Irritable Bowel Syndrome: Overlaps, Epidemiology, Diagnosis and Management

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Abstract:

Irritable bowel syndrome (IBS) is one of the most prevalent functional digestive disorders, diagnosis of patients might be difficult because IBS can be confused with the symptoms of other organic gastrointestinal disorders such as diarrhea, microscopic colitis, celiac and inflammatory bowel disease.

The primary clinical symptoms of IBS included changed bowel habits, pains, and recurrent abdominal discomfort. The pathogenesis of IBS is very complicated, there was several factors like environment, heritability, genetic, diet or intestinal inflammation, social learning, and disorders in the neuroendocrine system (NES) of the gut. The treatment must be tailored to each patient specific symptomatology because may be difficult management of the disease, patients should be avoiding some foods such as fermentable saccharides that increase osmotic pressure that provide substrate for bacterial fermentation, which results in the production of gas, distension of the large intestine with pain and discomfort in the abdomen. Many studies approved the effect of probiotics by improvements of abdominal distension and flatulence, as well as a reduction in the composite IBS symptom. Probiotics bind to the epithelial cells, inhibit pathogens, and improve intestinal barrier function, also increase stabilization of the colonic microbiota and reduce colonic fermentation.

Keywords: Irritable bowel syndrome, Diagnosis, Treatment.

متلازمة القولون العصبي: التداخلات، وبائية المرض، التشخيص والعلاج

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الخلاصة

متلازمة القولون العصبي (IBS) هو أحد أكثر الاضطرابات الوظيفية انتشارا للجهاز الهضمي، من الصعوبة تشخيص المرض لكون اعراضه متشابهة مع القولون العصبي واضطرابات الجهاز الهضمي العضوية الأخرى مثل الإسهال والتهاب القولون المجهري ومرض الاضطرابات الهضمية والتهاب الأمعاء. وفقًا للتوصيات العالمية، فإن معايير روما IV هي المعيار الذهبي الحالي لتشخيص القولون العصبي. ان الأعراض السريرية الأولية لمرض القولون العصبي تشمل تقلبات في الأمعاء والآلام متكررة في القولون وعدم الارتياح. تاثير الكائنات الحية الدقيقة بما في ذلك فرط نمو البكتيريا المعوية الصغيرة، والتغذية يعتبر امرا هاما. مسببات مرض القولون العصبي معقدة للغاية، حيث تلعب عدة عوامل دورًا اساسيا في حدوث المرض: تشمل هذه العوامل الوراثة، البيئة، والنظام الغذائي، والالتهابات المعوية، ودرجة الوعي الاجتماعي واضطرابات في نظام الغدد الصم العصبية داخل القناة الهضمية حيث يتكون هذا النظام في الامعاء من جزئين: خلايا الغدد الصم المنتشرة بين الخلايا الظهارية للغشاء المخاطي بمحاذاة تجويف الأمعاء، والأعصاب المحتوية على الببتيدرج، وهرمون السيروتونين، وأوكسيد النتريك في الجهاز العصبي المعوي في جدار الأمعاء. يجب ان يكون علاج القولون العصبي متناسبا مع الأعراض المشخصة لكل مريض لأنه من المحتمل

صعوبة إلسيطرة على المرض، ويجب تجنب بعض الأطعمة من قبل المرضى مثل السكريات القابلة للتخمر التي تزيد من الضغط الأزموزي والذي يساهم في تطور القولون العصبي وزيادة التخمر البكتيري مما يؤدي إلى إنتاج الغازات، وانتفاخ الأمعاء الغليظة مع الألم وعدم الارتياح. اكدت العديد من الدراسات التأثير الايجابي للبروبيوتيك من خلال تقليل اثار انتفاخات القولون، بالإضافة إلى تقليل الأعراض المعقدة لمتلازمة القولون العصبي. ترتبط البروبيوتيك بخلايا بطانة الامعاء، وتمنع تطور المرض، وتحسين وظيفة الحاجزالمعوي، كما تزيد من استقرارية الكائنات الحية الدقيقة في القولون وتقلل تخمر القولون.

الكلمات المفتاحية: متلازمة القولون العصبي، التشخيص، العلاج.

