Evaluation of Different Bowel Preparations for Small Bowel Capsule Endoscopy: A Prospective, Randomized, Controlled Study

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ABSTRACT

Background and Study Aims
To obtain an adequate view of the whole small intestine during capsule endoscopy (CE) a clear liquid diet and overnight fasting is recommended. However, intestinal content can hamper vision in spite of these measures. Our aim was to evaluate tolerance and degree of intestinal cleanliness during CE following three types of bowel preparation.

Patients and Methods
This was a prospective, multicenter, randomized, controlled study. Two-hundred ninety-one patients underwent one of the following preparations: 4 L of clear liquids (CL) (group A; 92 patients); 90 mL of aqueous sodium phosphate (group B; 89 patients); or 4 L of a polyethylene glycol electrolyte solution (group C; 92 patients). The degree of cleanliness of the small bowel was classified by blinded examiners according to four categories (excellent, good, fair or poor). The degree of patient satisfaction, gastric and small bowel transit times, and diagnostic yield were measured.
Results The degree of cleanliness did not differ significantly between the groups (P=0.496). Interobserver concordance was fair (k=0.38). No significant differences were detected between the diagnostic yields of the CE (P=0.601). Gastric transit time was 35.7 ± 3.7 min (group A), 46.1 ± 8.6 min (group B) and 34.6 ± 5.0 min (group C) (P=0.417). Small-intestinal transit time was 276.9 ± 10.7 min (group A), 249.7 ± 13.1 min (group B) and 245.6 ± 11.6 min (group C) (P=0.120). CL was the best tolerated preparation. Compliance with the bowel preparation regimen was lowest in group C (P=0.008).

Conclusions
A clear liquid diet and overnight fasting is sufficient to achieve an adequate level of cleanliness and is better tolerated by patients than other forms of preparation.

Keywords
Capsule endoscopy; Bowel preparation; Polyethylene glycol electrolyte solution; Aqueous sodium phosphate

Abbreviations
CE Capsule endoscopy; ASP Aqueous sodium phosphate; PEG Polyethylene glycol electrolyte solution; CL Clear liquids.

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INTRODUCTION

Capsule endoscopy (CE) is a widely applied tool for evaluating small bowel pathologies [1]. It was initially thought that a 12-h fast and a clear liquid diet for 24 h was effective preparation for CE. However, it soon became evident that the capsule entailed two problems: on the one hand, the percentage of incomplete examinations—up to 15% of all those performed—due to a prolonged gastric or intestinal transit time [1], and on the other hand, the relatively frequent presence of intestinal content, particularly in distal segments of the small intestine. For this reason, it was believed that cleaning the small intestine prior to examination would improve visibility during the endoscopy and, as a result, the diagnostic yield of the technique. Therefore, proposals were put forward based on preparations for other types of explorations, such as colonoscopies [2].

There is no consensus regarding the necessity of intestinal preparation for CE [3, 4]. Moreover, the effect of each type of preparation on intestinal transit time is unclear [5]. Thus, it would be beneficial to establish guidelines for improving the efficacy and tolerability of this technique.

The primary aim of the present study was to evaluate, in a prospective manner, the degree of cleanliness in the small intestine following three different forms of bowel preparation in patients referred for CE examination. Secondary aims were the influence of each type of preparation on diagnostic yield, transit time and procedure tolerability.

PATIENTS AND METHODS

Study Design

A prospective, multicenter, randomized, blind study was carried out to evaluate the degree of small intestine cleanliness and level of patient tolerance related with three types of bowel preparation for CE.

Between December 2004 and May 2005, 291 patients from nine Spanish hospitals were consecutively assessed as potential subjects for the study. The following exclusion criteria were established: concomitant severe hepatic, cardiovascular or renal disease; intestinal obstruction or gastrointestinal perforation confirmed or suspected; hypersensitivity to any of the components of the preparation; age under 18 years; and pregnancy. Eighteen patients were not explored due to the following reasons: refusal to undergo the preparation (two patients), erroneous inclusion in the study (one patient), and failure to show up for the procedure (15 patients). Two-hundred seventy-three patients were finally included in the data analysis and were randomized into three groups using an information-technology system: group A (n = 92, 33.7%) followed the standard regime, consisting of 4 L of clear liquids (CL); group B (n = 89, 32.6%) received two doses (90 mL) of aqueous sodium phosphate (ASP) and were recommended to drink 4 L of liquid; and group C (n = 92, 33.7%) received 4 L of a polyethylene glycol solution (PEG).

Capsule endoscopy was performed using the M2A Capsule System (Given Imaging Ltd., Yoqneam, Israel). Bowel preparation took place over the 24 h before the CE procedure was scheduled to take place and subjects fasted for 8 h prior to ingestion of the endoscopic capsule. Thereafter, patients were free to return home and continue with

their regular activities. Ingestion of clear fluids was permitted after 2.5 h and a small amount of solids could be taken after 4.5 h. Patients returned 8.5 h after ingestion of the capsule to have the data recorder removed, at which point they were asked to report any adverse events and to verify the excretion of the capsule in the stool.

