Annals of Gastroenterology (2016) **29,** 196-200

Bowel preparation in "real-life" small bowel capsule endoscopy: a two-center experience

Amir Klein[a], Marianna Dashkovsky[a], Ian Gralnek[a], Ravit Peled[a], Yehuda Chowers[a], Iyad Khamaysi[a], Ofir Har-Noy[b], Idan Levi[b], Moshe Nadler[b], Rami Eliakim[b], Uri Kopylov[b]

Rambam Health Care Campus, Rappaport Family Faculty of Medicine Technion-Israel Institute of Thechnology, Haifa; Chaim Sheba Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Abstract

Background Video capsule endoscopy (VCE) is an established diagnostic tool for the investigation of small bowel (SB) pathology. Bowel preparation prior to VCE may improve visualization, transit time, and diagnostic yield. We aimed to evaluate the "real-life" experience comparing two different preparation protocols in patients undergoing SB VCE.

Methods We performed a retrospective analysis of prospectively collected data from SB VCE procedures, performed in two tertiary care medical centers in Israel. VCE procedures performed at "Sheba Medical Center" used a 2-L polyethylene glycol (PEG) bowel preparation (n=360) while VCEs performed at "Rambam Health Care campus" used a clear liquid diet plus 12-h fast protocol (n=500). A dichotomous preparation scale (adequate, inadequate) was used to classify cleansing quality. Data collection included patient and procedural details. The proportion of VCE procedures with adequate bowel preparation and the overall positive SB findings in the two different bowel preparation protocols were evaluated.

Results SB completion rates were higher in the PEG protocol (96% vs. 83%, P<0.001) and SB passage time was significantly faster in the PEG protocol (mean 217±73 vs. 238±77 min, P<0.001). Bowel preparation quality was similar between groups (8% vs. 7% inadequate preparation, P=0.591). Overall positive SB findings were similar between the two groups (57% clear liquid fasting only vs. 51% PEG protocol, P=0.119).

Conclusion In this large cohort, a 2-L PEG protocol had similar preparation quality and diagnostic yield compared with clear liquid fasting.

Keywords Capsule endoscopy, diagnostic yield, bowel preparation, polyethylene glycol

Ann Gastroenterol 2016; 29 (2): 196-200

Departments of [a]Gastroenterology, Rambam Health Care Campus, Rappaport Family Faculty of Medicine Technion-Israel Institute of Technology, Haifa (Amir Klein, Marianna Dashkovsky, Ian Gralnek, Ravit Peled, Yehuda Chowers, Iyad Khamaysi); [b]Gastroenterology, Chaim Sheba Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv (Ofir Har-Noy, Idan Levi, Moshe Nadler, Rami Eliakim, Uri Kopylov), Israel

Conflict of Interest: Our study was financed by the departments of Gastroenterology at the Rambam Health Care Campus and the Sheba Medical Center. Ian Gralnek is a consultant for GIVEN imaging and received research funding from GIVEN imaging. Rami Eliakim is a consultant for GIVEN imaging. Ravit Peled is employed by GIVEN imaging. Ravit Peled is an employee of Given Imaging.

Correspondence to: Uri Kopylov, Department of Gastroenterology, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel, Tel.: +97 235302660, Fax: +97 235303160, e-mail: ukopylov@gmail.com

Received 6 December 2016; accepted 22 December 2015

DOI: http://dx.doi.org/10.20524/aog.2016.0012

Introduction

During the past decade, video capsule endoscopy (VCE) has emerged as a clinically useful and patient-friendly diagnostic tool for the investigation of obscure gastrointestinal bleeding/iron deficiency anemia, suspected small bowel (SB) Crohn's disease, and SB polyposis syndromes/tumors. Overall, VCE provides a definitive diagnosis in approximately 50% of cases [1-7]. Furthermore, VCE has also been shown to have a superior diagnostic yield (DY) compared to the other imaging modalities for the diagnosis of SB lesions [8-16].

The DY of VCE can be impaired by the presence of turbid intestinal contents and/or air bubbles. Bowel preparation performed prior to VCE may improve visualization and lead to a more successful VCE examination. Bowel preparation recommended by the capsule manufacturers is an 8-12-h clear liquids diet only. Some studies have found that the use of purgatives prior to capsule ingestion may result in higher quality images and DY [17-22], whereas others have

failed to confirm these observations [23-26]. Thus, there is a lack of consensus regarding the role of bowel preparation prior to SB VCE. Among the polyethylene glycol (PEG)-based laxatives, a low-volume preparation has been shown to be at least equally effective when compared to high-volume regimens [21,27,28]. Therefore, a 2-L PEG-based preparation, administered the day before the VCE procedure, is an accepted practice. The aim of this study was to evaluate the effectiveness of two alternative bowel preparations in patients undergoing SB VCE.

