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Review Article

Management of ulcerative colitis: a clinical update



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ABSTRACT

The objective of this study was to evaluate the consensus of expert societies and published guidelines on the management of ulcerative colitis, and to compare with the experience of the authors, in order to standardize procedures that would help the reasoning and decision-making process of the physician. A search was performed in scientific literature, specifically in electronic databases: Medline/Pubmed, SciELO, EMBASE and Cochrane, and the following descriptors were used: ulcerative colitis, acute colitis, clinical treatment, surgery and randomized trial. It can be concluded that the goals of therapy in ulcerative colitis are clinical and endoscopic remission, deep, sustained remission without corticosteroids, prevention of hospitalizations and surgeries, and improved quality of life. The surgical indications are reserved for selected cases, ranging from medical intractability, complications (severe refractory acute colitis, toxic megacolon, perforation and hemorrhage) and malignancy. Information in this review article must be submitted to evaluation and criticism of the specialist responsible for the conduct to be followed, in the face of his/her reality and the clinical status of each patient.

The degree of recommendation and strength of evidence were based using the GRADE system (The Grades of Recommendation, Assessment, Development, and Evaluation) described below:

1. A: Experimental or observational studies of higher consistency.
2. B: Experimental or observational studies of lower consistency.
3. C: Case reports (non-controlled studies).
4. D: Opinion without critical evaluation, based on consensus, physiological studies or animal models.

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Tratamento da retocolite ulcerativa: atualização clínica

R E S U M O

Palavras-chave:

Colite ulcerativa
Colite aguda
Tratamento clínico
Cirurgia
Complicações

O objetivo deste trabalho foi avaliar os consensos de sociedades de especialistas e guidelines publicados sobre o manejo da retocolite ulcerativa, e confrontar com a experiência dos autores, a fim de padronizar condutas que auxiliem o raciocínio e a tomada de decisão do médico. Foi realizada busca na literatura científica, mais precisamente nas bases de dados eletrônicas: Medline/Pubmed, SciELO, EMBASE e Cochrane, tendo sido utilizado os descritores: ulcerative colitis, acute colitis, clinical treatment, surgery e randomized trial. Pode-se concluir que os objetivos da terapia na retocolite ulcerativa são: remissão clínica e endoscópica, a remissão profunda sustentada sem corticosteróides, evitar hospitalizações e cirurgias, e melhora na qualidade de vida. As indicações cirúrgicas ficam reservadas para casos selecionados que variam de intratabilidade clínica, complicações (Colite aguda grave refratária, megacólon tóxico, perfuração e hemorragia) e malignização. As informações contidas neste artigo de revisão devem ser submetidas à avaliação e à crítica do médico especialista, responsável pela conduta a ser seguida, frente à sua realidade e ao estado clínico de cada paciente.

O grau de recomendação e força de evidência foram baseados usando o GRADE system (The Grades of Recommendation, Assessment, Development, and Evaluation), descrito abaixo:

A: Estudos experimentais ou observacionais de melhor consistência.

B: Estudos experimentais ou observacionais de menor consistência.

C: Relatos de casos (estudos não controlados).

D: Opinião desprovida de avaliação crítica, baseada em consensos, estudos fisiológicos ou modelos animais.

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Introduction and epidemiology

Nonspecific ulcerative rectocolitis (NURC) is a chronic inflammatory bowel disease (IBD) with a not fully understood etiology that manifests itself preferably in young people and whose main symptoms are a mucous and bloody diarrhea, with or without abdominal pain (A).

Its symptoms depend on the extent and severity of the disease; when limited to the rectum (proctitis), NURC tends to exhibit intense mucorrhea, tenesmus, fecal incontinence and defecation urgency. In severe cases of colitis, other associated symptoms such as vomiting, fever, anorexia, bloating and abdominal distension can emerge.

The disease tends to begin in the rectum and then extends cranially, affecting uniformly and also continuously the proximal segments, presenting a distal gradient.

In recent decades, an exponential increase in IBD has been described worldwide. There is evidence that these diseases have a direct relationship with industrial progress, which would justify its increasing incidence in some countries in recent decades, even in those hitherto classified as of low frequency (B).

