



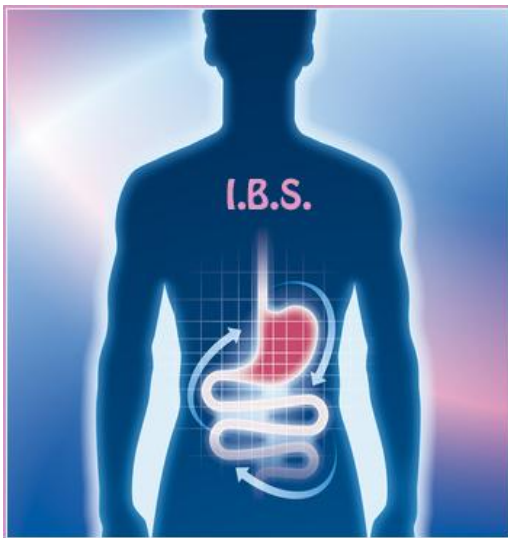
ASSIUT UNIVERSITY DRUG INFORMATION BULLETIN



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كلية الصيدلة

Irritable Bowel Syndrome



Irritable Bowel Syndrome (IBS) is a functional GI disorder characterized by abdominal pain and altered bowel habits in the absence of specific and unique organic pathology. The syndrome has been referred to as spastic colon, irritable colon, and nervous colon. Population-based studies estimate the prevalence of IBS at 10-20% and the incidence of IBS at 1-2% per year. In the past, IBS has been considered a diagnosis of exclusion; however, it is no longer considered a diagnosis of exclusion, but it does have a broad differential diagnosis. No specific motility or structural correlates have been consistently demonstrated; however, experts suggest the use of available guidelines can minimize testing and aid in diagnosis.

Etiology

The causes of IBS remain poorly defined, but they are being avidly researched.

Postulated etiologies of IBS

Abnormal transit profiles and an enhanced perception of normal motility may exist. Up to one third of patients with IBS may have altered colonic transit. Delayed colonic motility may be more common in patients with constipation-predominant IBS than in healthy controls. Similarly, accelerated colonic transit may be more common in patients with diarrhea-predominant disease than in healthy controls.

Causes related to enteric infection

Colonic muscle hyperreactivity and neural and immunologic alterations of the colon and small bowel may persist after gastroenteritis (postinfectious IBS). Psychological comorbidity independently predisposes the patient to the development of postinfectious IBS.

Infection with *Giardia lamblia* has been shown to lead to an increased prevalence of IBS, as well as chronic fatigue syndrome. In a historic cohort study of patients with *G lamblia*

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infection as detected by stool cysts, the prevalence of IBS was 46.1% as long as 3 years after exposure, compared with 14% in controls. ⁽¹⁾

Central neurohormonal mechanisms

A subset of patients with IBS has autonomic dysfunctions.⁽²⁾ Abnormal glutamate activation of *N*-methyl-*D*-aspartate (NMDA) receptors, activation of nitric oxide synthetase, activation of neurokinin receptors, and induction of calcitonin gene-related peptide have been observed.

The limbic system mediation of emotion and autonomic response enhances bowel motility and reduces gastric motility to a greater degree in patients who are affected than in controls. Limbic system abnormalities have been described in patients with IBS and in those with major depression.

Additional etiologic factors

It has been proposed that small bowel bacterial overgrowth provides a unifying mechanism for the common symptoms of bloating and gaseous distention in patients with IBS.

Bloating and distention may also occur from intolerance to dietary fats. Reflex-mediated small bowel gas clearance is more impaired by ingestion of lipids in patients with IBS than in patients without the disorder.

Studies of elimination and challenge diets have suggested that poorly absorbed short-chain carbohydrates, in the form of fructose and fructans, may create symptoms among patients with IBS.

Research suggests that neuronal degeneration and myenteric plexus lymphocytosis may exist in the proximal jejunum. Additionally, colonic lymphocytosis and enteroendocrine cell hyperplasia have been demonstrated in some patients.

