DE GRUYTER OPEN

ARS Medica Tomitana - 2018; 1(24): pag. 9 - 14
doi:10.2478/arsm-2018-0003

INFLAMMATORY BOWEL DISEASES: FOCUS ON THERAPY

Tocia Cristina[1], Achim Anda Carmen[1], Alexandrescu Luana[1], Dumitru Eugen[1]

[1] Faculty of Medicine, University "Ovidius" of Constanța

Cristina Tocia

Tomis Bvd. nr. 211, Bl. TS6b, Sc.C, Et.4, ap. 38,
Constanța, România
email: cristina.tocia@yahoo.com
phone: +40 740508441

ABSTRACT

INTRODUCTION: Medical management of Inflammatory Bowel Diseases is complex and tailored to disease activity. The primary goal is the induction of remission and maintenance of remission with long-term prevention of disease progression. AIM: to describe current drug treatment practices in Inflammatory Bowel Diseases in Dobrogea. MATERIAL AND METHOD: The retrospective and descriptive study included 128 patients: group 1 = Crohn's Disease (79), group 2 = Ulcerative Colitis (46) and group 3 = Unclassified Colitis (3). RESULTS: The phenotypic distribution was: 62% with Crohn's Disease, 36% with Ulcerative Colitis and 3 patients with Unclassified Colitis. CROHN'S DISEASE: According to Montreal Classification, the majority of patients were diagnosed after 40 years (58%); the most frequent involvement was ileo-colonic (47%) and the most frequent phenotype was inflammatory (60%). 40% patients had intestinal complications and 7% had extraintestinal complications. 16.4% required surgical interventions. 67% were treated at some point with aminosalicylates, 44% with immunosuppressive drugs (thiopurines), 80% with corticosteroids for the induction of remission (inaugural flare) and 50% of them received again corticosteroidssteroids in the evolution of the disease, and 29% with biologic therapy. ULCERATIVE COLITIS: Most common location was left colitis in 47% cases. One patient had intestinal complications and no extraintestinal complications were reported in this group. No patients required surgical interventions. 82.5% were treated at some point with aminosalicylates, 37% with immunosuppressive drugs (thiopurines), 17% with corticosteroids and 11% with biologic therapy. UNCLASSIFIED COLITIS: In this group were not reported intestinal and extraintestinal complications and also no patient required surgical interventions. 2 patients were treated at some point with aminosalicylates, all patients were treated with immunomodulators and only one patient was administered biologic therapy. CONCLUSIONS: Particularities of Crohn's Disease in our region are: widespread use of aminosalicylates, overuse of corticosteroids overtime, underprescribed biologic therapy.

Keyword: Inflammatory Bowel Diseases, Crohn's Disease, Ulcerative Colitis, biologic therapy

Introduction

Medical management of Inflammatory Bowel Diseases is complex and personalized depending on the presence of disease extension, severity of the lesions and associated complications. As these diseases evolve with a relapsing and remitting course, treatment is tailored to disease activity. The primary goal in treating IBD is the induction of remission and maintenance of remission with long-term prevention of disease progression.

There are several types of therapies used in the treatment of IBD: 5-ASA, corticosteroids, immunosuppressive drugs (thiopurines) and biologics. In our region we use 5-ASA (mesalamine-oral/enema/suppositories), intravenous hydrocortisone hemisuccinate or oral methylprednisolone, azathioprine and anti-TNF agents like Infliximab and Adalimumab.

Aim

The aim of the paper is to describe current drug treatment practices in IBD in Dobrogea.

Material and method

The retrospective and descriptive study included 128 patients with IBD admitted to Department of Gastroenterology of Constanța County Emergency Clinical Hospital „Sf. Apostol Andrei" and in outpatient clinic between 2014-2016. Information was collected from the medical software digital database for inpatients and outpatients. Characteristics of patients were introduced in a standard worksheet that included the following entries: name, age, sex, type of IBD: Crohn's Disease, Ulcerative Colitis, Unclassified Colitis, Montreal Classification for CD and extent of lesions for UC and Unclassified Colitis, if they had intestinal/extraintestinal complications, surgical interventions or not, and types of treatment.

Inclusion criteria: IBD (old and new cases) and age > 16 years.

Exclusion criteria: IBS and other types of colitis (infectious colitis, microscopic colitis, ischemic colitis, radiation colitis).

