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IRRITABLE BOWEL SYNDROME IN PREGNANCY AND BEYOND

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Abstract

Irritable bowel syndrome (IBS) tends to be an umbrella term for a variety of bowel disturbances of unknown origin, typically presenting with symptoms that include a change in bowel habit frequently with alternating constipation and diarrhea. Abdominal bloating and distension are common, sometimes accompanied by abdominal pain, which may be relieved by defecation, and sometimes a feeling of incomplete defecation. A diagnosis of irritable bowel syndrome is often reached when all organic disease has been ruled out by appropriate medical tests. The complexity of the condition increases during pregnancy because of the additional physical, hormonal, and psychological stressors associated with the condition.

The optimal treatment of IBS remains to be defined. The current recommendations for management of IBS depend on amelioration of the predominant symptoms. Almost inevitably, management does not address the cause of the condition, which in most cases is either unknown, involves more than one trigger, or is not amenable to treatment. Medications to control diarrhea, constipation, motility dysfunction, and psychological stress are often employed. Probiotics and dietary manipulation may have a useful role in therapy. Whatever the approach to management of IBS, the needs and safety of the mother and developing fetus must be paramount, which often poses challenges for both the sufferer and health care professionals involved in her care.

As with any medical condition, the unique needs of the pregnant mother and her developing fetus must be considered at all times when management strategies are instituted, especially if the protocols involve drugs, drastic changes in diet, or other interventions that may pose a risk.

Introduction

Irritable bowel syndrome (IBS) tends to be an umbrella term for a variety of bowel disturbances of unknown origin. It is sometimes referred to as "irritable colon", "spastic colon", or "nervous colon". The condition is often chronic, and with the abdominal changes associated with pregnancy can present a great challenge for both the sufferer and the health care professional involved in her care.

Characteristics of Irritable Bowel Syndrome

Symptoms of IBS typically include[1] a change in bowel habit frequently with alternating constipation and diarrhea. Abdominal bloating and distension are common, sometimes accompanied by abdominal pain, which may be relieved by defecation, and sometimes a feeling of incomplete defecation.

Other characteristic findings in IBS which tend to distinguish it from intestinal inflammatory bowel diseases (IBD) include[1] a lack of overt signs of structural damage to the wall of the intestine (frequently indicated by blood in the stool), no loss of weight, and nighttime fever is not experienced.

A diagnosis of irritable bowel syndrome is often reached when all organic disease has been ruled out by appropriate medical tests. The Manning Criteria or the Rome (I, II or III) classification system are often used for diagnosis[2].

Rome II and III Criteria for Diagnosis of IBS

The main points for diagnosis of IBS according to the Rome II and Rome II criteria include[3] abdominal pain or discomfort for 12 weeks or longer over the past 12 months, plus two of the following:

- Relief of discomfort with defecation
- Association of discomfort with altered stool frequency (diarrhea, or constipation, or alternating)
- Associated discomfort with stool form (hard, soft, loose, liquid etc)

Diagnosis of IBS in Pregnancy

Many women already have IBS before entering pregnancy, and the symptoms tend to continue, or sometimes become exacerbated during the pregnancy. When symptoms of IBS initially arise during pregnancy, the same diagnostic criteria as IBS without pregnancy are currently applied, although the accuracy and validity of the Rome criteria have not yet been studied in pregnancy. The usual directives include ruling out alarm symptoms of organic disease, such as blood in the stool, weight loss, fever (especially night-time), and abdominal masses which would indicate organic disease states other than IBS.

Tests for IBS in Pregnancy

The usual tests that are used in the differential diagnosis of IBS include[4], blood count; presence of indicators of inflammation such as sedimentation rate and inflammatory mediators; stool analysis for infections in diarrhea-associated symptoms such as the presence of ova and parasites and bacterial pathogens; indicators of celiac disease[5], such as presence of anti-endomysial antibodies

and anti-tissue transglutaminase (tTGA) antibody; indicators of lactase deficiency, such as the hydrogen breath test, blood glucose or galactose levels; and tests for thyroid function.