History

A meticulous history is the key to establish a diagnosis of IBS. The Rome criteria provide

Altered bowel habits

Constipation variably results in complaints of hard stools of narrow caliber, painful or infrequent defecation, and intractability to laxatives. Diarrhea usually is described as small volumes of loose stool, with evacuation preceded by urgency or frequent defecation. Postprandial urgency is common, as is alternation between constipation and diarrhea. Characteristically, one feature predominates in a single patient, but significant variability exists among patients.

Abdominal pain and distention

Descriptions are changeable. Pain frequently is diffuse without radiation. Common sites of pain include the lower abdomen, specifically the left lower quadrant. Acute episodes of sharp pain are often superimposed on a more constant dull ache. Meals may precipitate pain, and defecation commonly improves pain. Defecation may not fully relieve pain, however.

Pain from presumed gas pockets in the splenic flexure may masquerade as anterior chest pain or left upper quadrant abdominal pain. This splenic flexure syndrome is demonstrable by balloon inflation in the splenic flexure and should be considered in the differential of chest or left upper quadrant abdominal pain. Patients frequently report increased amounts of bloating and gas.

Quantitative measurements fail to support this claim. People with IBS may manifest increasing abdominal circumference throughout the day, as assessed by CT scan. They may also demonstrate intolerance to otherwise normal amounts of abdominal distention.

Additional symptoms consistent with IBS

Clear or white mucorrhea of a non inflammatory etiology is commonly reported. Epidemiologic associations with dyspepsia, heartburn, nausea, vomiting, sexual dysfunction (including dyspareunia and poor libido), and urinary frequency and urgency have been noted. Symptoms may worsen in the perimenstrual period, and fibromyalgia is a common comorbidity. Stressor-related symptoms may be revealed with careful questioning (emphasize avoidance of stressors).

Symptoms inconsistent with IBS

Symptoms not consistent with IBS should alert the clinician to the possibility of an organic pathology. Inconsistent symptoms include: onset in middle age or older, acute symptoms (IBS is defined by chronicity), progressive symptoms, nocturnal symptoms, anorexia or weight loss, fever, rectal bleeding, painless diarrhea, steatorrhea, lactose and/or fructose intolerance, gluten intolerance.

Criteria for Diagnosis

A consensus panel created and then updated the Rome criteria to provide a standardized diagnosis for research and clinical practice. The Rome III criteria for the diagnosis of IBS require that patients have had recurrent abdominal pain or discomfort at least 3 days per month during the previous 3 months that is associated with 2 or more of the following:

- Relieved by defecation
- Onset associated with a change in stool frequency
- Onset associated with a change in stool form or appearance

Supporting symptoms include the following:

- Altered stool frequency
- Altered stool form
- Altered stool passage (straining and/or urgency)
- Mucorrhea
- Abdominal bloating or subjective distention

Four bowel patterns may be seen with IBS. These include the following:

- IBS-D (diarrhea predominant)
- IBS-C (constipation predominant)
- IBS-M (mixed diarrhea and constipation)
- IBS-A (alternating diarrhea and constipation)

The usefulness of these subtypes is debatable. Notably, within 1 year, 75% of patients change subtypes, and 29% switch between constipation-predominant IBS and diarrhea-predominant IBS.

Treatment

Therapy is directed at specific symptoms. An effective therapeutic relationship is essential for effectively managing IBS. Patients should be invited to express not only their symptoms but also their understanding of their symptoms and the reasons prompting a visit to the health care practitioner (e.g., fear of serious disease). Patients should be educated about the disorder (e.g., normal bowel physiology and the bowel's hypersensitivity to stress and food) and reassured, after appropriate tests, about the absence of a serious or life-threatening disease. Appropriate therapeutic goals (e.g., expectations regarding the normal course or variability in symptoms, adverse effects of drugs, the appropriate and available working relationship between the physician and the patient) should be established. Finally, patients can benefit by being actively involved in

the management of their condition. When successful, this can enhance the patient's motivation to adhere to treatment, foster a more positive physician-patient relationship, and mobilize the coping resources of even the most chronically passive patients. Psychologic stress, anxiety, or mood disorders should be identified, evaluated, and treated. Regular physical activity helps relieve stress and assists in bowel function, particularly in patients with constipation.⁽²⁾

Dietary Measures

Fiber supplementation may improve symptoms of constipation and diarrhea. Individualize the treatment because a few patients experience exacerbated bloating and distention with high-fiber diets. Polycarbophil compounds may produce less flatulence than psyllium compounds.

