Original Article

Epidemiological profile and clinical characteristics of patients with intestinal inflammatory disease☆

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A B S T R A C T

According to several epidemiological studies, there is a significant increase in cases of inflammatory disease in developing countries.

Objective: To describe epidemiological data and clinical features of patients with inflammatory bowel disease in patients enrolled in Campo Grande, MS.

Method: A retrospective descriptive study with a database analysis of patients who were enrolled and renewed their process in the Exceptional Medications Program of the Health Department from January 2008 to December 2016.

Results: 423 patients participated in the study, 260 women and 163 men. Of these, 238 patients had Crohn's disease and 185 had ulcerative rectocolitis. The patients' mean age was 46 years. The most commonly used medication for both diseases was mesalazine and 34.3% of the patients needed to switch their medication during the treatment, most of them with Crohn's disease. In Crohn's patients, the most affected segment was the colon (40.6%) and in patients with ulcerative rectocolitis the entire large intestine was involved (78.8%) was more common. Of the total number of patients, 10.8% of the women and 18.4% of the men needed to use an anti-TNF.

Conclusion: Most people on treatment for IBD are female, with a mean age of 46 years and suffering from Crohn's disease. The most affected segments were the entire large intestine in URC cases and the colon in Crohn's disease cases. Mesalazine was the most used drug in both diseases. There was more drug replacement in Crohn's disease patients. In Crohn's disease, younger patients used infliximab more frequently.

Perfil epidemiológico e características clínicas dos pacientes com doença inflamatória intestinal

R E S U M O

De acordo com vários estudos epidemiológicos, há aumento significativo de casos de doença inflamatória nos países em desenvolvimento.

Objetivo: Descrever os dados epidemiológicos e características clinicas dos pacientes com doença inflamatória intestinal em Campo Grande - MS.

Método: Pesquisa descritiva retrospectiva, com análise dos prontuários em banco de dados, em pacientes que cadastraram e renovaram o processo no Programa de Medicamentos Excepcionais da Secretaria de Saúde, de janeiro de 2008 e dezembro de 2016.

Resultados: Participaram da pesquisa 423 pacientes, 260 mulheres e 163 homens. Deste total, 238 possuíam doença de Crohn e 185 Retocolite Ulcerativa. A média de idade foi de 46 anos. O medicamento mais utilizado em ambas doenças foi a mesalazina e 34,3% dos pacientes necessitaram realizar troca de medicamentos ao longo do tratamento, sendo a maioria portador da doença de Crohn. Nos pacientes com Crohn o segmento mais acometido foi o cólon (40,6%) e nos pacientes com RCU foi todo o intestino grosso (78,8%). Do total de pacientes, 10,8% das mulheres e 18,4% dos homens necessitaram utilizar anti-TNF.

Conclusão: A maioria das pessoas em tratamento para DII são do sexo feminino, com média de idade de 46 anos e portadores de Doença de Crohn. Os segmentos mais acometidos na RCU foi todo o intestino grosso e na Doença de Crohn o colo. A mesalazina foi o medicamento mais utilizado em ambas as doenças. Houve mais troca de medicamentos na Doença de Crohn. Na Doença de Crohn pessoas mais jovens utilizaram mais o infliximabe.

Introduction

Inflammatory bowel disease (IBD) represents a group of idiopathic chronic inflammatory bowel disorders. This nomenclature encompasses two main nosological categories: Crohn's disease (CD) and ulcerative rectocolitis (URC), which are characterized by an overlapping of clinicopathological manifestations and by other clearly different features.[1]

IBDs occur throughout the world and represent a serious health problem since these disorders affect preferentially young people, lead to frequent recurrences and take up clinical forms of high severity.[2]

It is believed that the etiopathogenesis of the disease, although not well understood, is related to the abnormal immune response to the bacterial microbiota of the intestinal lumen, which would be associated with changes of the mucosal barrier function. There are genetic, socioenvironmental, microbiological and immunological factors that would also be involved as risk factors, and of the onset and maintenance of the disease.[3]

According to the literature, with regard to the epidemiology, one observes a prevalence of IBD in white people, who are between 20 and 40 years, with a second peak of the disease starting at age 55, and with a similar distribution in both genders, except for CD, in which women are more often affected.[4]

Brazil is still considered an area of low IBD prevalence, despite a significant increase in the registries of these diseases in the Brazilian literature. In the last 20 years, CD has generally exceeded URC in incidence rates. In developing countries where IBDs are emerging, URC is more common than CD.[5]

In our working context, we noticed that there has been a great increase in the demand for medical care of people with IBD, and the epidemiological and morbidity data in the literature are insufficient to evaluate the profile of these patients.