There is wide variation between the incidence rates of IBD. In Europe, incidence rates range from 4.1/100,000 (Romania) to 81.5/100,000 (Faroes Islands).¹ With regard to ulcerative colitis, one recent systematic review estimated that the incidence in Europe ranged from 0.4 to 24.3 new cases diagnosed per 100,000 inhabitants (A).² In Asia and the Middle East, on the other hand, the incidence was lower: 0.1–6.3/100,000.² On the

other hand, in North America the incidence of NURC had intermediate rates, ranging from 0 to 19.2/100,000 population.³

As the prevalence of NURC, the most recent data available in the literature are from a population-based study published at the beginning of 2014 that showed a slight increase in Scandinavia (C).⁴ Currently there are about 61,000 patients diagnosed with IBD in Sweden, and most patients are carriers of NURC, with a prevalence of 0.35% (95% CI: 0.34–0.35).⁵ It has also been observed that the prevalence of IBD is higher in countries of the northern hemisphere, that is, those closer to the Arctic.⁶ In Finland the prevalence of NURC was higher in Oulu and Tampere, cities located further north, compared to Helsinki, a city located further south in that Scandinavian country (C).⁷

In Brazil, an epidemiological study conducted by the Botucatu Medical School evaluated the incidence and prevalence of IBD in a micro-region of São Paulo state. During the period from 1986 to 2005, an increase in incidence was observed over this time, but with lower values when incidence rates were compared worldwide, that is, the incidence rate in this region is low, matching Latin America and southern Europe countries (C).⁸ It is noteworthy that its incidence has an inverse relation with smoking.

Signs and symptoms

NURC usually affects young patients in the second to the fourth decade of life, regardless of gender. The inflammatory process is restricted to colorectal mucosa and submucosa and can manifest itself from a mild form to a severe colitis with

Frequency of bowel movements 0 = Normal for the patient 1 = 1-2 stools/day in addition to the usual 2 = 3-4 stools/day in addition to the usual 3 = >5 stools/day beyond the usual	Rectal Bleeding 0 = No blood 1 = Blood streaks in less than half of evacuations 2 = Evidence of fresh blood in most of the evacuations 3 = Bowel movements with fresh blood
Endoscopic findings 0 = Normal mucosa or inactive disease 1 = Mild disease (enantherma, loss of vascular pattern, mild friability) 2 = Moderate disease (obvious enantherma, loss of vascular pattern, friability, erosions) 3 = Severe disease (spontaneous bleeding, ulceration)	
Global Medical Assessment^a 0 = Normal 1 = Mild disease 2 = Moderate disease 3 = Severe disease	
Scores (Points) ≤ 2 and no subscore >1 3-5 6-10 11-12	Disease severity Clinical remission Mild activity Moderate activity Severe activity

^aThe global medical evaluation takes into account the daily complaint of the patient with regard to abdominal discomfort, pain, a feeling of well-being (normal, above or below the average), physical examination findings and the patient's performance of daily activities.

Fig. 1 – Mayo Clinic Score: severity index of ulcerative colitis.

systemic involvement. The disease can be limited to the rectum (proctitis); can involve the left semicolon (left colitis) or often extends throughout the colon (pancolitis).

Thus, the signs and symptoms vary according to the extent and intensity of the inflammatory process, although there is not always proportionality between the extent of disease and severity of symptoms (A).

The clinical picture consists of episodes of diarrhea of moderate to severe intensity, most often accompanied by fresh blood and/or mucus, usually preceded by abdominal cramps, and with relief after defecation. This increase in bowel rhythm can occur during the day or at night. Other symptoms may be present, such as anorexia, fever, asthenia, defecation urgency, flatulence, and tenesmus; the severity of diarrhea tends to correlate with the extent and severity of colonic inflammation (A).

The abdominal pain varies according to the intensity of inflammation, being generally of mild to moderate type, but may become severe in complications such as fulminant colitis and toxic megacolon.