In each centre, a single researcher was responsible for visualization of the CEs (AM, BG, EPC, IFU, JV, PM, SF, VP). All were blind to the group to which patients belonged. The global degree of cleanliness of the small intestine and the colon (usually the cecum and proximal colon) was evaluated according to the four categories shown in Table 1.

Gastric emptying time (GET) and small intestinal transit time (SITT) were recorded. GET was defined as the length of time the capsule remained in the stomach (i.e. the time between the first gastric image and the first duodenal image). SITT was defined as the period of time during which the capsule remained in the small bowel (i.e. the time between the first duodenal image and the first cecal image in patients in whom the capsule reached the cecum, and the time between the first duodenal image and the last small-intestinal image in patients in whom the capsule did not reach the cecum). Diagnosis of CE and the influence of each type of preparation on the diagnostic yield of the technique were analyzed.

Thirty-one of the 273 studies performed were selected at random in order to perform a concordance study. These were visualized by two of the researchers (JV and VP), who were blind to the result of the first visualization.

Patient Comfort

Tolerability of the preparation was assessed via a questionnaire and a visual analogical scale. Immediately before the procedure, a nurse questioned each patient about their level of satisfaction with the preparation. Patients were asked how it had affected their daily activity and nocturnal rest, and degree of compliance was analyzed with relation to the type of preparation.

Ethical Guidelines

The study protocol complied with the principles of the Declaration of Helsinki and was approved by our institution’s ethics committee. All patients signed an informed consent form at the time of enrolment.

Statistical Analysis

It was calculated that, in order to ensure a 5% type I error with a statistical power of 80%, each group would need to include 78 patients. We expected that 10% of the patients would not eventually be assessed, mainly due to the capsule not having reached the cecum. Continuous variables were compared by means of the Kruskal–Wallis’s test, and categorical variables were compared using the chi-square test. In order to detect differences between the three preparation groups and to analyze the secondary objectives, Snedecor’s F distribution was used for independent mea-sures (ANOVA with one factor) in the case of normally distributed continuous data and Kruskal–Wallis’s test was employed when requirements were non-parametric. Significance was accepted at a value of $P<0.05$. The Spearman rank correlation was used to quantify interobserver agreement. Statistical analysis was performed with the SPSS program, version 14.

RESULTS

Patient Data

Two-hundred seventy-three patients were analyzed over a 17-month period. Table 2 shows the characteristics of the patients included in each group. Significant differences were not detected between the three groups, except with respect to the percentage of bed-ridden patients, which was higher in group C (P=0.002). CE was recommended due to obscure gastrointestinal bleeding of unknown origin in 72.9% of the cases (27.8% overt and 45.1% occult) and because of suspected Crohn's disease in 10.3% of the patients (Table 3).

Quality of Case-Study Cleanliness

The percentage of patients in which the quality of the study was excellent was 7.6% in group A, 16.1% in group B and 13.3% in group C. The most frequent evaluation of the preparation was "good", with no differences being detected between the groups (Table 4). There was a trend towards a higher level of cleanliness in group B (ASP), but statistical significance was not reached. A fair concordance was found in the second visualization of 31 case studies (k = 0.38).

Gastric and Small-Intestinal Transit Time of the CE

Gastric transit time was 35.7 ± 3.7 min (mean ± SD) in group A, 46.1 ± 8.6 min in group B and 34.6 ± 5.0 min in group C (P=0.417). The small-intestinal transit time was 276.9 ± 10.7 min in group A, 249.7 ± 13.1 min in group B and 245.6 ± 11.6 min in group C (P=0.120). The cecum was visualized in 74, 68 and 75 patients in groups A, B and C, respectively (P = 0.507).

Diagnostic Yield of VCE

The CE revealed findings in 84% of the explorations conducted, and these findings were considered causes of the symptomatology in 68% of cases (Table 5). Angiectasia of the small intestine was the most frequent diagnosis (28.4%), followed by ulcer of the small intestine (6.6%) and lesions suggestive of Crohn's disease (5.9%). The result of the study was normal in 12.5% of cases. Significant differences were not detected with regard to the diagnosis established by the CE (P = 0.601).

Tolerability of the Procedure

The degree of inconvenience caused by each preparation was evaluated by a visual analog scale (mean ± SD) and was shown to be highest in group B (1.9 ± 0.1), followed by group C (1.5 ± 0.1) and group A (0.8 ± 0.1), in which the preparation was best tolerated (P\0.001) (Fig. 1). The preparation interfered with the patients' daily activity and nocturnal rest least in the liquid diet group (P=0.001). Compliance was lower in group C (PEG) than in group A (P=0.002) and group B (P=0.019), but was similar in the latter two groups (P=0.441).

