Indications for gastrointestinal endoscopy in children

Indikacije za gastrointestinalno endoskopijo pri otrocih

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Abstract

Gastrointestinal endoscopy has revolutionized the diagnosis and management of many gastrointestinal diseases and is now an integral part of the evaluation and treatment of gastrointestinal diseases in children and adolescents.

Endoscopic gastrointestinal procedures are now common in most major pediatric centres and they can be safely performed in small infants, including newborns.

Over the past few years, experts in committees and scientific societies have been working to establish indications for performing gastrointestinal endoscopy in children.

With the development of pediatric gastroenterology new diseases emerged and indications for performing endoscopies had changed.

The aim of the present review article is to summarize the most recent data on the indications for performing endoscopy in the most common pediatric gastrointestinal disorders.

Izvleček

Gastrointestinalna endoskopija je bistveno vplivala na diagnostiko in zdravljenje mnogih bolezni prebavil in je danes sestavni del ocenjevanja in zdravljenja bolezni prebavil pri otrocih in mladostnikih.

Gastrointestinalne endoskopske metode se danes pogosto uporabljajo v večini večjih pediatričnih centrov in jih je mogoče varno izvesti tudi pri majhnih dojenčkih, vključno z novorojenčki.

V zadnjih nekaj letih so si strokovnjaki v odborih in strokovnih združenjih prizadevali vzpostaviti indikacije za opravljanje gastrointestinalnih endoskopij pri otrocih.

Hkrati z razvojem pediatrične gastrologije so se pojavile nove bolezni in indikacije za izvajanje endoskopij so se spremenile.

Namen tega preglednega članka je povzeti najnovejše podatke o indikacijah za izvajanje endoskopije pri najpogostejših boleznih prebavil pri otrocih.

Introduction

Over the past 20 years, there was a dramatic improvement in performing endoscopy, due to the advances in fiberoptic and video technology. The following diagnostic and therapeutic endoscopy procedures are performed: esophagogastroduodenoscopy, colonoscopy, dilation, variceal sclerotherapy or banding, polypectomy, percutaneous endoscopic gastrostomy, foreign body extraction and capsule endoscopy. Their number is increasing year by year.[1] Pediatric endoscopy has become an important diagnostic procedure in the evaluation of gastrointestinal bleeding, dysphagia, severe pain disorders, inflammatory bowel disease, and radiographic abnormalities, as well as in taking biopsy specimens, removal of foreign bodies, and other clinical situations. Endoscopy should be performed by a physician with competence in pediatric gastroenterology. Endoscopy is useful only when it leads to correct diagnosis and proper treatment. Studies of diagnostic accuracy have shown that endoscopy is superior to radiography in the detection of peptic ulcers, polyps and other mucosal abnormalities, and it offers an

opportunity for histopathological diagnosis or concomitant treatment.

Methods

Electronic databases, such as PubMed, Medline, Cochrane Database of Systematic Reviews, were searched for relevant articles using the key words: "pediatric" and each of the following: "endoscopy", "gastroscopy", colonoscopy", "capsule endoscopy", "celiac disease", "GERD", "Helicobacter pylory" and "Eosinophilic esophagitis", "IBD", "polyps", polyposis", "digestive bleeding", "foreign bodies". The search was supplemented by accessing the "related articles" feature of PubMed, as well as scanning the reference lists for additional relevant studies. The analyzed main papers were clinical practice guidelines, review articles and original studies.

Results

Indications for endoscopy – first position paper

Over the past few years, experts from committees and scientific societies have been working to establish criteria for selecting the patients to benefit most from endoscopy. Because endoscopy, especially upper gastrointestinal endoscopy, has become easier to perform, pediatricians often recommend it in children with various nonspecific symptoms, leading to its overuse.

In 1996, The North American Society for Pediatric Gastroenterology and Nutrition (NASPGAN) published a position statement with recommendations on the indications for endoscopy in infants, children and adolescents.[2]

General indications for performing diagnostic, periodic and therapeutic upper endoscopy and colonoscopy with biopsy are presented in Table 1 and 2.

The development of adult gastroenterology was rapidly followed by the development of pediatric gastroenterology as a subspecialty focused on disorders of the pediatric gastrointestinal (GI) tract. The most frequently performed, mainly diagnostic, procedures are upper endoscopy and colonoscopy. New technologies, such as video capsule endoscopy (VCE) or double balloon enteroscopy, were developed and facilitated diagnosing small bowel disorders.

