# Treatment of Ulcerative Colitis; Update

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Ulcerative Colitis [UC] is a chronic debilitating inflammatory process that is usually confined to the mucosa and on occasions submucosa of the large bowel. It affects all age groups but is more common at 15-30 years and spares no sex. Typically the disease has relapsing-remitting course. Bloody diarrhea forms the cardinal clinical hallmark symptom of the disease, whereas the histopathological hallmark of the disease is diffuse infiltration of lamina propria with inflammatory cells, crypt abscesses and distortion of the mucosal architecture.

Extension of the disease to the muscular layers is unusual. The small bowel is never involved except in backwash ileitis, whereas the rectum is affected in around 95% of cases. The disease may present with extra-intestinal features as ocular, oral, skin, joints, liver, biliary disease and others. Beside the physical disability the disease has psychological consequences and considerable diminution of quality of life. The etiology of UC is obscure. Nonetheless, some postulations concentrating on the immune system were put foreword. One of these suggests disturbance of the intestinal immune system-of unknown cause- results in injury of the mucosa that predispose it to invasion by microorganism. On the other hand some believe that the disease is rather due to abnormal immune response to antigens of intestinal microorganisms[1,2]. It appears that the T cell lymphocytes play a fundamental role in the inflammatory process that characterizes the disease. Cigarette smokers were found to be less affected by UC, this points to the role of environmental factors in the pathogenesis of UC [3,4].

The disease that starts at the rectum is divided depending on its extent in the bowel into: ulcerative proctitis when it is limited to the rectum; left-sided colitis when it ascends to the splenic flexure; pancolitis if it goes more proximally.

Truelove and Witts classification are used to evaluate the severity of the disease[5]. Based on the clinical presentation the disease was classified into: mild when there is mild infrequent abdominal pain and diarrhea without fever or weight loss; moderate when the abdominal pain is not severe, the fever is of low grade and the anemia dose not require blood transfusion; when the disease presentation extends beyond that i.e. patient has a high grade fever, profuse bleeding, frequent loose motions and significant weight loss the disease will be categorized as severe.

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Fulminant disease is a medical emergency that requires hospital admission and special care.

It was reported that not more than 50% of patients with ulcerative colitis will be at clinical remission at any time and similar percentage
have a relapse yearly[6,7]. To improve this figure some effort-comparable to that done in management of Crohn's disease- has to be done. Nevertheless, current medical and surgical treatment including immunosuppressive drugs and the ileo-anal pouch procedure is relatively safe and effective for controlling different stages of the disease. Finding safer- especially on long term management- effective, and cheep treatment modality remain a challenge for clinicians and researchers.

In this review highlights were put on medical treatment of UC with light touch on screening for colorectal carcinoma. Details of the clinical, endoscopic, histopathological pictures as well as the local and systemic

complications are out of the scope of this article.

**What are the Goals of UC Treatment?**

In order to improve the quality of life and prevent the expected complications; induction and maintenance of remission together with close monitoring for complications and side effects of drugs were taken as target goals for treatment of UC that need be achieved.

**Current Treatment For Ulcerative Colitis**

To date there is no curative treatment for UC apart from panproctocolectomy. Effectiveness of current medical treatment depends on the proper consideration of extent of the disease and its severity when choosing the modality of treatment. It worth mentioning that clinical remission occurs as twice as endoscopic and histopathological remission in each clinical setting.

**Aminosalicylates:**

Aminosalicylates form the corner stone for management of UC. 5-aminosalicylic acid [5-ASA] forms the active ingredient of these compounds utilized for treatment of UC. Its desired action is supposed to be in the large bowel. Because of its excellent absorption and extensive first pass metabolism to the inactive compound N-Ac-5ASA some work was done to protect 5-ASA from absorption, and metabolism in the stomach and proximal small bowel by changing the formula to delay or control the release of the drug to be in the large bowel as in Asacol, Salofalk, Mesasal, Claversal, and Pentasa or add some other compound (pro-drug) to ‘ carry’ the active ingredient to its site of action as in sulfasalazine, olsalazine and balsalazide. It is important to note that there is no difference in colonic absorption between different formulas of aminosalicylates[8].