DISCUSSION

This study is the first to compare, in a prospective, randomized and blind manner, three different preparations for cleaning the small bowel prior to performing a CE. Preliminary results have already been published by our group [6]. Although similar studies exist (Table 6), none of the three abovementioned preparations have been

compared in a randomized way, and have only been analysed in short series [5, 7, 8] or retrospectively [8]. A review of the related literature by Franchis et al. [3] highlights the fact that studies published about this subject are scarce and provide inconsistent results.

Previous reports have compared different preparations with fasting, but few have evaluated the effect of a liquid diet adhered to throughout the day prior to CE. The most recent reports indicate that preparation with laxatives does not provide any advantage over fasting. Viazis et al. [7] carried out a prospective study of 80 patients randomly administrated 2 L of a PEG versus CL on the day prior to CE. No effect on the gastric or intestinal transit of the CE was detected, though a higher level of cleanliness was observed in the patients who had received PEG, among whom there was a statistically significant improvement of the diagnostic yield. Niv et al. [8] published an analysis of the use of ASP in 46 versus 23 patients whose bowel preparation consisted solely of overnight fasting. The authors recommended preparation with ASP after observing a higher level of cleanliness. However, it must be noted that the study in question was retrospective and based on a relatively small series of patients whose results did not justify the general application of said preparation. Similar results were obtained by Dai et al. [5], who compared a 4-L PEG solution versus a 12-h period of fasting.

The combination of several products has also been evaluated. Although ASP and bisacodyl (stimulant laxative) are reported to induce an increase of luminal fluid in the small bowel (documented in colon preparation), their coadministration has not proven to be effective as a preparation for CE [9]. Nevertheless, a combination of simethicone and PEG does appear to improve visibility of the small intestine [10]. Simethicone was not used in this study.

Ben-Soussan et al. [11] failed to observe a difference between the results achieved with a preparation of 2 L of PEG solution versus 12-h fasting. Indeed, they reported that the former approach increased the time of gastric emptying, which does not favor an effective small bowel examination.

Recently, Lapalus et al. [12] have evaluated the effect of bowel preparation with ASP. In a randomized trial of 127 patients requiring CE due to obscure gastrointestinal bleeding, no difference was detected in the quality of the bowel preparation between those administered ASP and those who simply fasted for 8 h. Likewise, no differences were found in gastric transit time, small-bowel transit time or detection of lesions.
Equally, our study does not demonstrate differences between the degree of cleanliness achieved with the three preparations employed. The quality of the preparation was considered “good”in the majority of patients in all three groups. The good results obtained in group A could be related with the consumption of a large amount of clear liquids (4 L) over the 24 h prior to the capsule endoscopy. Patients prepared with ASP were also recommended to drink the same amount of liquid (4 L) in order to obtain a good level of cleanliness and prevent the nephotoxicity of this product. Nevertheless, a trend towards a higher number of excellent results (16% as opposed to 7.6 and 13.3%) was observed in the group prepared with ASP, though this difference did not reach statistical significance. This suggests that preparation of distal sections of the intestine (ileum and cecum) with ASP is the most effective of the three methods employed. It is possible that future studies with longer series, or an evaluation of different degrees of cleanliness will tilt the balance in favor of this preparation.

We observed no differences in the diagnostic capacity of CE in any of the three preparations. In the same way, Van Tuyl et al. [13] compared a clear liquid diet with 1 and 2 L PEG in 90 patients. The PEG solution allowed a significantly better mucosal visualization, although the diagnostic yield was not significantly modified.

We must not ignore the disadvantages of each of the different types of intestinal preparation for CE. Postgate et al. [14] have reported that bowel purgatives and prokinetics do not improve the quality of vision during CE and reduce patient compliance. The results of our study demonstrate a liquid diet to provide good results and to be the best tolerated of the three preparations evaluated. Some studies have demonstrated that bowel preparation has a negative influence on gastric emptying and intestinal transit time, but there is a lack of uniformity among their results. In fact, there is also evidence that bowel preparation has no effect on these parameters [7, 15, 16]. We did not observe differences in gastric or intestinal transit after any of the three preparations. Visualization of the cecum was achieved in 70% of our subjects. Contrary to the reports of other authors, the cecum was visualized in more patients receiving the PEG preparation, which contained a higher percentage of bed-ridden patients, than in those in the remaining two groups.

There is no universally accepted scale that allows us to accurately quantify and compare levels of intestinal cleanliness. This makes any comparison of results difficult. Brotz et al. [17] described and validated three scales for grading small bowel cleansing prior to CE (quantitative index and qualitative evaluation). They reported a strong association between all three scales, though intraobserver reliability was moderate. The scale used in the present study is based on a global qualitative evaluation with four degrees of classification. This permits a considerable level of simplicity and a fair concordance.

