

A REVIEW ON INFLAMMATORY BOWEL DISEASE**CHINMAY DEVIDAS DESHMUKH***Department of Pharmacology, School of Pharmacy, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra, India.
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ABSTRACT

The gastrointestinal tract commonly known as the digestive tract is one of the most important canals in the body. It consists of the passage from mouth to anus including organs that help in the digestion. The food is taken into the mouth and all essential nutrients, and vitamins are absorbed from the digestive tract. The tract consists of important digestive organs such as the pharynx, esophagus, stomach, intestine, and rectum. Although the word gastrointestinal includes the entire tract, most commonly it is the stomach and intestine. The process of digestion is complex including a variety of minor processes. This includes mastication of food, mixing with saliva to form a bolus, mixing with various gastric enzymes to form chyme, mixing with intestinal, pancreatic and hepatic juices, absorption, and extraction, removal of water and fecal compaction and elimination. These processes are very disciplined, round-the-clock, and systematic. However, there may be chances of certain problems in this routine work such as infections, inflammation, irritation, acidity, or diseases. Constipation, diarrhea, inflammatory bowel disease (IBD), fissure, piles, fistulas, and hemorrhoids are some of the common. The smooth and easy process of digestion of food and elimination of waste is disturbed due to any of these diseases. Certain environmental factors, genetics, gender and age, smoking, chair syndrome, and geographical factors are the main things of the development of IBD. IBD causes prolonged digestive tract inflammation. There are various other underlying symptoms of the disease which are discussed in the article. The two types of this disease are ulcerative colitis and Crohn's disease. There are possible complications of these diseases such as malnutrition, weight loss, colon cancer, fistula, perforation, bowel rupture, etc. If these are not managed well in advance, then it may lead to the death of the person. To know more about the disease, the present review is an attempt to focus on all possible causes, clinical presentation, diagnosis, complications, and management of IBD. The experimental induction models are also tried to discuss in the present article.

Keywords: Crohn's disease, Inflammatory bowel disease, Chair syndrome, Fistula.© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2023v16i6.47124>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>**INTRODUCTION**

The human digestive system is involved in various important functions such as digestion, absorption, and assimilation of nutrients. One of the functions is the protection of pathogens. There are various diseases of the digestive tract, one of them is inflammatory bowel disease (IBD) commonly referred to as IBD [1]. IBD is a set of all inflammatory conditions that result from any cause leading to mild-to-severe swelling to the gastrointestinal tract (GIT). This prolonged swelling or inflammation of the tract may damage the tract. Mainly, there are two forms of this inflammatory condition and Crohn's disease (CD). Moreover, ulcerative colitis (UC) and both the disease commonly have the same clinical manifestations. IBD presents with diarrhea, gastrointestinal bleeding, ulcer, stomach pain, bowel obstruction, perforation, and cancer. The CD is regarded as an autoimmune disease that can have an impact on any portion of GIT but most commonly the distal small intestine and colon. UC is a chronic inflammatory disease in which inflammation is occurring only in the colon (large intestine) and rectum [2]. IBD is often confused with irritable bowel syndrome (IBS). Both are different diseases. The former is a disease and the latter is a syndrome. The causes and treatment of both are different. In IBS, there is improper bowel function and no inflammation. The incidence of IBD is depending on geographical area. The United States, United Kingdom, Norway, and Sweden have the highest rates. The incidence of death of IBD is due to colon cancer. The IBD can occur in adults but children are also diagnosing the disease. Generally, symptoms of IBD can start under the age of 35. The exact pathophysiology of this inflammatory condition is not well known. Various factors are contributing to the risk of IBD such as changes in the immune system, genetic variation, bacterial contamination, and production of pro-inflammatory cytokines. Family history and smoking also is an important causes of IBD. Moreover, the consumption of tobacco, polyunsaturated fatty acids consumption of milk protein is also increasing the chances of IBD. Various tests, radiographic examinations,

and blood and stool tests are available to detect the severity of the disease. Medication such as corticosteroids, aminosaliclates, and immunomodulators is helpful in the management and treatment of disease. The medications are particularly aimed to diminish the symptoms and decrease colon inflammation [3]. Various experimental models are also available to induce IBD in animals. The present review is an effort to discuss more precisely the clinical presentation, diagnosis, complications, and currently available treatments of IBD.