The data regarding the effectiveness of fiber are controversial because 40-70% of patients improve with placebo. A Cochrane systematic review found no benefit from fiber/bulking agents on IBS symptoms or global assessment.

Judicious water intake is recommended in patients who predominantly experience constipation.

Caffeine avoidance may limit anxiety and symptom exacerbation. Legume avoidance may decrease abdominal bloating. Lactose and/or fructose should be limited or avoided in patients with these contributing disorders. Take care to supplement calcium in patients limiting lactose intake.

Medication Summary

The selection of pharmacologic treatment remains symptom directed. Agents used for management of symptoms in IBS (IBS) include anticholinergics, antidiarrheals, tricyclic antidepressants, prokinetics, bulk-forming laxatives, serotonin receptor antagonists, chloride channel activators, and guanylate cyclase C (GC-C) agonists.

A Cochrane systematic review found that several antispasmodics, including peppermint oil, pinaverium, trimebutine, and cimetropium/dicyclomine, significantly outperformed placebo at improving IBS symptom and global assessment scores.

The 2009 ACG (American College of Gastroenterology) position statement on management of IBS noted that the antidiarrheal agent loperamide effectively reduced stool frequency and improved stool consistency, but it did not relieve pain, bloating, or other global IBS symptoms.

Prognosis

IBS is a chronic relapsing disorder characterized by recurrent symptoms of variable severity; however, life expectancy remains similar to that of the general population. Clinicians must be forthcoming with patients because knowledge may help allay undue fears as their disease waxes and wanes. IBS does not increase the mortality or the risk of inflammatory bowel disease or cancer.

Patients with IBS may carry an increased risk of ectopic pregnancy and miscarriage, but not stillbirth. The reasons for this are unknown. Whether the risk increases because of the IBS itself, or because of another factor such as medications used for IBS, is also unknown.⁽¹⁾

References:

- 1) Lehrer JK. Irritable Bowel Syndrome [Internet]. *Medscape Reference, Drugs, Diseases & Procedures*; Mar 11, 2013 [cited May, 2013]. Available from: <http://emedicine.medscape.com/article/180389-overview>
- 2) Merck Sharp & Dohme Corp. Irritable Bowel Syndrome [Internet]. *The Merck Manual for Health Care Professionals*; Feb 2012 [cited May 2013]. Available from: http://www.merckmanuals.com/professional/gastrointestinal_disorders/irritable_bowel_syndrome_ibs/irritable_bowel_syndrome_ibs.html

Terminology

Dysarthria



A general term applied when weakness or incoordination of the speech musculature prevents clear pronunciation of words. The individual's speech may sound as if it is slurred or weak. It may be due to damage affecting the centers in the brain which control movements of the speech muscles, or damage to the muscles themselves. Examples of dysarthria may be found in strokes, Cerebral Palsy and the latter stages of Parkinsonism, Multiple Sclerosis (MS) and Motor Neurone Disease (MND). Whatever the cause, a speech therapist can assess the extent of the dysarthria and suggest exercises or an alternative means of communication.

Reference: Marcovitch H. 2005. *Black's Medical Dictionary*. 41th ed. London: A&C Black Publishers Limited. p 214.



FDA News

FDA approves Simponi to treat ulcerative colitis

The U.S. Food and Drug Administration today approved a new use for Simponi (golimumab) injection to treat adults with moderate to severe ulcerative colitis. Simponi works by blocking tumor necrosis factor (TNF), which plays an important role in causing abnormal inflammatory and immune responses. Previously approved to treat rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis (arthritis affecting the joints in the spine and the pelvis), Simponi is now approved to treat adults with