Classification of IBS

There have been attempts to classify the different presentations of IBS, based on the predominant bowel symptoms[6]. Presently three main categories are recognized, namely:

- IBS with constipation predominant features (IBS-C)
- IBS with diarrhea predominant features (IBS-D)
- IBS with alternating symptoms of diarrhea and constipation (IBS-A)

A further category is often encountered, based on the apparent etiology of the IBS, namely, post-infectious IBS (PI-IBS)

Etiology of IBS

The exact pathophysiology of IBS remains unclear. A number of factors appear to be involved in the onset of the condition, either singly or in combination. A genetic predisposition has been suggested to be present in a large number of cases[7]. Other predisposing factors include, changes in function following inflammatory conditions in the GI tract; fluctuations in hormone levels; psychosocial factors, especially stress; side-effects of medications; use of oral antibiotics which are suggested to result in changes in the composition of the resident microflora of the bowel; and adverse reactions to foods, such as food allergy and food intolerances.

Inflammatory conditions that have been implicated in the etiology of IBS include[8] infection in the GI tract that may be viral, bacterial, or parasitic (post-infective (PI)-IBS); intestinal pathology resulting from inflammatory bowel disease (IBD), such as Crohn's disease and ulcerative colitis;

and surgical procedures in the digestive tract that may result in persistent inflammation. The cell damage and hyperpermeability that are consequences of these situations are thought to cause or contribute to the chronic condition of IBS.

Celiac disease has been identified in a significantly large number of cases of IBS. Sensitivity to gluten is thought to be a predisposing factor in many cases of IBS in which celiac disease has not been identified by conventional testing methods[9]. Cell damage resulting from continued exposure to gluten in such sensitive individuals may contribute to an inflammatory process that triggers or exacerbates IBS.

Hormonal fluctuations have been demonstrated to affect gastrointestinal (GI) tract function. In women, hormone changes during the menstrual cycle and pregnancy modify GI function[10]. Increases in estrogen and progesterone tend to affect gastric slow wave rhythm; may delay colonic transit, especially during the third trimester of pregnancy[9]; and affect nociception (perception of pain)[11]. During certain phases of the menstrual cycle, women reported reduced thresholds for pain, which was assumed to involve the effects of hormones[12]. Similarly, hormone changes in pregnancy tend to alter the perception of pain and increase the distress associated with IBS.

Psycho-social factors causing dysregulation within the brain-gut axis are thought to be significant contributing factors in many cases of IBS[13] . Stress can play an important part in the clinical expression and outcome of the disorder. The authors of an excellent review of this aspect of IBS[12] point out that early life experiences, including major loss, abuse, family influences on illness behavior, and maladaptive coping, can influence the clinical expression and severity of IBS. These factors produce complex interactions that affect biological, psychological and social systems for the individual with IBS. Such stressors result in motor dysfunction that cause intestinal motility disorders, resulting in the typical outcomes of constipation, diarrhea, or a

combination of these conditions, as well as the sensory dysfunction that predisposes to an increase in pain perception.

Research suggests that an imbalance of the intestinal microbiota and a dysfunctional intestinal barrier might trigger irritable bowel syndrome (IBS)[14]. Alteration in the microbial flora of the digestive tract can result from diverse causes such as oral antibiotics; other oral medications and a change in substrate such as the type of food passing into the bowel. A change in the microbial flora may result in different products resulting from the action of micro-organisms on undigested food material, such as gases, organic acids and others which may adversely affect the internal environment.

Adverse reactions to food are thought to contribute to IBS. Because the function of the digestive tract is the processing and absorption of food materials, it is logical to assume that food should play a significant role in the symptoms of IBS. Although some studies suggest that IBS symptoms in one quarter of patients may be caused or exacerbated by one or more dietary components[15], convincing evidence that dietary components act as triggers or exacerbating factors in IBS is surprisingly meager[16]. Food allergy, defined as immunologically-mediated responses to components of the diet, results in the release of inflammatory mediators that may have an immediate impact on the GI tract. The symptoms of food intolerances such as lactose intolerance, or in rare cases sucrase/isomaltase deficiency mimic those of IBS, so such causes need to be ruled out when looking for food involvement in IBS.

The composition of the diet has been extensively scrutinized as a possible contributing factor in IBS[15]. Inadequate fiber, especially in constipation-dominant IBS; inappropriate fibre, especially in diarrhea-dominant IBS; high fat levels; gas-producing foods; and carbonated beverages, have all been suspects at one time or another. However, none of these has been identified

definitively as consistently being involved in either the etiology or exacerbation of IBS in any significant number of cases.

Increased sensitivity to pain may play a significant role in IBS. Altered central processing, abnormal gastrointestinal motility, and visceral hypersensitivity may be important components in the pathophysiology of irritable bowel syndrome (IBS)[17]. These factors affect each other and are probably associated with development of IBS symptoms. A lower pain threshold to colonic distension was observed in most of patients with IBS compared to healthy subjects. Evidence from laboratory studies seems to indicate that neuropeptides such as tachykinins generated by the central nervous system interact with neurokinin receptors on the spinal cord, resulting in an increased sensation of pain[18].

