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Alimentary Tract

Oesophageal motor function in chronic intestinal idiopathic pseudo-obstruction: A study with high-resolution manometry

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ABSTRACT

Background: Chronic intestinal idiopathic pseudo-obstruction (idiopathic CIPO) is a rare heterogeneous condition for which the different phenotypes are difficult to be established. Oesophageal motility has shown to be impaired in patients with idiopathic CIPO at traditional manometry, whereas no studies have assessed it by high resolution manometry (HRM).
Aims: To evaluate oesophageal motility by HRM in patients with idiopathic CIPO.
Methods: 14 patients with idiopathic CIPO underwent oesophageal HRM. Multiple rapid swallows (MRS) were performed in order to evaluate contraction reserve. The Chicago Classification 3.0 was used to classify the oesophageal motility disorders.
Results: One idiopathic CIPO patient had type-II achalasia, one aperistalsis and 12 had minor disorder of peristalsis (11 ineffective oesophageal motility and one fragmented peristalsis). These minor disorders were not significantly different from those of 50 other consecutive patients who underwent HRM for dysphagia or GERD and received the diagnosis of ineffective oesophageal motility. Three of the 12 idiopathic CIPO patients with minor disorder of peristalsis had no contraction reserve after MRS.
Conclusions: HRM is able to identify different grades of oesophageal motor impairment in patients with idiopathic CIPO. Presence of major oesophageal dismotility or absent contraction reserve suggest a more severe and widespread motor disorder.

1. Introduction

Chronic intestinal pseudo-obstruction (CIPO) is a rare disabling condition characterized by symptoms and signs of intestinal obstruction, such as small bowel or colonic dilation, but without the evidence of any lesion occluding the lumen of the gut [1]. In a nationwide epidemiological survey in Japan, the prevalence of the disease including the secondary forms was 0.9 per 100,000 [2]. The syndrome most commonly occurs secondary to such diseases (secondary CIPO) as: systemic sclerosis, amyloidosis or endocrine and neurological diseases [1]. In such cases the prognosis and treatment are mainly related to the underlying condition. It is less clear how to establish the diagnosis in the idiopathic form of CIPO (idiopathic CIPO) and whether different phenotypes of this condition have different prognosis and treatment.

On the basis of the histological examination, idiopathic CIPO can be classified as enteric visceral myopathies, neuropathies and mesenchymopaties [1,3–5]. Full-thickness tissue biopsies are required for histological classification, but the normal ranges of the cellular components of the enteric nervous system are not well defined and the histological alterations *per se* do not seem to have a clear role in directing management or establishing a prognosis [4,6,7]. In the presence of inflammatory neuropathies steroids alone or combined with other immunosuppressive therapies have reportedly improved the clinical picture even if such an indication is based on few cases [8]. Thus, other approaches have been attempted in order to characterize the patients without the risks of surgery including: antro-duodenal manometry [7,9], anorectal manometry [10], magnetic resonance enterography in response to neostigmine [11], anti-neuronal nuclear antibodies [7,10,12–14] and anti-GAD antibodies [15].

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Standard oesophageal manometry has also been used in patients with idiopathic CIPO [10,14,16,17]. In a large study evaluating both idiopathic and secondary forms of CIPO, oesophageal motor impairment provided a significant predicting value for survival and for home-based parenteral nutrition requirement, suggesting that oesophageal manometry should be systematically performed in CIPO patients [7].

Oesophageal high-resolution manometry (HRM) has been recently introduced in clinical practice giving physicians a detailed representation of the motor activity of the entire oesophagus [18]. Where available HRM provides a more accurate diagnosis of oesophageal motor disorder than standard manometry [19]. A standardized classification of primary oesophageal motor disorders has been created, thus improving the understanding of oesophageal pathophysiology in patients with oesophageal symptoms [20]. However HRM has not been applied yet in patients with idiopathic CIPO.

Multiple rapid swallowing (MRS) during HRM is a complementary test that evaluates the oesophageal contraction reserve function, which requires both intact neural and muscular integrity [21]. Recently, the loss of contraction reserve in response to MRS has shown to represent the most common manometric abnormality in patients with systemic sclerosis regardless of baseline oesophageal motility diagnosis [22], thus suggesting that this test may be more sensitive than standard single water swallows in the detection of oesophageal motor impairment, at least in selected groups of patients. The manometric response to MRS has not been reported yet in patients with idiopathic CIPO.

Therefore, the aim of our study was to evaluate the presence of major and minor motor disorders in a consecutive series of patients with idiopathic CIPO, who underwent HRM, and to evaluate their contraction reserve in response to MRS.