New diseases such as eosinophilic esophagitis (EoE) were discovered, and more knowledge on diseases like celiac disease (CD), inflammatory bowel disease (IBD), and gastroesophageal reflux disease (GERD) has been achieved. Indications for performing endoscopy in these GI diseases are summarized below.

Indication for endoscopy in celiac disease

New diagnostic criteria for celiac disease from the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) were published in 2012.[3] The definition of CD has changed from that of a mere enteropathy to a common systemic disease strongly dependent on human leukocyte antigen HLA-DQ2 and HLA--DQ8 and presence of CD-specific antibody tests. The diagnosis of CD is based on symptoms, positive serology and histology consistent with CD.

In 1969, ESPGAN has formulated the classical criteria for celiac disease diagnosis, also known as Interlaken criteria, which recommended performing 3 biopsies for the diagnosis of CD.[4]

The next ESPGHAN guidelines for the diagnosis of CD were published in 1990 after introducing the tissue transglutaminase antibodies.[5]

According to these guidelines, one biopsy was sufficient if associated with positive serology, except for children younger than 2 years. In 2005, North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) developed clinical guidelines for the diagnosis and treatment of CD in children.[6] In 2008, the UK National Institute for Health and Clinical Evidence (NICE) published the guidelines for the diagnosis and management of CD in general practice, where small-bowel biopsies still had the central role for diagnosing CD.

Briefly, below are some of the recommendations of ESPGHAN guidelines from 2012.[3]

A major goal of the guidelines was to answer the question of whether duodenal biopsies with characteristic histological changes consistent with CD could be omitted in some situations in the diagnosis of CD. A whole spectrum of histological changes may be present, from a normal villous architecture to severe villous atrophy. According to the Marsh classification, lesions include infiltrative, hyperplastic, and atrophic patterns.[7] Intraepithelial lymphocyte count (IELs) >25/100 epithelial cells suggests an infiltrative lesion. These changes are not pathognomonic of CD and may be present in cow's milk or soy protein hypersensitivity, intractable diarrhea of infancy, severe infestation with Giardia lamblia, immunodeficiencies, tropical sprue, and bacterial overgrowth.[8] Even the most severe changes should always be interpreted in the context of clinical and serological settings and with consideration of dietary gluten content. Only 10 % of subjects presenting with infiltrative changes have CD.[9] Positive antibody levels increase the likelihood of CD.

Table 1: Indications for performing diagnostic, periodic and therapeutic upper endoscopy (NASPGAN position statement, 1996)

General indications for performing diagnostic upper endoscopy with biopsy
► gastrointestinal tract (GIT) bleeding (variceal and non-variceal)
► dysphagia and odynophagia
► persistent refusal to eat or persistent chest pain
► upper abdominal pain and/or discomfort with signs or symptoms suggesting serious organic disease (e.g., weight loss, anorexia, anemia), associated with significant morbidity (e.g., prolonged absence of school, hospitalization, limitation of usual activities)
► pain or discomfort which persists despite a course of therapy for vomiting of unknown cause
► indications for sampling of esophageal, gastric, duodenal or jejunal tissue/fluid
► clarification of imaging studies of the upper GIT
► known or suspected ingestion of a caustic material
► unexplained iron deficiency anemia
General indications for performing periodic upper endoscopy with biopsy
► periodic surveillance for proven Barrett's esophagus
► follow-up of selected ulcers or mucosal abnormality
► follow-up for adequacy of prior sclerotherapy or other variceal treatment (e.g., banding, shunting)
► surveillance for gastric or duodenal polyps in polyposis syndromes
► rejection or other complications following intestinal transplantation
Therapeutic upper endoscopy
► removal of selected polypoid lesions
► sclerotherapy or banding of esophageal varices
► dilation
► placement of feeding tubes (percutaneous endoscopic gastrostomy, transpyloric)
► treatment of persistent bleeding unresponsive to medical therapy
► removal of esophageal or sharp, foreign bodies or objects retained in the stomach generally longer than two to four weeks or temporally related to symptoms (e.g., vomiting, pain); removal of button batteries