moderate to severe ulcerative colitis that is resistant to prior treatment or requires continuous steroid therapy. Ulcerative colitis causes inflammation and ulcers in the inner lining of the large intestine and is one of two main forms of chronic inflammatory bowel disease. The inflammation can lead to abdominal discomfort, gastrointestinal bleeding, production of pus and diarrhea. Simponi is an important new treatment option for patients with moderate to severe ulcerative colitis,. It is critical that patients suffering from the serious and painful symptoms of ulcerative colitis have additional treatment options since patients experience the effects of the disease and respond to treatments differently."The safety and effectiveness of Simponi for ulcerative colitis were established in two clinical studies .Results showed that a greater proportion of Simponi-treated patients achieved clinical response, clinical remission and, as seen during endoscopy, had improved appearance of the colon after six weeks compared with the placebo group. The most common side effects in patients treated with Simponi are upper respiratory infection and redness at the site of injection. Patients treated with Simponi are at increased risk of developing serious infections, invasive fungal infections, reactivation of Hepatitis B infection, lymphoma, heart failure, nervous system disorders and allergic reactions.

Reference: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm352383.htm>

Test Your Knowledge



1. An adult patient who ingested 30 acetaminophen tablets (325 mg/ tab) 6 hours ago should be treated with

- (A) EDTA infusion
- (B) ipecac syrup
- (C) activated charcoal
- (D) N-acetylcysteine
- (E) probenecid

2. Which one of the following benzodiazepines would be preferred as an anxiolytic drug for an elderly patient with a history of cirrhosis?

- (A) chlordiazepoxide (Librium)
- (B) oxazepam (Serax)
- (C) clorazepate (Tranxene)
- (D) diazepam (Valium)
- (E) prazepam (Centrax)

3. A nurse informs you that a patient has polydipsia. This refers to

- (A) excessive urination
- (B) excessive craving for food
- (C) excessive thirst
- (D) diarrhea
- (E) double vision

4. A patient's blood test reveals an excessively high level of amylase. This may indicate a disease of the

- (A) liver
- (B) heart
- (C) kidney
- (D) lung
- (E) pancreas

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional health team as well as from others. Here's one of the enquiries received at the center!

Enquiry received from Ph/ Hazem Abda- Assiut Univ. Hospital

Enquiry: What is the max administered dose of levofloxacin? Are there any interactions between levofloxacin and theophylline, or between ciprofloxacin and theophylline?

Summary of Answer:

It is given by mouth or intravenously for the treatment of susceptible infections in a usual dose of 250 or 500 mg once or twice daily. A regimen of 750 mg once daily is recommended in the USA for complicated skin infections and for hospital-acquired pneumonia. Doses should be reduced in patients with renal impairment.

Theophylline levels can be markedly increased in some patients by **ciprofloxacin**, and possibly pefloxacin. Norfloxacin, ofloxacin, pazufloxacin, or prulifloxacin normally cause a much smaller rise in theophylline levels. Fleroxacin, flumequine, gatifloxacin, gemifloxacin, **levofloxacin**, lomefloxacin, moxifloxacin, nalidixic acid, rufloxacin, sparfloxacin and trovafloxacin appear not to interact. Although problems do not develop in all patients taking theophylline and ciprofloxacin it would be prudent to be alert for this interaction in any patient. Some recommend an initial reduction in theophylline dose, in the order of 30 to 50% when ciprofloxacin is started. However, since a proportion of

patients will not require a dose reduction, others suggest that the dose should be modified based on the theophylline level on day 2 of ciprofloxacin use.

References:

- 1) Sweetman SC. 2009. *Martindale: The Complete Drug Reference, 36th ed.* London: Pharmaceutical Press. P3694.
- 2) McEvoy G. K. 2005-06. *AHFS Drug Information Essentials.* Bethesda: American Society of Health- System Pharmacists Inc. Pp 450-451, 1131-1134.
- 3) Rxlist.com
- 4) Baxter K .2008. *Stockley's Drug Interactions. 8th ed.* London: Pharmaceutical Press. p1192

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Complementary Medicine

Vitex agnus-castus

Vitex agnus-castus is a herb that has been used for hundreds of years in Europe for female reproductive system disorders, is well-tolerated, and has established efficacy in helping with some symptoms associated with premenstrual syndrome. The major active constituents of *V. agnuscastus* are iridoid glycosides, flavonoids, alkaloids, and essential oils. Its dominant pharmacological effect on the body is inhibition of prolactin secretion. *V. agnus-castus* is available in a variety of dosage forms and its use is gaining popularity in the United States. Although it has a low adverse-effect profile, women should avoid ingesting the herb while trying to become pregnant, during pregnancy, or while nursing.

