

# Management of Inflammatory Bowel Disease

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## ABSTRACT

*Inflammatory bowel disease (IBD) is an inflammatory disease, which involves the digestive tract with still unknown definite etiology. IBD cases are frequently underdiagnosed or even overdiagnosed. Delay in diagnosis often happen due to the unspecific intermittent symptoms. Principally, treatment of IBD is targeted to acute episodes and maintenance of therapy during remission phase. First line therapy drugs include 5-acetyl salicylic acid (5-ASA) and corticosteroids are systemic and topical. If failed, then second line therapy, which has immunosuppressive characteristic, is given such as: 6-mercaptopurine, azathioprine, cyclosporine, methotrexate, and anti-TNF (infliximab). Efforts to prevent recurrent inflammation in IBD are to maintain the remission phase as long as possible. Surgery management may be considered if conservative of pharmacological treatment fails or complication happens.*

**Keywords:** *inflammatory bowel disease, management, treatment*

## ABSTRAK

*Inflammatory bowel disease (IBD) adalah penyakit inflamasi yang melibatkan saluran cerna dengan penyebab pastinya sampai saat ini belum diketahui dengan jelas. Kasus IBD sering mengalami underdiagnosed maupun overdiagnosed. Penundaan diagnosis sering terjadi akibat hilang timbulnya gejala yang tidak spesifik. Pada prinsipnya, pengobatan IBD ditujukan pada serangan akut dan terapi pemeliharaan saat fase remisi. Obat lini pertama berupa 5-acetyl salicylic acid (5-ASA) dan kortikosteroid yaitu sistemik atau topikal. Bila gagal, maka diberikan obat lini kedua yang bersifat immunosupresif seperti 6-merkaptopurin, azatioprin, siklosporin, metotreksat dan anti-TNF (infliximab). Upaya pencegahan peradangan berulang IBD adalah dengan mempertahankan fase remisi selama mungkin. Tatalaksana pembedahan dapat dipertimbangkan bila pengobatan konservatif atau medikamentosa gagal atau terjadi komplikasi.*

**Kata kunci:** *inflammatory bowel disease, tata laksana, pengobatan*

## INTRODUCTION

Inflammatory bowel disease (IBD) is an inflammatory disease which involves digestive tract with still unknown definite etiology. Generally, IBD consists of 3 types, which are: ulcerative colitis (UC), Crohn's disease (CD), and indeterminate colitis.<sup>1</sup> UC appears as diffused intestinal mucosal inflammation which is limited to the colon. Meanwhile, CD appears as transmural, patchy inflammation, which may involve any parts of the gastrointestinal tract. Approximately

5% patients with IBD are difficult to be classified into UC or CD, although after thorough examinations including clinical, radiology, endoscopy, or even anatomy pathology examinations have been performed because these patients have several appearance which is in line with UC or even CD. This may be considered as indeterminate colitis.<sup>2</sup>

Incidence of UC ranges from 10-20 per 100,000 residents per year with the prevalence of 100-200 per 100,000 residents. Incidence of CD is approximately

5-10 per 100,000 residents per year with the prevalence of approximately 50-100 per 100,000 residents. UC and CD are diseases frequently experienced by young aged patients (between 10-40 year old). Although, it may also happen in any age of patients. Approximately 15% are suffered by patients aged > 60 year old when diagnosis is being confirmed.<sup>3,4</sup> There is no significant difference between male and female. IBD predominantly happens in high socio-economic group, nonsmoker, oral contraceptive users, and low fiber diet individuals. In Indonesia, there is no data available regarding the epidemiology of IBD.<sup>1</sup> IBD cases are often being underdiagnosed or even overdiagnosed. Delay in the diagnosis often occur due to the intermittent unspecific symptoms. Additionally, lack of facility or diagnostic tool in local hospital also contribute to underdiagnosing IBD.<sup>2</sup> Furthermore, IBD patients usually feel embarrassed of their diseases.