The knowledge of this epidemiological profile can provide a broader basis and more elements in order to elucidate the natural history of the disease, its main complications and therapeutic failures, which would help in the clinical and therapeutic management of the patients.

Objective

The general objective of the present study was to describe the epidemiological data and clinical characteristics of patients with inflammatory bowel disease.

Method

A cross-sectional and retrospective study was conducted through a descriptive research, with an analysis of the medical records entered in a database, performed in patients with IBD who were registered and who renewed their processes in the Program of Exceptional Medications of the Department of Health in the period from January 2008 to December 2016, that is, the period in which the medical records of the available data began.

This study was submitted to the approval of the Ethics and Research Committee of HRMS Regional Hospital and of Plataforma Brasil. The costs of this non-profit research were fully funded by the researcher.

The patients studied came from public and private health systems, residents of the city of Campo Grande in the state of Mato Grosso do Sul and suffering from CD or URC. The data studied were obtained from medical records duly registered in the Health Center linked to SESAU, and the diagnoses of the diseases were confirmed by laboratory and imaging studies, as well as by medical consultations, a necessary condition for dispensing higher-cost drugs. Patients who had inactive processes, who were transferred to another city, with their treatment discontinued, and diagnosed with an undetermined colitis, were excluded from the sample.

The pharmacological agents used for the treatment of inflammatory bowel diseases that are funded by the state are corticoids, salicylates, antibiotics, immunosuppressants, and anti-tumor necrosis factor (anti-TNF) antibody.

The variables studied were: age, gender, body mass index (BMI), diagnosis and localization of the disease, colonoscopy report, the therapy used and doses available, and also if the medication was changed.

Data were collected by the CEAF program – Specialized Component of Pharmaceutical Assistance of the Ministry of Health, based on the number of CNS of each patient registered; after that, these data were entered and accounted in tables from the Microsoft Excel program, with statistical analysis carried out with use of SPSS 19.0 (Statistical Package for the Social Sciences) software, with which one can calculate means, medians, percentages, and standard deviations. For the calculations, the UFPa Chi-Squared test was applied for the formulation of the tables, and ANOVA was used for the calculation of means. The statistical significance level adopted was $p < 0.05$.

Results

During the studied period, 423 active patients who renewed their clinical reports at the high-cost pharmacy of the Health Center of the city of Campo Grande were included in this study.

Table 1 – Places of bowel impairment in IBD.

Crohn's disease ($n = 208/238$)	n	%
Rectum	113	54.30
Small intestine	93	44.70
Colon	164	78.80
Right colon	84	40.40
Transverse colon	27	13.00
Left colon	84	40.40
URC ($n = 160/185$)	n	%
Rectum	38	23.80
Left colon	57	35.60
The entire large intestine	65	40.60

Table 2 – Medications used.

Medication	Crohn's disease		URC	
	n	%	n	%
Azathioprine	84	35.3	29	15.7
Infliximab	48	20.2	10	5.4
Mesalazine	123	51.7	153	82.7
Adalimumab	80	33.6	10	5.4
Sulfasalazine	3	1.3	3	1.6
Methotrexate	0	0.0	1	0.5

Of this total, 238 (56.3%) suffered from CD and 185 (43.7%) suffered from URC. A higher percentage of women (61.5%) *versus* men (38.5%) were observed; in relation to age, a mean of 46.01 years and a median of 44 years were found, with ages ranging from 9 to 97 years.

