

Impact of polyethylene glycol plus simethicone on intraluminal bubble score during colonoscopy: A randomized endoscopist blinded trial

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Abstract

Introduction and Aim: Colonic air bubbles and foam are major hurdle to a positive colonoscopy. Bubbles hinder mucosal visibility resulting in poor diagnostic precision. This study aimed to determine the efficacy and tolerability of Simethicone in reducing the occurrence of colonic bubbles that could interfere with colon visualization, when added to Polyethylene glycol bowel preparation regimen.

Materials and Methods: This is a prospective randomized observer blind interventional study comparing PEG vs PEG + simethicone. Adult outpatients aged 18 to 60 years undergoing colonoscopy were recruited in this study. The primary outcome was the reduction in bubbles measured by intraluminal bubble score. The secondary outcome measures were patients' tolerability and endoscopists ease.

Results: The incidence of Score 1 and 2 bubbles was much lower with PEG + simethicone compared with PEG group ($P < 0.0001$). Bubble scores in the control vs study group were significantly different in various segments of the colon. Of the 150 Segments of colon caecum, ascending colon, transverse colon, descending colon and rectosigmoid examined segments without bubbles in the control vs study group (38.4% vs 88% $P < 0.001$). There was no significant difference in the incidence and severity of adverse events between the groups. There were no significant differences in the colonoscopy findings between the groups. However, water shooting counts, cecal intubation time and cecal withdrawal time was significantly lower in the PEG-simethicone group compared to PEG group.

Conclusion: PEG plus simethicone was more effective in reducing bubbles and enhances the mucosal visualization during colonoscopy.

Keywords: Simethicone, Polyethylene glycol, Colonoscopy, Intraluminal bubbles, Bowel preparation.

Introduction

Colonoscopy is primarily used in the diagnosis of inflammatory bowel disease (IBD), consisting of ulcerative colitis (UC) and Crohn's disease, irritable bowel syndrome (IBS) which are prevalent intestinal disorders with significant co-morbidities. Additionally, screening of high risk patients for colon malignancy is performed by colonoscopy.¹ Efficiency and success of colonoscopy depends primarily on adequate bowel purgation.^{2,3} Presence of residual stools, bubbles, foam, debris, and other fluids such as chyme hampers mucosal visibility thereby decreasing the diagnostic accuracy. Polyp detection rate and cecal intubation rate which are key quality indicators of colonoscopy depend on colon cleansing.^{4,5} Furthermore endoscopy duration, fatigue of endoscopists, patients' intolerance

has been increased by insufficient bowel preparation. Hence an appropriate intestinal preparation is essential prior to colonoscopy.⁵

Most of the bowel preparations are based on polyethylene glycol (PEG). 4 litre PEG solution was used but many patients reported cramping and bloating. Over the years, a standard large volume preparation has been replaced by low volume bowel preparations to improve patient compliance and tolerance.⁶⁻⁹ Even though low volume bowel preparation has increased the bowel cleansing efficacy, higher incidence of bubble formation has been reported with these preparations. In effect one third of patients receiving PEG solution have bubbles at the time of colonoscopy.¹⁰ The existing standard of practice is to irrigate and suction simethicone infused

saline through the irrigation channels during the colonoscopy to enhance mucosal visualisation. There is concern regarding retention of simethicone within non-brushable irrigation channels during colonoscopy. Colonoscope manufacturers have recommended against simethicone irrigation into the working channels possibly to prevent contamination of the non-brushable colonoscope channels. Furthermore, endoscopists' time and effort is increased by flushing and suctioning simethicone into the colonoscope channels¹¹. Antifoaming agents are added to low volume bowel preparations thereby reducing the need of simethicone irrigation for reducing bubbles.¹² Previous studies has shown the effectiveness of simethicone preparations prior to gastroscopy and capsule endoscopy.¹³⁻¹⁵ Only partial data is available on simethicone addition to PEG for colonoscopy preparation regimens. The study aimed to compare the efficacy of the bowel preparation in reducing bubbles between patients receiving PEG and those receiving PEG plus simethicone. Safety and tolerability of the simethicone are the secondary outcomes measured in the study.

Materials and Methods

Study design

This is a randomized observer blinded comparative interventional study conducted at Department Of Medical Gastroenterology, Madras Medical College. Sixty outpatients were included and were assigned to one of the treatment groups. All the patients provided written informed consent. This study was approved by the Institutional ethics committee, Madras Medical College.

