Digestive Endoscopy

Usefulness of wireless capsule endoscopy in paediatric inflammatory bowel disease

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A B S T R A C T

Background: Small bowel endoscopy is critical in revealing an inflammatory bowel disease (IBD) previously undetected and in classifying the IBD patients, i.e. Crohn’s disease or ulcerative colitis.

Methods: A prospective paediatric study on the usefulness of wireless capsule endoscopy (WCE) was performed in 117 children (age range: 4–17 years) with established or suspected IBD and compared with non endoscopic imaging tools. All patients underwent upper and lower gastrointestinal endoscopy.

Results: In Crohn’s disease patients (CD, n = 44), small bowel lesions were revealed by imaging tools in 8 and by WCE in 18 patients, respectively (p < 0.01). No small bowel involvement was observed in 29 ulcerative colitis patients by both imaging tools and WCE. Of 26 unclassified IBD, small bowel lesions typical of Crohn’s disease were detected by imaging in 7 and by WCE in 16 (p < 0.05). Of 18 patients with suspected IBD, small bowel lesions typical of Crohn’s disease were observed in 9 with WCE, vs. only in 4 with imaging (p < 0.01). No cases of capsule retention occurred.

Conclusions: WCE is valuable in revealing small bowel lesions in children with a previous diagnosis of CD and unexplained clinical and laboratory data. It is also helpful in unclassified IBD patients. This tool can influence the management and the course of IBD.

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1. Introduction

An increased incidence of paediatric inflammatory bowel disease (IBD) has recently been reported in western countries, with almost 10–12 novel cases per 100,000/year [1,2]. Two disease subtypes, Crohn’s disease (CD) and ulcerative colitis (UC) are the classical forms of IBD, and their definite diagnosis is based on clinically, endoscopic, histopathologic and imaging criteria [3,4]. Establishing the subtype of IBD is crucial in predicting the disease course as well as in choosing appropriate treatment interventions. In the management of IBD patients, investigation of small bowel is fundamental since its involvement may definitely indicate the presence of CD; furthermore, assessing small bowel involvement in CD patients may be helpful both in making therapeutic decision and planning the follow up [5,6]. Evaluation of the small bowel is also mandatory in cases labelled as IBD unclassified (IBDU) for which traditional endoscopy and histopathology do not discriminate between CD and UC [7]. This entity, also known as indeterminant colitis (this term should be reserved for patients in whom surgical specimen of the gut are available) may occur in up to 1/5 of a paediatric population with IBD referred to a tertiary center [1]. Traditional imaging methods to evaluate small bowel are contrast X-ray examination, ultrasound and magnetic resonance imaging (MRI) [8]. The latter seems to have a great sensitivity and specificity and has recently gained a wide acceptance among paediatric gastroenterologists since it is radiation free and suitable both for the initial approach and the follow up of IBD [9]. Wireless capsule endoscopy (WCE) has dramatically changed the exploration of the intestine and has shown high diagnostic efficacy for various gut disorders [10]. Whereas WCE has been shown to improve the diagnostic yield in adults with IBD, paediatric reports are few, mostly retrospective [11,12] or include small number of patients [13,14].

In this study we aimed to assess prospectively the ability of WCE in refining the approach to a large cohort of children with
known or suspected IBD, referred to tertiary centers of Pediatric Gastroenterology for small bowel endoscopy.

2. Patients and methods

One-hundred and thirty-three paediatric patients with known or suspected IBD (median age: 11.2 years; range: 4–17 years) were consecutively referred to tertiary centers for small bowel endoscopy through WCE. Patients were not eligible for WCE if they had swallowing disorders, oesophageal stenosis, known GI motility abnormalities, small bowel strictures at ultrasonography ad/or MRI and/or X-ray contrast examination. One-hundred and seventeen patients were suitable for this investigation: 16 were discharged because of stenosis at imaging tools [6], previous surgery [4], lack of cooperation [4], high severity of the disease with systemic features and malnutrition [2].