The study included 3 groups of patients: group 1 = CD (79 patients), group 2 = UC (46 patients) and group 3 = Unclassified C (3 patients).

Data analysis with Microsoft Excel Analysis ToolPack was performed and descriptive statistics (mean value and standard deviation) were calculated.

Results

The phenotypic distribution was: 79 patients (62%) with CD, 46 (36%) with UC and 3 patients with Unclassified Colitis (Figure 1).

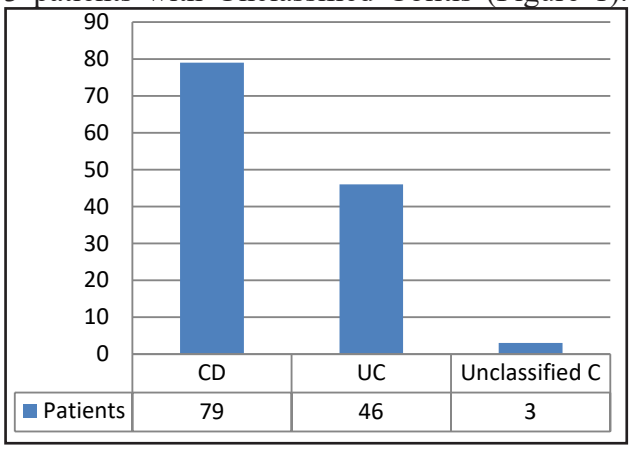

Figure 1. Phenotypic distribution of IBD

CROHN'S DISEASE

Montreal Classification

46 (58%) patients aged over 40 years were diagnosed (A3), followed by 32 (40.5%) aged between 17 and 40 years (A2) and only one patient of 16 years old (A1) (Figure 2).

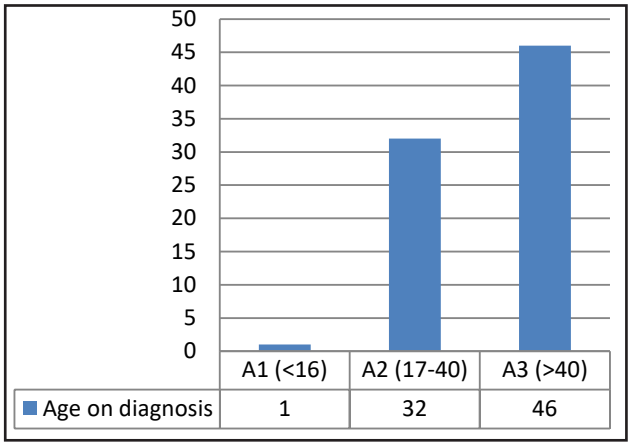

Figure 2. Age distribution on diagnosis

Regarding the location of the lesions, 37 (47%) patients had ileo-colonic involvement L3, 23 (29%) - ileal involvement L1 and 19 (24%) - colonic involvement L2 (Figure 3).

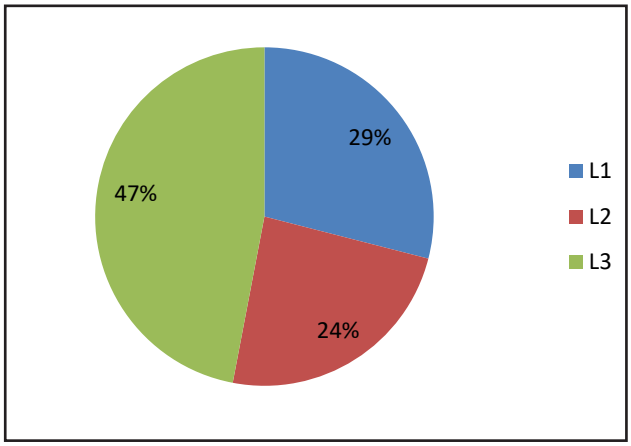

Figure 3. Disease location

The most frequent phenotype was inflammatory B1 in 48 patients (60%), followed by stenotic B2 in 21 (26%) patients and penetrant B3 in 10 (14%) patients (Figure 4).