Biopsies can be taken by upper endoscopy (recommended) or by suction capsule (performed in the past).[10] Although small-bowel biopsies obtained by suction capsule are usually of better quality, upper endoscopy has several advantages such as shorter procedure time, multiple biopsies obtained–given the possible patchy changes in CD. Endoscopy allows various patterns suggestive of CD to be visualized (e.g., absence of folds, scalloped folds, mosaic pattern of the mucosa between the folds). Reliability of these findings is limited to patients with total or subtotal villous atrophy.[11,12] The biopsy sampling site remains a matter for discussion. Sometimes, lesions may be limited to the duodenal bulb[13], although this is still controversial.[14]

Biopsies should be taken from the second/third portion of the duodenum (at least 4 samples) and from the duodenal bulb (at least 1 sample). Patients diagnosed as having CD do not need a histological re-evaluation on a gluten free diet (GFD). The disappearance of symptoms when present and/or normalisation of CD-associated antibodies are sufficient to support the diagnosis. If there is no clinical response to GFD in symptomatic patients, further biopsies may be required. In seronegative cases for anti-tissue transglutaminase type 2 antibodies (anti-TG2), endomysial antibodies (EMA) and antibodies against deamidated forms of gliadin peptides (anti-DGP), but with severe symptoms and a strong clinical suspicion of CD, small intestinal biopsies and HLA-DQ

Table 2: Indications for performing diagnostic, periodic and therapeutic colonoscopy (NASPGAN position statement,1996)

General indications for performing diagnostic colonoscopy with biopsy
► unexplained iron deficiency anemia
► unexplained gastrointestinal bleeding (e.g. melena or hematochezia of unknown origin)
► significant diarrhea of unexplained origin
► evaluation of inflammatory bowel disease
► abnormality on radiographic imaging (e.g., filling defect, stricture)
► intraoperative identification of a lesion that is not detected during surgery
► sexually transmitted diseases or rectal trauma (sigmoidoscopy only)
► ileal or colonic biopsies for diagnosis
General indications for performing periodic colonoscopy with biopsy
► surveillance for dysplasia/malignancy (e.g., IBD every 1–2 years in patients with pancolitis for more than 7–10 years and patients with left-sided ulcerative colitis for more than 15 years; Lynch syndrome after 20 years of age)
► patients with increased risk of colonic malignancy (e.g., after ureterosigmoidostomy)
► polyposis syndromes
► surveillance for rejection or other complications following intestinal transplantation
Indications for therapeutic colonoscopy
► polypectomy
► dilation of stenotic lesions
► treatment of bleeding vascular anomalies, ulcerations, or from a polypectomy site
► reduction of sigmoid volvulus
► removal of foreign body
► decompression of acute non-toxic megacolon

testing are recommended. If histology lesions are compatible with CD, but HLA-DQ2/HLA-DQ8 heterodimers are negative, then CD is not likely and an enteropathy of different etiology should be considered. Therefore, in these patients, CD could be diagnosed only after a positive challenge procedure with repeated biopsies.

Positive anti-TG2 or anti-DGP results should be confirmed by histology, unless certain conditions are fulfilled, which allow omitting the confirmatory biopsies.

In children and adolescents with signs or symptoms suggestive of CD and high anti-TG2 titers (levels >10 times ULN), the likelihood for villous atrophy (Marsh 3) is high. The option is to perform further laboratory testing (EMA, HLA), in order to diagnose CD without biopsies.

For an asymptomatic child or adolescent or for those with CD-associated conditions, the following approach is proposed. HLA testing should be offered as the first line test. The absence of DQ2 and DQ8 excludes CD. If the patient is DQ8 and/or DQ2 positive, then an anti-TG2 IgA test and total IgA should be performed, but preferably not before the child is 2 years old. If antibodies are positive, then duodenal biopsy is recommended. Demonstration of an enteropathy should always confirm the diagnosis of CD.

Indications for endoscopy in GERD

GER is the passage of gastric contents into the esophagus, with or without regurgitation and vomiting. GER is a normal physiologic process, occurring several times per day in healthy infants, children, and adults. GERD is present when the reflux of gastric contents causes troublesome symptoms and/or complications.

The NASPGHAN published the first clinical practice guidelines on pediatric GER and GERD in 2001.[15] Consensus-based guidelines on several aspects of GER and GERD were developed in Europe at about the same time, but were not officially endorsed by the ESPGHAN.[16,17]

In 2009, NASPGHAN and ESPGHAN developed an international consensus and evidence-based guideline for the diagnosis and management of GER and GERD in the pediatric population.[18] We emphasize the relevant recommendations from the guidelines about the indications for endoscopy in infants and children with GERD.

