Upper gastrointestinal findings detected by capsule endoscopy in obscure gastrointestinal bleeding


ABSTRACT

Objective: we analyzed our experience with the use of capsule endoscopy in areas that can be explored with gastroscopy to justify obscure bleeding, as well as the outcome after a new recommended gastroscopy in order to determine if a second gastroscopy before the capsule study can provide any benefit in the management of this disease.

Methods: we retrospectively studied 82 patients who were explored with capsule endoscopy for obscure gastrointestinal bleeding who had undergone previously only one gastroscopy.

Findings in the zones which were accessible by gastroscopy were normal, mild/known and severe/unknown. In the latter cases we recommended a second gastroscopy, and their treatment and outcome were subjected to further study.

Results: capsule endoscopy did not find any unknown esophageal findings. In 63% of cases, no gastric or duodenal lesions were shown; in 20%, lesions were mild or had been previously diagnosed, and in 17%, a new gastroscopy was recommended due to the discovery of an unknown condition which could be the cause of the obscure bleeding. This new information brought about a change in treatment for 78% of patients in this group, all of whom improved from their illness. Capsule endoscopy found significant intercurrent alterations in the small intestine in only 14% of cases.

Conclusions: the performance of a second gastroscopy, previous to capsule endoscopy, in the study of obscure gastrointestinal bleeding can offer benefits in diagnostic terms and may introduce therapeutic changes.

Key words: Capsule endoscopy. Obscure gastrointestinal bleeding. Gastroscopy.

INTRODUCTION

Obscure gastrointestinal bleeding (OGIB) accounts for up to 5–8% of all causes of digestive bleeding (1,2), and represents one of the main indications for intestinal wireless capsule endoscopy (WCE) (3-5). To formulate a preliminary diagnosis of OGIB (either overt or occult) according to the established definition, at least one diagnostic esophageal gastroduodenoscopy (EGD) and colonoscopy should have been performed (6). Although some published algorithms even suggest a repeat upper endoscopy before submitting the patient for WCE to complete the study of the small bowel (7), some authors postulate that the final decision should rely either on the preferences of the endoscopist performing the first EGD (8) or according to the findings of WCE once completed (9). This latter statement has been supported by results from some retrospective studies published in the last few years (10,11).

On the other hand, some common diseases, which can be cause of chronic anemia –e. g. severe gastroesophageal reflux (12) or esophageal varices screening in cirrhosis (13)–, usually require a repeat EGD (14). Performance of a repeat EGD is sometimes a matter of discussion with the patient, who might eventually reject this practice (15).

It is common to incidentally discover new findings in the gastrointestinal tract proximal to the second portion of the duodenum while performing WCE for OGIB (16) (17). These findings may be relevant enough either in
terms of therapeutic decisions or cost-effectiveness (17).

Our aim was to evaluate the clinical impact of repeat upper endoscopy after an initially negative procedure in patients with OGIB in terms of its role in reducing unnecessary WCE studies.

PATIENTS AND METHODS

We designed a descriptive retrospective study to identify pathologic findings in the regions considered within range of a standard EGD examination in patients referred to our center for WCE in case of OGIB (occult and overt) with a normal initial EGD. Patients with esophageal, gastric or duodenal abnormalities —proximal to the ampulla of Vater (18)— were recommended a new EGD. Baseline characteristics, new endoscopic findings, and follow-up of recruited patients were recorded, and a posterior analysis was carried out.

Clinical information on every patient was retrieved from the clinical report of the referring doctor. In case of missing data, the referring doctor was contacted via phone or fax. Information about symptoms of the upper digestive tract in the last month was obtained in person, on the day of WCE, including pyrosis, regurgitation and acute epigastric abdominal pain. Daily medication informations were obtained, paying particular attention to antiplatelet therapies, anticoagulants, proton-pump inhibitors (PPIs), non-steroidal anti-inflammatories (NSAIDs), and muscle-relaxants such as beta-adrenergic and alpha-adrenergic antagonists, calcium-channel antagonists, anticholinergics, contraceptives, benzodiazepines, nitrates, opiates, and xanthine. Smoking at least 10 cigarettes a day, and drinking over 20 grams of alcohol a day were the thresholds used for the definition of “tobacco” and “alcohol” use/intake, respectively.

Inclusion criteria included a prior and unique EGD 1 to 12 weeks before the day of the WCE study. Our endoscopy section is a referral unit for WCE in the region of Castile & Leon, comprising a total of 2.5 million inhabitants. Requesting forms were submitted mainly by gastroenterologists, followed by internists, surgeons, and hematologists.