Materials and methods

We retrospectively analyzed prospectively collected data from n=860 SB VCE procedures performed in two tertiary care medical centers in Israel (Rambam Health Care Campus, Haifa and Sheba Medical Center, Tel Hashomer). Data collection included patient demographics, VCE indication, capsule technical information including transition times between bowel segments, bowel preparation type and quality of preparation, and findings of the VCE examination.

We included all adult patients (age ≥18) referred to our centers for VCE between January 1, 2001 and December 31, 2012, for whom we had knowledge of the bowel cleansing protocol used. All VCE procedures, in both centers throughout the study period, were performed using the GIVEN Imaging video capsule (SB1 or SB2 capsule platforms) and RAPID VCE software (GIVEN Imaging/COVIDIEN Ltd).

VCE procedures performed at Sheba Medical Center used a 2-L PEG-based bowel preparation given the evening before the VCE procedure. The VCE procedures performed at Rambam Health Care Campus used only a clear liquid diet the day prior to VCE plus a 12-h fasting protocol prior to VCE ingestion. A dichotomous preparation scale (adequate or inadequate) was used to grade the quality of SB cleansing as designated by the reader of the study. In both centers, it was standard practice to explicitly document inadequate preparation quality in the VCE report. If no such documentation was made, or no recommendation for repeat VCE was made, bowel preparation quality was deemed to be adequate.

VCE reports routinely included documentation of anatomical landmarks identified such as "first gastric image", "first duodenal image" and "first cecal image". The gastric passage time was calculated as the elapsed time between the first gastric image and the first duodenal image. SB transit time was calculated as the elapsed time from the first duodenal image to the first cecal image. SB completion was defined as the capsule seen in the cecum.

At Rambam Health Care Campus, termination of a VCE procedure is based on the interpretation of the RAPID VIEWER after 6-7 h. At Sheba Medical Center, patients routinely continue the VCE procedure until the capsule's battery life is exhausted. The study was approved by the institutional review board (IRB code 0084-13-RMB). Data was analyzed as groups and individual patient consent was not sought as per IRB approval.

Statistical analysis

This was a retrospective study, therefore no statistical power calculations were performed *a priori*. Summary statistics (arithmetic mean, standard deviation and frequency) are presented for quantitative variables. Pearson's χ^2 test was used to evaluate differences between the two bowel preparation groups (i.e., 2 L PEG vs. clear liquid fasting only) for the detection of lesions in the SB. All applied tests were two-tailed with a significance assigned at 0.05. We analyzed the data using SPSS version 21.

Results

Eight hundred and sixty VCE procedures were evaluated (Rambam Health Care Campus n=500 and Sheba Medical Center n=360). Patient demographics, including gender and weight were similar between the two centers (P=0.40, P=0.80 respectively), however the mean patient age of the patients receiving PEG preparation was significantly older (52.6 years ± 19 vs. 48.4 years ±21 P=0.018), (Table 1). Indications for VCE included obscure gastrointestinal bleeding (14%), iron deficiency anemia (40%), and suspected Crohn's disease (40%). Other indications (weight loss, abdominal pain, diarrhea, refractory celiac disease, polyposis syndromes) accounted for 6% of referrals. There was significant heterogeneity between the centers in the distribution of the various indications within each study site (Table 2).

Gastric passage time was not significantly different between the two protocols (mean 25.0±21 min for clear liquid fasting vs. 22.7±21 min for PEG, P=0.077). However, SB passage time was significantly faster for the cohort receiving PEG (217±73 min vs. 238±77 min P<0.001). SB completion rates were also significantly higher in the PEG-receiving group (96% vs. 83%, P<0.001). The percentage of adequate SB preparation

Table 1 Clinical characteristics of patients that received a clear liquid fasting and PEG-based preparation for capsule endoscopy

Preparation	Mean	Standard deviation	P-value
Age			
2 L PEG	52.62	19.04	0.003
Clear liquid fasting	48.45	21.53	
Weight			
2 L PEG	74.63	17.76	0.819
Clear liquid fasting	75.41	23.11	
Height			
2 L PEG	167.61	12.38	0.031
Clear liquid fasting	172.82	9.59	
Male Gender			
2 L PEG	49%		0.409
Clear liquid fasting	52%		

PEG, polyethylene glycol

did not differ significantly between the groups (92% vs. 93% adequate cleansing in the clear liquid fasting and PEG groups respectively, (P=0.59). Finally, no significant difference in overall positive SB findings between the two preparation protocols was observed (57% clear liquid fasting only vs. 51% PEG, P=0.12), (Table 3).

