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ORIGINAL ARTICLE

Analysis of excessive corticosteroid use as an indicator of poor quality of care in patients with inflammatory bowel disease

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ABSTRACT

Aim To evaluate the clinical impact of corticosteroids (CS) overuse in inflammatory bowel disease (IBD) patients. Excessive use of CS could delay more efficacious treatment and may indicate poor quality of care.
Method This is a two-phase study that used Steroid Assessment Tool (SAT) to measure corticosteroid exposure in IBD patients. In the first phase data from 211 consecutive ambulatory patients with IBD (91 with ulcerative colitis, 115 with Crohn's disease, and five with unclassified inflammatory bowel disease) were analysed by SAT. In the second phase, one year after data entry, clinical outcome of patients with corticosteroids overuse was analysed.
Results Of the 211 IBD patients, 132 (62%) were not on corticosteroids, 45 (22%) were corticosteroid-dependent and 34 (16%) used corticosteroids appropriately, according to the European Crohn's and Colitis Organization guidelines. In the group of patients with ulcerative colitis, 57 (63%) were not on corticosteroids, 18 (20%) were corticosteroid-dependent, and 16 (16%) used corticosteroids appropriately; in the group of patients with Crohn's disease 70 (61%), 27 (23%) and 18 (16%), respectively. Overall, 24 (out of 45; 53%) patients with IBD could avoid the overuse of corticosteroids if they had a timely change of the treatment, surgery or entered a clinical trial.
Conclusion An excessive corticosteroid use can be recognized on time using the SAT. We have proven that excessive corticosteroid use could be avoided in almost half of cases and thus the overuse of CS may indicate poor quality of care in those patients.

Keywords: audit, quality of health care, steroid use

INTRODUCTION

Before approval and wider use of biologics for IBD indications, the cornerstone for the treatment of inflammatory bowel disease (IBD) was corticosteroids and 5-aminosalycilates (5- ASA) (1,2). Corticosteroids are very potent drugs and are often unavoidable in inducing remission for both Crohn´s disease (CD) and ulcerative colitis (UC) (2–5), but they are ineffective in maintaining remission (6,7). Unfortunately, due to the numerous side effects their use should be reduced to minimum, especially now when a novel therapy with biologics is widely available that is not only efficacious, but also has fewer side effects (3). The European Crohn's and Colitis Organization (ECCO) guidelines define corticosteroid dependency and excess as the inability to wean steroids below the equivalent of prednisolone 10 mg/day or budesonide 3 mg/day within 3 months of starting steroids, relapse within 3 months of stopping steroids, or the need for more than a single course of corticosteroid in 1 year (8). If feasible, patients should be switched to corticosteroid sparing therapy in order to achieve corticosteroid free remission (9). Due to numerous reasons the overuse of

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corticosteroids in everyday practice is still present, but official evidence is still scarce and not emphasized enough (10,11).

Many authors and organizations consider that use of corticosteroids is one of the measures for quality of care of IBD centres, and its overuse is one of the indicators of poor quality of care (12–14). Monitoring CS overuse through audits is one way to improve care of IBD patients (15,16).

Health care in Bosnia and Herzegovina (B&H) faces difficulties due to organizational issues as well as a lack of medical doctors (17). Consequently, there is a disparity in providing health care between centres, uneven practice in the treatment of IBD and non-adherence to guidelines. As there are no official internal nor external audits, management and decision-making is nearly always left to the discretion of individual physician, which is not unknown in many other countries facing similar problems (2,15).

A group of authors from the United Kingdom created a free internet platform called Steroid Assessment Tool (SAT), which is designed to evaluate the use and overuse of corticosteroids in IBD patients (11). As excess use of corticosteroids is an indicator of poor quality of care in IBD patients, SAT could be a useful tool in identifying pitfalls of healthcare system (18). In order to test this indicator of care quality, we decided to perform this study and offer scientific evidence of corticosteroid overuse in IBD patients by using SAT. This is the first study in BiH that is addressing this issue.

The aim of this study was to evaluate the excess use of corticosteroids and its clinical outcomes in ambulatory IBD patients in a single university centre in Bosnia and Herzegovina.

PATIENTS AND METHODS

Patients and study design

This two-phase prospective study was conducted in the periods from December 2018 to January 2021 at the University Clinical Centre Tuzla.

Eligible patients were ambulatory consecutive patients with a confirmed diagnosis of IBD that lasted for more than one year, and who had digital medical records of their clinical status, recent colonoscopy and the prescribed treatment in the year before data entry. The activity of the disease was assessed by experienced IBD physicians based on a combination of the clinical status and colonoscopy findings into four SAT preapproved categories (quiescent, mild, moderate and severe) using the Physician's Global Assessment (Grade 0 -3).