We used the same protocol for WCE in all patients, which excluded the use of any prokinetics or preparations of the intestine using cleaning solutions. The WCE system used was a Given Imaging M2A plus® with spatial location through 7 sensors placed in the abdomen, and the recording system was a Data Recorder TM Given®. The “M2A plus” capsule was swallowed by the patient with the help of less than 30 cc of water. This capsule is 26 x 11 mm in size and 3.45 gram in weight. The preparation for the procedure included a fasting period of at least 4 hours, except for some clear liquids. After swallowing the capsule, patients were suggested to walk as much as possible. The display of recorded data took place on the same week of the exploration and was performed by three doctors, all of them experimented in the technique.

The report was written using the standard, accepted terminology (19).

After WCE results, new upper digestive tract findings were noted (known abnormalities from prior EGD were excluded). Particular attention was paid to those cases in which the newly discovered lesions were located within the anatomic range of a standard EGD evaluation, and could possibly justify the origin of OGIB. Some examples were severe esophagitis, large esophageal varices, erosive gastritis or duodenitis with blood, significant vascular lesions, severe portal gastropathy, gastric or duodenal ulcers, and neoplastic lesions.

In any of these cases, even if a small-bowel alteration had been also observed during the WCE exam, a repeat EGD was recommended to the referring doctor. The completion of a repeat EGD was then confirmed by means of contacting the patient or referring doctor via a phone call. Any information obtained in the repeated EGD was registered, as well as new therapeutic orders and clinical follow-up.

RESULTS

In a period of two years, we prospectively studied 82 patients (49 men and 33 women). Their mean age was 61.3 years (range 28-83). The prevalence of alcohol consumption and smoking was 10 and 12%, respectively. Concerning the use of medications in this population, this was led by PPIs (52%) followed by muscular relaxants (41%), antiplatelet drugs (17%), and anticoagulants (7%). No patient used non-steroidal anti-inflammatory drugs. Only in 15% of these patients complained about upper gastrointestinal symptom.

All initial EGDS were normal or with a diagnosis that did not explain bleeding (small hiatal hernias, mild esophagitis, I-II/IV esophageal varices, mild portal hypertension associated gastropathy, esophageal papillomas, or non-eroded gastric polyps).

The average time recorded in the esophagus and stomach for the capsule was 35 minutes (range 1-142 minutes).

In the esophagus, we clearly recognized small esophageal varices and papillomas, but we could not identify mild esophagitis or hiatal hernias. WCE did not show any new esophageal findings.

WCE results showed no gastroduodenal lesions in 52 (63%) patients. In 16 cases (20%), some already diagnosed or new minor unimportant lesions (slight erosive gastro-duodenitis, slight gastric portal gastropathy, and non-eroded small polyps) were observed. In the remaining 14 (17%) patients, WCE showed relevant gastric and/or duodenal lesions not previously noted during initial EGD (Table I). Mean age in this group was 70 years (range: 22-80). Male proportion was 71.4%; the use of PPIs (57%) and antiplatelets (21%) was also increased in
comparison with the rest of the study population. Tobacco consumption was similar to the total population average (14%), and no case of alcohol use was observed. Of note, none of these patients reported any upper gastrointestinal tract symptoms. There were no significant differences in time intervals between EGD and WCE in this group with regard to the rest of patients.

In 8 of these 14 patients, gastro-duodenal lesions were the only pathological findings discovered in the digestive tract. In the remaining 4 patients (patient’s number 1 and 10 did not complete WCE), we observed lesions in the small bowel, but in only two of them with an entity that could explain the source of OGIB.

A new EGD was performed in 7 patients (7 refused). In 86% of them WCE findings were confirmed (Table I).

**DISCUSSION**

WCE has become one of the most important non-invasive diagnostic tests for the evaluation of the small bowel (20). Due to its straightforward procedural application and few complications, WCE is widely accepted by patients, in contrast to other procedures such as EGD (21). On the other hand, EGD is the most accurate endoscopic procedure for detecting and treating most diseases of the upper digestive tract. It is a safe and usually well tolerated technique that has a high diagnostic yield (22-24).