IBD may cause loss of employment opportunity, psychological problem, failure to thrive, and sexual developmental delay in young aged patients. Medications such as: corticosteroid or immunosuppressive drug may cause secondary health problem and surgical procedure may cause complications, including impotence or gastrointestinal function failure.<sup>5</sup> Impact of IBD to the society is quite high because the incidence frequency in young age and its potency to cause life-long health problem. The incidence of IBD in the hospital ranges from 45-90 cases per 300,000 population per year.<sup>6</sup> The mortality rate of UC (hazard ratio = 1.44; 95% CI = 1.31-1.58) and CD (hazard ratio = 1.73; 95% CI = 1.54-1.96) is very dependent to age and disease distribution.<sup>7</sup>

## MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

The etiology and pathogenesis of IBD are still unclear, therefore treatment is stressed on inhibiting inflammation cascade. General treatment in the form of antibiotic administration, intestinal lavage, binding bacterial products, resting the work of the intestine, and changing dietary pattern. Intestinal lavage can be performed by using physiologic fluid or even experiment using liquid sucralfate. Probiotic is expected to be able to bind to bacterial products. Several food which should be avoided as they may provoke attack, include wheat, cereal yeast, and dairy products.<sup>8,9</sup> Several constituents with antioxidant characteristic which have been reported to be beneficial in IBD cases are glutamine and short chain fatty acid.

In principle, IBD treatment is targeted to acute attacks and maintenance therapy during remission phase. The

first line drugs are 5-acetyl salicylic acid (5-ASA) and corticosteroid (systemic or topical). If failed, second line drugs which have immunosuppressive characteristics are given (such as: 6-mercaptopurine, azathioprine, cyclosporine, methotrexate and anti-TNF (infliximab)).<sup>1,2</sup>

Metronidazole have been adequately studied to be beneficial in CD in decreasing degree of disease activity in active condition if given in the dose of 1,500-3,000 mg once daily. While in UC, antibiotics are rarely being used as therapy towards proinflammatory agents.

Groups of drugs which can play role in treating active phase and inducing remission as soon as possible are corticosteroid and salicylate amino acid.<sup>10,11</sup> Corticosteroid is a potent anti-inflammatory agent for moderate-severe UC and CD, as well as relapse cases. Oral steroids are very effective to induce rapid clinical remission, but no effect in maintaining remission. In severe condition, parenteral corticosteroid may be given. To maintain remission, steroid dose can be decreased gradually following introduction of immunosuppressive drugs. Generally, the choices are prednisone, metilprednisolone, or enema steroid because they are cheap and affordable. To gain high steroid concentration in the intestinal wall with minimal systemic effects, currently non-systemic glucocorticoid drugs have been developed in IBD treatment (may use oral slow release budesonide or enema). Budesonide is a corticosteroid with poor systemic absorption and low bioavailability and has extensive first pass metabolism, therefore it has high topical effect with low systemic toxicity. The average dose to reach remission phase is equal to 40-60 mg prednisone, which is tapered down after remission is achieved in 8-12 weeks. Mechanism of action is through inhibiting several inflammation pathway, suppressing interleukin transcription, suppressing arachidonate acid metabolism, and stimulating lymphocyte apoptosis in lamina propria of digestive tract.<sup>12</sup>

Salicylate amino acid drugs group is drugs which have been used for a long time and potent to treat IBD, particularly as drugs to maintain remission. These drugs work on the intestinal epithelial cells through series of mechanism to decrease release of inflammatory mediators, cytokines, and reactive oxygen species (ROS). Sulfasalazine with the dose of 2-4 g/day (active phase IBD) is given to achieve remission and continued with maintenance dose according to patient's condition. After remission is achieved (generally after 16-24 weeks), the medication is followed with maintenance dose which is individual as preparations in the form of oral, systemic, and suppository or enema. Maintenance therapy may decrease colorectal cancer risk up to 75%

(OR = 0.25; 95% CI 0.13 - 0.48). and it is less effective to maintain remission in CD.<sup>11</sup> Adverse effects are 10-45% and are dose-dependent, such as: headache, nausea, epigastric pain, and diarrhea.<sup>2,13</sup> Mesalazine maintenance dose is 1.5-3 g once daily.