These indications are: infants with recurrent vomiting and poor weight gain, unexplained crying, irritability, or distressed behavior, children older than 18 months of age with chronic regurgitation or vomiting, heartburn, reflux esophagitis, Barrett esophagus, dysphagia, odynophagia, food refusal, difficulty in swallowing or pain with swallowing.[18]

Reflux is not a common cause of unexplained crying, irritability, or distressed behaviour in otherwise healthy infants. After excluding more common causes such as cow-milk protein allergy, neurologic disorders, constipation, and infection, additional investigations to diagnose GERD and esophagitis may be indicated (pH monitoring, impedance monitoring and endoscopy).

In some cases of chronic-relapsing esophagitis, repeat endoscopy or diagnostic studies may be indicated, if other causes of esophagitis have been ruled out.

Barrett esophagus (BE) occurs in children less often than in adults. Multiple biopsies in relation to endoscopically-identified esophagogastric landmarks are advised to confirm the diagnosis of BE and dysplasia.

Upper GI endoscopy allows direct visual examination of the esophageal mucosa and obtaining mucosal biopsies for histological evaluation.[19] Macroscopic lesions associated with GERD include esophagitis, erosions, exudate, ulcers, strictures, hiatal hernia (HH), esophageal metaplasia, and polyps. Endoscopy can detect strictures, but they are better seen on barium contrast study. That is why anatomic and motility disorders of the esophagus are better evaluated by barium radiology or motility studies. Recent global consensus guidelines define reflux esophagitis as the presence of endoscopically-visible breaks in the esophageal mucosa at or immediately above the gastroesophageal junction.[20] Mucosal erythema or an irregular Z-line is not a reliable sign of reflux esophagitis.[21] The Hetzel–Dent classificati-

on has been used in several pediatric studies for grading severity of esophagitis and response to treatment.[22-24] The Los Angeles classification is used for adults, however it can be used in children as well.[25] The presence of endoscopically-normal esophageal mucosa does not exclude a diagnosis of non erosive reflux disease (NERD) or esophagitis of other etiologies.[26,27] Multiple biopsy samples of good size and orientation should be obtained.[25,28] Histology may be normal or abnormal in NERD, because GERD is a patchy disease.[27] Eosinophilia, elongation of papillae (rete pegs), basal hyperplasia, and dilated intercellular spaces (spongiosis) are neither sensitive nor specific.[29-31]

GERD is likely the most common cause of esophagitis in children, however other disorders such as EoE, Crohn disease, and infections also cause esophagitis[32] (Table 3).

In children with documented esophagitis, normal esophageal pH monitoring suggests a diagnosis other than GER. EoE and GERD have similar symptoms and signs and can be best distinguished by endoscopy with biopsy, however not in all cases.

Indication for endoscopy in eosinophilic esophagitis

In 2007, the first consensus recommendations for the diagnosis and treatment of Eosinophilic esophagitis (EoE) were published,[26] which were updated in 2011.[33]

According to these new recommendations, "EoE represents a chronic immune/antigen mediated esophageal disease, characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation". The updated definition of the disease includes the histological presence of > 15 eosinophils per high power field (eos/hpf) in at least 1 endoscopic esophageal mucosal biopsy (peak value) taken at upper gastrointestinal endoscopy.[33]

Upper endoscopy for mucosal abnormalities is an integral part of the diagnostic workup in suspected EoE. The endoscopic mucosal changes may be seen through the entire length of the esophagus.

Typical endoscopic findings include esophageal rings, linear furrows and white exudates and less often, narrowing of the caliber of the esophagus. A normal esophagus

Table 3: Causes of esophagitis

► Gastroesophageal reflux
► Eosinophilic esophagitis
► Infections
► Candida albicans
► Herpes simplex
► Cytomegalovirus
► Crohn disease
► Vomiting, bulimia
► Pill induced
► Graft-versus-host disease
► Caustic ingestion
► Postsclerotherapy/banding
► Radiation/chemotherapy
► Connective tissue disease
► Bullous skin diseases
► Lymphoma

at endoscopy does not exclude the diagnosis of EoE. Mucosal breaks (erosions or ulceration) are not findings of EoE and are indicative for GERD, Crohn's disease or other diagnoses. According to Shah et al, at least three esophageal biopsy specimens taken from different parts of esophagus are necessary in order to achieve a diagnosis of EoE in 97 % of patients.[34] In their study, Gonsalves et al showed a sensitivity of only 55 % in 1 biopsy specimen compared to the sensitivity of 100 % in 5 biopsies.[35] To maximize diagnostic sensitivity, it is therefore recommended that at least 2–4 biopsies should be taken from both proximal and distal esophagus, regardless of the endoscopic appearance of the esophagus.[33]