Of the total number of patients studied (423), 55 patients were excluded due to a lack of information in the medical records regarding the affected intestinal segment (a colonoscopy report unavailable). Therefore, of the 208 patients with CD and with an available report, the most frequent location of the disease was the colon (78.8%), followed by the rectum (54.3%) and the small intestine (44.7%). Of the 160 patients with URC and with an available report, the entire large intestine (40.6%), followed by the left colon (35.6%) and the rectum (23.8%) have been the segments more often involved (Table 1).

Among the medications used by the patients, it was observed that, in the case of CD, the majority of the patients were being medicated with mesalazine (51.7%), followed by azathioprine (35.3%), adalimumab (33.6%), infliximab (20.2%), and sulfasalazine (1.3%). Of the patients with URC, the majority also used mesalazine (82.7%), followed by azathioprine (15.7%), infliximab (5.4%) adalimumab (5.4%), sulfasalazine, and methotrexate (0.5%) (Table 2).

Of the total number of patients studied, 34.3% switched their medication over time; however, it was not possible to establish the reason for these changes, or to assess the severity of the diseases. We could inquire that the changes were more frequent in patients with CD, 100 (42%), compared to patients suffering from URC, 45 (24.3%) ($p < 0.001$) (Table 3).

Analyzing patients with CD and with drug replacement, there was no difference between genders ($p = 0.57$). The mean age of the patients who underwent some change was 43.11

Table 3 – Factors associated with drug replacement in IBD.				
	Mean age	p	Mean BMI (kg/m^2)	p
Replacement × age and BMI				
Total				
Drug replacement	45.25	0.483	24.68	0.071
With no drug replacement	46.42		25.61	
CD				
Drug replacement	43.11	0.490	23.83	0.020
With no drug replacement	44.61		25.14	
URC				
Drug replacement	50	0.500	26.58	0.590
With no drug replacement	48.2		26.07	

	Male		Female		p
	n	%	n	%	
Replacement × gender					
Total					
Drug replacement	49	30.10	96	36.90	0.148
With no drug replacement	114	69.90	164	63.10	
CD					
Drug replacement	60	43.80	40	39.60	0.517
With no drug replacement	61	60.40	77	56.20	
URC					
Drug replacement	9	14.50	36	29.30	0.027
With no drug replacement	53	85.50	87	70.70	

	Rectum			Small intestine			Colon		
	n	%	p	n	%	p	n	%	p
Replacement in CD × affected segment									
Drug replacement	51	45.1	0.775	42	45.2	0.808	72	43.9	0.854
With no drug replacement	62	54.9		51	54.8		92	56.1	

	Right colon			Transverse colon			Left colon		
	n	%	p	n	%	p	n	%	p
Drug replacement	36	42.9	0.743	11	40.7	0.695	34	40.5	0.370
With no drug replacement	48	57.1		16	59.3		50	59.5	

years ($p = 0.49$). With regard to BMI, we found a mean of 23.83 kg/m^2 ($p = 0.02$). With regard to the affected segment, there was no statistically significant difference ($p = 0.808$) (Table 3).

When analyzing patients with URC and with drug replacement, a greater number of shifts occurred among women (29.3%) *versus* men (14.5%) ($p = 0.027$). The mean age of the patients was 50 years, with a BMI of 26.58 kg/m^2. Taking into account the affected segment, no relevant statistical difference was found (Table 3).

Among those patients who used the anti-TNF agent infliximab, the majority were men, 30 (18.4%) *versus* women, 28 (10.8%) ($p = 0.026$), but no statistical difference was observed between men with CD and URC. The mean age of patients with CD treated with the anti-TNF agent (37.63 years) was lower *versus* patients with CD who did not use this drug (46.79 years) ($p < 0.001$). Among patients who used the immunosuppressive drug azathioprine, there was no difference between genders ($p = 0.742$). The general mean age of the patients was 43.19 years ($p = 0.031$).

Discussion

In the studied sample, a greater number of women with IBD were observed, which agrees with the findings described in the literature.[2,6] The peak of incidence described varies between the third and fourth decades of life.[1] In the case of CD, the literature situates the highest incidence varying between the second and third decades of life.[7] In the present study, the means for IBD and CD fall into the fourth decade of life. These data lead us to believe that a period of high productivity of the population is compromised, due to the important repercussions on the patients' quality of life, motivated by the disease.