Immunosuppressive drugs used in the therapy with salicylate amino acid and corticosteroid fail to achieve remission. Examples of this group of drugs are 6-mercaptopurine, azathioprine, cyclosporine, and methotrexate. Azathioprine or its active metabolite 6-MP requires 2-3 months before showing its therapeutic effects. Generally used as inductor in dependent or refractory steroid cases. Usually, initial dose of 50 mg is given until substitution efficacy is achieved, then increased gradually 2.5 mg/kg body weight for azathioprine or 1.5 mg/kg body weight for 6-MP. The most common side effects are nausea, dyspepsia, leucopenia, lymphoma, hepatitis, and pancreatitis. Intravenous cyclosporine may be used as an acute management of severe steroid refractory UC cases with success rate up to 50-80%. CD cases with fistulation may close quickly. Unfortunately, conversion to oral dose frequently cause relapse. The most frequent side effects include nephrotoxicity, and opportunistic infection such as plasma cell pneumonia (PCP). Methotrexate is effective for CD-steroid dependent case and is good to maintain remission in UC. Induction dose is 25 mg/week subcutaneous/intramuscular (SC/IM) until steroid tapered-off is complete, then maintenance dose is considered to the limit no occurrence of side effects which is associated to immunosuppressive effects, such as: emergence of interstitial pneumonia and or liver fibrosis. Usually clinical effectivity response is seen in several weeks.<sup>13</sup>

Lately, several anti-tumor drugs (biological agents) are thought to be used in IBD treatment, such as: infliximab, adalimumab, certolizumab. These drugs are usually indicated for moderate and severe CD fistulated (steroid refractory). Preventive measures of recurrent inflammation in IBD are by maintaining remission phase as long as possible through 5-ASA maintenance dose which is individual or through introduction of immunosuppressive drugs, anti-TNF, and probiotics.<sup>13</sup>

Surgery is considered if conservative or pharmacological treatment failed or complication occurred, such as: massive bleeding, intestinal perforation, fistula, abscess, obstruction due to intestinal stenosis (fibrosis process), toxic megacolon (particularly in UC), or even malignant degeneration.<sup>10</sup> Several surgical procedures which need to be considered can be seen in Table 1 as follows.

**Table 1. Surgical procedures for inflammatory bowel disease<sup>11</sup>**

Disease	Procedures
Ulcerative colitis	Colectomy and ileal pouch formation Proctocolectomy with ileostomy Colectomy with ileorectal anastomosis
Crohn's disease	
Duodenal disease	Strictureplasty, duodenojejunostomy Balloon dilatation per endoscopy
Small bowel disease	Fistula: resection and damaged segment anastomosis Stricture: resection, strictureplasty, or balloon dilatation
Colorectal disease	Segmental colectomy for limited disease Proctocolectomy for diffused and extensive disease
Severe anorectal disease	Abdominoperitoneal resection with permanent end-colostomy

## EDUCATION IN THE MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

Comprehensively and simultaneously, management of IBD has to be understood by patient and family. Therefore, understanding towards cases, diagnostic, and therapeutic processes which are planned and required to be performed, always have to be informed and performed with consent of patient and his family, including the informed consent process and patient safety. In educating patient and family, also need to be informed about complications which may happen due to disease progression which is chronic exacerbation, also disease prognosis which is generally very much influenced by response degree to conservative treatment.

As clinical implication of a complication, possibility of surgical procedure also needs to be informed from the beginning and if surgical intervention will be started, procedure preparation in the form of surgery tolerance consultation including written informed consent should already be done.

## CONCLUSION

Important phase in treatment of IBD is maintenance during remission phase, with preventive efforts to maintain this phase as long as possible. Several groups of drugs, such as: corticosteroid and drugs with immunosuppressive characteristic as second line drugs, play important role in treating active phase and inducing remission phase as soon as possible. If conservative treatment failed, then surgery might be considered as a solution in management of IBD. One of the most important factors in management is education to the patient and family, starting from

disease awareness, treatment planning, until post treatment, such as: complication, which may happen due to disease progression.

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