Introduction

Overlaps

Irritable bowel syndrome (IBS) is common disease of gut-brain interactions, generally known as functional gastrointestinal disease (1). Most of cases occur in females and wealthy countries (2). It's diagnosed clinically depend on the self-reported symptoms of patients; and may be less common than functional dyspepsia (3). Irritable bowel syndrome (IBS) is classified as a chronic functional disease, and its effects mainly on the bowel functions with abdominal pains interfere with the patient capacity, it primarily affects young people; and overlaps with other functional gastrointestinal disease and causes a huge burden to life and economy of society (4). Because of variations in diet, culture, and diagnosis, prevalence varies significantly among nations. (2). The association between IBS and psychological discomfort, anxiety, and depression aligns with the replaced terminology of functional gastrointestinal disorders. by the term disorder of gut brain interaction (5) in order to ascertain the effectiveness of psychological therapy (6), overlap of this disease related to severe symptoms and impact on life quality (7). Individuals were distinguished by higher rates of psychological distress and worse sleep quality with regardless of age or sex, (8). Recently found that Irritable bladder disorders and headaches, particularly migraines, are associated with IBS (9,10). In addition to increased somatization and psychological distress in patients, functional diarrhea or constipation has also been linked to IBS (11).

Gut endocrine cells are found throughout the gastrointestinal tract, according to several years of studies when food and microbial metabolism stimulate the gut lumen, the cells release hormones into the lamina propria to act primarily through paracrine and afferent and efferent synaptic transmission. It also demonstrated the variations in IBS subtypes and how neurotransmitters may trigger abdominal pain through the hypothalamus and brain-gut axis (12). Additionally, it has found that IBS patients have higher levels of histamine, glutamate, noradrenalin, and γ-aminobutyric acid than healthy controls, which reduces gastrointestinal motility and abnormal colonic transit (13). Sensory microvilli are responsible for detecting gut pressure and gut contents. It was shown that bile acid and short-chain fatty acid metabolites are mostly linked to gastrointestinal malabsorption. (14)

Dietary and intestinal flora

Certain types of foods must be avoided by patients because they have a major impact on the disease's symptoms. In approximately sixty percent of cases IBS patients have worsening symptoms within 15 minutes of eating and ninety-three percent within 3 hours (15). It's reported specific foods as triggers such as milk and dairy products, in addition to wheat goods, onions, peas, beans, spicy spices, cabbage, specific meats, smoked products, fried food, and caffeine (16). Two years after receiving guidance on diet management, IBS patients had a different

diet profile. They avoided all FODMAP-rich food, consumed more food with probiotic supplements and did not avoid food sources that were crucial to their health (17). Foods contain short-chain carbohydrates, are poorly absorbed and end up in the distal small bowel and colon, once to improve the osmotic pressure and act as a substrate for bacterial fermentation, but also cause gas production, distension of the large intestine, and pain or discomfort in the abdomen (18). In reality, there was no evidence linking between food allergies such as sugar alcohols as well as apples, wheat, and milk which contain lactose and fructose and symptoms, clinical experience has shown that patients with increased fiber consumption are more likely to develop bloating, distension, and stomach pain compared to patients on low-fiber diets or placebos, but other studies recommended intake large amount of dietary fiber improve symptoms (19). it found that soluble fiber intake was effective in reducing overall IBS symptoms, while water-insoluble fiber did not improvement; This finding relates to how fiber and FODMAPs affect symptoms, which are linked to intestinal flora (20). Abdominal pain and discomfort can be caused by bacteria such as *Clostridium spp*., (16) which break down fiber and FODMAPs to produce gas can result in distension of the large intestine (21). Probiotics alter colonic fermentation and stabilise the colonic microbiota, and several studies on probiotics have shown improvements in flatulence and abdominal distension, with a reduction in the composite IBS symptom score (22). In addition, inhibition of Clostridia spp. which improving barrier function and binding to epithelial cells to prevent pathogen compliance, these bacteria also prevent gas production during the fermentation of carbohydrates, a lot of studies on probiotics have shown that they can reduce general IBS symptoms, including gas and abdominal distension (23),in addition to change colonic fermentation and stabilize the colonic flora (24).