Oral 5-ASA compounds were found to be less effective than enemas in inducing remission when the disease is confined to the rectum, but the more proximal disease mandates their addition to topical enemas/ suppositories to ensure adequate coverage of the inflamed mucosa. It was reported that when both oral and topical aminosalicylates were combined together, an additive increment in total 5-ASA dose was achieved with consequent more effective response than either alone[9-11]. Meta-analysis had shown that there is significant difference in successful withdrawal rate from treatment between patients taking some of these compounds and those on placebo.

5-ASA is found in different forms. PH dependent and time-control release 5-ASA are released in the small bowel. When combined with sulfa the active ingredient will be released only in the large bowel. However, the side effects of the new compound may overshadow its use. The majority of the side effects were due to the sulfa particles[12]. It is worth mentioning that 5-ASA may have as well serious- though infrequent- side effects in almost all systems of the body including pneomonitis, pericarditis, nephritis, bone marrow suppression, pancreatitis,
hepatitis, diarrhea and hair fall. One of the important side effects is colonic hypersensitivity which closely mimics and may be diagnosed as refractory UC. Newer 5-ASA compound were shown to be much safer. Meta-analysis studies did not show differences in efficacy between different 5-ASA containing compounds. However, different mucosal concentration of 5-ASA were detected a week after cessation of different formulae of the compounds. It is crucial to know that the mucosal concentration of 5-ASA was found to be inversely correlated to the endoscopic and histopathological findings. This can explain the differences in patency between various formulas of the same compound [7,13,14]. With these modalities of treatment clinical recovery is expected in few days, while endoscopic and histopathological improvement may take some weeks. Although 5-ASA compounds are effective as inducer of recovery in UC, they are used mainly for maintenance of remission. It was reported that 75% reduction of colorectal cancer risk occurred in patients with UC whose remission was maintained with 5-ASA.This highlights the importance of long term maintenance therapy especially in patients with extensive disease[7]. Maintenance

therapy may not be necessary after the first episode of mild localized disease[15].
Again because of frequent dosing and on occasions by a large number of tablet; inconvenience leading to noncompliance was found to be the major factor in reducing the efficacy of the these drugs[16,17].
Patients who are not refractory to these measures may need corticosteroids. Although less effective than aminosalicylates , topical or systemic corticosteroids form a good choice for induction of remission in these refractory patients. Although less convenient to patients, topical medication give quicker response and need lesser doses than oral ones. Patient's preference may guide the choice between the oral or topical modalities.

**Corticosteroids:**
Corticosteroids suppress inflammation at different points via multiple pathways including suppression of interleukin transcription, arachidonic acid metabolism and stimulation of apoptosis of lymphocytes within the intestinal wall together with induction of IkB that stabilizes the NFkB complex.
Topical and oral corticosteroids are used in patients who had inadequate response or intolerance to 5-ASA and in patients with moderate or sever UC. However, apart from the side effects, around 40% of patients may not respond to corticosteroids. This mandated looking for other alternatives[18]. Oral prednisolone is efficient inducer of remission in UC. When combined with rectal enemas/suppositories its action will be augmented. About 50% of topical corticosteroids are absorbed and may show the side effects. The newer corticosteroids like budesonide and prednisolone metasulphobenzoate are less absorbable and so they form a better choice to conventional ones[19,20]. The majority of corticosteroids side effects are dose dependent and rapid tapering of the dose may enhance rapid relapse of the disease.
Intravenous corticosteroids may be the first option as initial treatment for severe extensive UC. However, if there is no adequate response within 7-10 days, then immune modulators will be highly indicated[21]. Observational studies had shown response rate of 60% to 80% to IV corticosteroids, but this was not supported with double blinded placebo-controlled studies[22].

