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Finding the solution for incomplete small bowel capsule endoscopy

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Author contributions: Cotter J developed and coordinated the study, drafted and critically revised the manuscript and approved the final version to be submitted; Dias de Castro F reviewed the capsule endoscopy videos, performed data analysis and literature research and drafted the manuscript; Magalhães J participated in the design of the study and statistical analysis; Moreira MJ and Rosa B revised the manuscript and reviewed the capsule endoscopy videos; all the authors read and approved the final manuscript.

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Abstract

AIM: To evaluate whether the use of real time viewer (RTV) and administration of domperidone to patients with delayed gastric passage of the capsule could reduce the rate of incomplete examinations (IE) and improve the diagnostic yield of small bowel capsule endoscopy (SBCE).

METHODS: Prospective single center interventional study, from June 2012 to February 2013. Capsule location was systematically checked one hour after ingestion using RTV. If it remained in the stomach, the patient received 10 mg domperidone per os and the location of the capsule was rechecked after 30 min. If the capsule remained in the stomach a second dose of 10 mg of domperidone was administered orally. After another 30 min the position was rechecked and if the capsule remained in the stomach, it was passed into the duodenum by upper gastrointestinal (GI) endoscopy. The rate of IE and diagnostic yield of SBCE were compared with those of examinations performed before the use of RTV or domperidone in our Department (control group, January 2009 - May 2012).

RESULTS: Both groups were similar regarding age, sex, indication, inpatient status and surgical history. The control group included 307 patients, with 48 (15.6%) IE. The RTV group included 82 patients, with 3 (3.7%) IE, P = 0.003. In the control group, average gastric time was significantly longer in patients with IE than in patients with complete examination of the small bowel (77 min vs 26 min, P = 0.003). In the RTV group, the capsule remained in the stomach one hour after ingestion in 14/82 patients (17.0%) vs 48/307 (15.6%) in the control group, P = 0.736. Domperidone did not significantly affect small bowel transit time (260 min vs 297 min, P = 0.229). The capsule detected positive findings in 39% of patients in the control group and 49% in the RTV group (P = 0.081).

CONCLUSION: The use of RTV and selective administration of domperidone to patients with delayed gastric passage of the capsule significantly reduces incomplete examinations, with no effect on small bowel transit time or diagnostic yield.

Key words: Small bowel capsule endoscopy; Prokinetic drugs; Domperidone; Incomplete examination

Core tip: Incomplete small bowel capsule endoscopy (SBCE) is an important limitation of the technique and may occur in up to 20% of patients. Delayed gastric passage of the capsule is a major factor leading to incomplete SBCE. Selective administration of oral dom-
peridone to patients with delayed gastric passage of the capsule assessed with the real time viewer (RTV) effectively reduces the rate of incomplete SBCE. The administration of domperidone does not influence small bowel transit time of the capsule. There is an overall trend towards higher diagnostic yield of SBCE when domperidone is selectively administered. The use of the RTV should be adopted systematically in patients undergoing small bowel capsule endoscopy.


INTRODUCTION

Small bowel capsule endoscopy (SBCE) was introduced in clinical practice in 2001, and it proved to be a valuable non-invasive technique to examine the small bowel[9]. SBCE may be useful in a wide range of clinical settings, such as obscure gastrointestinal (GI) bleeding[2], suspected and known Crohn’s disease (CD)[3-5], celiac disease[6] and polyposis syndromes[7], with a higher diagnostic yield when compared to conventional diagnostic techniques[2,4,8-11]. An important limitation of SBCE is the possibility of incomplete examination of the small bowel, which occurs when the capsule does not reach the cecum within the recording time of approximately 9 h. The rate of IE is approximately 20% to 30% in most studies[12,13]. In such cases, the value of SBCE is limited by the fact that it may miss lesions located in the distal segments of the small bowel, eventually leading to the need for further examinations and increased costs[14]. Retrospective studies identified some factors that may be associated with incomplete small-bowel SBCE examination, such as inpatient status[15], previous abdominal surgery[16] and prolonged gastric transit time (GTT)[17], while the effect of age or medical conditions such as diabetes mellitus remains controversial[18]. Currently, there is no consensus regarding the use of prokinetic drugs in SBCE to reduce the rate of IE with SBCE[17]. In theory, prokinetics might be useful by improving gastric emptying, but their routine use in patients submitted to SBCE is not widely established[17]. Randomized prospective studies failed to demonstrate an improvement in SBCE completion rates with the use of metoclopramide, administered before the procedure[18,19]. One of the recent advances in the field of SBCE is the availability of a portable external viewer for direct monitoring of the images received during the procedure. The new Given® Data Recorder (DR3) with the real time viewer (RTV) enables real-time viewing during SBCE procedure (Figure 1). The European Society of Gastrointestinal Endoscopy (ESGE) recommended that patients at increased risk for IE might benefit from the use of the RTV peri-procedurally, with subsequent endoscopic placement of the capsule in the duodenum when indicated[20]. The aim of our study was to assess whether the prokinetic agent domperidone, in association with the RTV, could reduce the rate of IE and improve the diagnostic yield of SBCE.