Epidemiology

IBS prevalence ranges from 1.1% in France and Iran to 35.5% in Mexico, with varying regularity throughout Asia, according to Rome Center research, indicated that the incidence of IBS varies widely within countries (18), several researches don't used standardized diagnostic criteria or the same methodology, cultures, geography and populations as the reasons for different prevalence, global prevalence's of disease is still not accurate. thus, recently need more studies of epidemiology in several countries, the global epidemiological studies of Rome IV in 33 different countries, appeared the prevalence rates in Australia and Asia were slightly decrease than those in the United States, However, in Europe, they were comparable (25), of all the countries surveyed, Egypt had the highest prevalence rate in Albania. (26), in recent years, there were representative studies have been carried out in different countries (27) according to the Rome criteria (28). Overall, the prevalence in Africa is clearly higher than in other regions, and prevalence in the US and Europe based on Rome IV diagnosis is similar, on the other hand, the prevalence differs greatly between Asia and Europe according to questionnaire surveys, it was found IBS is more common in women than in males, according to the previous studies (29). It's interesting to note that IBS is equally prevalent in Asian women and men in recent years. (12) it's decreased with age while increase in younger people, with highest prevalence in the ifferent regions of the Saudi Arabia (30).

Clinical diagnosis

It was believed previously that IBS was a functional state with no clear causes or organic disease; however, with more study

and an update of the Rome criteria, the emphasis changed from functional to brain-gut interaction. Clinical studies on pathogenesis reveal that the microbiome, gastrointestinal endocrine cells, visceral hypersensitivity, and gastrointestinal motility disorders are observed in IBS patients and are the direct causes of abdominal discomfort, abdominal pain, or diarrhea. Recurrent abdominal pain, abdominal discomfort and alter bowel habits are the main clinical characterization of patients. it was found through experiments increased levels of fecal bile acids, short-chain fatty acids, and colonic mucosal Takeda G protein-coupled receptor 5 protein expressions (31,32). Tryptophan of aryl hydrocarbon receptor kynurenine pathway and methane gas productions associated with abnormal of colonic transit and evacuation lead to constipation and bloating. Additionally, disorder oroanal transit duration was related to methane and hydrogen concentrations, and more rapid abnormal oroanal transit time was linked to a increase severity of nausea, abdominal discomfort and rumbling (33). Specifically, abdominal pain can't be determined just on the presence of abdominal discomfort; also, the pain may be associated with a change in bowel movements (either pain alleviation or severity through defecation and/or a change in stool form) (34). The relationship to food or meals is not a diagnostic criterion for IBS, and is not associated with increase mortality, although it represents a significant proportion of morbidity and health care burden of quality of life, psychological distress, poor work performance, absenteeism, and others of activities of life (34). Due to the difficulties of diagnosis IBS and limited evidence-based treatment options, high prevalence of patients seeking for complementary and alternative medicine therapies. (35). Suggesting that IBS not a primary bowel disorder but a systemic disorder that based on reported symptoms by patients, emerging data suggest that retrospective recall of IBS symptoms (even >1 week) may exaggerated symptoms compared to reported of gastrointestinal symptoms that occurred within the past 3 to 6 months may be exaggerated (36).

Pathogenesis

Many factors implicated in the pathogenesis such as environment, heritability, genetic and dietary or intestinal microbiota, low grade inflammations and modifications in the NES (19). The gut's NES consists of two components: peptidergic, serotonergic and nitric oxide-containing nerves of the enteric nervous system in the gut wall and endocrine cells dispersed throughout the mucosal epithelial cells facing the gut lumen as showed in the figure (1).

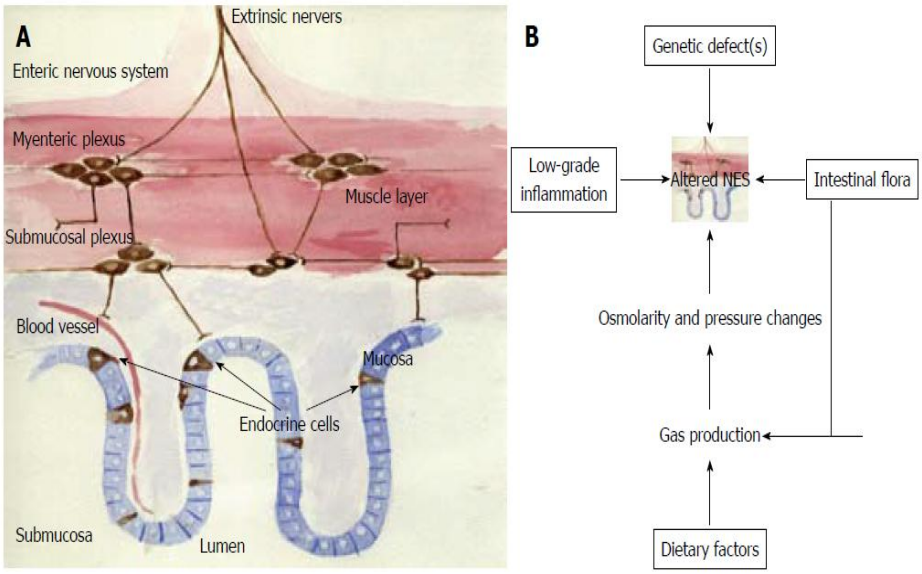

Figure (1): Schematic drawing to illustrate the neuroendocrine system of the gut and the possible pathogenesis of irritable bowel syndrome.
A: Schematic drawing of neuroendocrine system.
B: Possible pathogenesis of irritable bowel syndrome. (19)