Capsule endoscopy was performed for suspected Crohn's disease in 288/860, 33.5% of the patients. In these patients, the prevalence of relevant diagnostic findings (mucosal ulcers/erosions) was higher in patients prepared with clear diet (27.4% vs. 13.2%, P=0.03).

Discussion

In this retrospective study, we evaluated "real-life" experience with two different SB preparation protocols. We found no significant difference in the gastric passage time between the two protocols; however, we found a significantly shorter SB passage time and a higher SB completion rate in the cohort who received PEG. From our clinical experience, incomplete procedures are usually due to premature disconnection of the VCE recorder when content seen on the RAPID VIEWER significantly obscures the lumen and is mistaken for colonic content. In our study, the observed differences in capsule completion rates between the two centers are most probably attributable to the difference in the definition of study completion between the two centers, suggesting that the use of the rapid viewer as the lone standard for determining SB completion may not be appropriate. Importantly, with the introduction of new generation capsules such as SBIII with a battery time of approximately 12 h, the rate of capsule completion increased significantly. Theoretically, differences in completion rates may influence DY. In this study, the completion rate was higher for the PEG protocol, but this did not translate into a higher DY. Incomplete procedures in the clear liquid fasting protocol were due to "colon-like" luminal content seen on the RAPID viewer. In such cases, where adequate mucosal visibility cannot be obtained, the impact of early disconnection on DY is most likely marginal.

There were no significant differences between the two preparation protocols in regards to overall SB capsule findings (57% clear liquid fasting only vs. 51% PEG, P=0.12). In the 2-L PEG cleansing protocol, 93% of the procedures were considered to have had adequate preparation compared with 92% of the procedures in the clear liquid fasting only protocol (P=0.59). In a meta-analysis by Rokkas *et al* [18], data from 476 patients directly comparing different preparation protocols was analyzed. A significant benefit was demonstrated for those patients who received purgatives (for DY - OR 1.81, 95%CI 1.25-2.63, P=0.002) and for SB visualization quality (SBVQ) - OR 2.113, 95%CI 1.25-3.57, P=0.005). An additional meta-analysis by Belsey *et al* [21] evaluating 8 studies with 850 patients, concluded that compared with fasting alone, the use of any form of bowel preparation prior to VCE ingestion yielded significantly better visibility and DYs, (OR 2.31, 95%CI 1.46-3.63, P<0.0001 and OR 1.88, 95%CI 1.24-2.84, P<0.023 respectively). When per-treatment, *post-hoc* analysis was performed, only the PEG-based regimens demonstrated a benefit in DY (OR 3.11, 95%CI 1.96-4.94, P<0.0001). In 2009, the European Society for Gastrointestinal Endoscopy (ESGE) issued clinical recommendations on the use of VCE to investigate SB, esophageal and colonic diseases [28]. These guidelines state that a purgative bowel preparation given prior to VCE ingestion enhances the DY of SB VCE, but does not affect the SB capsule completion rate. However, there is no consensus or specific recommendation on the most appropriate type of bowel preparation. Finally, Vliegen *et al* [29], concluded that the use of a PEG-based regimen as preparation for VCE is recommended as first-line (level of evidence - Grade A). Our study did not employ a validated cleansing score for VCE. However, currently such score does not exist. Park *et al* [23] used a four-step scale based on the proportion of SB mucosa visualized and the extent of obscured visualization due to bubbles and turbid bowel content. Other studies [17,25,26,30] used a semi-objective two-step score based on the percentage of obscured SB mucosa. In a study by Van Tuyl *et al* [27], SB visualization of less than 75% was considered poor whereas visualization of more than 75% was considered good. In a meta-analysis by Rokkas *et al* [18], a significant heterogeneity in the visualization scores was demonstrated between the studies evaluated. Finally, a recent consensus guideline [29] concluded that validated scales for quality of cleansing are not yet available. Instead, we use a "real-life" practical definition on the assessment of the preparation appropriateness by the study reader.