MATERIALS AND METHODS

We conducted a single center prospective interventional study, comparing the use of domperidone in association with RTV in consecutive patients undergoing SBCE from June 2012 to February 2013 (RTV group) vs a control group of patients who had been submitted to SBCE following the standard procedure with no use of RTV or domperidone, from January 2009 to May 2012, in our Department. The RTV images were viewed by gastroenterologists with a large experience in SBCE to check the capsule position during the procedure. The RTV was used to confirm the passage of the capsule to the small-bowel one hour after ingestion. If the capsule remained in the stomach, 10 mg of domperidone were administered p.o. and the location of the capsule was rechecked after 30 min. if it still remained in the stomach, an additional dose of 10 mg of domperidone was administered orally and after another 30 min the location of the capsule was rechecked; then if still in the stomach the capsule was placed directly in the duodenum by upper endoscopy using a basket. All patients followed a 24 h clear liquid diet and 12 h fasting prior to SBCE (PillCam® SB2, Given® Imaging Ltd. Yoqneam, Israel), and were advised not to eat for 4 h after swallowing the capsule. No oral purge was administered. Patients with obstructive symptoms, known small bowel strictures and/or in whom some bowel purge or prokinetics were used did not enter the study. One experienced gastroenterologist, with more than 100 SBCE procedures, reviewed SBCE images using RAPID Reader® (Given® Diagnostic Imaging System, Given® Imaging). The completion rate was defined as the frequency of SBCE reaching the cecum within the battery life (approximately 9 h). Gastric transit time (GTT) was recorded from the first gastric image to the first duodenum image, and small-bowel transit time (SBTT) was recorded from the first duodenum image to the first cecal image, or alternatively the last image of the small bowel if the capsule did not reach the cecum within recording time.

Statistical analysis

Continuous variables were expressed as mean ± SD and analyzed with the unpaired t-test. Fisher’s exact test was used to compare incomplete examinations rate and diagnostic yield between the two groups. A P-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS® (version 17.0 for Windows®, SPSS inc®, Chicago, IL, USA). All patients gave their informed consent prior to their inclusion in
patients with IE than in patients with complete examination. Average gastric time was significantly longer in the group, where the capsule remained in the stomach 1 h after ingestion, while in the control group the proportion of patients with the capsule remaining in the stomach 1 h after ingestion was 48/307 (15.6%), P = 0.736. In the control group, a total of 359 SBCE were retrospectively reviewed. Forty procedures were excluded because patients received bowel preparation with polyethylene glycol prior to SBCE in the setting of a clinical trial, and another 12 patients were excluded because the capsule was immediately passed into the duodenum under endoscopic assistance using the AdvanCE delivery system. In the control group, a total of 82 patients using the RTV and 307 matched controls were included in the study analysis. The baseline clinical characteristics and indications for SBCE in both groups are summarized in Table 1. Variables such as age, gender, previous abdominal surgery, inpatient status and indication for SBCE were not significantly different between the two groups. The rate of IE was 15.6% (n = 48) in the control group vs 3.7% (n = 3) in the RTV group (P = 0.003). In the RTV group, no differences were observed in the SBTT among patients who received or did not receive domperidone (260 min vs 297 min, P = 0.229). In one patient (7.0%) out of the 14 patients in the RTV group in whom domperidone was administered, the capsule remained in the stomach two hours after ingestion, and an upper endoscopy was performed to deliver the capsule to the duodenum using a basket. SBCE positive findings were observed in 39% of the control group vs 49% of the RTV group (P = 0.081). None of the 14 patients who received domperidone had any side effect related to the drug.