Extra-intestinal conditions may be present, such as joint, dermatological, ophthalmologic, hepatobiliary and hematologic manifestations that may precede or appear after the intestinal event.

Classification of severity

The disease can be classified according to the clinical picture, in association with laboratory and endoscopic parameters. In the 1960s, a study published by University of Oxford (UK) investigators, produced the Truelove-Witts classification (1955).⁹ However, the English classification did not include critical parameters to assess the severity of the disease, as

well as endoscopic findings and the general condition of the patient. In 1987, the Mayo Clinic group in Rochester, Minnesota (USA),¹⁰ published a classification that has become the most widely used in the literature, both in clinical practice and in most of the trials involving patients with NURC (Fig. 1). The disease can be classified as mild, moderate or severe, and 2/3 of patients exhibit a mild-to-moderate picture (A).¹⁰ The treatment is based on the intensity and extent of the inflammatory process.

Diagnosis

There is no single test that can be considered the “gold standard” for the diagnosis of NURC. The diagnosis of this condition is based on data from the clinical history and physical examination, together with laboratory tests and radiological, endoscopic and histological studies. The main tests are colonoscopy, pathology, serum and fecal biochemical tests and radiological studies (D).¹¹

Colonoscopy

Unlike Crohn's disease, NURC is characterized by a diffuse mucosal and submucosal inflammation limited to the colon and rectum. A few patients may experience an inflammation of 5–10 cm from terminal ileum that was referred to as reflux ileitis or “backwash ileitis”; there is controversy as to whether this finding is related or not with disease severity.

Colonoscopy with biopsy of the mucosa is the test of choice, since it can establish the diagnosis and assess the extent and severity of the disease, and also allows the collection of material for histological analysis and cultures. In patients

with active NURC, one can observe a continuous and diffuse inflammatory process with edema, congestion, friability and granularity of the mucosa, and microulcerations that may or may not be covered by fibrin. In 95% of the time, the rectum is compromised by the inflammatory process; on the other hand, rarely the terminal ileum will be affected (5%). Another frequent endoscopic finding is the inflammation gradient, in which a more intense involvement in the rectum and a milder involvement in proximal segments are observed.

In addition, the histological evaluation is critical to the diagnosis of this disease, in staging procedures the degree of inflammation, in the follow-up after the beginning of treatment, and even to exclude dysplasia and cancer associated to NURC (B).^{11,12}

It is of the utmost importance a good integration between the surgeon, endoscopist and pathologist to improve diagnostic accuracy (A).¹¹

Complementary tests

Some tests may help in assessing the severity of inflammation. Serum levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are useful tests in the evaluation of the inflammatory process, but these are not specific and must be analyzed in conjunction with other clinical, endoscopic, radiological and histopathological data (B).^{11–13}

Some serological markers as pANCA and ASCA, although not specific, can predict years ahead (in case of a positive result) if the patient will develop inflammatory bowel disease; these markers are also valuable in differentiating colitis and Crohn's disease. There is also evidence that pANCA-positive NURC patients are at a higher risk of being colectomized, which may reflect greater disease severity (B).^{11–13}

Fecal calprotectin is a newly added test to the clinical armamentarium; this is a very sensitive test for the diagnosis of bowel inflammation, although with little specificity. Fecal calprotectin reflects the presence of inflammation, and there is a direct correlation of their levels with the severity and of the extent the inflammatory process.

Thus, this test is very useful in monitoring the response to treatment, as well as in the diagnosis of relapses. Negative levels should not be interpreted as a lack of bowel organic pathology, but as the absence of an inflammation caused by neutrophils (B).^{13,14}

In patients treated with biological agents and benefited with good clinical and endoscopic response, a sharp drop in fecal calprotectin level is observed, which shows good correlation with the mucosal healing process.^{11,14} It can be concluded that the clinical disease activity index, in association with serum and fecal markers, increases the accuracy in determining and predicting the acutization stage of the disease and to monitor the response to treatment.^{11,12}

Treatment

The treatment of ulcerative colitis is based on severity, activity, location and extent of the disease. Considering that in general NURC involves more distal segments of the large bowel (rectum and sigmoid), this disease can be classified, according to its location, into 3 groups (Montreal Classification, Table 1).