Motility dysfunction, resulting from changes in autonomic nervous system signals and from products of microbial fermentation may contribute significantly to IBS. New studies suggest that gut motility and defecation are regulated by psychical, somatic, and immune processes, strongly influenced by stress[19].

Alteration in the speed of food passing through the G.I. tract can result in disturbance of the normal process of digestion and absorption of nutrients. For example, an increase in the rate of movement will result in incomplete breakdown of food components in the small intestine, and an increase in fluid retention in the colon, contributing to diarrhea. A decrease in the speed of material passing through the digestive tract can result in prolonged fermentation of undigested food remaining in the colon, a reduction in fluid remaining in the colon, dry solid, stool, and constipation.

Gender-related Differences in GI Tract Function

There are differences in the way in which men and women respond to conditions in the GI tract. For example, colonic transit is generally slower in women than men, and may be affected by the phase of menstrual cycle[20]. GI tract symptoms tend to increase in the late luteal and menses phases of the cycle. In addition, gastric emptying into the duodenum tends to be slower in women than in men[21].

GI Tract Motility Changes During Pregnancy

Normal hormonal changes that occur during pregnancy may cause changes in GI tract function[22]. This 2003 review indicated that one third of pregnant women report an increase in stool frequency and 38% report constipation. The prolonged oro-cecal transit in the third trimester of pregnancy[23] tends to contribute to constipation.

Fermentation of Food Material in the Bowel

All food materials not absorbed through the lining of the small intestine pass into the large bowel. The normal microbial flora comprising millions of bacteria colonise the organ, which perform "end-stage digestion" of the residual food components. Under normal circumstances, products of microbial activity can be important nutrients, for example, producing some B vitamins (e.g. pantothenic acid; biotin) and vitamin K which are vital for human health. However, some of the products of microbial fermentation may be harmful, for example, when non-digested carbohydrates pass into the large intestine an osmotic imbalance may occur that leads to excess fluid in the lumen of the large bowel resulting in loose stool. In addition, bacterial fermentation may produce organic acids, such as acetic, lactic, butyric, and propionic acids that further contribute to the osmotic

imbalance, and gases such as carbon dioxide and hydrogen that result in abdominal bloating and flatulence[24]. The symptoms associated with excessive fermentation of carbohydrates in the bowel include abdominal fullness, bloating, and cramping pain, sometimes within 5-30 minutes, sometimes several hours after ingesting the carbohydrate, followed by a watery diarrhea from 5 minutes to 5 hours after ingestion.

A well-known example of fermentation of undigested dietary sugar is lactose intolerance. In this condition the milk sugar, lactose, is incompletely digested by the enzyme, lactase, which is produced in the brush-border cells lining the digestive tract. Lactose is a disaccharide which cannot be absorbed through the lining of the digestive tract until it is broken down into its constituent monosaccharides, glucose and galactose. The undigested lactose moves into the large intestine, where it causes osmotic imbalance, and provides a substrate for fermentation by the resident microflora. The lack of lactase reserves makes lactose particularly vulnerable to maldigestion.

Therapeutic Management of IBS

The optimal treatment of IBS remains to be defined[1]. The current recommendations for management of IBS depend on amelioration of the predominant symptoms. Almost inevitably, management does not address the cause of the condition, which in most cases is either unknown, involves more than one trigger, or is not amenable to treatment. A variety of medications are frequently employed in controlling the symptoms of IBS, which are designed to control diarrhea, relieve constipation, modulate disturbed motility, or are aimed at reducing psychological stress by treating the anxiety or depression that may be contributing to the condition.

IBS Medications and Pregnancy

During pregnancy, the use of medications is usually discouraged because of risk to the developing fetus[22]. There is a significant paucity of research studies on IBS in pregnancy and the effects of the medications usually employed to control its symptoms. Practitioners tend to recommend a balance between the benefit to the mother versus the risks to her fetus, but there is a lack of evidence-based research that would indicate either safety or harm associated with each medication. Consequently, IBS management in pregnancy tends to avoid drugs, and education that provides reassurance that the condition, although sometimes highly distressing, is not in itself likely to produce lasting harm. In addition, methods to attempt modification of the mother's attitude to distress, and a reduction in her stress levels wherever possible, together with dietary modifications to eliminate the most likely symptom triggers and substitute with foods of equivalent nutritional value provide the most effective methods for treatment at the present time[22].