DISCUSSION

SBCE emerged as a valuable non-invasive diagnostic technique to investigate the entire small-bowel. However, a major drawback is the rate of incomplete examinations, reaching up to 20% to 30%. Some conditions have been associated with incomplete small bowel examination, such as inpatient status or previous abdominal surgery, while the effect of age or medical conditions such as diabetes mellitus remain controversial. Importantly, delayed GTT has been consistently reported as a leading cause of incomplete small bowel examination. Our study supports the hypothesis that the systematic use of the RTV included in the new Given Data Recorder (DR3), in association with domperidone to overcome delayed gastric transit in selected cases, enhances the completion rate of SBCE. Domperidone is a type II dopamine antagonist similar to metoclopramide, with similar effects on gastric emptying but with lower central side effects. Domperidone is not approved by the FDA for use in the United States but is widely used in Europe. To our knowledge, none of the published studies in this area used domperidone as a prokinetic to improve cecal intubation rates. A recent randomized controlled trial which used intramuscular metoclopramide 15 min before capsule ingestion, reported a decrease in GTT with no change in SBTT or complete examination rate, reinforcing that it may also be influenced by other variables. In our study, domperidone significantly contributed to reduce the rate of IE. The drug was only administered in patients with delayed gastric passage of the capsule, documented with the RTV. Moreover, there was no significant difference in SBTT among patients who received or did not receive domperidone. The fact that the SBTT was similar in patients receiving or not domperidone (260 min vs 297 min, respectively, P = NS) is relevant, because it supports the hypothesis that delayed gastric emptying may be a more determinant factor leading to incomplete SBCE than delayed transit of the capsule in the small bowel; the fact that the transit time of the capsule in the small bowel is not significantly reduced by the prokinetic is also important, because a faster passage of the capsule through the small bowel has been associated with lower diagnostic yield.
of SBCE. Indeed, Westerhof et al. found a positive correlation between the diagnostic yield of SBCE and longer small bowel transit time, irrespective of whether the capsule reached the cecum within recording time. In our series, despite the reduction of IE, we did not find a significantly higher diagnostic yield in the RTV group (49% vs 39% in the control group). Recently, Gao et al. showed that delivering the capsule to the duodenum by upper endoscopy using a basket in patients with delayed gastric transit, identified with RTV, improved the rate of complete small-bowel examinations, resulting in higher diagnostic yield of SBCE. We could speculate whether it would be useful to routinely place the capsule in the duodenum with the AdvanCe from the beginning of the examination. However, this strategy would be both invasive and add costs to a procedure that is already expensive. Moreover, it is not possible to accurately predict to which patients it would be helpful, making it unsuitable to implement as a routine procedure in clinical practice.

In our study, only one patient in the RTV group required endoscopic-assisted placement of the capsule into the duodenum. Our results support that to overcome delayed gastric transit time identified by the RTV, non-invasive procedures such as selective administration of oral domperidone to patients with delayed gastric passage of the capsule documented with the RTV, should be the method of choice. This strategy has the merit of strictly selecting the patients to undergo pharmacological and/or flexible endoscopic intervention. Further studies are needed to support the association between complete examination and higher diagnostic yield of SBCE. Although this was not a prospective randomized clinical trial, both groups were homogeneous regarding the most common conditions associated with incomplete SBCE. In conclusion, our results support that the use of RTV to monitor the position of the capsule during SBCE and administration of domperidone in the case of delayed gastric passage, significantly enhances the completion rate of SBCE. Whether such strategy could contribute to improve the diagnostic yield of SBCE will require further investigation.