2. Methods

2.1. Patients

Fourteen consecutive adult patients with idiopathic CIPO (five males; median age 42 years; range 29–50; 13 Caucasians and one black African) underwent HRM from September 2011 to February 2016. The diagnosis of idiopathic CIPO was based on the presence of chronic symptoms of obstruction, radiological evidence of at least one gut segment distended with air-fluid levels and exclusion of any organic obstruction of the gut lumen [1,2,23,24]. Any patients with CIPO secondary to paraneoplastic and collagen diseases, including: systemic sclerosis, diseases of the central nervous system (mitochondrial neurogastrointestinal encephalomyopathy, myotonic dystrophy, parkinsonism, and multiple sclerosis) were carefully excluded as were those with spinal cord lesions, diabetic visceral neuropathy, hypothyroidism, hypoparathyroidism, and amyloidosis. Any patients with previous oesophageal and gastric surgery or eosinophilic oesophagitis were also excluded. None of the patients had travelled in countries where Chagas' disease is endemic or in East Africa.

All the patients with idiopathic CIPO underwent an abdominal CT or MRI scan and the appropriate endoscopic exams in order to exclude a mechanical obstruction and to define the magnitude of the gut dilation. The presence of anti Hu antibodies was assessed as previously described [10]. All the patients with colonic dilation underwent anorectal manometry to investigate the presence/absence of the rectoanal inhibitory reflex. Thirteen patients were followed up for a median time of 4 years (range 2–20 years) after diagnosis, whereas one was lost to follow-up.

2.2. Oesophageal high-resolution manometry

Oesophageal symptoms were recorded with a standardized questionnaire for all patients [25].

HRM was performed using a 4.2-mm outer diameter solid-state assembly with 36 circumferential sensors spaced at 1-cm intervals (Unisensor AG, Attikon, Swizerland). The manometric signals were visualized as isobaric contour plots on a dedicated screen, and were stored for subsequent analysis using commercial software (MMS Investigation & Diagnostic Software, Version 8.19, build 2188). Normal values were set according to Bogte et al. [26]. In all cases, the oesophageal manometry catheter was passed trans-nasally under topical anesthesia (Lidocaine spray 10%) after overnight fast, and positioned so that it straddled the lower oesophageal sphincter (LOS). The whole test was performed with the patients in a recumbent position on their right side. Each test started with ten five-mL single swallows (SS) of water at intervals of 20–30 s, followed by two 10-mL multiple rapid swallows (MRS) as follows: two-mL water swallows were administered through a syringe at intervals of two-three seconds, while the physician indicated the rhythm of swallowing.

2.3. Data analysis

2.3.1. Single swallows

For all the patients, there was acquisition of data about: the LOS (basal tone, measured during 30 s of resting at the beginning of manometry, and 4-s Integrated Relaxation Pressure, 4-s IRP), oesophageal body (Distal Contractile Integral, DCI) and peristaltic activity (number of weak and failed waves defined as DCI lower than 450 mmHg s cm and 100 mmHg s cm respectively) [20]. The Chicago Classification v3.0 of motility disorders was used.

2.3.2. Multiple rapid swallows

During MRS the following variables were assessed: (1) presence of motor inhibition, defined as the absence of any motor activity >20 mmHg of amplitude in the distal oesophageal body; (2) oesophago-gastric pressure gradient (OGPG), defined as the difference between intra-oesophageal and intra-gastric pressure, with the first being measured 3 cm above the upper border of the LOS during the last five seconds of MRS or, in the presence of contractions, during the last five seconds of suppressed motility [27,28]. After MRS the presence of any after-contraction of the oesophageal body (defined visually as the presence of peristaltic activity between the transition zone and the upper border of the LOS) was assessed and the ratio between the mean DCI of the identified after-contractions and the mean DCI of SS (the MRS/SS DCI ratio) was calculated in order to define contraction reserve. Absence of contraction reserve was defined as the absence of after-contractions or by a MRS/SS DCI ratio <1.

2.4. Patients with Ineffective Oesophageal Motility (IOM)

As the majority of idiopathic CIPO patients had minor disorders of peristalsis (i.e. IOM and fragmented peristalsis; see Results), their results were compared with those of 50 other consecutive patients (18 males; median age 53 years; range 39–68) who underwent HRM with the same protocol from July 2015 and December 2015 for dysphagia and/or symptoms suggesting of gastro-oesophageal reflux disease (GORD) and received a diagnosis of IOM according to Chicago Classification v3.0 [20].

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