Probiotics in Management of IBS

IBS involves dysfunction in a variety of complex interactive mechanisms, many of which involve microorganisms. There are interaction between different micro-organisms within the intestinal microflora; the interaction of microorganisms with the host; and interactions between microorganisms and the immune tissues within the gut resulting in inflammatory processes that lead to adverse effects within the gut, including hyperpermeability of the intestinal lining. Advantageous changes in the composition of the intestinal microflora may ameliorate some of these adverse effects. Such changes may be accomplished by the use of appropriate probiotics. If symptoms of IBS can be relieved by the use of non-drug therapies such as probiotics, the risk to mother and fetus in pregnancy would be avoided.

Probiotic management of IBS is in its infancy. Research studies have demonstrated the possible value of probiotics in short-term management of specific symptoms of IBS[25], namely, diarrhea, constipation, and abdominal bloating. However, the specific strains, dosage and viability of the microorganisms remain to be determined[26].

Preliminary studies indicate that *Bifidobacterium infantis* shows evidence of reducing flatulence and retarding colonic transit in cases of diarrhea[27],[28]. However, the authors of the study point out that the dosage, duration of treatment, and extent of clinical benefits in IBS remain to be determined.

A 2008 study[29] in women between the ages of 18 and 55 with and without functional constipation involving Activia yogurt containing 10(8) UFC/g of *Bifidobacterium animalis* and the prebiotic (microbial substrate) fructoligosaccharide (FOS) at a dosage of 2 units/day of Activia, or a placebo control of a lacteous dessert without probiotics for a period of 14 days indicated improvement in the quality of the stools, a reduced perception of straining effort during defecation, and a reduced perception of pain associated with defecation

A recent study using *Bifidobacterium bifidum* MIMBb75[30] involving a total of 122 patients, randomised to receive either placebo (N=62) or MIMBb75 (N=60) once a day for 4 weeks indicted that MIMBb75 significantly reduced the global assessment of IBS symptoms when compared with the placebo group based on a 7-point Likert scale[a]. MIMBb75 also significantly improved the IBS symptoms of pain/discomfort, distension/bloating, urgency and digestive disorder.

[a] A Likert scale is a psychometric rating scale commonly used in survey type questionnaires. Respondents specify their level of agreement or disagreement on an agree/disagree scale for a series of statements. Thus the scale captures the intensity of their feelings

Probiotics and Lactose Intolerance

Certain strains of bacteria, notably lactobacilli, bifidobacteria and *Streptococcus thermophilus*, synthesize a beta-galactosidase enzyme which breaks down lactose to its constituent monosaccharides[31]. These strains are commonly used in the manufacture of yogurt. Thus, active strains within the food product assist in reducing the symptoms of lactose intolerance in sensitive individuals. In addition to the effects of the enzyme, the fermented product is thicker in constituency and thus delays gastrointestinal transit, allowing a longer period of time in which both the human and microbial lactase enzymes can act on any remaining lactose.

Probiotics and Safety in Pregnancy

Although some studies show promise for the use of probiotics and prebiotics in control of IBS symptoms, many researchers urge caution. One recent (2009) review[32] indicates that most random controlled trials about the utility of probiotics in IBS have not used an appropriate study design and do not adequately report adverse events. Therefore, there is inadequate data to comment on the efficacy of probiotics in IBS. Furthermore, the safety of probiotic strains in pregnant and breast-feeding women have been inadequately studied, and at least one probiotic product widely used in the management of IBS[33] carries a warning on the label that the product is not suitable during pregnancy and lactation.

However, several studies suggest that probiotics are generally safe during certain stages of pregnancy. A meta-analysis and systematic review of 8 randomized control trials of probiotic use in more than 1500 pregnant women who began probiotic treatment with *Lactobacillus* spp alone or in combination with *Bifidobacterium* spp between 32 and 36 weeks' gestation and continued until delivery was published in 2009[34]. Compared to women who were given placebo,

there was no increase in the incidence of miscarriages or malformations (which was expected because probiotic use mostly occurred in the third trimester and was therefore unlikely to affect organogenesis), and no significant difference in birth weight, gestational age, or the incidence of cesarean section.