Since 2002, WCE has been considered a complementary tool in the study of the upper gastrointestinal tract (25,26). Of note, a new esophageal capsule endoscopy has been recently developed (27,28). Some studies show that this esophageal capsule and EGD can be quite concordant in their findings, and ECE can even discover abnormalities not revealed by EGD (29,30). The absence of gastric distension (among other reasons) makes capsule endoscopy a restricted procedure for the standard study of the stomach. However, technical improvements are promising, like those achieved in the colon (31).

WCE is an useful tool in the workup of OGIB, but certain issues, such as the limited effectiveness of medical therapies (32), development of new alternative endoscopic methods (double-balloon enteroscopy), and risk of capsule impaction (1.9%) during WCE (33) suggest that new prospective studies are needed to clarify the most effective strategy in the evaluation of OGIB (34). Some studies have addressed the importance of repeat EGD be-

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**Table I. Patients with upper tract bleeding diagnosed by capsule endoscopy, second EGD findings, and follow-up**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Antiplatelets</th>
<th>PPIs</th>
<th>WCE diagnosis in upper tract</th>
<th>Second EGD</th>
<th>Findings in the SB in WCE</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80</td>
<td>M</td>
<td>No</td>
<td>Yes</td>
<td>Inflammatory and hemorrhagic gastropathy</td>
<td>Not performed</td>
<td>WCE uncompleted</td>
<td>Asymptomatic with double dose of PPIs</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>M</td>
<td>No</td>
<td>No</td>
<td>Hemorrhagic gastritis</td>
<td>Not performed</td>
<td>SB normal</td>
<td>Asymptomatic with PPIs</td>
</tr>
<tr>
<td>3</td>
<td>74</td>
<td>F</td>
<td>No</td>
<td>No</td>
<td>Hemorrhagic gastritis</td>
<td>Not performed</td>
<td>SB normal</td>
<td>Asymptomatic with double dose of PPIs</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>M</td>
<td>No</td>
<td>No</td>
<td>Hemorrhagic gastritis</td>
<td>Not performed</td>
<td>SB normal</td>
<td>Asymptomatic with PPIs</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>M</td>
<td>No</td>
<td>No</td>
<td>Hemorrhagic gastritis</td>
<td>Yes. It did not confirm WCE findings</td>
<td>Slight enteropathy</td>
<td>Asymptomatic with PPIs</td>
</tr>
<tr>
<td>6</td>
<td>80</td>
<td>M</td>
<td>No</td>
<td>Yes</td>
<td>Hemanegious gastritis</td>
<td>Not performed</td>
<td>Vascular lesions in SB</td>
<td>Dead secondary to massive bleeding</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>M</td>
<td>No</td>
<td>Yes</td>
<td>Duodenal and gastric vascular lesion</td>
<td>Yes. It discovered gastric tumor</td>
<td>SB normal</td>
<td>Asymptomatic after surgery</td>
</tr>
<tr>
<td>8</td>
<td>79</td>
<td>M</td>
<td>AA</td>
<td>Yes</td>
<td>Duodenal ulcer</td>
<td>Not performed</td>
<td>SB normal</td>
<td>Dead (unknown cause)</td>
</tr>
<tr>
<td>9</td>
<td>22</td>
<td>M</td>
<td>No</td>
<td>No</td>
<td>Duodenal ulcer</td>
<td>Not performed</td>
<td>SB normal</td>
<td>Asymptomatic with PPIs</td>
</tr>
<tr>
<td>10</td>
<td>59</td>
<td>M</td>
<td>No</td>
<td>Yes</td>
<td>Tumoral stenosis in duodenum</td>
<td>Yes. It confirmed WCE findings</td>
<td>WCE did not go through the stenosis</td>
<td>Asymptomatic after surgery</td>
</tr>
<tr>
<td>11</td>
<td>76</td>
<td>F</td>
<td>No</td>
<td>No</td>
<td>Inflammatory duodenal stenosis</td>
<td>Yes. It confirmed WCE findings</td>
<td>Several ulcers and areas of marked lymphoid hyperplasia</td>
<td>Diagnosis of intestinal lymphoma</td>
</tr>
<tr>
<td>12</td>
<td>72</td>
<td>M</td>
<td>No</td>
<td>No</td>
<td>Gastric vascular lesion</td>
<td>Yes. It confirmed WCE findings</td>
<td>SB normal</td>
<td>Asymptomatic after argon and PPIs</td>
</tr>
<tr>
<td>13</td>
<td>77</td>
<td>F</td>
<td>AA</td>
<td>Yes</td>
<td>Watermelon stomach</td>
<td>Yes. It confirmed WCE findings</td>
<td>SB normal</td>
<td>Clinical improvement after argon-beam therapy</td>
</tr>
<tr>
<td>14</td>
<td>75</td>
<td>F</td>
<td>AA + clopidogrel</td>
<td>Yes</td>
<td>Watermelon stomach</td>
<td>Yes. Only one unlikely microerosion in jejunum</td>
<td>Poor response to argon-beam therapy</td>
<td></td>
</tr>
</tbody>
</table>