The main differential diagnosis for symptoms and histopathological findings is GERD, although other diseases that are also associated with esophageal eosinophilia, such as infectious esophagitis, esophageal achalasia, celiac disease, Crohn's disease, connective tissue disorders, graft-versus-host disease, drug hypersensitivity, and hyper-eosinophilic syndromes should also be excluded.[26,32,33]

Recently, Mulder et al proposed a scoring system of clinical and endoscopic features, which may be useful in older children and adolescents.[36] A very recent study reported that the measurement of eosinophil-derived proteins in luminal secretions could be used to distinguish children with EoE from those with GERD.[37] Recommendations for evaluation of management are presented below. It is outlined that in symptomatic children with histological findings of esophageal eosinophilia, a trial of PPIs is recommended for 8 weeks. A second upper endoscopy should be performed under PPI therapy in all children, even if symptoms resolve. If histology is still suggestive of EoE, then the diagnosis of EoE should be made. The efficacy of the dietary intervention and drug treatment should be monitored by symptomatic assessment and evaluation of endoscopic and histological response. In cases of clinical and histological remission, foods should be re-introduced, with drug titration or discontinuation. The lack of appropriate biomarkers to evaluate response to treatment and detect early relapse may require repeated endoscopy and biopsy during the course of the disease. Such biomarkers are currently under investigation.[38]

Endoscopy and Helicobacter pylori infection

We emphasize the best available evidence for children and adolescents with Helicobacter pylori infection and some of the recommendations where endoscopy is mentioned.[39]

In recommendations 1 and 2, it is stressed that diagnostic testing for H pylori infection is not recommended in children with functional abdominal pain. There is inadequate evidence supporting a causal relation between H pylori gastritis and abdominal symptoms in the absence of ulcer disease. Therefore, cases of abdominal pain consistent with the diagnostic criteria of functional pain[40] should not be investigated for H pylori, unless upper endoscopy is performed during the diagnostic workup in search for organic disease.[41-47]

In recommendation 4, it is outlined that in children with refractory iron-deficiency anemia in which other causes have been ruled out, testing for H pylori infection and endoscopy should be performed.

Recommendations 6 and 7 point out that for the diagnosis of H pylori infection during endoscopy, gastric biopsies (antrum and corpus) for histopathology are taken. Initial diagnosis of H pylori infection should be based on either positive histopathology, positive rapid urease test or a positive culture. Two biopsies are taken from both the antrum and the corpus for histology. Presence of H pylori is patchy. It is highly recommended to take not only biopsies for histopathology but also for a rapid urease test and culture. The diagnosis of the infection is based also on the macroscopic findings of a nodular mucosa in the antrum or bulbus and/or gastric or duodenal erosions or ulcerations.

Endoscopy and histology in cow's milk protein allergy

The recently published evidence-based guideline provides recommendations and practical algorithm for the diagnosis and management of suspected cow's-milk protein allergy (CMPA).[48] If CMPA is suspected by history and examination, then strict allergen avoidance is initiated. A controlled oral food challenge (open or blind) under medical supervision is required to confirm or exclude the diagnosis of CMPA. In patients with otherwise unexplained significant and persistent gastrointestinal symptoms, failure to thrive, or iron deficiency anemia, upper and/or lower endoscopies with multiple biopsies are appropriate. However, macroscopic lesions and histological findings, such as mucosal atrophy or eosinophilic infiltrates, are neither sensitive nor specific for CMPA, and these should be interpreted in the context of medical history and oral challenges. The diagnostic yield of these procedures is higher for finding diagnoses other than CMPA.