**Immunomodulators:**
It had been estimated that circulating antibodies were present in around 60% of patients with ulcerative[23]. Using immunomodulators for treatment of the disease is therefore not a surprise. Because of their tremendous side effects, these drugs are not routinely used to initiate or maintain remission. Their main role is sparing corticosteroids when higher doses of the latter are needed or be used when there is resistance to corticosteroids. They may also be used for maintenance in patients whose remission was induced by cyclosporine[24]. Understanding the potential toxicity and the appropriate way for monitoring are imperative before prescribing these medicines. When given even cautiously, close observation for evidence of pancreatitis, bone marrow suppression and hepatotoxicity is mandatory. These toxic effects were reversible with withdrawal of the drugs[25]. Bone marrow suppression will indirectly predispose the patients to opportunistic and different viral infections. Life-threatening disseminated varicella zoster and CMV pneumonitis were reported[26,27].
.The beneficial effect of azathioprine [AZA] in induction and maintenance of remission were reported, and it had been proved that this effect was augmented when an aminosalicylate was added to therapy [28]. Thiopurine methyltransferase is an important enzyme for the metabolism of mercaptopurine [MP]. Current data show that higher levels or activity of this enzyme are associated with resistance to AZA/MP therapy. Determining the level and or activity of this enzyme prior to initiation of therapy is therefore important to avoid an unnecessary exposure to these notorious drugs. This will not ameliorate the need for close monitoring of patients for the side effects[29].

Patients on these drugs were also susceptible to develop lymphoma particularly EBV-mediated lymphoma[30]. Nevertheless, this risk of developing extra-intestinal malignancies which was advocated earlier was not supported by following reports. Non-melanoma skin cancer is well documented in these patients [31,32] .

**Cyclosporine:**

Intravenous and oral cyclosporine had shown an excellent effect (83%) and (63%) respectively in patients who are corticosteroid refractory. In such patient this drug plays an important role to bridge the patient to other modality of maintenance therapy [33]. Some studies had shown no difference between IV corticosteroids and low or high dose cyclosporine. Cyclosporine side effects remain a concern to treating teams. Hypomagnesaemia, renal failure and opportunistic infection with reported mortality rate of 1%-2% are among the serious ones. This will definitely be augmented by the concomitant use of other immune modulators and may be good reasons to advocate surgery over these drugs[34-36].

**Oral methotrexate:**

Initial reports on oral methotrexate for treatment of UC were disappointing. However, the small dose of the drug used in such patients could explain those results. Consequent trials using larger doses of oral or intramuscular methotrexate showed promising results regarding both induction and maintenance of remission. When combined with folic acid a tremendous reduction of antiproliferative side effects was seen[37,38].

**Potential Treatments For Ulcerative Colitis:**

Control of symptoms, cure of the disease, without the sequential late complications is the goal of treatment of UC. To date there is no "ideal" drug to achieve that. A drug that induces effective clinical, endoscopical and histopathological remission which can maintain that without serious side effects is still a dream. Current drugs including aminosalisalates, corticosteroids, antimetabolites, infliximab and others have all failed short of achieving those goals.

A large number of drugs were on the horizon. Hopefully these drugs will pass efficacy and safety testing and will soon be a new additional option for the patients.

**Inflammatory cytokine inhibition:**

The role of tumour necrosis factor alpha(TNFα) in inflammatory bowel disease is well established. Drugs to modulate or block this effect including the mouse/human (chimeric)
monoclonal antibody infliximab, the humanized monoclonal antibody CDP571, the fully human monoclonal antibody adalimumab, the human soluble TNF p55 receptor , thalidomide and the MAP kinase inhibitor CNI-1493 are coming up rapidly[39].