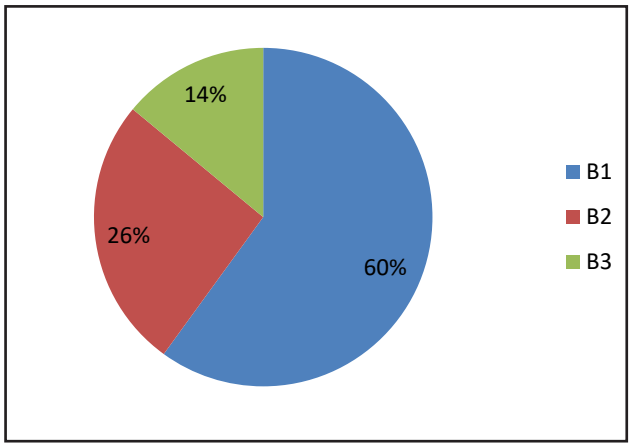

Figure 4. Disease behaviour

Complications

32 (40%) patients had intestinal complications and 9 (7%) patients had extraintestinal complications (Figure 5).

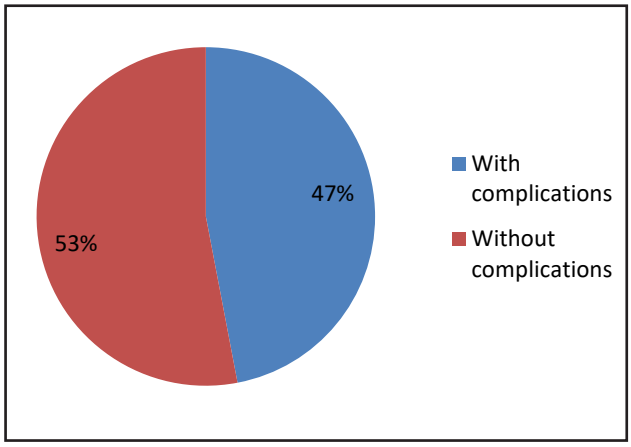

Figure 5. Distribution of complications

Surgery

13 (16.4%) patients required surgical interventions.

Types of treatment

The treatments administered to patients overtime, anytime in the course of their disease, were analyzed: 53 (67%) patients were treated at some point with aminosalicylates, 38 (44%) with immunosuppressives, 63 (80%) with steroids for the induction of remission (inaugural flare) and 40 (50%) of them received again steroids in the evolution of the disease, and 23 (29%) - biologic therapy with the predominance of Adalimumab (20 patients) (Figure 6).

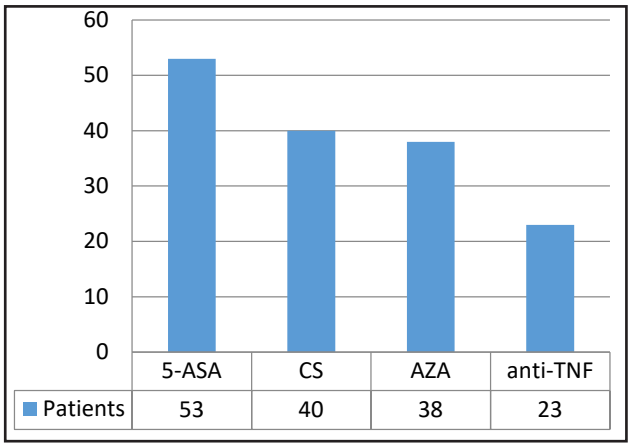

Figure 6. Types of treatment

ULCERATIVE COLITIS

Disease extension

Most common location was left colitis E2 in 22 (47%) patients, followed by proctitis E1 in 18 (40%) patients and extensive colitis E3 in 6 (13%) patients (Figure 7).

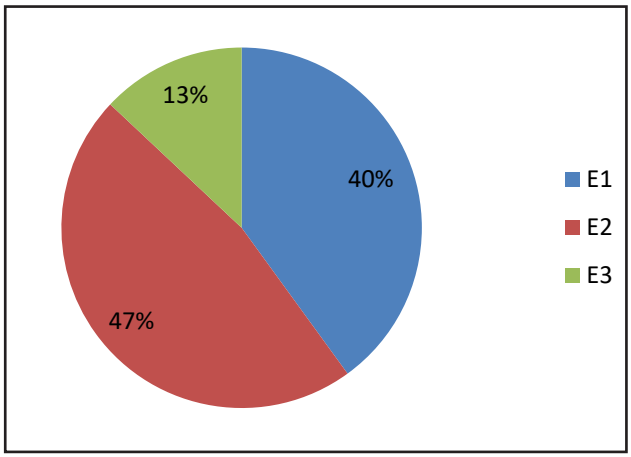

Figure 7. Disease extension

Complications

One patient had intestinal complications (rectovesical fistula) and no extraintestinal complications were reported in this group.