Study population

Adult patients aged 18 to 50 years irrespective of gender undergoing colonoscopy for ulcerative colitis, Irritable bowel syndrome or Suspected new growth in the large intestine were recruited to the study. Baseline characteristics of the participants are presented in table 1. Patients allergy to Polyethylene glycol and Simethicone, Pregnant and lactating women, H/o alimentary tract surgery in the past six months, Patients with Ileus, Suspected bowel obstruction, Toxic colitis or Megacolon, Patients with chronic

liver, renal and cardiac failure were excluded from the study.

Study procedure

Patients were randomly assigned to one of the treatment arms, PEG or PEG plus simethicone. Participants were allocated randomization numbers through computer generated randomization list. Colonoscopy performed by a single gastroenterologist to avoid interobserver variability and the gastroenterologist did not participate in the randomization process.

Drug preparations

Diet instructions were identical for both the study groups. The day before colonoscopy, patients were permitted a low residue breakfast up to 9:00 AM, followed by clear liquids upto 3 hrs before the colonoscopy. Patients received specific instructions regarding a low-residue diet, including list of acceptable and unacceptable foods. The study preparation was PEG plus simethicone. Subjects were given 1 sachet of standard drug dissolved in 2 litres of water, to which 50 mg of simethicone dissolved in 1 ml of water is added. Subjects were advised to drink 200 ml of this solution every 10-15 minutes and complete it in 2 hour. The process was completed 3 hours prior to Colonoscopy. Colonoscopies and patient assessments were performed by the gastroenterologist on the day of the procedure.

Evaluation of Bowel Preparation

The primary outcome was measured based on the Visual Analog Scale. The Bubble Scale used for this study graded 5 segments of the colon cecum, ascending colon, rectosigmoid, transverse colon and descending colon. Each colon segment was graded using a 4-point scale where Minimal or no bubbles-Score 0, Bubbles covering half the lumen-Score 1, Bubbles covering the entire circumference-Score 2, Bubbles filling the entire lumen- Score 3.^{16,17} To minimize intraobservers variability gastroenterologist was familiarized with the scale and score assigned to respective observation. Colonoscopy procedure parameters and colonoscopy findings were recorded. Patients were monitored for adverse events by the

investigator during preparation for colonoscopy. Mild events were classified as Nausea, vomiting, abdominal pain, bloating and flatulence. Serious events were classified as rash, swelling, itching, difficulty in breathing and dizziness.

Statistical analysis

The obtained data was analyzed statistically. Distribution of age was analysed using One Way ANOVA Sex distribution was analyzed by Chi square test. The biochemical parameters and bubble scores were analyzed using One Way ANOVA p value < 0.05 was considered to be statistically significant.

Results

In total, 126 subjects were screened 46 were excluded and 20 subjects withdrew consent. 60 subjects were enrolled. Of the 60 subjects, 30 subjects were assigned each to control group and study group respectively. 60 subjects underwent colonoscopy [female and male (40% vs 60%; P=0.5)] with no significant gender difference between control and study groups. Baseline characteristics of the study subjects are presented in table 1. Score 0 was more and scores 1, 2 and 3 were less in study group. This signifies that incidence of bubbles was less in study group. There was a statistically significant difference in the incidence of bubbles between the groups in various segments of colon i.e, in ceacum, rectosigmoid, ascending colon, transverse colon and descending colon. (p< 0.0001)

Totally 150 segments (areas) of the colon were examined in each group. Figure 3 represents segments of colon with and without bubbles in both the groups. The counts of water shooting for cleaning the lens of colonoscope was significantly lower in the simethicone group. Cecal intubation time and cecal withdrawal time were significantly different in both the group and are presented in Table 2. Table 3 represents colonoscopy findings in both the groups. Incidence of adverse drug reaction was less in the study group compared to the control group (10% vs 26.6%). Nausea (13.3%), vomiting (3.3%), abdominal bloating (3.3%) and flatulence (6.6%) were the adverse drug reactions reported in the control group. Nausea (10%) was the only adverse drug reaction in study group.