Our study has additional limitations. As described before, our two populations were heterogeneous and differed in several baseline characteristics such as mean age and distribution of the various indications for VCE within the cohort. While this undoubtedly presents a bias in this study, we believe that the

Table 2 Indications for capsule endoscopy stratified by preparation regimens

Preparation	Indication (%)				P-value
	Anemia	Bleeding	CD	Other	
2 L PEG	65	7	24	5	<0.0001
Clear liquid fasting	30	17	46	7	

PEG, polyethylene glycol; CD, Crohn's disease

Table 3 Procedure characteristics and outcomes stratified by preparation regimen

	Clear liquid fasting	2-L PEG	P
Mean gastric passage time (min)	25±21	22.7±21	0.077
Mean small bowel passage time (min)	238±77	217±73	0.001
Completion rate (%)	83	96	<0.001
Adequate cleansing (%)	92	93	0.591
Positive findings (%)	57	51	0.119

PEG, polyethylene glycol

clinical significance of these differences are minor and the size of the cohort enables us to draw conclusions regarding the primary study endpoint, which was to assess whether in a real-life setting, bowel preparation type influences bowel visualization and VCE DY.

We did not have access to the detailed patient files and some of the indications listed can in fact be generalized into broader categories; e.g., a patient referred for chronic diarrhea and weight loss can also be regarded as a "suspected Crohn's disease" indication. In addition, some of the patients had more than one indication specified; e.g., anemia and diarrhea, which can both be grouped into the "suspected Crohn's disease" indication or be viewed as two separate indications possibly stemming from two different pathological entities. This made the categorization process somewhat variable. However, we are not aware of any published literature suggesting that VCE procedure indication may influence bowel preparation, DY or transit time and therefore we believe that this observed heterogeneity between the two cohorts should not have interfered with the measured outcomes. Interestingly, the percentage of positive findings was lower in patients receiving PEG preparation if the indication for the test was suspected Crohn's disease. We do not have a good explanation for this result, however, it may further emphasize the low practical diagnostic value of PEG-based preparation that did not appear to have any positive impact on the DY in our study.

In conclusion, we found no significant difference in overall DYs and quality of bowel preparation. The results of this study reflect 10 years of "real-life" experience with this unique technology, which may often be more generalizable than the data acquired during clinical trials, hence its importance. More prospective data is needed.

Summary Box

What is already known:

- Video capsule endoscopy (VCE) is a prime diagnostic modality for small bowel pathologies
- Bowel preparation improves VCE visibility
- The impact of polyethylene glycol (PEG)-based bowel preparation on the diagnostic yield is still debatable

What the new findings are:

- In this large retrospective cohort, PEG-based preparation was not associated with a superior diagnostic yield compared with overnight fasting and clear fluids
- Bowel preparation quality was similar between the groups
- No clinical benefit of PEG-based preparation in VCE was demonstrated

References

1. Scapa E, Jacob H, Lewkowicz S, et al. Initial experience of wireless-capsule endoscopy for evaluating occult gastrointestinal bleeding and suspected small bowel pathology. *Am J Gastroenterol* 2002;**97**:2776-2779.
2. Lewis BS, Swain P. Capsule endoscopy in the evaluation of patients with suspected small intestinal bleeding: Results of a pilot study. *Gastrointest Endosc* 2002;**56**:349-353.
3. Fireman Z, Mahajna E, Broide E, et al. Diagnosing small bowel Crohn's disease with wireless capsule endoscopy. *Gut* 2003;**52**:390-392.
4. Urbain D, De Looze D, Demedts I, et al. Video capsule endoscopy in small-bowel malignancy: a multicenter Belgian study. *Endoscopy* 2006;**38**:408-411.
5. Rondonotti E, Spada C, Cave D, et al. Video capsule enteroscopy in the diagnosis of celiac disease: a multicenter study. *Am J Gastroenterol* 2007;**102**:1624-1631.
6. Rondonotti E, Pennazio M, Toth E, et al. Small-bowel neoplasms in patients undergoing video capsule endoscopy: a multicenter European study. *Endoscopy* 2008;**40**:488-495.
7. Koulaouzidis A, Rondonotti E, Karargyris A. Small-bowel capsule endoscopy: a ten-point contemporary review. *World J Gastroenterol* 2013;**19**:3726-3746.
8. Triester SL, Leighton JA, Leontiadis GI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with obscure gastrointestinal bleeding. *Am J Gastroenterol* 2005;**100**:2407-2418.
9. Saurin JC, Delvaux M, Gaudin JL, et al. Diagnostic value of endoscopic capsule in patients with obscure digestive bleeding: blinded comparison with video push-enteroscopy. *Endoscopy* 2003;**35**:576-584.
10. Saperas E, Dot J, Videla S, et al. Capsule endoscopy versus computed tomographic or standard angiography for the diagnosis of obscure gastrointestinal bleeding. *Am J Gastroenterol* 2007;**102**:731-737.
11. Ell C, Remke S, May A, Helou L, Henrich R, Mayer G. The first prospective controlled trial comparing wireless capsule endoscopy with push enteroscopy in chronic gastrointestinal bleeding. *Endoscopy* 2002;**34**:685-689.
12. Triester SL, Leighton JA, Leontiadis GI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. *Am J Gastroenterol* 2006;**101**:954-964.
13. Eliakim R, Fischer D, Suissa A, et al. Wireless capsule video endoscopy is a superior diagnostic tool in comparison to barium follow-through and computerized tomography in patients with suspected Crohn's disease. *Eur J Gastroenterol Hepatol* 2003;**15**:363-367.
14. Costamagna G, Shah SK, Riccioni ME, et al. A prospective trial comparing small bowel radiographs and video capsule endoscopy for suspected small bowel disease. *Gastroenterology* 2002;**123**:999-1005.
15. Caspari R, von Falkenhausen M, Krautmacher C, Schild H, Heller J, Sauerbruch T. Comparison of capsule endoscopy and magnetic resonance imaging for the detection of polyps of the small intestine in patients with familial adenomatous polyposis or with Peutz-Jeghers' syndrome. *Endoscopy* 2004;**36**:1054-1059.
16. Mata A, Llach J, Castells A, et al. A prospective trial comparing wireless capsule endoscopy and barium contrast series for small-bowel surveillance in hereditary GI polyposis syndromes. *Gastrointest Endosc* 2005;**61**:721-725.
17. Viazis N, Sgouros S, Papaxoinis K, et al. Bowel preparation increases the diagnostic yield of capsule endoscopy: a prospective, randomized, controlled study. *Gastrointest Endosc* 2004;**60**:534-538.
18. Rokkas T, Papaxoinis K, Triantafyllou K, Pistiolas D, Ladas SD.

