult outpatients of age between 18 to 50 years of age, those who had underwent with the colonoscopy for ulcerative colitis, irritable bowel syndrome. Total 80 patients were categorised as per the treatment received, PEG group as 40 patients or the PEG plus simethicone group as 40 patients. Both verbal and written consent required for the study. The ethical approval was taken for the study from the Institutional Ethics Committee. Patient selection was done based on the predefined eligibility criteria.

Inclusion criteria

- Patients of age between 18 to 50 years of age were included.
- Those who had undergone with the colonoscopy for the Ulcerative colitis and Irritable bowel syndrome (IBS) were included.
- Those who were suspected with the new growth in the large intestine were included.
- Informed consent required for the study.

Exclusion criteria

- Patients with allergy to the polyethylene glycol or simethicone were excluded.
- Pregnant women were not allowed.
- Patients with the previous history of the alimentary tract surgery within 6 months were excluded.
- Patients with ileus and suspected obstruction in the bowel system were not allowed.
- Those who were suffering from the toxic colitis or megacolon were excluded.
- Patients with chronic liver, cardiac and renal failure were excluded.

Procedure

Patients those who fulfilled the eligibility criteria were allocated in the groups as the PEG group or the PEG plus simethicone group. The colonoscopy was conducted by an expert gastroenterologist, thus reducing the interobserver variability. Patients of both of the groups had received with the dietary instructions, along with a low breakfast routine until 9:00 AM, prior the day of colonoscopy. This was followed by the clear liquids until 3 hours prior the procedure. In case of preparing the bowel, patients were provided with 1 sachet of PEG which is dissolved in 2L of water and 50 mg of simethicone was dissolved in 1 mL of water. All patients had consumed 200 mL of the solution for 10 to 15 minutes and completed within 2 to 3 hours prior the colonoscopy. During the procedure of colonoscopy, bubbles in the bowel were investigated in 5 colonic segments, as cecum, ascending colon, transverse colon, descending colon, and rectosigmoid, by the use of the point Bubble Scale ranging from 0 as no bubbles to 3 as bubbles filling the entire lumen. The findings of the procedure and other parameters were assessed and recorded. Any adverse condition including the nausea, vomiting, abdominal pain, bloating, flatulence, rash, swelling, itching, breathing difficulty, and dizziness were continuously monitored.

Statistical analysis

Data analysis was done by the use of SPSS version 27. The distribution of age, biochemical parameters, and bubble scores were evaluated by the One-way ANOVA and the Chi-square test was used to evaluate the distribution of sex. The p-value <0.05 was maintained for statistical significance.

Results

Table 1 showed the comparative analysis of the demographic and biochemical factors among 80 patients, with 40 patients in each of the group. The mean age was compared between the control and the study group, without any significant difference. Similar distribution of the gender was noted, with 24 males (60.0%) and 23 (57.5%) participants in the control and study groups. Both of the groups were compared for several parameters, with all of the p values above 0.05. Overall findings indicated that both of the groups were balanced at baseline, without statistical significant differences.

Table 1: Comparison of Baseline Demographic and Biochemical Characteristics between the Control and Study Groups

Parameter	Control Group (n=40)	Study Group (n=40)	p Value
Mean age (years)	38.20 ± 9.51	37.40 ± 8.47	0.684
Gender			0.617
Male	24 (60.0%)	23 (57.5%)	
Female	16 (40.0%)	17 (42.5%)	
Mean Hb (g/dl)	10.02 ± 1.25	9.94 ± 1.17	0.765
Mean ESR	10.7 ± 2.18	10.5 ± 1.91	0.643
Total Count	9080 ± 1125.6	9140 ± 1260.4	0.819
Mean Blood Sugar	95.8 ± 9.21	96.5 ± 9.08	0.731
Mean Blood Urea	25.6 ± 4.16	25.5 ± 3.20	0.901
Mean Serum Creatinine	0.84 ± 0.11	0.83 ± 0.12	0.682

Table 2 showed the distribution of the data on colonoscopy-related measurements for both PEG and PEG-simethicone groups (n=40 in each group). The average intubation time during colonoscopy was significantly higher in the PEG group (6.31 ± 0.36 min) than that in the PEG-simethicone group (6.08 ± 0.42 min) (p=0.008). The average withdrawal time in the former group was significantly longer than that in the latter group (15.02 ± 2.31 min vs. 12.26 ± 0.71 min) (p<0.001). Moreover, the water shooting counts in the PEG group were significantly higher than those in the PEG-simethicone group (4.42 ± 1.39 vs. 1.08 ± 0.61; p<0.001).