EPIDEMIOLOGY

UC is occurring more commonly in South Asia and South East Asia, whereas CD is a rare disease [4]. It is also found that Ashkenazi Jews have greater chances of IBD. The incidence of IBD is higher in North America and Northern Europe than that in Southern Europe. People living in Urban and Industrialized areas have greater chances because they eat more fat and processed food. Similarly, chair syndrome can also have an impact on the development of IBD. In Asia, the cases of IBD rising but not as compared to Europe. As per recent studies, Haryana and Punjab had some cases of IBD. The task force of IBD was set up in 2003 and collected data from various gastroenterologists across the nation. It is observed that CD was much higher in the South than in East as compared with other regions. The data was collected through a questionnaire and it was hospital-based [5,6].

PATHOGENESIS

The exact cause of IBD is unclear. It is believed that genetics, environmental factors, lifestyle, stress, and diseases of the immune system may contribute to IBD. Family history or inheritance is the main cause of IBD, especially CD. Genetic variations and mutations are responsible for IBD, for example, NOD2, TLR, OCTN1/2, ATG16L1, and IRGMIL23R, IL12B. These all genes maintain homeostasis in the intestinal flora and regulate inflammation [7,8] In addition, certain

bacteria are also causing inflammation changing the intestinal microflora. For example, *Firmicutes*, *Bacteroidetes*, *Streptococcus* spp., *Lactobacillus* spp., *Proteobacteria* [9]. Another factor is the Western style diet, i.e., processed food, refined carbohydrate, and saturated fatty acids also cause enteritis [10].

CLINICAL PRESENTATION

Maximum gastrointestinal diseases have the same symptoms including diarrhea, pain, and bleeding. The typical symptoms of IBD are diarrhea, rectal bleeding, abdominal pain, and tenesmus. The symptoms may be severe depending on the extent of the disease. The symptoms are present for weeks or months. If the disease extends to the rectum, bleeding is there through the feces. Sometimes, mucus and pus are also observed in stools. Nocturnal or postprandial diarrhea is observed. Severe cramping pain is also there. These all symptoms may accompany a fever, weight loss, loss of appetite, and anemia due to blood loss. These symptoms can eventually lead to peritonitis, perforation, proctitis, pancolitis, and proctosigmoiditis [11,12].

CAUSES

The exact underlying cause is difficult to discuss but bacteria, viruses, and antigens trigger the immune response of the body to produce an inflammatory response in the GIT. A recent study reported that some hereditary, genetic, and environmental factors may also contribute [13].

Risk factors

Age, ethnicity, genetics, medication, and smoking are risk factors for both UC and CD. The anti-inflammatory drug can also cause or worsen IBD [13].

COMPLICATIONS

IBD if left untreated can eventually turn into a severe life-threatening disease. 1% of severe patients present with massive hemorrhage. Toxic megacolon is noted with hastrations, especially in UC. 10% of patients have obstruction caused by benign stricture formation with one-third of stricture (narrowing of the bowel) occurring in the rectum [8]. Anal fissures, perianal abscesses, or hemorrhoids are occasionally developed in UC patients and extensive perianal lesions occur in CD patients. In addition to the above symptoms, profuse bleeding from ulcers, perforation or bowel rupture, fistula, malnutrition, weight loss, and anemia due to bleeding are occurring commonly. UC has a more increased risk of colon cancer. Blood clot formation, cholangitis, and bowel obstruction are also some complications. IBD is not only linked with colon complications, but it can also have an impact on the skin, and joints, and may result in eyes, liver, kidney, and bone disorders. Arthritis is more common [14].