Another study reported the results of diet and probiotic use starting in the first trimester of pregnancy[35]. 256 women were randomised at their first trimester of pregnancy into a control and a dietary intervention group. The intervention group were randomized, double-blind to receive probiotics (*Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12) or placebo. No adverse effects of the probiotic based on pregnancy outcome and fetal and infant growth during the 24 months' follow-up were reported.

Nevertheless, the unqualified recommendation for the use of probiotics in the control of IBS in pregnant women must await further well-controlled trials on their safety and effectiveness.

Diet in the Management of Irritable Bowel Syndrome

There is no evidence that food of any type causes IBS. However, food passing through the "damaged organ" may prolong or exacerbate the condition. Components of food interact with gastrointestinal tissues both immunologically (for example in allergy and food protein enteropathy) and non-immunologically (for example in intolerances such as lactase deficiency). It is likely that a variety of factors are contributing to the symptoms in an individual sufferer. A practical approach to the dietary management of IBS takes into account as many of these factors as possible.

A 2007 study in Canada[36],[37] determined that diet is the primary factor manipulated by women with IBS to manage their condition. All 8 participants identified foods and/or beverages

that caused exacerbation of their symptoms, and all participants identified individual foods that they perceived to be responsible for triggering their symptoms.

Dietary Fiber and IBS

Increased dietary fibre has been a mainstay of therapy for patients with IBS following an article that appeared in 1984[38]. The basis for this approach was an attempt to achieve a decrease in colonic pressure, and an acceleration of oro-anal transit. However, more rigorous research has revealed that in fact, increasing the amount of fiber in the diet is of little value in the treatment of IBS. Studies indicated that there was little difference between treatment group and placebo, and no relief of abdominal pain, while some types of fiber, specifically corn and wheat bran, may actually worsen the symptoms[39]. Abnormal bacterial fermentation of the undigested fibre in the colon can cause excessive gas production, bloating and abdominal pain and worsen the clinical outcome in IBS[40],[2]. The current recommendations from the American College of Gastroenterology Functional Gastrointestinal Disorders Task Force recommends the use of fibre in patients with constipation, but not for the treatment of IBS[41].

Dietary Management of IBS

Most IBS sufferers tend to react adversely to a variety of foods, which differ between individuals. Successful management of IBS involves accurate identification of any offending foods and their replacement with those of equivalent nutritional value. It is particularly important that the nutritional needs of the pregnant women and her developing fetus be optimally supplied. To ensure the nutritional health of the pregnant woman, any elimination diet attempted during pregnancy must be supervised by a registered dietitian or other suitably qualified health care professional.

Typically, foods that trigger or exacerbate symptoms of IBS may include[42] the patient's food allergens; intolerance triggers; food additives that enhance the release of inflammatory mediators, such as tartrazine and benzoates; and other GI tract irritants such as alcohol, caffeine and other methylxanthines, and a reduction in fermentable substrate to relieve symptoms in the large intestine. In reducing indigestible and highly fermentable foods, the FODMAP[b] diet[43] has been reported to be successful in some cases of IBS and other functional gastrointestinal diseases (FGID)[44]

Guidelines for Dietary Management of IBS

The aim is to reduce "irritation" in all parts of the digestive tract by avoidance of known inflammatory triggers, and to reduce the amount of fermentable substrate passing into the colon[42]. The elimination phase of the diet, which is designed to eliminate the most likely offending foods is typically followed for a period of four weeks. This is usually followed by "challenge" of each eliminated food, with careful monitoring for the development of symptoms. The final diet will consist of the tolerated foods, with alternative sources of any excluded nutrients supplied from alternative dietary sources. The whole procedure should be supervised by a registered dietitian or other suitably qualified health care professional to ensure optimal nutrition during all phases of the process.

[b] The acronym, 'FODMAP'—Fermentable Oligo-, Di- and Mono-saccharides and Polyols—was coined to describe a previously-unrelated group of short-chain carbohydrates and sugar alcohols (polyols which putatively have three common functional properties: poorly absorbed in the small intestine; osmotically-active molecules; rapidly fermented by bacteria.

Summary

IBS is a complex condition with many different triggers and exacerbating factors. The complexity of the condition increases during pregnancy because of the additional physical, hormonal, and psychological stressors associated with the condition. Management strategies are typically designed for symptomatic relief rather than cure. Medications to control diarrhea, constipation, motility dysfunction, and psychological stress are often employed. Probiotics and dietary manipulation may have a useful role in therapy. Whatever the approach to management of IBS, the needs and safety of the mother and developing fetus must be paramount, which often poses challenges for both the sufferer and health care professionals involved in her care.

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