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Predictors of steroid dependence and resistance in patients with ulcerative colitis

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ABSTRACT *AIM: to detect predictors of steroid dependence (SD) and steroid resistance (SR) in ulcerative colitis (UC).*
PATIENTS AND METHODS: a retrospective study was done. The medical documentation of 1,105 patients, who underwent inpatient treatment from 2018 to 2021, were analyzed. Sixty-nine percent of patients (n = 762) received systemic steroid therapy for UC. In accordance with inclusion and non-inclusion criteria, the medical documentation of 170 patients was selected for statistical analysis. Depending on the steroid status of patients, three groups were identified: group 1 (n = 56) with steroid dependence, group 2 (n = 56) with steroid resistance and group 3 — controls (n = 58), who got systemic GCS without the further SD and SR.
RESULTS: the incidence of SD was 33.9% (259/762), and SR was 22.04% (168/762). We identified the following predictors and SD risk factors: age of the disease onset < 30 years old (AOR = 0.960; 95% CI = 0.928–0.993; p = 0.019), start dose of prednisolone < 60 mg (AOR = 2.369; 95% CI = 1.030–5.441; p = 0.042), prescription of systemic GCS ⩾ 2 courses per year (AOR = 2.988, 95% CI = 1.349–6.619, p = 0.007), Mayo Index Score < 10 points (AOR = 0.631; 95% CI = 0.492–0.809; p < 0.001). The risk of SR statistically significant when Mayo Index Score ⩾ 10 points (AOR = 2.573, 95% CI = 1.094–6.050, p = 0.030), albumin level < 37.1 g/l (AOR = 4.571; 95% CI = 1.567–13.330; p = 0.005), CRP ⩾ 47.1 mg/l (AOR = 2.641; 95% CI = 1.102–6.328; p = 0.029).
CONCLUSION: it is rational to predict an individual response to GCS in patients with UC. With a high risk of SD and SR, it is advisable to consider early administration of biological and target therapy, avoiding re-prescription of GCS.

KEYWORDS: *ulcerative colitis, steroid dependence, steroid resistance*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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LIST OF ABBREVIATIONS

IBD — inflammatory bowel diseases
GCS — glucocorticosteroids
SR — steroid resistance
SD — steroid dependence
CRP — C-reactive protein
UC — ulcerative colitis
OCED — optimal clinical effective dose

INTRODUCTION

Systemic glucocorticosteroids (GCS) have been widely used in the treatment of ulcerative colitis (UC) since the middle of the XX century [1]. Nowadays, despite the emergence of new classes of drugs for the treatment of inflammatory bowel diseases (IBD), systemic corticosteroids remain the basic therapy for the induction of remission in moderate, severe and acute severe forms of UC. More than 50% of patients with UC have at least one course of systemic therapy of GCS during their lifetime [2]. Having a wide range of pharmacological effects, GCS inevitably have an undesirable effects, and therefore their use as maintenance therapy is unacceptable. According to Russian and foreign guidelines for UC, achieving steroidal remission is one of the fundamental goals of conservative approach, and the duration of systemic steroid therapy should not exceed 12 weeks [3–5]. Nevertheless, according to real clinical practice, the duration of GCS courses in IBD is on average

13–30 weeks, which significantly exceeds the recommended duration [6]. And in 34% of patients, there is a need to re-prescribe GCS within a year [7].

In assessing the effectiveness of UC treatment, the main aspect is the clinical, laboratory and endoscopic response to systemic steroid therapy.

When describing the hormonal status, the concepts are distinguished:

- Steroid resistance (SR) — the absence of positive shifts in clinical and laboratory indicators in severe UC attack against the background of the use of systemic GCS at a dose equivalent to 2 mg/kg of prednisolone per 24 hours for more than 7 days; or in the case of a moderate attack — the preservation of the activity of the disease with oral administration of GCS at a dose equivalent to 1 mg/kg of prednisolone, for 14 days.
- Steroid dependence (SD) — an increase in the activity of the disease with a decrease in the dose of GCS against the background of achieving initial improvement within 3 months from the start of treatment; or the occurrence of the disease recurrence within 3 months after the end of systemic steroid therapy [5].

According to a large epidemiological study of ESCApe in Russia in 2011, the incidence of SR in UC was 23%, and SD — 21%, i.e. almost half of the patients had an absence or loss of response to GCS [8].