Surgery

No patients required surgical interventions.

Types of treatment

The treatments administered to patients overtime, anytime in the course of their disease, were analyzed: 38 (82.5%) were treated at some point with aminosalicylates, 17 (37%) with thiopurines, 8 (17%) with steroids and 5 (11%) with biologic therapy: 3 patients - with IFX and 2 patients with Adalimumab (Figure 8)

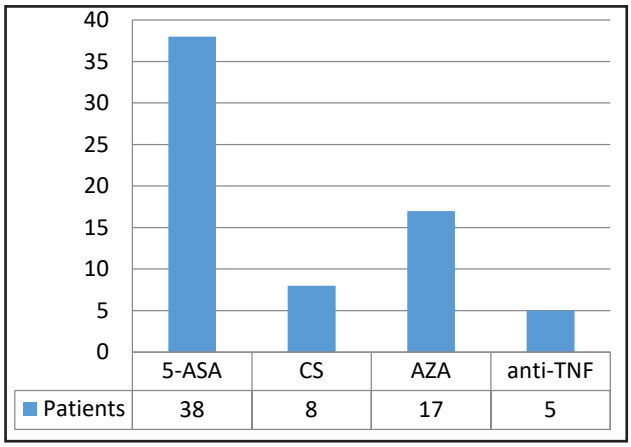

Figure 8. Types of treatment

UNCLASSIFIED COLITIS

In this group were not reported intestinal and extraintestinal complications and also no patient required surgical interventions.

Types of treatment

2 patients were treated at some point with aminosalicylates, all patients were treated with thiopurines and only one patient received biologic therapy (Adalimumab). The patients from this group were not treated with steroids.

Table 1. Types of treatment in IBD

Types of treatment	CD (79 patients)	UC (46 patients)
Aminosalicylates	67%	82.5%
Corticosteroids	50%	17%
Thiopurines	44.5%	37%
Biologic Therapy	29%	11%

Discussions

CROHN'S DISEASE

In our study we observed widespread use of 5-ASA drugs (mesalamine) in CD (67% being a high percentage) despite high-level evidence indicating marginal benefit at best and international guidelines recommending limited indications (even in the colonic disease). ECCO Guidelines don't recommend the use of mesalamine in CD (1). ESCAPE Study also reported the trend of introducing 5-ASA in the treatment of patients, but in a lower percentage (34%) (2). The results of ECCO EpiCom Study in Eastern Europe showed the early introduction of 5-ASA in CD, in the first months after the diagnostic despite the fact that a small number of patients had colonic involvement. The same practice was noted in a recent study conducted in Hungary (3). A possible reason for the use of 5-ASA could be its antineoplastic role sustained by some studies that suggest a lower risk for the development of colon cancer in CD with colonic involvement (4), but current evidence and guidelines don't recommend routine prescribing of these drugs to reduce or prevent the risk of developing neoplasia.

Corticosteroids are best suited for short-term control of symptoms and disease activity. Current evidence suggest that these drugs should not be used as primary therapy for long periods of time because they are not effective in preventing complications or progression of disease. These medications are indicated in moderate and severe disease activity but are not effective for maintenance of remission (1). In our study, 80% were treated with steroids at the inaugural flare for the induction of remission and 50% of them received again steroids for acute flare-ups of disease. 50% is a high and worrying percentage considering the limited indications of these drugs and their side effects and risks, which increase with repeated or long-term use. Analyzing these results, we conclude that the need for repeated courses of steroids indicated that a patient's primary CD medication was insufficient and a change would have been useful (maybe these patients would have had indications for immunosuppressive drugs or biologic therapy).

Almost half of the patients (44.5%) were treated at some point with immunosuppressive drugs - Azathioprine - the thiopurine derivate used in our region. ECCO Guidelines recommend the use of thiopurines for the maintenance of remission (1). Our results are in concordance with our neighbours' from Hungary (3).

