

Simethicone adjunct to polyethylene glycol improves small bowel capsule endoscopy imaging in non-Crohn's disease patients

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Abstract

Background Currently, there is no standardized protocol for bowel preparation before small bowel capsule endoscopy (SBCE). This study aimed to investigate the effect of simethicone combined with polyethylene glycol (PEG) on the visualization quality (VQ) of the SBCE in patients with or without known or suspected Crohn's disease (CD).

Methods This observational, prospective, single-center study included consecutive patients undergoing a SBCE between 2007 and 2008. Patients received either a standard bowel cleansing preparation of 2 L PEG and 80 mg simethicone orally 12 and 1 h before SBCE respectively (Group A) or only PEG (Group B). VQ, based on scores for luminal bubbles in frames taken from the small intestine, examination completeness, SBCE diagnostic yield, gastric and small bowel transit times were recorded.

Results Of the 115 patients finally included (Group A, n=56 and Group B, n=59) the cecum was visualized in 103 (89.6%). Simethicone overall improved the VQ in the proximal [OR: 2.43 (95%CI: 1.08-5.45), P=0.032] but not in the distal bowel segment (P=0.064). Nevertheless, this effect was not observed in patients undergoing SBCE for either known or suspected CD.

Conclusion Simethicone as an adjunct to PEG for bowel preparation in patients undergoing SBCE significantly improved the VQ in non-CD patients.

Keywords Small bowel capsule endoscopy, simethicone, visualization quality, Crohn's disease

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Introduction

Small bowel capsule endoscopy (SBCE) is a revolutionary modality which allows full visualization of the small bowel and provides invaluable information regarding the diagnosis and management of obscure gastrointestinal bleeding and non-stricturing small bowel Crohn's disease (CD) [1,2]. However, the diagnostic yield (DY) of SBCE may be compromised by poor bowel preparation which affects the visualization quality (VQ), and the gastric (GTT) and small bowel intestinal transit times (SBTT) which may influence the examination completeness (EC) [3-6].

Until now, there is no consensus regarding the ideal small bowel preparation that would allow excellent VQ and EC

resulting in optimal DY of the SBCE test. Thus, in the absence of established guidelines, due to limited and/or contradictory data, small bowel preparation for SBCE in routine clinical practice remains still empirical [1,3-10]. Most centers use a regimen that consists of a combination of clear liquid diet followed by a 8-h fasting period and an oral purgative, either polyethylene glycol (PEG) or sodium phosphate, 12 h prior to the examination, although timing and dosing are not yet clearly defined [9,11-14]. Furthermore, in order to improve VQ and EC, additional preparation substances have been used, such as detergents that may disrupt intraluminal air bubbles (simethicone) and prokinetics, such as erythromycin, but again results are either inconclusive or controversial [15-20]. These discrepancies may be due to different methods of assessing the visibility of small intestinal mucosa by SBCE as there is no widely accepted, standardized, easy to apply and time-saving scoring system for the quality of bowel preparation that would render the results of clinical trials comparable [21,22].

Our primary aim was to investigate the effect of simethicone on VQ of SBCE in patients with or without known or suspected CD, while secondary objective was to study the impact of simethicone on EC, DY, GTT, and SBTT.

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Conflict of Interest: None

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Patients and methods

Study design

This was an observational, prospective, single-center study which included consecutive patients undergoing a VCE study (PillCam SB[®] capsule endoscopy system, Given Imaging Ltd., Yokneam, Israel) between 2007 and 2008. Exclusion criteria were known or suspected small intestinal strictures, gastric surgery, diabetes mellitus, pregnancy, paralysis or impaired mobility and the use of medications affecting gastrointestinal motility. All videos were reviewed blindly by two independent, experienced capsule endoscopists (KP, IT). The study was approved by the Ethics Committee of Evaggelismos hospital.

Patients, bowel preparation and definitions

All patients during the first 3 days followed a fiber-free diet, whereas during the fourth day they received only clear liquids. Additionally, they received a standard bowel cleansing preparation of 2 L PEG (Klean Prep PEG+ E[®]; Kite Hellas, Greece) 12 h before SBCE and either 80 mg simethicone (Gas-X[®], Novartis Consumer Health, Inc.) orally 1 h before the SBCE (Group A) or not (Group B). All patients with proven or suspected CD prior to the aforementioned procedure had undergone patency control, using a standard small bowel patency capsule (AGILE[™] patency system Given Imaging Ltd., Yokneam, Israel).