In conclusion, based on the present results, we affirm that adherence to a liquid diet throughout the day prior to CE, in combination with fasting, constitutes an effective preparation for achieving a good level of cleanliness in the small intestine. Furthermore, this procedure is well tolerated and, thus, more accepted by the patient. In this sense, our findings confirm the benefits of a liquid diet as opposed to other types of preparation. However, if in the future a product is developed that achieves an adequate level of cleanliness in both the small intestine and colon and is also well tolerated by the patient, the recommended protocol for carrying out these diagnostic tests will no doubt be modified, not only in the case of SB capsule endoscopies, but also in that of colon capsule endoscopies and even colonoscopies, in which bowel preparation continues to be a stumbling block.

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Table 1. Score used to evaluate the level of intestinal cleanliness	
Grading	**Description**
Poor	Intestinal content impeding evaluation
Fair	Liquid or solid intestinal content allowing evaluation
Good	No intestinal content or some content in the terminal ileum and/or cecum
Excellent	No intestinal content in any part of the small intestinal tract (including ileum) or the cecum

Table 2. Characteristics of the patients included in each group				
Groups	**Characteristics**			
	N	**Mean age ± SD (years)**	**Male/female**	**Bed-ridden (%)**
Group A	92	57.8 ± 2.02	33/59	12 (13.0%)
Group B	89	55.6 ± 1.9	37/52	6 (6.7%)
Group C	92	57.4 ± 1.8	47/45	23 (25%)
P value		0.69	0.109	0.002

Table 3. Indication for capsule endoscopy (CE)		
Indication	**Frequency**	**Percentage (%)**
Obscure gastrointestinal bleeding (occult)	123	45,1
Obscure gastrointestinal bleeding (overt)	76	27,8
Suspicion of Crohn’s disease	28	10,3
Surveillance of polyposis syndromes	10	3,7
Chronic abdominal pain	8	2,9
Diarrhea	6	2,2
Malabsorption	6	2,2
Suspicion of small-bowel tumors	4	1,5
Other	11	4,0

Table 4. Quality of case-study cleanliness			
Rating	**Group A**	**Group B**	**Group C**
Excellent	7 (7.6%)	15 (16.8%)	12 (13.0 %)
Good	59 (64.1%)	53 (59.5%)	60 (65.2 %)
Fair	23 (25.0%)	16 (17.9%)	15 (16.3 %)
Poor	3 (3.3%)	5 (5.6%)	5 (5.4 %)

Table 5. Capsule endoscopy diagnosis	
Capsule endoscopy diagnosis	**Percentage (%)**
Small bowel angiectasia	28.4
Small bowel ulcer	6.6
Suggestive of Crohn’s disease	5.9
Small bowel polyp	5.5
Small bowel angioma	4.4
Blood in the small bowel	3.3
Stenosis with ulceration	2.8
Small bowel submucosal tumor	2.6
Small bowel villous atrophy	2.6
Active bleeding in jejunum	2.2
Chronic stenosis	1.1
Gastritis	1.1
Duodenitis	0.7
Active colonic bleeding	0.4
Meckel’s diverticulum	0.4
Total	68

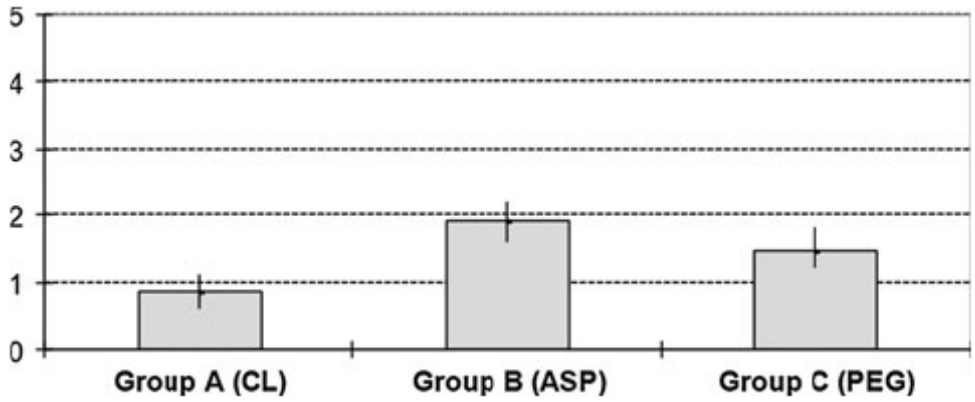

Figure 1. Degree of inconvenience of the preparation (mean, IC95). CL clear liquids, ASP aqueous sodium phosphate, PEG polyethylene glycol.