Table 1 – Classification of Montreal (2006) – according to URC location.

Ulcerative rectocolitis – URC	Classification of Montreal
E 1 – Proctitis	Limited to rectum (30%)
E 2 – Left Sided Colitis	Affects the rectum and left colon (distal to the splenic flexure) (40%)
E 3 – Pancolitis	Affects the rectum and colon proximal to the splenic angle (30%)

As to the severity of the disease, it can be considered mild, moderate or severe, based on the aforementioned criteria. It is noteworthy that the vast majority of patients experience mild-to-moderate illness (85%) and the rest presents with the severe form (15%).^{15–17}

The main goals of NURC management are clinical remission of active disease, remission maintenance without corticosteroids, prevention of complications, and improvement of the quality of life. However, since the advent of the management with biological agents (and in line with the management of Crohn's disease), the healing process of the inflamed intestinal mucosa must be an objective to be pursued, since there is evidence that an effective control of inflammation is associated with a decrease in rates of recurrence of the disease, reducing the need for hospitalization and even in the number of colectomy indications (B).¹⁷

Table 2 lists the main drugs, routes of administration, and dosages.

The treatment of NURC is based on the extent and activity of the disease.^{17,18}

Proctitis

The first-line therapy for active colitis limited to the rectum (proctitis) is topical mesalazine (A).⁹ A systematic review from of 38 clinical trials from Cochrane database on proctitis and left colitis management confirmed the superiority of this therapy *versus* placebo for the induction of clinical remission, besides endoscopic and histological improvement. In a head-to-head comparison, topical mesalazine, is also better than oral mesalazine, being more effective than topical corticosteroids to achieve clinical, endoscopic and histological remission (A).^{19,20}

Mesalazine 1g/day in suppository is the initial treatment for mild or moderate proctitis; one alternative is the use of mesalazine enema (A).^{19,20} In this sense, the suppository is better tolerated, its application is easier and shows the better rectal distribution of the drug, with no difference in the application in a single *versus* divided dose.

The combined use of oral and topical mesalazine, or with a topical steroid, may be tried in those cases with no initial improvement; this is the second treatment option (A).^{18–20} In the staggered therapeutic sequence, if the aforementioned therapies were unsuccessful, the physician can suggest the use of immunosuppressants and/or biological therapy.^{17,18}

Table 2 – Main drugs used to treat ulcerative colitis.

Drug	Commercial brand	Presentation	Initial dose	Maintenance dose
Mesalazine	Pentasa	Tablets 500 mg Sachets de 1 g and 2 g	3 g–4 g	1 g–2 g
Mesalazine	Pentasa	Suppository	1 g	500 mg
Mesalazine	Pentasa	Enema 1 g	1 g	1 g
Mesalazine	Mesacol	Tablets 400 and 800 mg	2.4–4 g	1.6–2.4 g
Mesalazine	Mesacol	Suppository 500 mg	1 g	500 mg
Mesalazine	Mesacol MMX	Tablets 1.2 g	3.6–4.8 g	1.2–2.4 g
Sulfasalazine	Azulfin	Tablets 500 mg	4–5 g	2 g
Sulfasalazine	Azulfin	Suppository	1 g	500 mg
Azathioprine	Imuran	Tablets 50 mg	2–2.5 mg/kg	2–2.5 mg/kg
Infliximab	Remicade	Ampoules 100 mg	5 mg/kg weight at weeks 0, 2 and 6	5 mg/kg every 8 weeks
Adalimumab	Humira	Prefilled syringe 40 mg	160 mg SC at weeks 0 and 80 mg at week 2	40 mg SC every 2 weeks

Left Sided Colitis

The treatment of choice in cases of mild-to-moderate left sided colitis is a combination of oral and topical mesalazine; there is evidence that the concentration levels of 5-ASA in the rectal mucosa are greater in the combined therapy *versus* monotherapy with this agent (A).^{19,20}