EC was defined as cecum visualization. The VQ of the small intestinal lumen was assessed in frames of both the proximal (starting with the first image immediately after passage of the capsule through the pylorus) and the distal (beginning 1 h before passage through the ileocecal valve) small bowel video segments, with each one of these lasting about 1 h, and was rated according to the absence or presence of luminal air bubbles as excellent (grade 0, total absence of bubbles), good (grade 1), fair (grade 2), and poor (grade 3, bubbles which did not allow visualization of the small bowel) as has been described previously [23,24]. For further study analysis purposes, adequate VQ was defined as a score of 0 or 1, whereas insufficient as a score of 2 or 3. GTT was defined as the time intervening between the first gastric and the first duodenal image, whereas SBT[™] was defined as the time intervening between the first duodenal image and the first cecal image, for cases in which the capsule reached the cecum. The DY of the SBCE was assessed according to Costamagna *et al*, as previously described [25]. Briefly, the findings of SBCE were considered positive if they explained the symptoms for which the test was performed, assisted the further management of the patient, or were subsequently confirmed by other diagnostic modalities, whereas of uncertain significance if they failed to completely explain the symptoms, thus necessitating further investigation. When no abnormality was detected, despite definite indications for the presence of a lesion, the test was considered as having 'no findings' [25].

Statistical analysis

Descriptive statistics were provided with medians and interquartile range (IQR) for continuous variables and frequency and percentage for categorical variables. Agreement between categorical measurements was assessed using Kappa statistics. Categorical variables were compared between patients' groups with the chi-square or the Fisher's exact test as appropriate, while continuous variables were compared with the Mann-Whitney U-test. Statistical analysis was performed using the SPSS 22.0 (SPSS Inc., Chicago, IL, USA). A P-value <0.05 was considered as statistically significant.

Results

A total of 115 patient's SBCE videos were finally evaluated. Compliance with bowel preparation was excellent. Simethicone was well tolerated and none of the patients discontinued the preparation or reported any side effects. Fifty-six patients (48.7%) received simethicone premedication (Group A) and 59 patients (51.3%) did not (Group B). Patient groups were similar in demographic, clinical data and indications for SBCE (Table 1).

The capsule was not retained in any of the patients. Overall the cecum was visualized in 103/115 (89.6%) patients. Inter-observer agreement on cecum visualization was 100% and agreement on the bowel preparation VQ was almost perfect for the proximal ($k=0.822$, $P<0.001$) and substantial for the distal small bowel video segments ($k=0.727$, $P<0.001$).

Simethicone overall improved the VQ in the proximal bowel segment [OR: 2.43 (95%CI: 1.08-5.45), $P=0.032$], but not in the distal segment, although a trend was observed

Table 1 Patients' demographic and clinical data

	Group A	Group B	P-value
N	56	59	
Male, (%)	30 (53.6)	29 (49.2)	0.710
Age (years, median, IQR)	45 (28-72)	45 (31-66)	0.531
Smoking, (%)	5/38 (13.2)	11/43 (22.6)	0.263
BMI (kg/m ²)	26 (23.2-29)	25 (23-26.5)	0.381
Indications, (%)			
CD	17 (30.4)	21 (35.6)	0.560
Suspected small-bowel CD	8 (14.3)	11 (18.6)	0.619
Iron-deficiency anemia	19 (33.9)	15 (25.4)	0.414
Chronic diarrhea	5 (8.9)	2 (3.4)	0.264
Recurrent abdominal pain	1 (1.8)	2 (3.4)	1.000
Recurrent melena	0 (0)	2 (3.4)	0.496
FAP	1 (1.8)	1 (1.7)	1.000
Miscellaneous disease	5 (8.9)	5 (8.5)	1.000

IQR, interquartile range; BMI, body mass index; CD, Crohn's disease; FAP, familial adenomatous polyposis

($P=0.064$) (Fig. 1, Table 2). Subgroup analysis showed that the addition of simethicone had no effect on the VQ of patients undergoing SBCE either for known CD or suspected (and eventually confirmed) CD ($P=0.507$); however, simethicone premedication improved significantly the VQ in the proximal bowel segment in non-CD patients [OR: 2.93 (95%CI: 1.06-8.08), $P=0.047$] (Table 2).

There was no statistically significant difference between groups A and B regarding EC, DY, GTT and SBTT (for cases where the capsule reached the cecum) of the SBCE (Table 3). The percentage of lesions in the proximal bowel in groups A and B was 55.2 and 48.4%, respectively.

Discussion

Currently, in the absence of established guidelines and/or recommendations, bowel preparation prior to SBCE remains still empirical. Simethicone has been frequently used in order to improve the quality of gastrointestinal mucosa visualization during endoscopy as this detergent can disrupt intraluminal air bubbles from the lumen. Supplemental use of simethicone before SBCE either alone [16,21,23,24] or in combination with purgatives [17,26,27] was found to improve the VQ of small bowel, especially in the proximal part of the small intestine [23,24]. However, data are somehow contradictory [13,18,28], probably due to the great diversity of indications for SBCE in different patient groups and in scoring systems used to classify the VQ of SBCE [22].