In the first phase data from 211 consecutive ambulatory patients with IBD (91 with ulcerative colitis, 115 with Crohn's disease, and five with unclassified inflammatory bowel disease) were analysed by SAT. In the second phase, one year after data entry, clinical outcome of patients with corticosteroids overuse was analysed.

The study was approved by the Ethics Committee of the University Clinical Centre Tuzla (No. 02-09/2-57/21) and due to the nature of the study (an audit study), using anonymous data of a single centre, an informed consent was not required.

Methods

For the analysis of corticosteroid use and overuse we used the Steroid Assessment Tool (SAT). It is a secured web-based database, created and validated by UK gastroenterologists (11,14), designed to analyse treatment and steroid exposure in patients with IBD (11,14).

The tool uses data on patients' disease, disease activity, current and previous treatment, corticosteroid use in the year before data entry, number of courses and ability to reduce dosing in order to identify an excess use of steroids.

SAT is secured by password and authorized in one name, so a single physician was allowed to enter patients' data. The analysis of the questions that can be seen in the supporting information where SAT methodology is first described (14) was made by the online algorithm after entering all necessary data in the SAT.

The overuse of CS was defined by the European Crohn's and Colitis Organization (ECCO) guidelines (8). After SAT identified patients with CS overuse, those patient records were unblinded and additionally reviewed to assess the treatment outcomes one year after their data entry. Outcomes were defined as actions in the following year performed in order to wean them off corticosteroids. Those actions were grouped as: change in medical treatment (introduction of biologics or switch to other biologic), surgery, stepwise weaning off corticosteroids without a change in medical treatment or entering phase III of clinical trials where patients got a chance to receive new medical treatment as a part of efficacy and safety multicentric double blind placebo-controlled research of new drugs for IBD indications. If those actions led to corticosteroid free remission, it was considered that those patients' use of corticosteroids was avoidable if they had a timely change of treatment. If they were still corticosteroid dependent that meant their disease could not be treated differently with the timely change in treatment, which meant their corticosteroid overuse was justified and could not be avoided.

Statistical analysis

SAT analysed all variables and provided results presented as absolute numbers and percentages. An $\chi 2$ test was used to compare categorical variables between the groups. A difference was considered significant with $p<0.05$.

RESULTS

The total cohort consisted of 211 patients with IBD, of which 91 (42%) had UC, 115 (56 %) had CD and five (2%) had undetermined IBD. Since there were only 2% of patients with UIB, only data from CD and UC cohort (total of 206 patients) were further analysed.

A disease activity between two cohorts was different: UC cohort had more patients with mild disease and CD one had more patients with more severe disease (p=0.01) at the time of data entry. Hence, patients with UC used more 5-ASA medications, while patients with CD used more azathioprine, methotrexate and inhibitors of tumour necrosis factor (anti TNF), which is consistent with differences in their disease activity (Table 1).

Of the 211 IBD patients in the year before data entries, 132 (62%) were not on CS, 45 (22%) were CS-dependent, and 34 (16%) used CS, but according to the ECCO guidelines they were not CS dependent. There was no statistical difference between those two groups (Table 2).

Out of 45 patients with CD who used steroids, 27 (60 %) were steroid-dependent. Most of those patients with CD had to use CS for longer than 3 months (19/27), could not reduce the dose under 10 mg (17/27), and five patients had a relapse within 3 months after CS withdrawal. Out of 34 patients with UC who used corticosteroids, 18 (53 %) were CS dependent. Most of them were not able to reduce the dose under 10 mg of prednisolone (11/18), four had a relapse within 3 months after corticosteroid withdrawal. There was no statistical difference among cohorts regarding duration of steroid use in months (p=0.3) (Table 3).

Both UC and CD patients with mild disease were less likely to use steroids and patients with moderate/severe disease used it more often (p <0.05 for CD, and p<0.000001 for UC) (Table 4).

Bone protection medicines were prescribed to 27 (60%) of CD and 22 (66%) of UC patients on corticosteroids.