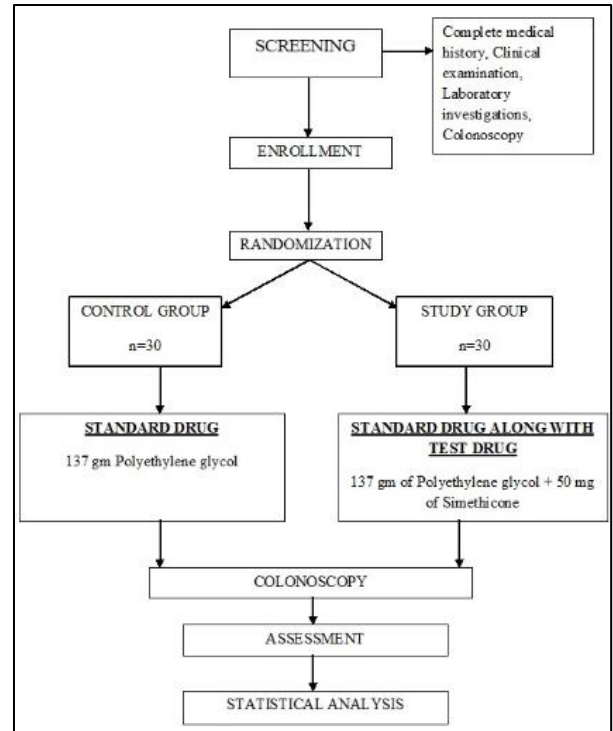


Fig. 1: Study flow chart

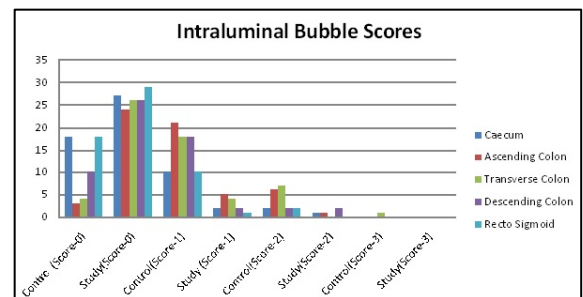


Fig. 2: Intraluminal bubble scores in various segments of colon

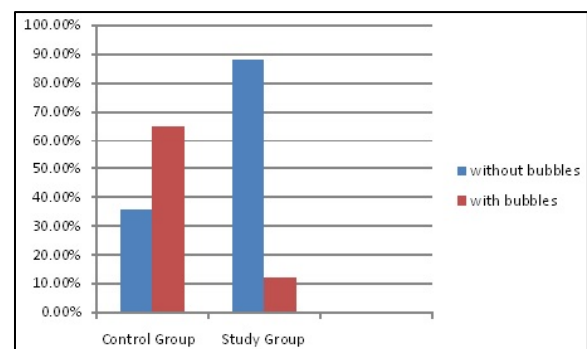


Fig. 3: Shows the percentage of segments in the in the control and study group with and without bubble

Table 1: Baseline Characteristics of the participants

	Control Group	Study Group	p Value
Mean age (in years)	38.50 ± 9.69	37.10 ± 8.323	0.551
Gender			
Male	18	18	0.5
Female	12	12	
Mean Hb (g/dl)	9.99 ± 1.28	9.97 ± 1.14	0.957
Mean ESR	10.8 ± 2.23	10.4 ± 1.88	0.175
Total Count	9100 ± 1100.9	9120 ± 1273.9	0.513
Mean Blood sugar	95.6 ± 9.33	96.7 ± 9.15	0.927
Mean Blood Urea	25.8 ± 4.28	25.4 ± 3.12	0.13
Mean Serum Creatinine	0.84 ± 0.11	.83 ± .13	0.67

Table 2: Colonoscopy procedure parameters

Colonoscopy parameters	PEG (n=30)	PEG-Simethicone (n=30)	P value
Colonoscopy intubation time (mean ± SD), min	6.37 ± 0.33	6.12 ± 0.45	<0.019
Withdrawal time (mean ± SD), min	15.14 ± 2.42	12.18 ± 0.63	<0.001
Water shooting counts	4.57 ± 1.44	1.02 ± 0.57	<0.001

Table 3: Colonoscopy findings

Colonoscopy findings	PEG (n=30)	PEG- Simethicone (n=30)
Normal, n (%)	14(46.7)	13(43.3)
Polyps, n (%)	10(33.3)	14(46.7)
Cancer, n (%)	1(3)	1(3)
Colitis, n (%)	2(6)	1(3)
Nonspecific, n (%)	4(13.3)	2(6)

Discussion

Quality indicators of colonoscopy including cecum intubation time, withdrawal time, number of endoscopically detected polyps, adenoma detection rate (ADR) and advanced neoplasia detection rate (ANDR) are directly impacted by adequate bowel preparation. Colonic bubbles are encountered by the endoscopists and to date bubbles are addressed by adding simethicone to their flushes. Several studies have compared the bowel cleansing of various purgatives with or without simethicone.^{12,18,19} There is underestimation of impact of bubbles on bowel preparation adequacy. A previous study has shown the incidence of bubbles with PEG-ELS is 32% and 30% with split dose sodium phosphate liquid administered on the day of colonoscopy. In a prior prospective study bubbles interfering with polyp identification were detected in 35% of patients.^{16,20} In our study there is significant reduction in the bubbles in the simethicone group similar to the previous studies.