ULCERATIVE COLITIS

In this group, 82.5% were treated with aminosalicylates, 37% with immunosuppressive drugs, 17% with corticosteroids and 11% with biologic therapy. Mesalamine is the standard first-line therapy for mild-to-moderate UC. Our results follow the current guidelines

which indicate that 5-ASA is a highly effective treatment for induction and maintenance of remission in UC (5). Similar with other studies (2), main therapy was with 5-ASA (mesalamine) alone or in combination with other medications. 37% were treated with thiopurines (azathioprine) and a small percentage 17% with corticosteroids. We noticed that the need for corticosteroids in UC was reduced and lower than in CD. These results together with the absence of intestinal and extraintestinal complications, perianal disease, surgical interventions and the small number of extensive colitis highlight the benign course of UC in our region.

Biologic therapy for IBD

Nowadays, advances in treatments for IBD have included biological therapies, based mainly on monoclonal antibdodies, such as anti-TNF drugs. These medications show a high index of remission, enabling a significant reduction in cases of surgery and hospitalization. In our study, the need for biological therapy was identified in 28 patients (22.6%) and it was more often prescribed for CD (23 patients). The reason could be that CD had a more severe disease progression in our region: stenotic and penetrating behaviour were present in 40% of the cases and the need for surgery was identified in 16.4% of the patients. Bringing up into discussion the overprescribing corticosteroids in CD, we suggest that biologic therapy is underprescribed in our region because not only stenotic and penetrating behaviour would require this kind of medication, but also a part of the patients with inflammatory phenotype and severe disease that didn't respond to conventional therapy. Only 5 patients with UC were treated with biologics (suggesting once again the benign course of UC in our region).

A study published in 2014 showed that the total number of patients treated with biologics at that time in Romania was 903 (also included here pediatric patients); 253 of them were diagnosed with CD and 650 with UC (6). In contrast with this study, in Dobrogea, biologics are more often prescribed for CD because CD is predominant.

Conclusions

Particularities of CD in our region are: widespread use of aminosalicylates (although many studies showed limited effectiveness in CD even in cases with colonic involvement), overuse of corticosteroids overtime, underprescribed biologic therapy and severe disease progression. This last statement is sustained by the frequent presence of stenotic and penetrating behaviour, complications occurred, surgery needed in this group and the high use of steroids. Also, biological therapy is more frequent used in CD than in UC, but it is suboptimal in CD. We conclude that the need for repeated courses of steroids indicated that a patient's primary CD medication was insufficient and a change would have been useful (maybe these patients would have had indications for immunosupresive or biologic therapy).

Particularities of UC in our region are: the benign course sustained by the low number of extensive colitis, the absence of intestinal, extraintestinal complications and surgery, low use of corticosteroids and biologic therapy, achieving disease control with other medications, mainly with 5-ASA as guidelines recommend.

References

1. Gomollon F, Dignass A, Annese V, Tilg H, Van Assche G, Lindsay JO, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. J Crohns Colitis. 2017;11(1):3-25.
2. Krstic M, Tarabar D, Bojic D, Nagorni A, Hadnadjev L, Dugalic P, et al. P421 Epidemiological study of occurrence, clinical course and treatment options of IBD in Serbia. Results of ESCApe study. Journal of Crohn's and Colitis. 2012;6:S177.
3. Kurti Z, Vegh Z, Golovics PA, Fadgyas-Freyler P, Gecse KB, Gonczi L, et al. Nationwide prevalence and drug treatment practices of inflammatory bowel diseases in Hungary: A population-based study based on the National Health Insurance Fund database. Dig Liver Dis. 2016;48(11):1302-7.

4. Williams C, Panaccione R, Ghosh S, Rioux K. Optimizing clinical use of mesalazine (5-aminosalicylic acid) in inflammatory bowel disease. Therapeutic advances in gastroenterology. 2011;4(4):237-48.
5. Dignass A, Lindsay JO, Sturm A, Windsor A, Colombel J-F, Allez M, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 2: current management. Journal of Crohn's and Colitis. 2012;6(10):991-1030.
6. Rencz F, Pentek M, Bortlik M, Zagorowicz E, Hlavaty T, Sliwczynski A, et al. Biological therapy in inflammatory bowel diseases: access in Central and Eastern Europe. World J Gastroenterol. 2015;21(6):1728-37.