CD can affect any part of the gastrointestinal tract, but often the most affected segments are the terminal ileum and the colon.[7–9] In our sample, we observed a higher number of patients with colon involvement, a finding which disagrees with the findings in the literature.

With reference to URC, the literature reveals that in approximately 45% of the patients the disease is limited to the

rectosigmoid, 35% to the left colon, and up to 20% of the patients suffer from pancolitis, in cases where the disease has spread beyond the splenic flexure.[10] In the present study, we observed a higher frequency of pancolitis, which agrees with the findings reported in the study by Cabral et al.[6] We were not able to classify the severity of the disease; however, in the evaluation that took into account the extension of the affected segment, we noticed that the sample studied could be at greater risk for the development of colorectal dysplasia and neoplasia, since the risk varies according to the extent of the disease.[10]

The group of patients medicated with mesalazine constitutes the majority in both diseases evaluated in the present study. According to the literature, the treatment of choice for URC is done with aminosalicylates; usually, these drugs, alone or in combination with corticosteroids, maintain the disease in remission.[9,11,12] In the present study, we observed a lower need for drug replacement in patients with URC.

In patients with CD, even though oral mesalazine has proved beneficial in the past, new evidence suggests that this approach is minimally effective *versus* placebo, and less effective than budesonide or conventional corticosteroids.[7] Published clinical trials were not sufficient to adequately compare mesalazine *versus* sulfasalazine. A meta-analysis of three major studies with mesalazine (4 g/day) showed a significant, but not clinically relevant, statistical difference compared to placebo.[7] Therefore, in the present study, it was seen that many patients suffer from CD and use mesalazine, a therapy with no consistent efficacy.

For CD patients, the therapy is chosen according to the location of the disease, its severity, and extraintestinal complications.[1,5,7,9]

Immunosuppressants and biological agents are the most relevant pharmacological classes for this purpose.[12] The tumor necrosis factor alpha is a critical cytokine for the origin, amplification, and maintenance of the inflammatory dysfunction observed in CD patients.[13]

Due to the genetic heterogeneity of the disease, CD patients are expected to have a greater need for drug replacement, dose adjustment, or even surgical indication.[11,12] Our sample is similar to those found in the literature. However, a greater use of aminosalicylates has been observed in patients with CD, different from what is recommended as a better therapy to induce remission of this disease, which could support the high number of drug replacements in CD patients.

Unfortunately, there is no cure for CD, and the patient depends on therapeutic approaches for the induction and maintenance of its symptomatic control, improvement of the quality of life and minimizing long-term complications.[7] Even in the face of these facts, a technical review evaluated the safety and efficacy of immunomodulatory and biological agents as inductive therapies for remission and maintenance in patients with CD.[14]

The therapy with biologicals allows mucosal healing and is one of the treatments most often used in the current therapeutic management of CD.[12,15] Infliximab (IFX) is a chimeric monoclonal antibody in which 25% of its structure consists of murine protein and 75% of human protein, with intravenous administration. Adalimumab (ADA) is a 100% human monoclonal antibody, administered subcutaneously.[16]

Despite the initial benefit achieved with the short-term use of anti-TNF, the literature shows that up to 30% of patients fail to respond throughout the treatment, and in the long term, up to 40% do not show sustained benefits.[12] In these situations, strategies for rescue therapies were and are still being studied for the remission of the disease, either with an increase of the dose or reducing the interval of use of the medication. In the literature, there are reports that show greater efficacy with the continuous use of anti-TNF treatment, in relation to its episodic use.[18]

In the studied group, 148 patients (34.9%) were being medicated with this pharmacological class and, of this total, 128 (86%) suffered from CD. When analyzing the number of patients studied in this paper, the number of patients using biological agents is still small, given the high cost of this medication, its side effects, and contraindications to its use.

Conclusion

Most people on treatment for IBD are women, with a mean age of 46 years, and are CD patients. The most affected segments were the entire large intestine in URC patients and the colon in CD patients. Mesalazine was the most used drug in both diseases. There were more drug replacements in CD patients. Infliximab was most commonly used by CD patients; in this group, younger people used infliximab more often.

Conflicts of interest

The authors declare no conflicts of interest.

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