Does purgative preparation influence the diagnostic yield of small bowel video capsule endoscopy?: A meta-analysis. *Am J Gastroenterol* 2009;**104**:219-227.
19. Niv Y. Efficiency of bowel preparation for capsule endoscopy examination: a meta-analysis. *World J Gastroenterol* 2008;**14**:1313-1317.
20. Kotwal VVS, Attar BBM, Gupta S, Agarwal R. Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. *Eur J Gastroenterol* 2014;**26**:137-145.
21. Belsey J, Crosta C, Epstein O, et al. Meta-analysis: efficacy of small bowel preparation for small bowel video capsule endoscopy. *Curr Med Res Opin* 2012;**28**:1883-1890.
22. Wi JH, Moon JS, Choi MG, et al. Bowel preparation for capsule endoscopy: a prospective randomized multicenter study. *Gut Liver* 2009;**3**:180-185.
23. Park SC, Keum B, Seo YS, et al. Effect of bowel preparation with polyethylene glycol on quality of capsule endoscopy. *Dig Dis Sci* 2011;**56:**1769-1775.
24. Ben-Soussan E, Savoye G, Antonietti M, Ramirez S, Ducrotté P, Lerebours E. Is a 2-liter PEG preparation useful before capsule endoscopy? *J Clin Gastroenterol* 2005;**39**:381-384.
25. Pons Beltrán V, González Suárez B, González Asanza C, et al. Evaluation of different bowel preparations for small bowel capsule endoscopy: a prospective, randomized, controlled study. *Dig Dis Sci* 2011;**56**:2900-2905.
26. Postgate A, Tekkis P, Patterson N, Fitzpatrick A, Bassett P, Fraser C. Are bowel purgatives and prokinetics useful for small-bowel capsule endoscopy? A prospective randomized controlled study. *Gastrointest Endosc* 2009;**69**:1120-1128.
27. Tuyl SAC Van, Ouden H Den, Stolk MFJ, Kuipers EJ. Optimal preparation for video capsule endoscopy : a prospective, randomized, single – blind study. *Endoscopy* 2007;**39**:1037-1040.
28. Ladas SD, Triantafyllou K, Spada C, et al. European Society of Gastrointestinal Endoscopy (ESGE): recommendations (2009) on clinical use of video capsule endoscopy to investigate small-bowel, esophageal and colonic diseases. *Endoscopy* 2010;**42**:220-227.
29. Mathus-Vliegen E, Pellisé M, Heresbach D, et al. Consensus guidelines for the use of bowel preparation prior to colonic diagnostic procedures: colonoscopy and small bowel video capsule endoscopy. *Curr Med Res Opin* 2013;**29**:931-945.
30. Nouda S, Morita E, Murano M, et al. Usefulness of polyethylene glycol solution with dimethylpolysiloxanes for bowel preparation before capsule endoscopy. *J Gastroenterol Hepatol* 2010;**25**:70-74.