Our study demonstrated that simethicone combined with PEG improved the VQ of the SBCE only in the proximal bowel segment, in agreement with a recent meta-analysis [29]. However, subgroup analysis showed that this effect was mainly seen in non-CD patients and simethicone did not exert any beneficial effect on VQ in patients with established CD or patients with suspected CD, eventually diagnosed with this disease based on various diagnostic tests including SBCE. This discrepancy may be related to the fact that CD patients often display marked gastrointestinal motor disorders preventing normal propulsive activity [30].

Moreover, simethicone did not have any effect on the EC, DY, GTT and the SBTT of the SBCE, as indicated also by the majority of the previous studies with the exception of Dai *et al* who showed that, in addition to a better visualization of small

bowel mucosa, simethicone shortened the procedure time and led to a higher rate of EC [11].

Limitations of the study were the small sample size and the lack of randomization. Strength of our study was that all SBCE videos were evaluated blindly by two independent, experienced viewers having an excellent inter-observer agreement.

In conclusion, our study showed that simethicone administered as an adjunct to PEG for bowel preparation

Table 2 Small bowel capsule endoscopy visualization quality

	Group A (n=56)	Group B (n=59)	P-value
VQ adequate, (%)			
Proximal	43 (76.8)	34 (57.6)	0.032
Distal	37/50 (74)	29/53 (54.7)	0.064
VQ adequate, (%) (non-CD patients)			
Proximal	28/37 (75.7)	17/33 (51.5)	0.047
Distal	25/34 (73.5)	18/30 (60)	0.111
VQ adequate, (%) (patients with known or suspected CD*)			
Proximal	15/19 (78.9)	17/26 (65.4)	0.507
Distal	12/16 (75)	11/23 (47.8)	0.294

*Who were eventually diagnosed with CD based also on positive SBCE findings

VQ, visualization quality; CD, Crohn's disease; SBCE, small bowel capsule endoscopy

Table 3 Small bowel capsule endoscopy completeness of examination and diagnostic yield

	Group A	Group B	P-value
GTT (median, IQR, min)	26 (11-67)	24 (8-68)	0.871
SBTT (median, IQR, min)	274.5 (196-346)	261 (213-324)	0.682
EC, (%)	50 (89.3)	53 (89.8)	1.000
DY, (%)			
Positive findings	18 (32.2)	21 (35.6)	0.897
Uncertain findings	11 (19.6)	10 (16.9)	
No findings	27 (48.2)	28 (47.5)	

GTT, gastric transit time; SBTT, small bowel transit time; EC, examination completeness; DY, diagnostic yield

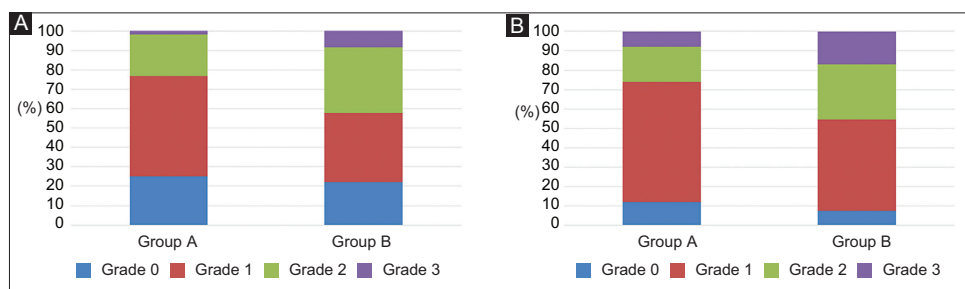


Figure 1 Small bowel capsule endoscopy visualization quality based on a 4-scale grading system regarding both the proximal (A) and the distal (B) bowel

Summary Box**What is already known:**

- Small bowel capsule endoscopy (SBCE) is useful for the diagnosis and management of obscure gastrointestinal bleeding and non-stricturing small bowel Crohn's disease (CD)
- A bowel preparation is needed in order to improve visualization quality of the SBCE

What the new findings are:

- Simethicone as an adjunct to polyethylene glycol for bowel preparation in patients undergoing SBCE improved the VQ in non-CD patients

before SBCE improved the VQ, at least in the proximal small bowel segment in non-CD patients. For patients undergoing SBCE to evaluate or confirm suspected CD, simethicone premedication did not appear to improve the VQ of the small bowel. Larger, prospective studies are warranted to define the role of simethicone as part of the bowel preparation in different patient populations.

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