### COMMENTS

**Background**

In up to 20% of patients undergoing small bowel capsule endoscopy (SBCE) the examination is incomplete. This is a major limitation of this expensive technique, leading to further examinations and expended time and resources. There is ongoing debate on which factors are associated with incomplete examinations and what are the optimal strategies to overcome this issue.

**Research frontiers**

It has been consistently shown that delayed gastric passage of the capsule is a major factor leading to incomplete examinations. The authors evaluated the effect of the prokinetic drug domperidone for improvement of completion of SBCE, with the routine use of real time viewer (RTV) included in the Data Recorder DR3.

**Innovations and breakthroughs**

After confirmation with RTV for the presence or absence of the capsule in the stomach at 1 h, selective administration of 10 mg domperidone to those patients with delayed gastric passage of the capsule has the effect to decrease gastric transit time and leads enough to bring down the rate of incomplete examinations, without affecting small bowel transit time.

**Applications**

This simple and very practical method significantly reduced the rate of incomplete examinations of SBCE. Thus, the authors suggest that the use of the RTV and administration of domperidone for those patients with delayed gastric passage of the capsule should become the standard of practice.

**Terminology**

SBCE incomplete examination occurs when the capsule does not reach the cecum within the battery lifetime. The RTV is included in the Data Recorder DR3 (Given*), allowing for the real time location of the position of the capsule inside the GI tract. Domperidone is a type II dopamine antagonist which may be used to promote gastric emptying.

**Peer review**

In this study, Cotter et al. demonstrate that the systematic use of RTV to recognize patients with delayed gastric passage of the capsule, and selective oral administration of Domperidone to these patients is not only an easy and very practical method but also is beneficial for significant reduction of the rate of IE, without affecting small bowel transit time.

### REFERENCES


5. Long MD, Barnes E, Isaacs K, Morgan D, Herfarth HH.

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**Table 1 Control group vs real time viewer group: Baseline characteristics and outcomes**

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<th>Clinical indication</th>
<th>Control group</th>
<th>RTV group</th>
<th>(p)-values</th>
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<tr>
<td>Age (mean ± SD), yr</td>
<td>(49.7 \pm 20.7)</td>
<td>(48.2 \pm 20.5)</td>
<td>0.518³</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>(136/171)</td>
<td>(32/50)</td>
<td>0.452³</td>
</tr>
<tr>
<td>History of abdominal surgery</td>
<td>24 (8)</td>
<td>12 (15)</td>
<td>0.083³</td>
</tr>
<tr>
<td>Inpatient status</td>
<td>38 (12.3)</td>
<td>10 (12.2)</td>
<td>1.0³</td>
</tr>
<tr>
<td>Clinical indication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OGIB-occult</td>
<td>117 (36)</td>
<td>26 (32)</td>
<td>0.079³</td>
</tr>
<tr>
<td>OGIB-overt</td>
<td>46 (15)</td>
<td>6 (7)</td>
<td></td>
</tr>
<tr>
<td>Suspected CD</td>
<td>83 (27)</td>
<td>29 (35)</td>
<td></td>
</tr>
<tr>
<td>CD staging</td>
<td>33 (11)</td>
<td>11 (14)</td>
<td></td>
</tr>
<tr>
<td>Other indications</td>
<td>28 (9)</td>
<td>10 (12)</td>
<td></td>
</tr>
<tr>
<td>Incomplete examination</td>
<td>48 (15.6)</td>
<td>3 (3.7)</td>
<td>0.003³</td>
</tr>
<tr>
<td>Positive findings</td>
<td>120 (39)</td>
<td>40 (49)</td>
<td>0.081³</td>
</tr>
</tbody>
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\(p\)-values were calculated using unpaired \(t\)-test, Fisher’s exact test (b) and Pearson \(z\)-test. OGIB: Obscure gastrointestinal bleeding; CD: Crohn’s disease; RTV: Real time viewer.


**P-Reviewers**: Aung W, Handa O, Loeve AJ

**S-Editor**: Wen LL

**L-Editor**: A

**E-Editor**: Liu XM