Table 1. Characteristics and therapy of patients with ulcerative colitis and Chron's disease

Variable		Number (%) of patients in the group		p
		Ulcerative colitis (n=91)	Crohn´s disease (n=115)	
Disease severity	Quiescent	2 (2.22)	2 (1.74)	0,01
	Mild	32 (35.15)	15(13.04)	
	Moderate	44 (48.35)	74 (64.35)	
	Severe	13(14.28)	24 (20.87)	
Current/ previous use of medication				
Mesalazine (5 ASA)	Current	91 (100)	94 (81.74)	0.00009
	Previous	0 (0)	20 (17.39)	
	Never	0 (0)	1 (0.87)	
Azathioprine	Current	26 (28.57)	75 (65.22)	0.000000001
	Previous	8 (8.79)	18 (15.65)	
	Never	57 (62.64	22 (19.13)	
Other immunosuppression (methotrexate)	Current	1 (1.1)	8 (6.96)	0.0057
	Previous	0 (0)	7 (6.09)	
	Never	90 (98.9)	100 (86.95)	
Anti-tumour necrosis factor (Anti TNF)	Current	7 (7.69)	32 (27.83)	0.0012
	Previous	5 (5.49)	5 (4.35)	
	Never	79 (86.8)	78 (67.82)	
Anti-integrin	Current	3 (2.73)	2 (1.75)	0.47
	Previous	0 (0)	0 (0)	
	Never	88 (96.7)	113 (98.25)	

Table 2. Corticosteroid use in ulcerative colitis and Crohn's disease

Corticosteroid usage	Number (%) of patients in the group		p
	Ulcerative colitis (n=91)	Crohn´s disease (n=115)	
No steroids	57 (62.6)	70 (61)	0.795
Appropriate	16 (17.6)	18 (15.5)	
Overuse	18 (19.8)	27 (23.5)	

As a result of the second phase of the study we determined that 6 (out of 18; 33%) patients with UC and 18 (out of 27; 66%) with CD (overall 24 out of 45; 53%) could probably avoid overuse of corticosteroids if they had a timely change of treatment, timely surgery, or entered a clinical trial. There was a statistical difference between UC and CD patients (p<0.05), meaning that more patients with Crohn's disease could have been treated differently in order to reach corticosteroid free remission (Table 5).

Table 3. Duration of corticosteroid use in ulcerative colitis and Crohn's disease cohorts

Duration of corticosteroid usage (months)	**No (%) of patients in the group**		**p**
	Ulcerative colitis (N=33)	**Crohn's disease** (N=46)	
<3	15 (45.5)	20 (43.5)	0.307
3-12	16 (48.5)	18 (39.1)	
>12	2 (6)	8 (17.4)	

Table 4. Corticosteroid use according to disease severity in ulcerative colitis and Crohn's disease

Activity of disease	**Number (%) of patients in the group**							
	Ulcerative colitis (N =91)			**p**	**Crohn's disease** (N=115)			**p**
	NO use	**Appropriate use**	**Overuse**		**NO use**	**Appropriate use**	**Overuse**	
Quiescent	2 (2.2)	0	0	0.000001	2 (1.7)	0	0	<0.05
Mild	27 (29.7)	5 (5.5)	0		12 (10.4)	2 (1.7)	1(0.9)	
Moderate	27(29.7)	9 (9.8)	8 (8.8)		43 (37.4)	13 (11.3)	18 (15.7)	
Severe	1 (1.1)	2 (2.2)	10 (11)		12 10.4)	4 (3.5)	8 (7)	

Table 5. Outcome of steroid dependent patients one year after detection of their steroid overuse

Clinical outcome of steroid dependent patients	**Number (%) of patients in the group**					
	Ulcerative colitis (N=18)			**Crohn's disease N=27**		
	Number of patients	**Steroid free**	**Still on steroids**	**Number of patients**	**Steroid free**	**Still on steroids**
Change of medical treatment (introduction to biologics or switch to other biologics)	7 (39)	3 (16.6)	4 (22.2)	10 (37)	7 (26)	3 (11.1)
Colectomy/resection (surgery)	1 (5.6)	1 (5.6)	0	7 (26)	6 (22.2)	1 (3.7)
Clinical trial	3 (16.5)	2 (11.1)	1 (5.6)	0	0	0
Used for other conditions	2(11.1)	0	2(11.1)	2 (7.4)	0	2 (7.4)
No change in treatment	1 (5.6)	0	1 (5.6)	2 (7.4)	0	2 (7.4)
Weaned of steroids gradually during prolonged period	0	0	0	5 (18.5)	5 (18.5)	0
Lost to follow up	4 (22.2)	unknown	unknown	1 (3.7)	unknown	unknown
		Yes	NO		Yes	NO
Steroids could be avoided if patients were managed differently		6 (33.4)	12 (66.6)		18 (66.6)	9 (33.4)

DISCUSSION

There are many measurements of the quality of care for patients with IBD, but analysing the overuse of corticosteroids is one of the most important ones considering well known adverse effects of steroids (13). In our study we have confirmed that SAT is a good internet platform that can be used in single centres to analyse the use and overuse of steroids as a measurement of the quality of care of their IBD patients and therefore act as a surrogate for internal audit.