So, it's important to suggest that altered neuroendocrine system, can result in abnormal GI motility, secretion, and sensation, these disorders characterized symptomatic of IBS, in other hand: low-grade inflammation, dietary variables, intestinal flora, or hereditary factors, are responsible for the modification in the neuroendocrine system and development of illness (19).In clinical practice, the idea that IBS is a psychiatric condition is crucial. (37). Rectal stimulation is linked to increased activation of the anterior cingulate cortex, insula, thalamus, prefrontal cortex, and cerebellum in IBS patients, whereas abdominal discomfort are linked to structural qualities of the brain in these individuals (38). Patients with abdominal discomfort have increased activation of the prefrontal cortex, anterior cingulate cortex, insula, thalamus, and cerebellum, which has been linked to changes in the brain. Furthermore, it primarily revealed an increase in gray matter volume and cortical thickness in the primary somatosensory cortex, secondary somatic sensory cortex, and subcortical regions, while diminishing gray matter volume, surface ara, and cortical thickness in the posterior insula and superior frontal gyrus.. Significant abnormalities were showed in the gut flora of IBS patients, as demonstrated in the Figure (2) *Escherichia coli, Enterobacteria, Ruminococcus gnavus, Anaerobes, and Bacteroides*, appear more prevalent in IBS patients compared to *Coli, Lactobacilli, Collinsella, and Bifidobacteria.* (39)

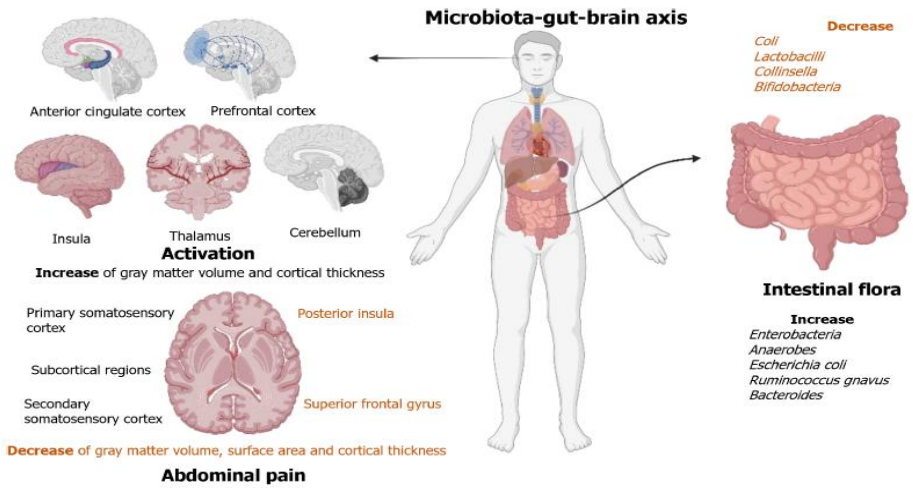

Figure (2): The mechanism action of the gut-brain-microbiota axis(39)