The reasons for performing WCE were: (1) children with an established CD (44 cases; median age: 11.0 years; range: 6–17) in most of which clinical and laboratory signs (i.e. diarrhoea, haematochezia, severe abdominal pain, fever, refractory anaemia, low serum albumine, high plasma levels of acute phase reactants) were not fully explained by features revealed by conventional endoscopy; (2) children with previous diagnosis of UC (29 cases; median age 11.6; range: 5–17), needing to definitely exclude CD colitis; (3) further classification of a group of IBD children (26 cases; median age 10.0 years; range: 4–16) who had received a diagnosis of IBDU; (4) children with haematochezia and signs of small bowel disorders (18 cases; median age: 10.5 years; range: 5–17), without a definite diagnosis with traditional gastrointestinal (GI) endoscopy.

All patients underwent diagnostic work-up including ileocolonoscopy and upper GI endoscopy under general anaesthesia or conscious sedation. Diagnosis and classification of IBD were based on commonly agreed criteria [3,4]. Infectious and immunological diseases as well as malabsorption syndromes and food allergy were excluded in all. Intestinal obstruction had been excluded with MRI or small intestine contrast ultrasonography (SICUS). The methodology of MRI has been published elsewhere [9]. The SICUS was performed after ingestion of a macrogol solution enabling to visualise and measure wall thickness and lumen diameter along the small bowel [15,16].

In order to optimise visualisation of the jejunum and ileum by WCE, patients were given no more than 1L of PEG 4000 oral solution, administered in 100–200 mL increments every 10 min in the early morning of the examination after an overnight fast. Patients were allowed to resume their usual activities and drink clear liquids 1 h and 3 h, respectively, after ingesting the capsule. The WCE used in this study was the PillCam small bowel video capsule (Given Imaging, Israel) that measures 11 mm × 25 mm and weighs less than 4 g, with a recording system consisting of a data recorder and a workstation equipped with image processing software. In patients unable to swallow the capsule, the latter was released in the proximal duodenum with a paediatric video-gastroscope (Olympus PCF Q180), in which the capsule had been loaded using a foreign body Roth Net (US Endoscopy, Mentor, OH). All patients underwent WCE within one week from the completion of the upper and lower GI video-endoscopy. Imaging tools of the ileum (ultrasonography, MRI, small bowel follow through) were performed few days before WCE. Capsule retention was defined as failure of passage of the capsule from the gastrointestinal tract for 2 or more weeks [10]. The examination was considered as incomplete if the capsule did not reach the caecum within 8 h [12].

The capsule images were independently interpreted by two members of the staff (S.O. and M.E.R.), with a great training in GI endoscopy and unaware of the clinical history, previous investigations and diagnosis. The study was judged to be negative if no abnormalities were seen and positive if clear abnormalities of the small bowel mucosa (i.e. ulcerations, erosions, polyps, vascular lesions, bleeding lesions) were observed. There was a 100% concordance between the observers in classifying the study as positive or negative.

Features detected by WCE were considered as diagnostic of active CD if >3 diffuse small bowel ulcerations or multiple ulcerations were seen. Features of ≤3 ulcerations were considered suggestive but not diagnostic of small bowel CD. If no abnormalities or non specific findings (such as erythematous spots or mucosal breaks) were seen the examination was considered as non specific or normal [15]. White lesions within a crater with surrounding erythema were considered ulcers, whereas small superficial white lesions, even with surrounding erythema, were considered erosions.

This was a prospective study and the primary end-point was to compare the usefulness of WCE for assessing small bowel in suspected or established IBD in comparison with non endoscopic imaging tools.

Informed consent for all diagnostic procedures was obtained by parents (or caregivers) and also by children. The latter were informed with an appropriate text reporting descriptive figures. The ethical committee of each hospital approved the diagnostic procedures.

2.1. Statistical analysis

We performed comparisons between two procedures by using the Fisher exact test. Data were analysed using GraphPad InStat 3.1 for Mac OSX; p ≤ 0.05 was considered statistically significant. All tests were 2-tailed.

3. Results

The WCE procedure was well tolerated by all patients; no cases of capsule retention occurred. Eighteen patients (median age 7.0 years; range: 4–12) were unable to swallow the capsule: the latter was inserted through the videogastroscope using a foreign body going WCE.