Current Promoted Uses

Uses of *V. agnus-castus* relate to treatment of disorders of the female reproductive system such as short menstrual cycles, premenstrual syndrome (PMS), and breast swelling and pain (mastodynia/ mastalgia). It has been approved for irregularities of the menstrual cycle, premenstrual complaints, and mastalgia). Recent randomized, placebo-controlled studies have been conducted and found *V. agnus-castus* to be effective and well-tolerated for the relief of PMS symptoms, especially the physical symptoms of breast tenderness/fullness, edema, and headache. *V. agnus-castus* is not considered effective for PMS-related symptoms of abdominal bloating, craving sweets, sweating, palpitations, or dizziness. *V. agnus-castus* is not used in foods and is not recommended for use in children, adolescents, pregnant women, or women who are breastfeeding. *V. agnus-castus* should be avoided in patients receiving exogenous sex hormones, including oral contraceptives as *V. agnus-castus* may counteract the effectiveness of birth control pills by its effect on prolactin.



References: Tracy T. S., Kingston .R. L. 2007. *Herbal products ,Toxicology and Pharmacology 2nded.* New Jersey ed.. Humana Press Inc. P.245, 246.

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Health News

Sugary Sodas, Fruit Punches, & Kidney Stone Risk

WebMD News (Health Day)

It's important to stay hydrated. Drinking large amounts of sugary sodas and fruit drinks might raise the odds for painful kidney stones. Although drinking extra fluids usually helps

prevent stones from forming, researchers warn that beverages may come with varying risks or benefits. Coffee, tea and orange juice, for example, are associated with a lower risk of kidney stone formation. On the other hand; higher consumption of sugar-sweetened drinks was associated with a higher incidence of kidney stones. Researchers found that those who drank one or more servings of sugar-sweetened soda daily had a 23 percent higher risk for kidney stones than those who drank less than one serving per week. This was also true for those who drank sugary beverages other than soda, such as fruit punch. Adults need to consume 6 to 8 cups of fluid a day to maintain proper hydration and help prevent kidney stones. Cutting sugar-sweetened beverages out of those fluids might also help ward off stones. So what is the healthiest way to stay hydrated? "In general, water is still the best hydrant and certainly, for kidney stone prevention, the preferred beverage, experts say.

Answers:

Q1: D) Because the drug was ingested 6 hours ago, the likelihood of removing a large amount of drug from the stomach with ipecac syrup is small. Activated charcoal effectively binds acetaminophen if given soon after ingestion, but its use here is also unlikely to be of value because of the elapsed time. N-acetylcysteine serves as a glutathione substitute that effectively binds the toxin and permits it to be excreted in the urine. N- acetylcysteine is given orally or by lavage tube.

Q2: B) Oxazepam and lorazepam are metabolized by glucuronidation, a process that is much less dependent on liver function than on oxidation. Furthermore, the metabolites of oxazepam and lorazepam are inactive. But diazepam, clorazepate, prazepam and chlordiazepoxide are all metabolized by oxidation in the liver to desmethyldiazepam, an active metabolite with a very long half-life.

This process is impaired in the elderly and in the presence of liver disease e.g., cirrhosis resulting in drug accumulation and the risk of over sedation.

Q3: C) excessive thirst

Q4: E) pancreas

A Cooling Compress for Migraine

- 1 quart ice-cold water
- 2 drops peppermint essential oil
- 1 drop ginger essential oil
- 1 drop marjoram essential oil

Pour the water into a 2quart glass bowl and add the essential oils. Soak a clean cloth in the water and apply it to the head, forehead, or neck at the first sign of a migraine. Do not allow the compress to come into contact with the eyes. An ice pack applied over the compress will help keep it from getting warm.



Reference: Hoffmann David. 2003, Medical herbalism : the science and practice of herbal medicine, Rochester, Healing Arts Press p.371.

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