Endoscopy in inflammatory bowel disease

The diagnosis and classification of IBD are provided in the Porto criteria for the diagnosis of pediatric IBD[49], the Paris pediatric modification of the Montreal classification of IBD[50], and the NASPGHAN working group review.[51] In ulcerative colitis (UC), there are specific guidelines for management.[52]

These criteria are the result of the consensus reached by the ESPGHAN inflammatory bowel disease working group. Diagnosis of Crohn disease, ulcerative colitis and indeterminate colitis is based on clinical signs and symptoms, endoscopy, histology and radiology (imaging). Every child suspected of IBD should undergo a complete diagnostic program consisting of colonoscopy with ileal intubation, upper gastrointestinal endoscopy and (in all cases except in definite ulcerative colitis) radiologic contrast imaging of the small bowel. Multiple biopsies from all segments of the GI tract are required for a complete histological evaluation.

Histological evidence of Crohn's disease in the upper GI tract can be present in up to 30 % of cases, even in the absence of upper GI symptoms. Unlike adults, more than 90 % of children with UC have a pancolitis, making full colonoscopy advisable. Sigmoidoscopy does not have a role except in severe UC where the risk of bowel perforation is higher, making flexible sigmoidoscopy a safer option. Histology of terminal ileal biopsies may help to exclude other diagnoses (eg, tuberculosis, Behcet syndrome, lymphoma, vasculitis). A diagnosis of indeterminate colitis cannot be made unless a full diagnostic program has been performed.[53,54]

Endoscopy is a crucial tool in the management of IBD. There is a spectrum of situations when an endoscopy may be of value in IBD, extending from initial diagnosis to differentiating between Crohn's disease and ulcerative colitis to long term management of both conditions. The role of colonoscopy in the management of IBD can be summarized as follows: (1) to establish a diagnosis; (2) to assess the disease extent and activity; (3) to monitor disease activity; (4) for surveillance of dysplasia or neoplasia; (5) to evaluate ileal pouch and ileorectal anastomosis; (6) to provide endoscopic treatment, such as stricture dilation/stent placement.

The endoscopic findings of active UC range from erythema, loss of the usual vascular pattern due to oedema, granularity of the mucosa and friability/spontaneous bleeding to erosions/ulceration. The endoscopic hallmark of Crohn's disease is the heterogeneous patchy nature of inflammation or skip lesions (areas of inflammation interposed between normal mucosa).

Macroscopic endoscopic differences between Crohn's disease and ulcerative colitis are presented in Table 4.

Colonoscopic surveillance for neoplasia is recommended by most gastroenterology and endoscopy societies. The British Society of Gastroenterology guidelines propose that patients with UC or Crohn's colitis should have a colonoscopy 10 years after the initial diagnosis to define the extent and activity of the disease. The advent of capsule and both single- and double-balloon-assisted enteroscopy is revolutionizing small-bowel ima-

ging and has major implications for diagnosis and classification.[54,55]

The main advantage of small bowel video capsule endoscopy (VCE) is the potential to visualize the entire length of the small bowel. It is less invasive and better tolerated. Compared to radiological investigations (CT or MR enterography), VCE appears as very sensitive in detecting early mucosal lesions. Recent studies showed the following sensitivity for diagnosis of Crohn's disease of the terminal ileum: 100 % by VCE, 81 % by MR enterography, and 76 % by CT enterography, respectively.[56,57]

Video capsule endoscopy

Video capsule endoscopy (VCE) is a diagnostic tool especially useful in imaging the small intestine. VCE technology offers greater magnification than traditional endoscopy, while also providing excellent resolution. It is a clinically useful tool for detecting occult bleeding[58] and superficial lesions that are not radiographically observed.[59,60] Much of the small bowel is not accessible with traditional endoscopy or even push endoscopy (which allows imaging up to 80–120 cm beyond the ligament of Treitz), however it can be visualized with the capsule endoscopy. In 1999, the first volunteer studies were performed and high-quality images from volunteers were published in the literature shortly thereafter.[61] In 2001, VCE was approved by the US Food and Drug Administration (FDA) for use in patients in the United States. In 2004, VCE was approved as a diagnostic tool for children older than 10 years of age. Supported by additional experience in children as young as 10 months of age, in 2009 the FDA expanded the role for VCE use to children 2 years and older and approved the use of a patency capsule (PC) for the same age group.[62]

The main indications for VCE are obscure GI bleeding,[63] suspected Crohn's disease, celiac disease, small bowel neoplasia, polyps etc.

Most obscure GI bleeding is due to lesions in the small intestine, a region that has traditionally been difficult to image adequately. Before VCE, the standard procedure comprised a combination of diagnostic methods, including upper endoscopy, colonoscopy, and push enteroscopy, as well as enteroclysis, nuclear bleeding scans, angiography, and small-bowel follow-through studies.