**Infliximab:**

Although the initial reports on Infliximab-which is a well established mode of treatment in some diseases including CD- gave controversial results when tried with UC[40, 41]. By binding to membrane- bound TNF Infliximab facilitates lysis of these cells and it also induces apoptosis of activated T cells[42,43]. Infliximab is given as three doses to induce remission and then one injection every eight weeks for maintenance[44]. Recent studies had proved the good clinical response to infliximab accompanied with significant mucosal healing. This adds to the benefits of this drug as mucosal healing was thought to be the most important single predictor of reduced risk of colonic cancer in patients with UC. Smaller doses of infliximab were found to be as effective as large doses with no significant differences in side effect. Close observation and vigorous search for serious infections had to be implemented as fatalities were reported[44,45], relatively recent reports have clearly demonstrated the benefits of this drug, with significant rates of clinical and endoscopic remission even in severe cases of the disease [44,46]. Nevertheless, the questions of when and in which patient shall the treatment be applied remain to be answered. The problem of development of antibodies against Infliximab has complicated the matter

more. Antimetabolites have to be used concomitantly with Infliximab to prevent the emergence of antibodies. In such conditions, it will be very difficult to estimate the real role played by each of Infliximab and the antimetabolites in remission[47]. Some reports had demonstrated the reduced likelihood of going to surgery in patient who had a single dose of infliximab. This may advocate the use of this drug over other ones including cyclosporine, steroids and antimetabolites. However, more studies looking particularly on where to put this drug in the therapeutic algorithm of UC, the long term out come and potential complications are mandatory [46].

**Selective Leukocyte Adhesion Molecule Inhibitors**

The exact role played by WBCs in the pathogenesis of UC is debatable. Nevertheless, the interaction between WBCs and inflamed vascular wall is well known. Recent therapeutic trials had proved the significant contribution of at least some subsets of T lymphocytes in the pathogenesis of UC and the mechanisms advocating that were postulated[48]. Complex reactions involving many mediators were thought of as possible contributors in this pathological process. Building on that, 'blockers' of those pathways we acceptable therapeutic options for the disease[49, 50].

The α4β7 integren molecules subtypes that are present on the cell surface of a small proportion of T lymphocytes were highly selective for the gut wall and so they direct the leukocytes towards that wall. Blocking these α4β7 molecular receptors has become the sites of interest to the investigators. Initial reports on such blockers gave promising results. This was supported by the good results of these drugs in treatment of Crohn's diease[48,51-53].

**Thiazole Derivatives**

In animal models with colitis, Tetomilast had shown some efficacy and its safety was demonstrated before. The primilinary reports on this drug when used for treatment of UC were encouraging[54, 55].

**Tacrolimus (Fk-506):**

This is an orally well absorbable calcineurin inhibitor, initially it was used for treatment of eczema and later became widely used in transplantation medicine. It has an excellent tolerability and had shown efficiency in induction of remission in refractory UC similer to that of cyclosporine and infliximab beside being a corticosteroid sparing agent. Being taken orally is an advantage for this drug[56].

**Other Agents:**

Recently etanercept which specifically binds and blocks TNF was assessed for its efficacy against naturally occurring cell surface TNF receptors. None consistent results were obtained[57]. Natalizumab has emerged as a promising active drug in treatment of UC. Unfortunately this was downgraded by the serious side effects of the drug including leukoencephalopathy which had severely over shadowed its benefits[58-60]. Visilizumab which selectively and instantaneously depletes T lymphocytes had shown a unique potential capability in treating severe and steroid refractory UC. Controlled trials on this agent are still going on. Like other T cell targeting agent rigorous attention has to be paid to opportunistic infection and lymphoma[61].

Recombinant interferon-β-1a has failed to show convincing activity in patients with UC. On the other hand enemas of epidermal growth factor that promote mucosal healing had shown promising effectiveness in patients with left-sided UC. Abut 83% of treated patients had clinical remission in two weeks time and had significant histopathologicl improvement. The long term response, complication and risk of cancer and lymphoma have to be sorted out by large controlled studies[62,63].

LMP-420 is a purine-based compound that strongly inhibits production of both TNF mRNA and protein. It is non-toxic to white blood cells or intestinal epithelium.. This give this compound an advantage over infliximab as it will not lead to lysis of the cells and hence it will not predispose the patient to reactivation or infection with tuberculosis[64,65].

