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Small bowel cleansing for capsule endoscopy in paediatric patients: A prospective randomized single-blind study

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ABSTRACT

Background: Small bowel cleansing by capsule endoscopy has never been addressed in children.
Methods: Randomized controlled trial to evaluate the effect of five bowel preparation regimens on the mucosal visibility surface (as percentage of visualized surface area). Group A: a clear liquid diet for 12 h on the day before; Group B: high volume polyethylene glycol (50 mL/kg, up to 2 Lt/die); Group C: low volume polyethylene glycol (25 mL/kg up to 1 Lt/die); Group D: 20 mL (376 mg) of oral simethicone; Group E: 25 mL/kg (up to 1 Lt/die) of polyethylene glycol solution plus 20 mL (376 mg) of oral simethicone.
Results: Overall, 198 patients (53% male, median age 13 years) were enrolled. Preparation regimen visualization scores were 14.1 ± 4.2, 18.9 ± 5.1, 17.8 ± 5.5, 14.9 ± 4.8 and 20.9 ± 4.6 in groups A, B, C, D and E, respectively ($P < 0.01$). Positive findings were found in 172 cases (87%), but no significant differences were observed in the diagnostic yield and tolerability. Interobserver agreement, $k = 0.89$ (95% CI 0.83 ± 0.71).
Conclusion: This is the first report in children that supports the use of 25 mL/kg (up to 1 Lt/die) of polyethylene glycol solution plus 20 mL (376 mg) of oral simethicone as the preparation of choice for capsule endoscopy.

1. Background

Capsule endoscopy (CE) is a well-known, non-invasive, diagnostic tool to evaluate small bowel disease in adults and children. Unfortunately, CE is unable to suction fluid or to wash the small bowel mucosa, so that its diagnostic yield is likely to be limited by debris, biliary secretion, bubbles and blood, especially in the distal small bowel [1]. In addition, CE sometimes fails to reach the cecum within the battery life of the capsule, resulting in a failure to visualize the distal portion of the small intestine.

It has been suggested that cleaning the small intestine prior to examination may improve mucosal visibility at CE and, as a result, the diagnostic yield of the technique. Therefore, CE-preparation regimens – mainly based on the same products adopted for colonoscopy preparation – have been proposed [2]. However, previous studies on adult populations reached controversial results. Although there is some evidence to support bowel preparation for CE, the optimal preparation regimen is still unclear [3–6]. In addition, no study addressed such an issue in children so that overnight fasting before the examination represents the only modification recommended for paediatric CE [7,8].

The primary aim of this prospective, randomized and controlled study (ClinicalTrials.gov – NCT01783782) was to evaluate the effect of five bowel preparation regimens on small-bowel cleansing in the paediatric population. The secondary endpoints were to evaluate the effects of preparation on diagnostic yield and tolerability.

2. Patients and methods

Consecutive patients, aged 4–18, referred for CE for various indications, between November 2005 and September 2012 were evaluated. Exclusion criteria included intestinal obstruction, suspicious impaired intestinal motility, and history of gastrointestinal surgery. After signed informed consent, patients were randomized by one of the investigators to one of the five preparation regimens by consecutive assignment using a computer-generated list of random numbers (0, 1, 2, 3 and 4).

Group A followed the standard regimen consisting of a clear liquid diet for 12 h on the day before CE, followed by an overnight fast. Group B received a high volume regime consisting of a 50 mL/kg (up to 2 Lt/die) of polyethylene glycol (PEG) solution the evening before the examination, followed by an overnight fast. Group C (low volume regimen) received 25 mL/kg (up to 1 Lt/die) of PEG solution

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the evening before the examination, followed by an overnight fast. Group D received 20 mL (376 mg) of oral simethicone (Panamir, DMG, Italy) and 200 mL water 30 min before capsule ingestion, and group E received 25 mL/kg (up to 1 Lt/die) of PEG solution followed by an overnight fast plus 20 mL (376 mg) of oral simethicone and 200 mL water 30 min before capsule ingestion. For all patients, age, sex, body mass index, and indication for CE were recorded.

All CE examinations were performed with the Pillcam SB capsule endoscopy system (Given Imaging Co. Ltd., Yoqnem). All patients in the 5 groups ingested the capsule on morning of the examination day. In patients unable to swallow the capsule, the latter was released in the proximal duodenum with a paediatric videogastroscope (Olympus PCF Q180), in which the capsule had been loaded using a foreign body Roth Net (US Endoscopy, Mentor, OH). After swallowing the capsule, patients were allowed to drink and eat a light meal at 2 and 4 h later. The recorder was disconnected after expiration of the CE battery, and data were downloaded to a workstation. Two experienced reviewers (SO and GDN) blinded to the preparation and to the result of the other evaluation, analyzed each capsule study using Rapid Reader 5 software (Given Imaging Co. Ltd.). The primary outcome measure was the visibility of the mucosal surface at CE according to the five different regimens of preparation.