Crohn's disease affects the small bowel in most individuals; in 30 % of patients, the disease is limited to the terminal ileum.

When used to evaluate IBD, capsule endoscopy allows visualization of lesions (e.g., small bowel erosions and ulcerations) in areas that other types of endoscopy[59] or radiography would not visualize. Capsule endoscopy can localize Crohn's disease in the small bowel.

A meta-analysis comparing the diagnostic yield of capsule endoscopy with that of other modalities (e.g., barium studies, colonoscopy with ileoscopy, computed tomography [CT] enterography or enteroclysis, and small-bowel magnetic resonance imaging [MRI]) found capsule endoscopy to be superior in the diagnosis of a recurrence in nonstricturing small-bowel Crohn disease.[64,65]

In accordance with adult and small number of pediatric studies,[66-69] NASPGHAN concluded that VCE is increasingly being used in the detection of obscure small bowel lesions and now has a proven role in the identification of Crohn's disease of the small intestine.[51]

Table 4: Differences in the macroscopic appearance between Crohn's disease and ulcerative colitis

Macroscopic features	UC	Crohn's Disease
Erythema	+ + +	+ +
Loss of vascular pattern	+ + +	+
Granularity of mucosa	+ + +	+
Cobblestone appearance	–	+ +
Pseudo polyps	+ + +	+ + +
Aphthous ulcers	+	+ + +
Deep ulcers	–	+ + +
Patchy inflammation	–	+ + +
Ileal ulcers	–	+ + +
Rectal involvement	+ + + +	+ +

UC – ulcerative colitis

Small bowel neoplasia occurs in 75 % of patients with Peutz-Jeghers syndrome (PJS) and 90 % of patients with familial adenomatous polyposis (FAP). Capsule endoscopy is superior to barium contrast study in detecting small-bowel polyps in patients with hereditary polyposis syndromes.

Capsule endoscopy has been considered an alternative diagnostic tool for diagnosis of celiac disease because the magnification it provides is sufficient for imaging the villi and detecting villous atrophy.

Rondonotti et al found that capsule endoscopy had a sensitivity of 87.5 % and a specificity of 90.9 % for findings such as flattened mucosa, mosaic appearance, and scalloped duodenal folds, compared with the biopsy results.[70]

Contraindications for VCE include swallowing disorders, small bowel obstruction, and small bowel stenosis. When the patient can not swallow the capsule due to any reason (including swallowing disorders, dysphagia, gastroparesis), the capsule can be safely introduced in the duodenum using various techniques and a standard endoscope. The safety and efficacy of capsule endoscopy in the pediatric population have not yet been established, though the literature includes a few positive case reports.[71]

Conclusion

Pediatric gastrointestinal endoscopy has evolved in the last decades. It developed from an infrequent procedure to a routine, safe and effective diagnostic tool. Children of all ages including premature newborns can be examined, enabling diagnoses of well known diseases (like GERD, IBD or celiac disease) and emerging disorders (for example, EoE). The new techniques, such as capsule endoscopy, have been established and are used more and more in pediatric patients.

International and national committees for pediatric gastroenterology have issued numerous guidelines that clarify the indications for performing endoscopy in various clinical conditions.

List of abbreviations:

- anti-TG2–anti-tissue transglutaminase type 2 antibodies
- anti – DGP–antibodies against deamidated forms of gliadin peptides
- BE–Barrett's Esophagus
- CD–celiac disease
- CMPA–cow's-milk protein allergy
- CT–computed tomography
- EoE–eosinophilic esophagitis
- EMA–endomysial antibodies
- ESPGHAN–European Society of Paediatric Gastroenterology Hepatology and Nutrition
- FAP–familial adenomatous polyposis
- FDA–Food and Drug Administration
- GERD–gastroesophageal reflux disease
- GI–gastrointestinal
- GFD – gluten free diet HH–hiatal hernia
- IBD–inflammatory bowel disease
- IELs–intraepithelial lymphocytes
- MRI–magnetic resonance imaging
- NASPGHAN–North American Society of Pediatric Gastroenterology Hepatology and Nutrition
- NERD – nonerosive reflux disease
- PJS–Peutz-Jeghers syndrome
- PPI – proton pump inhibitor
- UC–ulcerative colitis
- VCE–video capsule endoscopy

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