Overall, colonoscopy with exploration of the terminal ileum (TI) had been performed in all 44 patients with CD: the TI was involved in 33 (27 also with colonic lesions), in 9 the disease was localised at the large bowel only, whereas it involved the gastroduodenal tract alone in 2. Table 1 reports the clinical characteristics and the disease localisation of CD patients. CD lesions in the small bowel mucosa, previously undetected, were revealed by WCE in 18 patients (41%) and by non endoscopic procedures (MRI and/or SICUS) in 8 (18.1%) (p < 0.01); in all patients with colonoscopic TI ulcerations, the latter were also shown by WCE. All 18 CD patients with small bowel involvement exhibited clinical and/or laboratory data unexplained.
by features detected with conventional endoscopy that suggested a mildly active or quiescent disease: low serum albumine and anaemia in 10, severe abdominal pain with diarrhoea, fever and haematochezia in 14, high plasma levels of acute phase reactants (CRP, ESR, ferritine and fibrinogen) in 12.

Both WCE and non endoscopic procedures did not detect specific small bowel lesions in all 29 patients with a previous diagnosis of UC. The latter was subsequently confirmed at a long term follow up. In 10 patients WCE revealed non specific lesions such as areas of hyperaemia intermingled with granularity, both in small bowel areas close to the TI and in the latter: in all cases histology revealed a mild mixed inflammatory infiltrate of the lamina propria without crypt distortion and epithelial changes.

Of 26 patients with a diagnosis of IBDU, small bowel lesions diagnostic of CD were detected in 7 by non endoscopic procedures (26.9%) and in 16 by WCE (61.5%) (p < 0.05): the disease was re-classified as CD in them. The diagnosis of CD was then confirmed by endoscopic and histological findings at the single-balloon enteroscopy performed not later than 2 months after WCE study. In 10 patients with no lesions at WCE the diagnosis of IBDU was confirmed.

Of 18 patients investigated because of recurrent haematochezia and clinical signs of GI disorders, small bowel lesions diagnostic of CD were seen by WCE in 9 (50%), but only in 4 by MRI and/or SICUS (22.2%) (p < 0.01): in all of them upper and lower GI endoscopy as well as histology had not revealed specific inflammatory lesions. Of the remaining patients, WCE showed polyps in 2, drug-related lesions in 3, nodular hyperplasia related to multiple food allergy in 3, vascular abnormalities in 1. The CD diagnosis in this group of patients was subsequent confirmed by endoscopic and histological features as detected by single balloon enteroscopy.

In all investigated patients there were no features detected at MRI or SICUS but not visualised by WCE. The exam was incomplete in 5 patients (all with a previous diagnosis of CD): however it was thought to be valuable because most of the small bowel was clearly visualised.

4. Discussion

Currently, in the management of IBD, WCE is thought to be a third stage examination, useful to define the extent and the severity of already known CD, as well as for detecting small bowel lesions in cases of suspected CD [6]. The WCE is also of value in subjects with obscure GI symptoms in whom traditional endoscopy and imaging tools are negative [18–20]. A large meta-analysis study has shown that WCE has an overall diagnostic yield better than other non endoscopic imaging techniques in managing patients with definite or probable IBD [21].

Whereas previous reports have mainly highlighted the usefulness of WCE in patients with obscure GI bleeding or undefined intestinal disorders, less studies have been focused on IBD, only a minority of them including paediatric patients [22–26]. We investigated paediatric subjects both with a previous diagnosis of IBD and with signs suggestive of IBD. Of the CD group, small bowel lesions were disclosed by WCE in a significantly higher percentage of patients than by non endoscopic imaging: these subjects were characterised by clinical features and laboratory findings unexplained by conventional endoscopy that had revealed features indicating a mildly active or quiescent disease. Of the non endoscopic tools commonly used in the management of IBD, MRI and SICUS have recently been reported as reliable methods to document small bowel inflammation in CD, mainly if transmural damage occurs [8,9,15]. It is conceivable that most small bowel lesions in our patients were superficial, thus more detectable through a direct endoscopic inspection. However, prospective studies comparing WCE and non endoscopic tools in assessing small bowel involvement in IBD are warranted. Results in our patients with a previous CD diagnosis are in accordance with a statement from a recent international consensus that small bowel endoscopy in CD is not a routine procedure and should be performed in cases with unexplained symptoms and inconclusive imaging and ileo–colonoscopy [6].