Currently, the use of immunosuppressors (azathioprine, mercaptopurine, cyclosporine), genetically engineered biological and targeted therapy is available for the treatment of steroid-dependent and steroid-resistant forms of ulcerative colitis [5]. According to the mechanism of action, the following groups of drugs for the treatment of UC are distinguished: blockers of tumor necrosis factor alpha (infliximab, adalimumab and golimumab), a selective antagonist of integrin receptors (vedolizumab), an inhibitor of IL12/23 (ustekinumab), a modulator of sphingosine-1-phosphate receptors (ozanimod), as well as small molecules — inhibitors of JAK kinases (tofacitinib and upadacitinib).

Over the past three decades, foreign and Russian researchers have been trying to identify factors and develop criteria that could predict the effectiveness of conservative therapy and the risks of colectomy in UC. At the same time, the authors study clinical, laboratory, endoscopic and radiological parameters [9]. The Oxford Index [10], the Swedish Index [11], the ACE (Albumin, CRP and Endoscopy) index [12], which mainly assess the risks of colectomy against the background of systemic steroid therapy in acute severe UC, received the greatest prevalence in clinical practice.

It is noteworthy that many indices and criteria [10,11,13] were developed in the era of pre-biological therapy, and the dosages of GCS in these studies differ from those prescribed today. It is also worth noting that there is limited data in the literature on predictors of the SD formation. For example, Skrzypczak-Zielinska M. [14] and colleagues studied the genetic predictors of the response to steroid therapy, and the association of polymorphism of the FKBP5 gene and deletion of the MAPK14 gene with the development of SD in patients with UC was revealed. In some studies, it was found that the positivity of the serological marker p-ANCA is associated with a high risk of developing SD [15,16]. However, the use of genetic and serological markers is difficult in real clinical practice due to their high cost and low availability. A work on clinical predictors of the SD formation has been published in the Russian literature. According to Koinova, I.A. and co-authors, SD in UC is combined with frequent recurrences, a high score as per the Mayo index and the presence of extra-intestinal manifestations [17].

Some Russian experts in IBD associate the lack of response to systemic steroid therapy with the prescribed doses of the drug. According to Kharitonov A.G., one of the reasons for SR is the administration of low doses of GCS, insufficient to relieve inflammation with high activity of UC [18]. Alekseeva O.P. and co-authors studied construction dose-effect relationship in the first and repeated courses of systemic steroid therapy in patients with moderate and severe attacks of IBD. The optimal clinical effective dose (OCED) of prednisolone with statistical parameters of 50.70 ± 0.65 mg (p = 0.05) during the first course of therapy was determined. For repeated courses of prednisolone, the OCED

Table 1. *Characteristics of the patients*

Factors	SD (*n* = 56)	SR (*n* = 56)	Control (*n* = 58)	*p*
Gender, abs. (%) – Male – Female	 38 (67.9%) 18 (32.1%)	 32 (57.1%) 24 (42.9%)	 36 (62.1%) 22 (37.9%)	 0.504 0.504
Age, years, Me (Q1–Q3)	35 (30–43)	36 (30–44)	39 (34–50)	**0.03**
Course of the disease, abs.(%) – Acute – Chronic recurrent – Chronic permanent	 2 (3.6%) 5 (8.9%) 49 (87.5%)	 10 (17.9%) 14 (25%) 32 (57.1%)	 11 (19%) 20 (34.5%) 27 (46.5%)	 0.029 < 0.001 0.005
Extent of lesion, abs.(%) – Left-sided – Total	 10 (17.9%) 46 (82.1%)	 8 (14.3%) 48 (85.7%)	 8 (13.8%) 50 (86.2%)	 0.807 0.807
Previous therapy, abs. (%) – 5-ASA – immunosuppressors – cyclosporine – biological ± immunosuppressors – without specific therapy	 27 (27.3%) 23 (41.1%) 0 (0%) 6 (10.7%) 0 (0%)	 31 (31.3%) 8 (14.3%) 1 (1.8%) 10 (17.9%) 6 (10.7%)	 41 (41.4%) 9 (15.5%) 0 (0%) 5 (8.6%) 3 (5.2%)	 0.045 < 0.001 0.359 0.423 0.040
Body Mass, kg, M ± SD	69 ± 16	64 ± 15	70 ± 14	0.122

was 51.43 ± 1.55 (48.24–54.61) mg (p = 0.05), but the effectiveness of the therapy was 42% lower, which, according to the authors, indicates an insufficient effect of repeated courses of systemic steroid therapy for a period of 3 to 12 months [19].

So, we started our own study, the purpose of which was to identify predictors of SD and SR in patients with UC.

