FUNCTIONAL GASTROINTESTINAL DISORDERS

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RESUMEN

Los trastornos funcionales digestivos hacen parte de la patología gastrointestinal pediátrica. Son una combinación de síntomas gastrointestinales crónicos y recurrentes inexplicables secundarias a anomalías estructurales o bioquímicas. Involucran un espectro de entidades variadas, algunas de ellas consideradas como normales en el desarrollo del niño, y en las que los factores anatómicos, y afectivos cobran una especial importancia.

Palabras clave: Trastornos digestivos funcionales, Niños

SUMMARY

The digestive functional disorders are part of the pediatric gastrointestinal pathology. They are a combination of secondary inexplicable chronic and recurrent digestives symptoms to structural or biochemical anomalies. They involve a series of varied entities, some of considered them like normal in the development of the children, and in whom the anatomical, and affective factors receive a special importance.

Key words: Functional digestive disorders, Children

Functional gastrointestinal disorders (FGIDs) are defined as a group of conditions with variable combination of recurrent or chronic gastrointestinal symptoms in the absence of any clinical evidence of structural or anatomical abnormalities. In clinical practice, most children consulting for chronic or intermittent gastrointestinal pain have a FGID without any objective evidence of a pathologic condition. They are considered to have one of the most common GI conditions, functional abdominal pain. The Rome criteria distinguish four diagnoses within abdominal pain related FGIDs: functional dyspepsia, irritable bowel syndrome, childhood functional abdominal pain and abdominal migraine. Despite their frequent occurrence, the pathophysiology of most of these conditions remains unclear. The biopsychosocial model theorizes that differently than in the biomedical model in which each disease is caused by a single etiology, FGIDs result from the interaction of multiple biological, psychological and social factors. Among the multiple factors involved in the pathogenesis of FGIDs are genetic and environmental factors including familiar learning behavior and modeling. The results of twin studies support a genetic contribution. These studies have shown that concordance for Irritable bowel syndrome (IBS) was significantly greater in monozygotic (17.2%) than in dizygotic (8.4%) twins[1]. The responses from parents towards child's abdominal pain may reinforce or discourage future sick role behaviors. Studies have shown that solicitous responses from the parents towards the child's pain reinforce the child's symptoms and increase the health care-seeking behaviors[2].

Early life experiences also influences an individual's susceptibility to FGIDs. The early neonatal period is a vulnerable time. During this period nociceptive neuronal circuits are formed. The formation of neuronal circuits requires use-dependent activity for appropriate development. The presence of noxious stimuli during this critical period may affect their development resulting in decreased pain thresholds later in life. Therefore, early life events affect the

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developing brain and nervous system at a vulnerable age of great plasticity which may lead to modifications in future behavior towards pain. During this period of great plasticity, the alteration of synaptic input to central neurons can lead to permanent changes that manifest later in life. Animal studies have shown that in the neonatal period, colonic irritation results in chronic visceral hypersensitivity that persists through adulthood, findings that validate the possible role of early life events as proposed in biopsychosocial model. In humans, a cohort study has shown an association between gastric suction at birth and the child developing FGID later in life[3].