**Miscellaneous**

**Probiotics:**

It was believed that disturbance of the normal bacterial flora of the bowel plays an important role in inflammatory bowel disease. By deliberate introduction of beneficial micro-organisms to the bowel, attempts were made to restore the balanced flora and hence induce remission and possibly cure of this disturbing disease[66].

By producing predominately IL-2, IFNc and TNFa, stimulated T helper 1[Th1] cells were believed to play an important role in the pathogenesis of UC. It is found that Th 1 and T helper 2[Th2] down regulate each other. Consequently if Th 2 were promoted this will automatically demote Th1 and so reduce the pro-inflammatory factors IL-2, IFNc and TNFa. This phenomenon has led the researchers to look for clinical use of stimulator of Th2. One of the postulated stimulators of Th2 is the intestinal parasitic helminths. It was noted that UC is less in areas of high helminths prevalence. Nevertheless, this may be simplification of the matter as many other immunological factors have to be considered. Controlled studies may clarify this condition[67].

**Leukocytapheresis:**

After showing significantly higher effectiveness than prednisolone in the recent years, leukocytapheresis is emerging as an effective, practical, applicable, with few side effects and possibly as a standard treatment in cases of severe and refractory UC in order to avoid surgery[18, 68]. The patients who had this modality of therapy showed clinical improvement, reduced need for corticosteroids and on occasions total withdrawal of corticosteroids[18]. In addition to reducing lymphocytes, leukocytapheresis was found to reduce the level of some pro-inflammatory cytokines including TNF-α, Interleukin [IL]1β, IL -2, IL -8 and interferon-γ which are usually elevated in patients with UC[69].

**Weight reduction**

UC is characterized by the presence of elevated levels of several inflammatory modulators including IL-1, IL-6, TNF-a, and C-reactive protein. These same modulators were elevated in obese patients. Cases that had clinical improvement following weight reduction were reported[70].

**Medical treatment of Mild and Moderate Distal Colitis:**

**Proctitis and Left sided colitis:**

Around 30% of patients with UC present with proctitis. Rectal bleeding and urgency in the absence of diarrhea indicate limited distal colitis where 5-ASA suppositories form the best modality of treatment to induce and maintain remission, whereas enemas and foams are given to more proximal disease. The vast majority of patients respond to treatment. However, 5% of patients may not respond even to oral or intravenous corticosteroid and total colectomy could be the solution to improve the quality of life. Partial colectomy is not a good choice as the disease will eventually recur in the remnant of the colon[71]. Relief of constipation is occasionally helpful in patients with proctitis and this may need to be targeted. On the other hand antidiarrheal medications do not reduce the frequency of motions. In fact they predispose the patient to toxic megacolon and so better be avoided[72].

When the disease extends to the distal colon, the patients have more frequent diarrhea. Without systemic symptoms, topical 5-aminosalicylic acid (5-ASA) enemas and/or suppositories are effective and probably form the drugs of choice as initial treatment to induce and maintain remission in these patients[73-75]. There are no convincing data to support which are the best options in cases of failure to induce remission by aminosalisaltes[76]. However, in some patients hydrocortisone foams or enemas may form a reasonable alternative option, but their side effects occasionally jeopardize their usage. Budesonide is a poorly absorbed synthetic corticosteroid. Because of its extensive first pass metabolism, it has a short bioavailability and consequently better safety profile, thus favoring its usage over hydrocortisone and prednisolone when corticosteroids are needed.

Although meta-analysis of some studies had shown superiority of 5-ASA enemas to corticosteroid enemas, the decision of which drug to use will partially be influenced by other factors including the tolerability, availability and cost [20,77, 78]. The most important concern –beside the adverse effects- to treating physicians in topical treatment of UC is being inconvenient to many patients. This usually led to non-compliance. Compliance and long term remission are of utmost importance in this disease where meta-analysis data had shown development of colorectal cancer in 18% of patients with long standing [30-years] disease. Good persistent compliance was observed to reduce this risk by two folds[79-81].