We have proved that a total of 22 % of IBD patients were corticosteroid dependent, which is more than 14.9% reported from the UK. (11,14). In our study no statistical difference among CS overuse between patients with UC and CD was found similarly with UK study from 2017 (14). We have also proved similarly to UK authors (14) that UC patients had less severe course of disease, used rarely azathioprine, other immunosuppressant and anti TNF, but they still used CS in almost the same percentage as patients with CD.

In our country advanced therapy could be used only in university clinical centres such as our centre. We did not use data from smaller centres that did not even had that option. If we did so, the number of patients with excessive corticosteroid use could be even higher. In one single tertiary centre from Romania, where most patients were on biologics, CS were used in excess; they used SAT in 2019 and 2020 and managed to reduce the use of excess CS from 20.4% to 5.95 %, proving that this online tool is helpful in detecting problems with therapeutic management and the regular use could improve adherence to guidelines recommendations (18,19).

In Bosnia and Herzegovina biologics are approved by the Ministry of Health of both entities (Federation of BiH and Republic of Srpska) and in District Brčko. In recent years not all patients that required the drugs could get them on time with a waiting list for some patients of more than a year. The delay in approving biologics is probably one of the important reasons for excessive usage of steroids.

Even though the updated national guidelines for the treatment of IBD exist, there is no internal nor external audit. Many doctors have a lot of experience with the treatment of IBD patients with steroids and since there are a lot of organizational and financial problems, they still base their treatment primarily on corticosteroids. This is consistent with Dorrington et al. study (2) where logistical and financial barriers, as well as the lack of experience in the management of steroid sparing agents, were found as factors associated with the risk of steroid exposure.

According to our results the total of 53% of patients could avoid corticosteroids if they had a timely adequate therapeutic intervention, similarly with the UK study (14). Almost 18% of patients who were CS dependent had surgery in the following year in the University Clinical Centre. Timely surgery could lead to a better overall outcome, better quality of life and reduction of unnecessary therapy, primarily corticosteroids (20–22). Pharmacological therapy should be given not to avoid surgery, but to improve the quality of life (23). In our centre, surgery is used only as the last option, which is a line with other authors (24). We are planning to form a multidisciplinary team (MDT) with qualified surgeons and gastroenterologists with more interest in IBD in order to make better and more informed decisions for each patient individually.

In developed countries, especially in centres with good quality of care, where patients with IBD are put early on biologics and are not on prolonged corticosteroid use, an adequate candidate for some clinical studies is lacking (25). Among our patients who were steroid-dependent, three (out of 18) patients with UC entered multicentric clinical trial where they received a study drug (upadacitinib). Two (out of three) were weaned off steroid. Since eligible candidates for some clinical trials are difficult to find we consider that SAT could be used as a tool to locate those patients. Our findings proved that less resourceful countries like ours could be a valuable location for performing clinical trials in which many of these CS dependent patients could take part.

SAT also analysed the use of 5-ASA medications and one of the interesting results of this study is the fact that 82% of CD patients use continuously 5-ASA, which is not recommended by the ECCO guidelines. It is in concordance with prescribing habits reported by other authors (26–28). It is based on the fact that there are many patients who have been on 5 ASA for years, even decades. Gastroenterologists would be reluctant to change their prescribing habits in those patients. An inadequate treatment with 5 ASA in CD and overtreatment with CS could lead to a delay in more efficacious treatment (29), as well as avoid unnecessary side effects and financial cost.

The main point of this study is that we have identified that one of five patients with IBD overused corticosteroids. This is unacceptably high in the era of advanced treatment. It has also proved that a timely change of treatment strategy could reduce overuse of corticosteroids by half.

The limitation of this study is that SAT platform was not designed to analyse age, gender, IBD phenotype or disease duration, which are all important factors that could contribute to corticosteroid overuse and it is not designed to assess the use of steroids in any other disease or condition other than IBD.

In the time when there is a global shortage of medical staff, different e-platforms such as SAT and other more advanced artificial intelligence, platforms/neural networks could be used as assistance in everyday work. E-platforms can improve decision making and could alert physicians to different medical problems or to alternative treatment pathways. This relatively simple and easy-to-use SAT has shown to us that our centre has a problem with steroid overuse, which is an indication of potential low quality of care for IBD patients. Using SAT helped to initiate different actions for solving this such as emphasizing the importance of MDT meetings and organizing audits for the treatment of IBD. We are planning to use it in the future to continue to drive improvements in patient care.

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TRANSPARENCY DECLARATION

Conflict of interests: None to declare.

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