Later in life, various triggering factors either at the CNS or GI tract levels or both may also result in the manifestation of FGIDs. Pain may result from psychological or social aggressions or noxious stimuli affecting the wall nerve terminals, ENS or dorsal neurons in the spine, or higher structures. Stressful events may trigger symptoms of FGIDs. Patients undergoing stressful situations frequently complain of feeling like having "butterflies in the belly". Children who are high achievers and those who are bullied at school have a higher incidence of FAP in comparison to their peers[4-6]. The higher seasonal prevalence of functional abdominal pain symptoms during winter months may result from the interaction of various pathogenic factors such as school stressors, and cold weather that limits children's ability to be distracted by playing outdoors. Dysregulation of the hypothalamus-hypopituitary-adrenal axis can mediate the effects of stress on gastrointestinal function. The activation of brain corticotrophin-releasing factor (CRF) pathways plays an important role not only in the behavioral but in the visceral responses to stress. Experiments in CRF 1 knockout mice demonstrated the role of CRF_1 receptors in stress-related endocrine[7], behavioral (development of anxiety and depression)[8] and autonomic[9] responses. Animal studies showed that corticotrophin releasing hormone (CRH) antagonists abolish the increased gut sensitivity to stress. Studies have shown that CRF_1 signaling in the gut and the brain plays a role in the comorbidity of depression and anxiety in patients with IBS[10]. CRF gene expression is up-regulated by stress[11] which in turn results in delayed gastric emptying, dysmotility of the small intestine and colonic hypermotility[12]. Animal studies have shown that stress increases pain in response to rectal distension via neuronal pathways involving CRF and intestinal mast cells[13]. The role of CNS in modulating visceral pain and motility can be studied by using imaging modalities like position emission tomography (PET) and functional magnetic resonance imaging (fMRI). Studies on visceral hypersensitivity (a proposed "biological marker" of IBS) have demonstrated an important involvement of central and peripheral neurons in the pathogenesis of FGIDs. Recent findings indicate that gut inflammation may result in sensitization of parietal mechanoreceptors[14]. Barbara et al. have shown increased numbers of degranulating mast cells in close vicinity to mucosal nerves in colonic biopsies taken from IBS patients[15]. The frequency and severity of abdominal pain correlated with the proximity of the nerves to the mast cells and their degranulation products. Chemical or mechanical colonic stimuli in leads to chronic visceral hypersensitivity, with characteristics of allodynia (a painful response to a usually non-painful stimulus) and hyperalgesia (increased sensitivity to pain) associated with central neuronal sensitization[16]. Central sensitization constitutes an important mechanism of neuropathic pain. Studies have shown enhanced spinal cord processing in IBS patients with hyper excitability of spinal nociceptive neurons[17]. Sensitization of spinal sensory neurons may lead to enhanced neurotransmission as well as increased neuronal spontaneous activity and decreased firing threshold[18]. Interestingly, animal studies showed that central sensitization and visceral hypersensitivity to distal colonic and rectal balloon distention may result from the injection of irritants in the gastrocnemius muscle, areas that are innervated by common dermatomes. These findings exemplify the existence of a viscerosomatic convergence that includes synaptic input from afferents of the somatic

domain. Animals subject to this experiment during the neonatal period developed chronic somatic and visceral hyperalgesia[16].

The bidirectional interplay of peripheral and central effects is another important factor in the development of visceral hypersensitivity (brain-gut axis)[19]. CNS affects the peripheral activity through the modulation of the peripheral input. fMRI studies show detectable differences in regional cerebral blood flow in IBS patients when compared to healthy controls, suggesting abnormal cerebral sensory processing in response to colonic distention in IBS patients[20-23]. IBS patients have an amplification of pain, involvement of areas related to emotions and hypervigilance and a lower ability to down regulate the pain through the inhibition of the dorsal spinal neurons[24]. Studies in IBS patients show a greater degree of activation of areas associated with the cognitive processing of the sensory input[21,22]. These and other findings further prove the importance of the interactions of the brain gut axis, the biopsychosocial model for pathogenesis of FGIDs in the understanding that these conditions do not result of a single etiologic agent and that similar symptoms in different patients may result from different mechanisms[25].

Infectious agents may play a role in the pathophysiology of FGIDs. Studies have shown that IBS can develop as a sequel of an acute bacterial gastrointestinal infection[26]. Gut motor and sensory changes persist even after resolution of inflammation[31]. Saps et al. found a significantly higher prevalence of dyspepsia (24%) and IBS (87%) in children exposed to bacterial gastrointestinal infections (Shigella, Salmonella and Campylobacter), compared to the controls[27]. In this study, 36% of exposed children and 11% of control subjects complained of abdominal pain years after the resolution of the acute gastrointestinal infection. Adult studies have shown that patients with post infectious bacterial IBS have decreased gut transit time and enhanced rectal sensitivity than controls[28]. Rectal biopsies obtained from patients who developed post-infectious IBS showed greater expression of interleukins[29] and increased number of T lymphocytes[30]. Although, the role of bacteria in post infectious-IBS seems to be gaining acceptance, the possible effect of viral infections in the causation of post infectious IBS still remains unclear[27].

An adequate quantity and qualitative composition of the gut flora is necessary for the correct function of the GI tract. Gut flora may affect gut sensation and motor functions. Although the role of gut flora in pathogenesis of IBS remains unclear, a study found increased flora in up to 80% of patients with IBS[32-34].

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