Our study has shown more polyp were detected in the simethicone group. Simethicone is inactive

nontoxic silicone based polymer. It cannot be absorbed in the gastrointestinal tract when administered orally.²⁰ Simethicone reduces the surface tension of the gas bubbles and hence enable in bubble breakdown.²¹ Simethicone is generally used to treat symptoms caused by excess gas in the intestinal tract. Simethicone is inexpensive antifoaming agent with established safety. Of the 150 segments of colon examined 88% of the segments were without bubbles in the study group whereas only 35.4% in the control group were without bubbles. Air bubble reduction results in markedly enhanced visibility and, possibly, improvement in the quality of the colonoscopy. In caecum, the incidence of score 0 bubbles was more in the study group when compared with the control group, and the incidence of score 1 and 2 bubbles was also less in the study group with a significant p value (0.024). This shows that the incidence of bubbles was less in the study group. Similarly in ascending, transverse, descending and recto-sigmoid colon, the incidence of score 0 bubbles was more in the study

group when compared with the control group. *p* values were statistically significant showing that the incidence of score 1 and score 2 bubbles was less in the study group ($p < 0.0001$). In the control group, 90% of the examined ascending colon segments, 86.7% of the examined transverse colon segments, 40% of the examined caecum segments, 66.7% of the examined descending colon segments and 40% of the examined rectosigmoid segments, had either score 1, 2 or 3 bubbles. This shows that the problem of bubbles was more in ascending colon and transverse colon. The incidence of bubbles in the PEG group was 66.5%, whereas the incidence of bubbles in the PEG plus Simethicone group was only 11.9%. This shows that there is a significant reduction in the incidence of bubbles in the study group and indicates that simethicone may be responsible for this. This is in accordance with the studies conducted earlier.

Simethicone effect on cecal intubation time and cecal withdrawal time has generated varied results. Rishi et al have demonstrated simethicone premixed with PEG did not significantly reduce the cecal intubation time and cecal withdrawal time.¹¹ Yoo et al evaluated significant reduction in the cecal withdrawal time in the simethicone group. Though there was no significant reduction in the cecal intubation in the simethicone group.²² Our study demonstrated significant reduction in the mean cecal intubation time and mean withdrawal time in the simethicone group. Yoo et al, demonstrated significant reductions in the water shooting counts with addition of simethicone to PEG. The group receiving simethicone has significantly reduced the counts of water shooting during colonoscopy in our study. Incidence of adverse drug reactions was less in the study group (10%) when compared with the control group (26.6%). All the Adverse Drug Reactions were categorized as possible under WHO causality assessment scale. According to Modified Hartwig and Siegel severity assessment scale all Adverse Drug Reactions were mild. This shows that the Polyethylene glycol and Simethicone combination was tolerated better. There are few limitations to our study. One of the major limitations is that this randomized comparative trial was done in single center and included limited number of patients. Randomized multicenter trial with large

sample size required for further evaluation. Though there were significant differences in the secondary outcomes measured between the groups, this study was not powered for the secondary outcomes assessed. Also, to evaluate safety parameters biochemical and hematological analysis of patients' blood were not done. No vital signs were recorded before and after colonoscopy.

Conclusion

The addition of simethicone to PEG solution resulted in a significant reduction in intraluminal bubbles that could impede with the colon visibility. Larger studies are required to study the addition of simethicone to PEG in terms of greater polyp detection, adenoma detection, improved endoscopists' efficiency and reduced adverse events.

Source of Funding

None.

Conflict of Interest

None.

References

1. Telford JJ. Inappropriate Uses of Colonoscopy. *Gastroenterol Hepatol (N Y)* 2012;8(5):342–4.
2. Rex DK, Imperiale TF, Latinovich DR, Bratcher LL. Impact of bowel preparation on efficiency and cost of colonoscopy. *Am J Gastroenterol* 2002;97(7):1696–700.
3. Hassan C, Fuccio L, Bruno M, Pagano N, Spada C, Carrara S, et al. A Predictive Model Identifies Patients Most Likely to Have Inadequate Bowel Preparation for Colonoscopy. *Clin Gastroenterol Hepatol* 2012;10(5):501–6.
4. Harewood GC, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. *Gastrointest Endosc* 2003;58(1):76–9.
5. Froehlich F, Wietlisbach V, Gonvers J-J, Burnand B, Vader J-P. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc* 2005;61(3):378–84.
6. Spada C, Cesaro P, Bazzoli F, Saracco GM, Cipolletta L, Buri L, et al. Evaluation of Clensia®, a new low-volume PEG bowel preparation in colonoscopy: Multicentre randomized controlled trial versus 4L PEG. *Dig Liver Dis* 2017;49(6):651–6.
7. Cesaro P, Hassan C, Spada C, Petruzzello L, Vitale G, Costamagna G et al. A new low-volume isosmotic polyethylene glycol solution plus bisacodyl versus split-