This combined effect is more significant when the disease extends by at least 50 cm above the anal margin, that is, a proctosigmoiditis.^{12,13} A recent meta-analysis showed that mesalazine is superior to placebo in inducing and maintaining clinical remission in patients with NURC (number needed to treat [NNT]=6). Doses of mesalazine over 2 g/day were more effective than doses < 2 g/day in the prevention of clinical recurrence.¹⁹

Furthermore, the ASCEND II study demonstrated that mesalazine 4.8 g/day produced better scarring process/clinical response rate *versus* 2.4 g/day.²¹ As to enemas, the recommended dose is 1 g/day, with no difference between large- or low-volume enemas, the latter being better tolerated by patients (A).^{13,22} Although there is controversy among some meta-analyze, the use of rectal corticosteroids (enema) seems to be equivalent to the topical use of 5-ASA.^{22,23} Adherence to treatment with salicylates is a serious problem that can impact about 40–60% of patients. There is evidence that low adherence to treatment regime is related to a dosing regime higher or equal to 3 daily doses (A).^{13,20}

With the new formulations of mesalazine (mesalazine in sachet, or MMX®), patients can take a higher dose, and the result is a smaller number of daily doses, thus improving adherence to treatment.

The MOTUS study compared the use of mesalazine (sachet) 4 g taken in two doses of 2 g every 12 h *versus* a single dose of 4 g per day. Clinical remission at 8 weeks for patients treated with a single dose of mesalazine was 52.1% compared to 41.8% in those treated with two daily doses ($p=0.14$). The rates of mucosal healing and the improvement in symptom scores (UC-DAI) were statistically better *versus* in those patients treated with 2 doses/day²⁴ (B).

In cases not benefited with a good clinical response with the use of salicylic derivatives after 14–21 days of treatment, or in cases of disease exacerbation, corticosteroids can be added.

Prednisone is the corticosteroid most often used, with a suggested dose of 0.75–1 mg/kg/day, with a maximum dose of 60 mg/day. Prednisone is a synthetic glucocorticoid of intermediate power, being converted in the liver into prednisolone, the active form. The average daily dose is 40 mg/day for 1–2 weeks or until the occurrence of clinical remission; at this point, the corticosteroid must be reduced (10 mg/week, until 5 mg/kg/day), when the drug will be gradually reduced (5 mg each week) until its complete discontinuation.²³

If, during the corticosteroid weaning process, the disease relapses, the dose should be increased to the penultimate dose preceding that in which the relapse occurred; afterwards, the gradual discontinuation of procedure will be carried on. The salicylic derivatives should be maintained for long periods, in order to minimize the chance of relapse. In case of steroid dependence (inability to reduce the dose of 20 mg/day without the occurrence of relapse) or in cases of refractoriness to corticosteroids (no response to treatment with prednisone 60 mg/day after 4–6 weeks of therapy) the physician should suggest the use of immunomodulators (azathioprine, 6-mercaptopurine) (A).²⁴

Azathioprine at a dose of 2–2.5 mg/kg/day is the main immunomodulator or immunosuppressant used in clinical practice. Azathioprine is a synthetic analog of purine and was developed in the final years of the 1950s. This is a pro-drug of 6-mercaptopurine and acts by inhibiting DNA synthesis in proliferating cells, for instance, B and T lymphocytes.^{25,26}

The side effects of immunomodulation agents (azathioprine and 6-mercaptopurine) occur in around 12–15% of cases, and may be of allergic (fever, skin rash, nausea, vomiting, abdominal pain, diarrhea, hepatitis, or pancreatitis) or non-allergic (bone marrow depression, infections and neoplasia) origin. The most severe side effect is bone marrow aplasia, especially in those patients with deficiency of the enzyme thiopurine S-methyltransferase (TPMT). The full effect of the drug occurs 12–16 days after the beginning of treatment, considering its delayed action. The drug should not be used in inducing clinical remission, but in a therapy of maintenance.