DIAGNOSIS

There are various diagnosis techniques to examine the severity and stage of the disease. This aids physicians to locate, examine, and detect the inflammation. The techniques can be discussed as under:

Capsule endoscopy

The pill-sized capsule is swallowed by the patient. The colon must be empty for this procedure. The capsule can take pictures of GIT and endoscopic images of small erosions and ulceration and thereby physicians can locate this site. Similarly, a traditional endoscopy or endoscopic ultrasound is also used to detect the severity of the disease. A barium process is involved, in which the patient is allowed to drink barium sulfate solution. On X-ray, this solution appears white so the intestinal lining can be highlighted. When capsule endoscopy shows abnormalities or failure of detection precisely, then balloon-assisted endoscopies are preferred to look into the small bowel where a normal endoscope does not pass [15].

Colonoscopy and sigmoidoscopy

This technique is used to examine the colon with a colonoscope or sigmoidoscope. The swelling or ulcer can be determined and viewed through this method. There is a camera attached to the instruments [16].

Upper endoscopy

In this upper part of GIT such as the esophagus, stomach, and duodenum can be examined in case the patient is having nausea and vomiting.

Blood tests

In a blood test, white blood cell and sedimentation rates are tested. If both of these are elevated, then it confirms the intestinal inflammation. A complete blood count may reveal anemia which is caused by Vitamin B₁₂ deficiency or even infection. Moreover, serological markers may also be examined in blood tests to differentiate between UC and CD [17].

Stool test

To have an idea of occult blood (hidden) blood in feces, stool examination can be preferred.

Magnetic resonance and X-ray computed tomography

These magnetic scans can deeply examine the part of the intestine so abdominal complications such as fistulas, abscesses, obstruction, and bleeding can be detected. These techniques involve multidetector scanners of high resolution for observation of mucosa, bowel wall, and lumen of the intestine. Not only this, the fibrofatty proliferation, sacculation, fat deposition, and shortening of the bowel wall can also be determined with this technique. The magnetic resonance technique also assists in the determination of wall thickening, and edema in the intestine. A simple abdominal X-ray can also help to determine the perforated colon [17].

Biopsy

The biopsy technique involves the removal of a piece of the affected part and examining it microscopically. Such determination critically detects the type and severity of inflammation, mucosal damage may or may not be characterized by focal infiltration of leucocytes into the epithelium. Granuloma, which is more specific to CD can also be detected with biopsy. Histology can also be performed to examine the pieces more precisely [18].

MANAGEMENT AND TREATMENT

The main objective of managing this disease is to reduce inflammation and maintain remission.

Anti-inflammatory and immunomodulator drugs

This can be achieved by using anti-inflammatory drugs such as corticosteroids and 5 aminosalicylic acids, other drugs are immunomodulators, such as adalimumab, infliximab, natalizumab, azathioprine, mercaptopurine, methotrexate, and certolizumab. These compounds efficiently trigger a Th2-mediated response that dampens Th1-mediated inflammation to regulate the immune system. This drug suppresses the immune system so that inflammation-inducing chemicals are not released. These drugs also neutralize the protein in the body that causes inflammation.

Antibiotics

Ciprofloxacin and metronidazole can also be prescribed to eradicate the infection if any.

Other drugs

To give more relief to the patient, antidiarrhea drugs, painkillers, and nutrient and vitamin supplements are often prescribed to the patient. As diarrhea is a common symptom, it should be treated.

Special diet

In cases that are accompanied by weight loss, the gastroenterologist may recommend a special diet that can be induced through a feeding tube. Care is taken that no food particle can struct in GIT and cause blockage.

Surgery

In severe cases, the colon part or entire colon is surgically removed when other options of treatment do not work. If the damaged portion is removed, then the remaining normal portion of the intestine is

reconnected. In case the entire colon is removed, the surgeon creates a permanent opening in the abdomen called an ileal stoma through which stools pass in the bag [19].

Lifestyle modification

Home-based remedies are also found useful in some cases of IBD. The symptoms may be relieved. There is no evidence of food that can affect IBD but limiting dairy products, limiting meals, drinking plenty of fluids, multivitamins, and mineral supplements are found useful. In addition, stress management, smoking cessation, relaxation, and breathing exercises are proven beneficial [19].