Aminosalisaltes are not recommended for induction of remission in patients with severe forms of UC, not only that; even their role in treatment of moderately severe form of the disease has been doubted by relatively recent reports[82]. However, because of tolerability and safety they are still tried before shifting to corticosteroids[83,84]. In such patients corticosteroids remain to be the drugs of choice for induction of remission. However, a lot of debate is still going on regarding their optimal dosage, rout of administration and duration of treatment. This is mainly because of the serious side effects of these drugs. Moreover, it had been reported that only 30% of patients who had clinical remission to these drugs, show as well endoscopic remission and most of the patients will become either steroid dependent or need surgical intervention[85]. For these reasons clinicians started using corticosteroid sparing drug although the data supporting this practice are scanty[86].

**Maintenance therapy:**

One of the essential goals of management of UC is maintenance of clinical remission indicted by the continuation of absence of abdominal pain, diarrhoea, bleeding, passage of mucopus and rectal urgency and also maintenance of intact mucosa on endoscopy with absences of ulcerations, significant friability, granular appearance and crypt abscesses. Also maintenance therapy aims to prevent relapse of the disease. One of the simple signs of rectal compliance recovery is the ability of the patient to pass flatus without soiling the underwear. These clinical and histopathological remissions were found to be associated with reduced risk of relapse[28,87].

It is crucial to get sure of complete induction of remission before promoting to maintenance therapy. Maintenance therapy has to be individualized.

The aminosalicylates and purine antimetabolites form the classical compounds used worldwide for maintenance of remission[88]. Other drugs are under trials and probably will be soon approved for general use. However, we have to underscore that corticosteroids are not used for maintenance of remission. The extent of the disease and the drug history of the patient in particular his adherence to medication and the side effects during induction and the finance of the patient have to be considered before selecting the drug.

Aminosalicylates compounds are the drugs of choice for maintenance of remission regardless of the way or the drug that had induced the remission apart from when corticosteroids were used for induction of remission where their role remains a quiz. Emerging data indicate that they have a significant chemoprotective role against dysplasia and colorectal cancer[89]. They are always recommended for long term utility except in case of mild attack that responded completely to the initial therapy. The patient has to be aware of the importance of strict adherence to treatment in order to have better life quality and to avoid complications.

Sulfa containing aminosalicylates e .g. sulfasazine , were found to be more efficient than other aminosalicylates compounds like olsalazine or mesalazine in this regard but the side effects-which are occasionally dose related- may be alarming[90].

**Maintenance of remission in distal colitis:**

Topical (suppositories or enemas) aminosalicylates are effective in patients with proctitis and may be used for distal colitis. Every third day dosing was found to maintain remission in around 60% of patients[10].

Patients who are not responding to conventional maintenance therapy need special consideration. Compliance of patient with medication, local infection or co-existing disease like irritable bowel syndrome has to be looked for beside the search for development of colorectal cancer before labeling the condition as refractory to treatment. In such patients high dose of topical aminosalicylates- when the disease is confined to distal colon- in addition to oral aminosalicylates or antimetabolites may give good results in 3-6 months period[87]. If the optimal dose of 5-ASA and immunomodulator failed to maintain remission, then infliximab or colectomy has to be highly considered.

**Management of mild-moderate extensive colitis:**

Oral aminosalicylates in addition to topical ones form the main stay of induction of remission in this group of patients where the response is dose related. A round 80% of patients show good response to high doses of oral aminosalicylates[91]. Oral corticosteroids with / without topical therapy are reserved for refractory conditions, and for patients who demand rapid improvement. There is no consensus on the initiation dose or when and how to taper corticosteroids. However, doses between 20and 60mg of prednisolone were found to be effective. Higher doses will be overshadowed by the systemic side effects. Bone mass density measurement is mandatory in patients who are on long term corticosteroids in order to early detect and treat osteoporosis. Failure to respond to this remedy may necessitate the use of oral immune-modulators [9] Surgery will remain a choice for those who did not respond to these measures[87].