The image quality was evaluated only in cases in which the capsule reached the cecum within the examination period. There is not a standardized or validated scoring system for the quality of small-bowel cleanliness. The mucosal visibility was assessed as the percentage of visualized bowel surface area as follows: 1: <25%; 2: 25–49%; 3: 50–74%; 4: 75–89%; 5: >90% [9]. The small bowel record was divided into five segments by time, and the score for each segment was evaluated. Images from each segment were serially selected at 5-min intervals (1 frame/5 min), manually, by use of the RAPID system. If the capsule became stuck or remained in the same place for more than 5 min, those frames were only scored once and not repeated. Mean scores for each segment were obtained by summing the scores of all selected images and dividing the sum by the number of frames examined. The overall score for each patient was obtained by adding the scores for each individual segment. A higher score was taken as better image quality. The completion rate to the cecum was assessed based on the CE images.

Secondary outcome measures were the following: the number of positive findings and the overall diagnostic yield. A positive finding was defined as the presence of a visible finding, whether incidental or clinically relevant. A positive yield at CE was assumed if the visible finding was considered relevant to the indication for CE. Where appropriate, this was confirmed by further evaluation (repeated upper-GI or lower-GI endoscopy, single-balloon enteroscopy (SBE), laparotomy, or cross-sectional imaging). All patients were evaluated with a questionnaire, based on a numerical scale between 0 and 10 (with 10 being no burden at all and 0 indicating an intolerable procedure), about the impact of the bowel preparation and their level of satisfaction [10]. Interobserver agreement between two investigators (SO and GDN) in evaluating mucosal visibility was also calculated.

3. Statistical analysis

Patients were randomized by means of a list of three randomly generated numbers. Parametric results were compared by analysis of variance (ANOVA). Nonparametric data were compared with the Kruskal ± Wallis test. Group proportions were compared using the *c*2 test or Fisher's exact test where appropriate. Differences between groups and effects in time were analyzed by repeated-measures ANOVA with post-hoc Bonferroni tests. A *P* value below 0.05 was considered significant. Interobserver agreement was assessed by *k* statistics. Statistical analysis was performed with the SPSS program for Mac OSX.

4. Results

Of two hundred seven patients eligibly for the study, 204 were randomized and only 198 (53% male, mean age 13.3, range 7–18 years) were analyzed. Three were excluded because not meeting inclusion criteria, and the remaining six were eliminated because the capsule did not reach the cecum (Fig. 1). However, it was always excreted 24–48 h after ingestion. CE was performed for the analysis of suspected small-intestinal inflammatory bowel disease in 84 (42%) of patients, for obscure gastrointestinal bleeding in 65 (33%), and for other reasons (e.g. surveillance of polyposis syndromes, malabsorption, diarrhoea, etc.) in 49 (25%) (Table 1). No significant differences regarding sex, age, or indication for CE were found within the five groups.

The gastric transit time was 25 ± 10 min in group A, 27 ± 9 min in group B, 23 ± 7 in group C, 29 ± 11 in group C and 31 ± 13 min in group E (P = NS). The small-intestinal transit time was 185 ± 70 min in group A, 175 ± 90 min in group B, 183 ± 87 in group C, 193 ± 77 in group C and 181 ± 63 min in group E (P = NS). The cecum was visualized in 39 (95%), 40 (97%), 40 (97%), 40 (97%) and 39 (97%) patients in groups A, B, C, D and E, respectively (P = NS).

The scores related with the visualized bowel surface area were 14.1 ± 4.2, 18.9 ± 5.1, 17.8 ± 5.5, 14.9 ± 4.8 and 20.9 ± 4.6 in groups A, B, C, D and E, respectively ($P < 0.01$). The mean value of Group E was statistically significantly higher than that of all other groups ($P < 0.05$), whilst no other inter-group difference emerged from our analysis (Fig. 2). In the first two segments, no significant difference was found regarding the mean value of preparation score (P = NS), whilst the biggest differences are evident in three successive

Table 1
Patient characteristics, indications and diagnostic yield in the different study groups.

	Group A *N* = 39	Group B *N* = 40	Group C *N* = 40	Group D *N* = 40	Group E *N* = 40
	No prep	PEG 50	PEG 25	Simethicone	PEG + S
Age, years	13.3 ± 3.1	14.3 ± 2.7	13.9 ± 3.5	14.1 ± 3.3	13.5 ± 2.8
Male gender	19 (48.7%)	20 (50%)	22 (55%)	23 (57.5%)	21 (52.5%)
Indication *n* (%)					
IBD	17 (43%)	19 (48%)	15 (38%)	17 (43%)	16 (41%)
Obscure GI bleeding	13 (34%)	11 (28%)	15 (38%)	12 (31%)	14 (36%)
Other	9 (23%)	10 (24%)	10 (24%)	11 (28%)	9 (23%)
Diagnosis					
Definite	26 (67%)	28 (70%)	31 (77%)	28 (70%)	32 (81%)
Probable	7 (18%)	6 (15%)	4 (10%)	7 (17%)	3 (9%)
No diagnosis	6 (15%)	6 (15%)	5 (13%)	5 (13%)	4 (10%)

PEG, polyethylene glycol; S, simethicone; IBD, inflammatory bowel disease; GI, gastrointestinal.