EXPERIMENTAL MODELS FOR INDUCING IBD

To test any drug over IBD, we need to induce IBD first in the experimental animals. There are various experimental models or methods to induce colitis in rabbits, guinea pigs, and rats. These models involve intraluminal administration of caustic agents such as ethanol, formalin, or organic acids to initiate the inflammatory response. We have discussed the following models to induce experimental colitis.

Acetic acid-induced colitis

In this model, the dilute solution of acetic acid is intrarectally administered to induce colitis in rats. This colitis is not having similarities to human UC but it is observed that the biopsies obtained from human UC are very similar to the pattern of acetic acid-induced mucosal arachidonate metabolism. In this case, there is the introduction of the acetic acid proton into epithelium where it liberates protons and causes epithelial injury. Further cyclooxygenase and lipoxygenase pathways are activated [20].

Indomethacin-induced colitis

In this model, Indomethacin is given subcutaneously in rats to produce colitis. This colitis is affecting the middle portion of the small intestine including the jejunum and proximal ileum and also cecum. The inflammation is not continuous and shows some patches of normal tissues (skip areas). This model is similar to CD.

The pathogenesis of the lesions produced by Indo is not clear. The mechanism is thought to involve prostaglandin-related enteropathy in rats. Local changes in intestinal microflora are also observed. Inhibition of protective prostaglandins such as PGE and PGE and prostacyclin may be one mechanism by which Indomethacin induces injury and inflammation [21].

Iodoacetamide-induced colitis

In this model, such as glutathione which is an endogenous sulfhydryl (SH) compounds, contribute to the protection of gastric mucosa. The introduction of SH blockers in the colon can cause colitis in the mucosa. This is caused by decreasing the amount of SH compounds that are defensive [22].

Trinitrobenzene sulphonic acid (TNBS)-induced colitis

Colitis can also be occurred by one more compound. Treatment with a 2, 4, 6-TNBS in the colon can cause colitis. In this method, TNBS enema is given to animals following ethanol enema in the mucosal layer of the intestine. Susceptibility to TNBS is different among various mice, but some developed hapten-induced delayed-type hypersensitivity caused chronic colitis [22].

Oxazolone colitis

Oxazolone also causes colitis as that of TNBS. Here, the body weight loss and diarrhea are seen on the 2nd day after the enema. These symptoms diminish after 10–12 days. Ulcers and colitis are most commonly found in the distal colon. Microscopically it is observed that there is a reduction in the number of goblet cells, epithelial cells as compared with controls [22].

Dextran sulphate solution (DSS) induced colitis

It is also documented that the DSS also induces colitis. The administration of DSS dissolved in water to mice or rats caused body

weight loss, mucosal ulcers and infiltration of neutrophils shortening of the intestine hematochezia, acute colitis, which occurred during the administration of DSS and chronic colitis, which occurred a little time after the administration of DSS, was seen in this model [22].

DISCUSSION AND CONCLUSION

There is no complete cure for IBD. Drugs can dampen intestinal inflammation by several mechanisms. The review provides an overview of the disease under all possible headings. Some drugs can reduce inflammation by inhibiting the proliferation of cytokines but have potential side effects such as nausea and vomiting. The immunomodulation drugs also dampen Th1-mediated inflammation by regulating the immune system. As per the latest study, Anti-TNF- α antibodies are also used to reduce inflammation caused by TNF- α . Artificial cell encapsulation is another ray of hope which involves the delivery of the compound to a specific target site in the body in a time-dependent manner. This may consist of DNA, drugs, enzymes, and antibodies which when introduced into the body reduce intestinal inflammation. This is due to the reduction of the level of proinflammatory cytokines and the limiting of the side effect. These all results are encouraging. But still, there is the need for validation of more effective, efficacious drug treatment for making commercializing newer IBD therapies. The information obtained from ongoing and completed clinical trials will surely be helpful to us the understanding the pathophysiology of inflammation in the colon and may have an excellent impact on treating the disease.

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The author has collected the information required for this paper from various sources such as PubMed, Science Direct, research gate, and Wikipedia. Various books and theses have been referred for publication in this article. He has also collected information from surveys conducted by Physicians in Pune and from hospital patients.

CONFLICT OF INTEREST

The authors declare that there is not any conflict of interest in the publication of this paper.

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