PPIs: proton pump inhibitors; WCE: capsule endoscopy; SB: small bowel; AA: acetylsalicylic acid; EGD: esophago-gastro-duodenoscopy.
fore recommending WCE. Other authors recommend a second EGD when WCE was normal (35).

Our group has tried to confront the question of the clinical impact of repeat EGD during workup for OGIB in our local population. Due to technical and ethical limitations (performing a repeat EGD just before WCE was not considered in our institution), our results have some limitations.

All the raised lesions observed in the esophagus during the first EGD were confirmed by WCE. According to Sharma et al., this single fact would support the inclusion of capsule endoscopy in the diagnostic armamentarium for the esophagus (28). New design features in ECE will provide a complete view of the esophageal lumen, obtaining a superior number of frames from other sites like the cardia (36-38). Our results show that, although with some limitations in the identification of mild esophagitis and the cardia, WCE results allowed us to not recommend repeat EGD.

When considering our results in the stomach and duodenum, WCE was able to capture images for an average of 30 minutes, similar to data obtained in prior studies in the same population (39), but less than reported recently (40). Despite the technical limitations of WCE to evaluate the stomach and the duodenum, it provided information in 30 patients (37%): 14 without a previous diagnosis and 16 with mild lesions previously diagnosed during the first EGD. These findings were considered significant enough to explain OGIB and recommend repeat EGD in 14 patients (17%). In 8 cases, the gastro-duodenal findings observed during WCE were the only identifiable abnormalities in the digestive tract to explain the origin of bleeding. So we propose that performing a second EGD might have prevented the need for WCE in these cases. Although the prevalence of gastric and duodenal lesions in our local population diagnosed with OGIB is slightly superior to other series, the results are similar enough to make them consistent with present literature references (10,11,41,42). In our country other studies with WCE have shown gastro-duodenal lesions in 3.4-9% of subjects (43,44).

In only 2 patients, we found synchronous bleeding lesions in the upper tract and the small intestine, which prevented us from correlating these pathologies and attributing them to interactive or systemic factors.

Some of the limitations of this study are the possible different skills set between endoscopists performing initial and second EGDs (8), time interval between procedures, the possibility of intercurrences (45), the population heterogeneity considered for OGIB (46), and discrepancy between WCE accuracies according to OGIB type (47). The different time intervals between tests (due to the waiting list) can be an important limitation too, although, in most cases, it was between two and eight weeks. On the other hand, we are aware of the value of our study would achieve in case we would performed a second EGD procedure to the entire group on the same day of WCE. For us, it was impossible to carry out. However, in our opinion, our results are relevant and reportable; WCE discovered significant lesions in areas accessible to standard EGD in a considerable number of patients (14/82), particularly in those with antiplatelet treatment; these being in 8 of them the only abnormality found. We think that performing a second EGD might have prevented the need for WCE in these cases.

These results did have a clinical impact on the diagnostic and therapeutic strategies for twelve patients. Of these twelve patients, six were diagnosed with peptic disease (not confirmed in the only one who underwent a second EGD) and their treatment was modified either by starting therapy with PPIs or by increasing prior doses with good results. Six patients with neoplastic or vascular lesions underwent a second EGD, and in all of them the WCE diagnosis was confirmed. Surgical or endoscopic therapy was decided according to those findings. Five of these six cases improved.

Although the detailed analysis of the stomach and duodenum using WCE provided benefit in our patients, we think that one of the most relevant points to improve the cost-benefit of this test in OGIB is a right indication, using it only after a rigorous exam of the mucosa during the initial EGD (and repeating it if necessary).

In conclusion, performing a second EGD before indicating a WCE study may increase the diagnostic yield and improve the cost-effectiveness of WCE in patients with OGIB. These findings would probably be enough to establish a final diagnosis, since the rate of synchronous bleeding-source lesions in the upper tract and the small bowel has proven quite low. A detailed, careful analysis of the upper tract frames from WCE is therefore recommended, since it may provide relevant new diagnostic information.

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