A meta-analysis of the Cochrane Foundation revealed that the use of azathioprine is effective in maintaining remission in patients with NURC whose treatment with salicylates failed, or requiring several treatments with steroids to obtain the induction of remission. The long-term use of corticosteroids

must be avoided, as well as its frequent reintroductions. However, the study concluded that there is little evidence that the use of azathioprine, as a maintenance drug, is superior to salicylates (A).²⁵

Other immunomodulatory drugs such as 6-mercaptopurine (1–1.5 mg/kg/day) and methotrexate (15–25 mg/week) can also be used in refractory cases. A meta-analysis published recently showed that about 2/3 of patients refractory to azathioprine may benefit from the use of 6-mercaptopurine in maintaining remission in patients with NURC (B).²⁶

Pancolitis or extensive colitis

Mild-to-moderate cases of pancolitis should be treated similarly to the treatment given to patients with left colitis, that is, with oral mesalazine 4–4.8 g/day associated with mesalazine enema 1 g/day (A).^{13,17,22}

Likewise, if the symptoms persist after 14–21 days of treatment or if a sustained relief of symptoms has not been achieved after 30–40 days of treatment with mesalazine, one can introduce an induction therapy with oral corticosteroids (prednisone) at an average dose of 40 mg/day (0.75–1 mg/kg/day – not exceeding 60 mg/day). The maintenance treatment is carried out with mesalazine 2–2.4 g/day (A).^{23,24}

Patients with proctitis, left colitis or mild-to-moderate pancolitis refractory to conventional therapy with salicylates and immunomodulators should be treated with biological agents combined with azathioprine, or as monotherapy (B).^{13,25,27,28}

Proctitis, left colitis or moderate-to-severe pancolitis refractory to conventional treatment

Infliximab is a chimeric monoclonal antibody anti-TNF (tumor necrosis factor), being indicated for patients with NURC refractory to conventional therapy. (B) Two randomized, placebo-controlled studies published in 2005, ACT 1 and ACT 2, showed that the use of infliximab at a dose of 5 mg/kg was superior to placebo in the treatment of patients with moderate-to-severe ulcerative colitis refractory to conventional therapy with salicylates and azathioprine.^{28,29}

Patients treated with infliximab had a better clinical response and improved clinical remission and mucosal healing *versus* patients treated with placebo. Infliximab should be used intravenously at a dose of 5 mg/kg body weight, with an induction dose at week 0, another dose 2 weeks after the first, and a third dose 6 weeks after the initial dose (Induction therapy: weeks 0, 2 and 6). Maintenance therapy must be performed with infusions every 8 weeks at a dose of 5 mg/kg.^{28,29}

Currently, there is evidence that the use of infliximab in combination with azathioprine is superior to monotherapy with infliximab or with azathioprine in patients with moderate-to-severe NURC refractory to salicylates, corticosteroids, and immunomodulators.³⁰

The SUCESS study revealed that patients treated with infliximab combined with azathioprine had a better clinical response, clinical remission and a mucosal healing process, when compared with those who received monotherapy (B).³⁰

Recently, at the end of 2014, ANVISA approved the use of adalimumab, another anti-TNF agent, indicated for the treatment of moderate-to-severe NURC refractory to conventional therapy. Adalimumab is a fully human monoclonal antibody which binds effectively to soluble and transmembrane TNF. The pivotal studies ULTRA (Ulcerative Colitis Long-Term Remission and Maintenance with Adalimumab) 1 and 2 evaluated patients with NURC refractory to conventional therapy treated with adalimumab and compared them with those treated with placebo. As observed in studies with infliximab, NURC patients refractory to conventional therapy and treated with adalimumab had a better clinical response and improved clinical remission, besides a better mucosal healing *versus* those treated with placebo. Adalimumab should be used subcutaneously at a loading dose of 160 mg given at week 0, with 80 mg administered at week 2. The maintenance dose is 40 mg SC administered every 2 weeks.^{23,31,32}