**Maintenance of remission in mild-moderate extensive colitis:**

Oral aminosalicylates are again the drugs of choice for maintenance of remission. When the patient did not respond to corticosteroids or require large dose for induction that is difficult to taper or was dependent on them for maintenance of remission; he will be considered to have chronic UC and such patients may require antimetabolitis as part of their maintenance treatment[92].

If the patient had two flare-ups in one year then failure of maintenance of therapy will be declared and immunomodulotory therapy or probiotics has to be added. Patients who required cyclosporine or azathiprine for induction of remission were found to perform well when put on antimetabolites as maintenance therapy[87]. Although patients who are smokers were noted to be less likely to develop UC, studies have failed to demonstrate significant beneficial role for nicotine in maintenance of remission[93]. Azathioprine or 6-mercaptopurine may be used as corticosteroid sparing in refractory cases or can be continued as maintenance regimens if they were used to induce remission[9].

**Management of sever colitis:**

Hospital admission and resuscitation are fundamental steps in these patients. Maximal dose of oral aminosalicylates, oral or intravenous steroids are usually tried to induce remission.

Failure of clear response in 7-10 days is an indication for parentral immunomodulator including azathioprin and cyclosporine, or infliximab[94] or colectomy as the disease will be considered as refractory to conventional therapy. A bout 40% of patients will have this fate so close observation and collaboration with expert surgeons is vital[95]. There are no data to support the benefit of continuous corticosteroids infusion over pulse therapy in such cases[9]. One well designed study showed an excellent response in 82% of corticosteroids- refractory patients to intravenous cyclosporine[33]. Addition of azathioprine or 6-MP to cyclosporine has augmented the response[96]. In order to avoid surgery, patient with fulminant UC may need to have similar chance of cyclosporine therapy. Changing the position may help to evacuate air and decompress the bowel in these patients. Because of the risk of co-existing infection, it is common practice to prescribe parentertal broad spectrum

antibiotics to these patients despite the lack of convincing supportive data. This also holds true for total parenteral nutrition[97-99]. After induction of remission in such patients they will be subjected to maintenance therapy regimens similar o that used moderate extensive colitis.

Surgery is invariably indicated in cases of massive or continuous hemorrhage, perforation and if there is cancer. Patients with severe refractory colitis with or without toxic megacolon, and those with disabling symptom even in less severe conditions may also be candidates for surgery[9].

**Colectomy:**

Colectomy may be the ultimate fate in 9% of patients within the first five years of diagnosis of UC. This figure will increase to 35% in patients with pancolitis mainly because of failure of medical therapy[100].

Creation of ileoanal pouch following colectomy has greatly popularized surgery, as it has ameliorated the inconvenience of ileostomy/ colostomy. However, pouchitis developing in 50%, pouch failure in 10%, reduction of female fertility by 80% and nocturnal fecal incontinence in 24% of patients are a major concern and challenge to treating team[101-104].

**Surveillance for Colonic Carcinoma in UC:**

Colorectal cancer (CRC) is a well recognized complication of UC. One of the goals of management of UC is to avoid or treat CRC if it developed in these patients. The risk increases with the duration and extent of the disease. It is curable when detected early and this highlights the importance of early detection. Therefore screening of CRC is of utmost importance to achieve this goal. Several methods do exist for screening including fecal occult blood tests and radiological screening with barium enema or CT colonography. Sigmoidoscopy and or colonoscopy although semi-invasive are of particular importance as they allow for tissue diagnosis of suspected lesions[105]. Only 57.3% of the patients with UC had screening for CRC indicating underutilization of these screening methods. Patients' awareness, availability, possible complications and cost of these tests markedly influence the rate of screening[106]. The initial reports of increased risk of lymphoma in patients with UC were contrasted with recent researches. This had strongly pointed to the medications used in management of UC as the most likely suspect [107].

**Relapses:**

Relapses of the disease are common. Exclusion of other causes of bloody diarrhea has to be made before diagnosing relapse. Pathogens are present in a high percentage [50%] of patients with UC who had relapse of the disease. Investigating stool by culture is therefore important to avoid unnecessary delay in managing these patients[72].

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