Management of IBS

Since diet therapy has shown important etiopathological features, it is crucial for reducing the symptoms of IBS, although there were some unintended effects, it has been demonstrated that the low-FODMAPS diet can be useful in reducing symptoms (40). The dietary management approach for IBS widely accepted over the last ten years, it needs to be more updated based on self-reported symptoms and food triggers, or results of breath tests and carbohydrate-digesting enzyme analyses (3). Although this approach not extensively tested for efficacy, it is likely to improve patients' dietary compliance and lower their risk of malnutrition in the hypervigilant patient subset (41). It must require to assess novel approaches to diet management, for instance, a lower histamine diet study could be necessary for individuals with allergic IBS, less intake of food antigen hypersensitivity may result decreased abnormal intestinal permeability and improved symptoms of IBS, perhaps in conjunction with a high-fiber diet to strength protective intestinal mucus layer(3). Although Probiotics are live microorganism and generally very safe, some are potential dangers should be considered, including infection, immunomodulatory changes, the capacity for antibiotic resistance, and adverse metabolic effects such as the accumulation of bile salts. The effectiveness of probiotics in treating irritable bowel syndrome (IBS) and the efficacy of its are less well understood (3). FDA-approved pharmacologic treatments for IBS diarrhea and constipation are prevalent in GI practice, but they show very limited therapeutic benefits compared with placebo (42, 43). Pharmaceutical therapies for IBS with nonabsorbable antibiotics for the microbiome are not considerable. Diet therapy can identify the etiopathological factors by offering an excellent basis for managing IBS, for example, the low FODMAP diet is an essential test to distinguish between the role of osmotic imbalance and bacterial gas production in luminal distention and the degree of visceral hypersensitivity (3). Dietary management of IBS will be more tailored to the patient's history and symptoms; for example, completely different dietary approaches may be warranted in patients who have dietary triggers compared to those who have a history of anxiety, bile acid infection and atopic IBS, or dietary antigen hypersensitivity (3). It should be

more sensitive microbiome and metabolomic analysis of these alternatives in clinical trials and needed to be understand whether microbes in the colon or small intestine play a role in IBS and whether changing the bacterial enterotype effects on the pathophysiology condition. (44). It suggests that interventions like probiotics, prebiotics, synbiotics, and dietary changes can mitigate IBS symptoms (45). It is expected that in five years studies in the futures, more individualized approach of diagnosis and treatment will have been developed, probably a single diagnostic biomarker not have been identified, only with combination of dietary guidelines, biomarkers (microbiome, metabolomic, immune), and more exact symptom criteria will be preferred. The subclassification of IBS is more likely to be related to its etiology than to a simple stool form (3) and evidence of IBS "clusters" based on symptoms and psychological distress (46-48).Anti-inflammatory medications are prescribed for ulcerative colitis, particularly in cases of mild to severe illness (49). These medications target inflammations induced by elevated nuclear factor kappa B (NFκB) (50) and macrophages, which are involved in the beginning of inflammations (51). Routine diet treatment programs based on biomarkers which be the best line of therapy for each individual with IBS (52), Functional foods and dietary fiber supplements that partially hydrolyzed guar gum and human milk oligosaccharides (HMO) have been tested, it's found fiber combinations may be recommended for the improvement of gut flora and symptoms. It is possible through next five years of studies, microbiota profiles may be utilized as biomarkers to guide appropriate therapy of patients (53), understanding of microbial metabolic pathways may significantly improve our understanding of IBS pathogenic mechanisms, therefore can predict which best diet for IBS symptoms for each individual based on their metabolomic, nutrigenomic and transcriptomic profile, this may relegate medication to second-line therapy (3). Also, should be avoid higher levels of free radical synthesis and lower antioxidant capacity, which causes oxidative damage to cellular constituents (54,55).

Conclusions

1- IBS is a common gut-brain disorder that can be influenced by diet and microbiota proliferation in the small intestine.
2- The degree of symptoms differs significantly from patient to patient which includes diarrhea, constipation, or a combination of the two, with abdominal pain or discomfort occurring concurrently with abdominal distension and the degree of symptoms varies from feasible to severe, it overlaps with organic gastrointestinal conditions, such as celiac disease, inflammatory bowel disease, microscopic colitis, or bile acid diarrhea.
3- The etiology of IBS is complicated because interaction with many factors such as genetics, and environment, intestinal microbiota, diet, low-grade inflammation, and disruptions in the gut's neuroendocrine system (NES).
4- Long-term use of pharmacological to relief pain, diarrhea, or constipation is not recommended, therefore alternative therapies have been suggested including cognitive behavioral therapy and gut-directed hypnotherapy, other nonpharmacological treatment of IBS should be tailored to avoid certain food items, like Fermentable monosaccharides, disaccharides, polyols (FODMAPs) and oligosaccharides to get beneficial effects on IBS patients' symptoms and quality of life.
5- Patients with both IBS and lactase intolerance should undergo routine

serologic testing for celiac disease and food sensitivity. In contrast, patients with bloating should avoid foods like celery, beans, onions, carrots, raisins, apricots, bananas, and plums.

Recommendations

1. More updates of the diagnosis and pathophysiology with early colonoscopies for first-degree related colorectal cancer are recommended.
2. Further studies highlight the impact of coffee, green tea, and spicy foods on individuals with IBS and illustrate the role of anxiety and depression in the illness's development.

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