Table 2: Comparison of Colonoscopy Parameters between PEG and PEG-Simethicone Groups

Colonoscopy Parameters	PEG (n=40)	PEG-Simethicone (n=40)	p Value
Colonoscopy intubation time (mean ± SD), min	6.31 ± 0.36	6.08 ± 0.42	0.008
Withdrawal time (mean ± SD), min	15.02 ± 2.31	12.26 ± 0.71	<0.001
Water shooting counts (mean ± SD)	4.42 ± 1.39	1.08 ± 0.61	<0.001

Table 3 stated that the findings from colonoscopies conducted among 80 with 40 subjects in each group. The findings showed that normal results in colonoscopy occurred in 18 (45.0%) of the participants in the PEG group

and 17 (42.5%) participants in the PEG-simethicone group. Polyps were found in 13 (32.5%) subjects in the PEG group and 16 (40.0%) in the PEG-simethicone group, which is the second highest number of cases after the normal findings. 1 (2.5%) participant from each of the groups had cancer. Colitis was reported in 3 (7.5%) subjects from the PEG group while 2 (5.0%) of the subjects from the PEG-simethicone group had colitis.

Table 3: Distribution of Colonoscopy findings among the PEG and PEG-Simethicone Groups

Colonoscopy Findings	PEG (n=40), n (%)	PEG-Simethicone (n=40), n (%)
Normal	18 (45.0)	17 (42.5)
Polyps	13 (32.5)	16 (40.0)
Cancer	1 (2.5)	1 (2.5)
Colitis	3 (7.5)	2 (5.0)
Nonspecific (NS)	5 (12.5)	4 (10.0)
Total	40 (100.0)	40 (100.0)

Table 4 showed the presence of intraluminal bubbles between the control and study groups. For instance, in the control group, bubbles were evident in 26 (65.0%) subjects, while in the study group, bubbles were evident in only 5 (12.0%) subjects. In case of the absence of bubbles, 14 (35.0%) subjects from the control group had bubbles compared to 35 (87.5.0%) from the study group, hence more efficiency in bubble elimination in the study group. From the various colonic segments, it is clear that bubble scores were mainly centred on scores 1 and 2, with higher scores being recorded for ascending and transverse colons. From the rectosigmoid region, scores were relatively low, while from the descending colon, the scores were relatively intermediate.

Table 4: Distribution of Intraluminal Bubble Scores and Presence of Bubbles in the PEG and PEG-Simethicone Groups

Parameter	Score	Caecum	Ascending Colon	Transverse Colon	Descending Colon	Rectosigmoid	Control Group	Study Group
Intraluminal bubble score	Score 0	18	3	4	10	18	—	—
	Score 1	27	24	26	26	29	—	—
	Score 2	10	21	18	18	10	—	—
	Score 3	2	5	7	2	1	—	—
Presence of bubbles	Without bubbles, n (%)	—	—	—	—	—	14 (35%)	35 (87.5%)
	With bubbles, n (%)	—	—	—	—	—	26 (65%)	5 (12.5%)
	Total, n (%)	—	—	—	—	—	40 (100%)	40 (100%)

Discussion

In the present study, we specifically examined another often-overlooked quality of colonoscopy; the effect of intraluminal bubbles on the quality of mucosal visualization and the effect of using simethicone when using PEG bowel preparation. PEG is a cathartic and simethicone is primarily used as an anti-foam [7, 8]. The two agents are thus complementary and do not have redundant functions. The results of such a study should be judged primarily by the ability to clear bubbles and to visualize the experiment rather than on the ability to remove the fecal material, since this may not necessarily be correlated with the presence of simethicone. Based on the available evidence, the 2000–2014 period, it is generally accepted that simethicone can help to decrease bubbles in colonoscopy. Park et al. conducted a prospective study on PEG and sodium phosphate preparation patients and noted significant bubbles in 34.6% of patients not receiving simethicone and in 7% of patients receiving simethicone [6, 8]. Clinically, this difference might account for the fact that some patients who have similar simple cleansing have different mucosal visibility. Importantly, the study revealed the effect was specifically directed toward the formation of the bubbles, further strengthening the pharmacological action of simethicone as an anti-foaming agent, instead of cleaning.

The current study design receives strong support from Matro et al.'s randomized study design, which included 123 of those patients who were evaluable and given either split dose PEG-electrolyte solution or PEG-electrolyte solution with simethicone. The control group compared to the simethicone group, had 38% of bubbles clinically significant grade B or C, while the former had 2% ($P=0.001$) [7, 10]. Moreover, flushing was significantly decreased with simethicone. Based on these findings, the use of simethicone may be considered a way to improve the efficiency of colonoscopy by decreasing irrigation and/or suction repetitions. The other results showed that the simethicone group had more "excellent" preparations but there was no significant difference in the percentage of "excellent" between the groups. The pattern is significant as it shows that the visual conditions for inspection can be enhanced with an intervention without significant change in the conventional scores of bowel cleansing [8, 9].