We conclude that there is strong scientific evidence regarding the effectiveness of anti-TNF agents (infliximab and adalimumab) in the management of moderate-to-severe NURC refractory to conventional treatment. Recent meta-analysis with over 2200 patients enrolled in randomized trials showed that, in patients treated with infliximab or adalimumab, a lower number of hospitalizations and fewer complications occurred. Those who were treated with infliximab also were less likely to be colectomized. Furthermore, the use of anti-TNF agents in patients with NURC was not associated with an increased risk of serious adverse effects (A).³³

Severe acute colitis of any extent

Severe acute ulcerative colitis is a potentially fatal condition that has been described by Truelove & Witts in 1954, who used the following criteria for its definition: bloody diarrhea (> episodes/day), anal bleeding, fever (>37.8°C), tachycardia (HR >90 bpm), anemia (Hb <10.5 g/dL) and increased erythrocyte sedimentation rate (ESR >30 mm).⁹ Other clinical parameters must be evaluated at admission: degree of hydration, anemia, and malnutrition. All patients meeting criteria for severe colitis should be hospitalized for treatment in the intensive care unit with a multidisciplinary approach (coloproctologist, gastroenterologist, a nutrition specialist, psychologist, and nurse). Despite the fact that cases of severe acute colitis often are associated with inflammatory bowel disease, this disease can have other causes that should be investigated at admission and, if present, treated: infectious colitis by *Clostridium difficile*, cytomegalovirus, shigella, salmonella, and enterohemorrhagic *E. coli*, among others.

Prevention of thromboembolic disease is mandatory. Where required, patients should receive enteral or parenteral nutritional support, intravenous corticosteroids and broad-spectrum antibiotics.

In acute or fulminant colitis, the drug of choice is hydrocortisone 300–400 mg/day or methylprednisolone 60 mg/day, which may be administered by continuous infusion or divided into 3–4 applications. (B) The patient should be reevaluated 2–3 times a day, and complications such as toxic megacolon, profuse bleeding, and intestinal perforation should

be averted. Toxic megacolon is characterized by an acute dilation of the colon (colon >5.5 cm diameter), in association with signs of toxemia (fever, tachycardia, pain, bloating, confusion, anemia and leukocytosis). In the face of a diagnostic suspicion, one should avoid using narcotics, nonsteroidal anti-inflammatory drugs, and antidiarrheals, which can worsen the clinical picture. Furthermore, barium enema and colonoscopy should also be avoided. The treatment consists of supportive measures, fasting, hydration, intravenous corticosteroids, antibiotics (ciprofloxacin 1–1.5 g/day) and metronidazole 20–30 mg/kg/day and ceftriaxone 2 g/day + metronidazole 20–30 mg/kg/day; and, if needed, a blood transfusion. On the other hand, an acute perforated abdomen is an indication of emergency surgery.

The patient severely affected should be evaluated carefully; and in the absence of clinical and laboratory improvement after 3–4 days of parenteral corticosteroid therapy, a rescue therapy (cyclosporine or infliximab) should be instituted (B).^{34,35} The use of infliximab in this scenario, at a dose of 5 mg/kg of body weight, has been shown to be effective in preventing colectomy both in short- and long-term (B).^{36,37}

Thus, it is critical that all patients with severe IBD (Crohn disease or NURC) or frequent relapses undertake screening tests (PPD-Mantoux reaction and chest Rx), serology for hepatitis, and – in emergency situations – collection of samples for tests in the face of any need for biologic or immunosuppressive therapy. For this purpose, it is important to be with vaccination updated.

If, after 48–72 h, no improvement with salvage therapy was observed and if the patient's condition worsens, or also if a bowel perforation was diagnosed, the surgical option will be mandatory. In emergency situations with peritoneal contamination and in patients who require surgery and who are being treated with prednisone/prednisolone (dose >20 mg/day for over 6 weeks), the surgery must be performed in 2 or 3 surgical times. (B) In a first surgical time, total colectomy with ileostomy and burial of the rectum at the level of (or slightly above) the peritoneal reflection; and in a second time, with the reconstruction of bowel transit.^{38,39}

Conflicts of interest

Dr. Fabio Vieira Teixeira is a speaker of Janssen, Ferring, Nestlé, Abbvie and Hospira.

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