In a previous retrospective study on WCE in 28 IBD children, 4 of 5 UC patients and 1 of 2 IBDU patients changed their diagnosis in CD, whereas in 13 of 21 CD a more extensive small bowel disease than previously thought was revealed [27]. The use of WCE has also been reported in a group of 50 adult patients with known or suspected IBD and no evidence of active disease on classical investigation: WCE revealed features diagnostic or suspected of CD in 20 and 10, respectively; the examination was normal or nonspecific in the remaining 20 [17].

We also investigated children with a previous diagnosis of UC: in none of them WCE revealed specific small bowel lesions. This
outlines the appropriateness of the diagnostic criteria adopted in our study [3,4]. Indeed, the UC diagnosis was subsequently confirmed in all subjects at a long term follow up. It is widely agreed that the diagnosis of UC does not require small bowel endoscopy with WCE; however, these patients had been referred for small bowel endoscopic evaluation due to some diagnostic uncertainties related either to the aspect and the topography of colonic endoscopic lesions or to the type and distribution of the inflammatory infiltrate at histology. Interestingly, in 10 UC patients areas of granularity and hyperaemia were observed in the TI and in more proximal areas: histology revealed only a mild mixed inflammatory infiltrate of the lamina propria and no epithelial or crypt change, thus excluding CD.

Interestingly, 26 subjects had been diagnosed as IBDU, due to lack of endoscopic and histological criteria discriminating between CD and UC. Of these patients, 16 were reclassified as CD because of peculiar small bowel lesions at WCE; imaging tools detected ileal inflammatory lesions suggesting CD in only 7 of them. In a previous multicenter study in 30 adults with IBDU and negative serology, WCE was useful for categorising them whereas a normal small bowel imaging could not exclude a diagnosis of CD [22]. Interestingly, a previous report in adults with UC or IBDU who underwent WCE has shown that small bowel lesions consistent with CD could be detected in almost 16% of investigated subjects [28]. The unclassified forms of IBD are peculiar of the paediatric age since IBD in childhood not uncommonly exhibits clinical, endoscopic and histological phenotypes that do not allow a clear differentiation between UC and CD, with consequent uncertainty in choosing therapeutic options and in the long term prognosis [3]. In paediatric series, the prevalence of IBDU ranges from 5% to 30%, suggesting a variation in classification criteria [3].

In 18 patients evaluated for haematochezia and signs of chronic enteropathy, WCE revealed a CD in 9, whereas other entities were detected in the remaining patients. These data confirm the diagnostic value of WCE in subjects with undefined GI disorders [20]. Previously, in children with obscure small bowel disorders, WCE detected lesions consistent with CD in almost 50% of the patients, with a sensitivity higher than imaging tools [29].

Our study confirms that WCE is well tolerated and safe in paediatric patients. We did not observe any capsule retention, whereas data from previous paediatric studies indicate a WCE retention rate ranging from 2% to 5% [11], that is comparable with data from adult patients. In our study, we did not observe any capsule retention, whereas data from previous paediatric studies indicate a WCE retention rate ranging from 2% to 5% [11], that is comparable with data from adult patients.

In conclusion, WCE is a very useful approach to children presenting with symptoms suggesting IBD or with an established IBD. It is of particular helpful in identifying small bowel ulcerations in children with CD exhibiting clinical and laboratory features unexplained by conventional GI endoscopy and imaging tools. It is also critical in reclassifying children with IBDU. While it is widely agreed that WCE in IBD should be recommended as a third stage examination after conventional upper and lower GI endoscopy, it remains unsettled how this examination will influence the management of IBD and how it should be used in conjunction with other investigatory modalities (i.e. MRI, ultrasound). Finally, one important issue will be how to integrate capsule endoscopy with balloon assisted enteroscopy, a novel technique that allows both endoscopic exploration of the small bowel and histological assessment as well as therapeutic interventions.

Conflict of interest statement
None declared. Dr. Laura Stronati, Research Assistant at ENEA, is performing several research projects on paediatric IBD at the Department of Pediatrics of the Sapienza University in Rome.

References