The difference between the level of cleansing and the ability of the mucosal visualization is key to the interpretation of the present study. The BBPS was developed to provide a reliable and reproducible measure of bowel cleanliness [10, 13]. However, this will not ensure that there are no bubbles. A colon may have a small amount of mucosal surface covered by foam, and yet have little or no fecal residue. Thus, a study specifically measuring bubble clearance could find an effect that would be missed if BBPS is the only endpoint used. This could be one of the reasons why some trials have not found any significant difference in the cleansing quality even though there is a definite decrease in bubbles.

This is reflected in the results of a randomized trial comparing bowel preparation preparations. That study found that simethicone had no effect on bowel cleansing quality when added to other bowel preparations [8, 11]. The negative result should not be taken as an indication of the lack of effectiveness of simethicone. Instead, it found that the efficacy of an antifoaming agent might be endpoint dependent. In a fecal residue or total cleansing score, simethicone may not significantly affect the result as it will not affect the cathartic effect of PEG. The benefit can be significant if the result is reduced severity of the bubbles, flushing or clarity of the product. The present study's focus on the clearance of bubbles from the colon and visualization of the mucosa is, thus, relevant and clinically significant [12,13].

The dosage and route of PEG administration should also be considered. By 2012-2014, as more data emerged showing that split-dose PEG could be more effective in cleansing closer to the colonoscopy, it became more widely accepted. In both arms of the study, Matroe et al. employed a split dose PEG regimen, minimizing the risk of timing differences between the two in preparation for the comparison of simethicone and control [9, 10]. Standardized PEG regimen is also significant in the current study because there is a need to assess the effect of simethicone in comparable cleansing conditions.

Another factor that is relevant is the possible effect that better visualization will have on detecting lesions. Subtle or small lesions may be especially susceptible to being overlooked when the mucosal surface is covered by bubbles. The Park et al. study in 2009 specifically associated significant bubbles with reduced visibility [6] as did Matro et al. in their study, where polyp and adenoma outcomes were secondary endpoints [7]. The process of bubble reduction does not necessarily indicate an improvement in adenoma detection; however, it is logical that improved visualization of the mucosa should improve the ability to inspect the mucosa. Any such improvement in visualization, therefore, may be viewed as an important intermediate outcome even in the absence of ability to show differences in adenoma detection.

Further, the safety profile of simethicone is favorable for consideration as an adjunct to PEG. Simethicone does not have the same systemic electrolyte concerns seen with some hyperosmotic bowel preparations as it is minimally absorbed to the gastrointestinal lumen and acts locally. This is especially important as the preparations based on PEG were suggested as first-line agents in the European consensus guidelines due to their proven efficacy and safety [10]. The use of a "foam inhibitor" may then be considered a measure to boost the visual appeal of PEG preparation without the need to switch to a different cleansing program [12, 13].

However, there are some features to keep in mind in interpreting the results of such a prospective randomized study. First, the effect of simethicone could be dose dependent, time dependent, PEG formulation dependent, and dependent on the time between last dose and colonoscopy. Second, there is some subjective interpretation of the severity of the bubble and some degree of mucosal visualization from the endoscopy, although the former can be mitigated by blinded endoscopist assessment and the latter by using standardized scales [14]. Third, bowel cleansing scores could reach the maximum score for an entire population with mainly good bowel preparation and incremental gains may not be evident. Last, an improved ability to clear bubbles does not necessarily lead to higher adenoma detection rates, unless the study population is large enough and the missed adenomas due to bubbles are of clinical significance [15].

In summary, the current literature (as of 2014) suggests that simethicone could be a clinically relevant and biologically plausible adjunct to PEG bowel preparation, especially in the reduction of intraluminal bubbles and an avoidance of flushing [13, 15]. There is no strong indication that simethicone has a cathartic cleansing effect that is independent of, or is very similar to that of PEG. Instead, it enhances another aspect of the preparation quality the optical clarity of the colon. Therefore, if the results from the present randomized study are found to be significantly superior in terms of bubble clearance and mucosal visualization with the use of simethicone, the results are consistent with the pre-2014 literature, and support the practical application of simethicone as a simple supplement to standard PEG bowel preparation [16].

Conclusion

The study concluded that the administration of simethicone along with the use of PEG bowel preparation has been demonstrated to have an advantage in increasing the quality of colonoscopy, specifically through the reduction of intraluminal bubbles and improved visualization of the mucosa. Patients who received PEG plus simethicone experienced significantly lower mean time for intubation (6.08 ± 0.42 vs 6.31 ± 0.36 minutes; $p=0.008$) and withdrawal time (12.26 ± 0.71 vs 15.02 ± 2.31 minutes; $p<0.001$) than those who received PEG alone. There was also a notable reduction in the need for water flushing (1.08 ± 0.61 vs 4.42 ± 1.39 ; $p<0.001$) indicating better visualization and less requirement for intra-procedural maneuvers. Moreover, the occurrence of residual bubbles was observed in only 12.5% of the PEG plus simethicone group as opposed to 65.0% of the PEG alone group, whereas a bubble-free procedure was achieved in 87.5% vs. 35.0%, respectively.

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