- dose 4 L polyethylene glycol for bowel cleansing prior to colonoscopy: a randomised controlled trial. *Dig Liver Dis* 2013;45(1):23–7.
8. Repici A, Cestari R, Annese V, Biscaglia G, Vitetta E, Minelli L, et al. Randomised clinical trial: low-volume bowel preparation for colonoscopy - a comparison between two different PEG-based formulations. *Aliment Pharmacol Ther* 2012;36(8):717-24.
 9. Valiante F. Bisacodyl plus split 2-L polyethylene glycol-citrate-simethicone improves quality of bowel preparation before screening colonoscopy. *WJG* 2013;19(33):5493.
 10. Matro R, Tupchong K, Daskalakis C, Gordon V, Katz L, Kastenber D et al. The Effect on Colon Visualization During Colonoscopy of the Addition of Simethicone to Polyethylene Glycol-Electrolyte Solution: A Randomized Single-Blind Study: Clinical and Translational *Gastroenterol* 2012;3(11):e26.
 11. Rishi M, Kaur J, Ulanja M, Manasewitsch N, Svendsen M, Abdalla A, et al. Randomized, double-blinded, placebo-controlled trial evaluating simethicone pretreatment with bowel preparation during colonoscopy. *WJGE* 2019;11(6):413–23.
 12. Tongprasert S, Sobhonslidsuk A, Rattanasiri S. Improving quality of colonoscopy by adding simethicone to sodium phosphate bowel preparation. *WJG* 2009;15(24):3032.
 13. Fang Y, Chen C, Zhang B. Effect of small bowel preparation with simethicone on capsule endoscopy. *J Zhejiang Univ Sci B* 2009;10(1):46–51.
 14. Ahsan M, Babaei L, Gholamrezaei A, Emami MH. Simethicone for the Preparation before Esophagogastroduodenoscopy. *Diagn Ther Endosc* 2011;2011:1–4.
 15. Keeratichananont S, Sobhonslidsuk A, Kitiyakara T, Achalanan N, Soonthornpun S. The Role of Liquid Simethicone in Enhancing Endoscopic Visibility Prior to Esophagogastroduodenoscopy (EGD): A Prospective, Randomized, Double-Blinded. *Placebo-Controlled Trial* 2010;93(8):6.
 16. Sudduth RH, DeAngelis S, Sherman KE, McNally PR. The effectiveness of simethicone in improving visibility during colonoscopy when given with a sodium phosphate solution: A double-blind randomized study. *Intestinal Endosc* 1995;42(5):413-5.
 17. McNally PR, Maydonovitch CL, Wong RK. The effectiveness of simethicone in improving visibility during colonoscopy: a double-blind randomized study. *Gastrointest Endosc* 1988;34(3):255-8.
 18. Altıntaş E, Uçbilek E, Sezgin O, Sayici Y. Alverine citrate plus simethicone reduces cecal intubation time in colonoscopy - a randomized study. *Turk J Gastroenterol* 2008;19(3):174-9.
 19. Lazzaroni M, Petrillo M, Desideri S, Porro GB. Efficacy and tolerability of polyethylene glycol-electrolyte lavage solution with and without simethicone in the preparation of patients with inflammatory bowel disease for colonoscopy. *Alimentary Pharmacol Ther* 1993;7(6):655-9.
 20. Shaver WA, Storms P, Peterson WL. Improvement of oral colonic lavage with supplemental simethicone. *Dig Dis Sci* 1988;33(2):185-8.
 21. Brečević L, Bošan-Kilibarda I, Strajnar F. Mechanism of antifoaming action of simethicone. *J Appl Toxicol* 1994;14(3):207-11.
 22. Yoo IK, Jeon YT, Kang SH, Lee JH, Kim SH, Lee JM, et al. Improving of bowel cleansing effect for polyethylene glycol with ascorbic acid using simethicone: A randomized controlled trial. *Med* 2016;95(28):e4163

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