PATIENTS AND METHODS

A retrospective single-center study included 1,105 patients with UC in 2018–2021. Of these, 69% of patients (n = 762) underwent systemic steroid therapy for UC during their lifetime, including repeated courses of GCS in history. When analyzing medical documents, in most cases there was no comprehensive information about the duration and doses of systemic steroids, which were previously prescribed to patients in other medical institutions. In accordance with the inclusion criteria (established diagnosis of UC and administration of systemic steroid therapy in anamnesis) and non-inclusion criteria (age < 18 years, absence in primary medical documentation of data on the number and duration of courses of systemic steroid therapy, prescribed doses of GCS, absence of clinical laboratory and endoscopic data at the time of administration of systemic steroid therapy, and also, the transformation of the main diagnosis in the anamnesis), we selected the medical documentation of 170 patients for further statistical processing. Depending on the steroid status of patients, three groups were identified: group 1 (n = 56) with SD, group 2 (n = 56) with SR, and group 3 — control (n = 58), who were prescribed systemic therapy of GCS without further development of SD and SR. The following factors were analyzed as possible predictors of SD and SR:

- Clinical and demographic (gender, age of the patient, including at the time of the onset of the disease, heredity, smoking status, extent of lesion, presence of extra-intestinal manifestations, Mayo index);
- Laboratory (erythrocytes, hemoglobin, platelets, leukocytes, neutrophils, rod-shaped and segmented, lymphocytes, monocytes, ESR, total protein, albumin, globulins, albumin/globulin ratio, CRP, fibrinogen);
- Schemes of systemic steroid therapy (administration of topical corticosteroids in anamnesis,

Table 2. *Regression analysis to identify predictors and risk factors for steroid dependence*

Indicators	SD is present (*n* = 56)	SD is absent (*n* = 114)	HR	95% CI	*p*
Males, abs. (%)	38 (67.9%)	68 (59.6%)	1.428	0.728–2.804	0.3
Females, abs. (%)	18 (32.1%)	46 (40.4%)	0.7	0.357–1.324	0.3
Age of patient, years, Me (Q1-Q3)	35 (30.00–43.25)	37 (31.25–48.00)	0.971	0.943–0.999	**0.044**
Disease debut age, years, Me (Q1-Q3)	26 (21.00–32.00)	31 (23.00–41.75)	0.959	0.931–0.989	**0.007**
Heredity, abs. (%)	3 (5.7%)	5 (5.1%)	1.094	0.281–4.764	0.905
Smoking, abs. (%)	12 (22.0%)	11 (12.4%)	2.026	0.824–4.983	0.124
Lesion extent, abs. (%) – Left-sided – Total	 10 (17.9%) 46 (82.1%)	 16 (14.0%) 98 (86%)	 1.331 0.751	 0.561–3.161 0.316–1.782	 0.516 0.516
Acute course, abs.(%)	2 (3.6%)	21 (18.4%)	0.164	0.037–0.727	**0.017**
Extra-intestinal manifestations, abs. (%)	13 (23.2%)	21 (18.4%)	1.339	0.613–2.921	0.464
Starting dose of prednisolone < 60 mg, abs. (%)	23 (42.6%)	19 (18.4%)	3.280	1.575–6.835	**0.002**
Total number of GCS courses, Me (Q1-Q3)	2 (2–4)	1 (1–2)	1.537	1.204–1.962	**0.001**
⩾ 2 courses of GCS per year, abs. (%)	30 (53.6%)	29 (25.4%)	3.382	1.725–6.633	**< 0.001**
Prednisolone administration < 1 mg/kg, abs. (%)	22 (39.3%)	23 (20.4%)	2.532	1.251–5.124	**0.01**
Prednisolone administration > 2 mg/kg, abs. (%)	4 (7.1%)	12 (10.6%)	0.647	0.199–2.106	0.470
The course of GCS < 4 weeks, abs. (%)	13 (23.2%)	28 (29.8%)	0.713	0.333–1.527	0.383
The course of GCS > 12 weeks, abs. (%)	15 (26.8%)	10 (8.8%)	3.768	1.565–9.070	**0.003**
Escalation of the dose of GCS, abs. (%)	23 (41.1%)	23 (20.2%)	2.758	1.366–5.562	**0.005**
Administration of topical GCS (budesonide MMX), abs. (%)	10 (17.9%)	16 (14%)	1.331	0.561–3.161	0.516
Mayo Index, points, Me (Q1-Q3)	9 (7–9)	10 (8–11)	0.648	0.524–0.802	**< 0.001**

the starting dose of the first course of corticosteroids in terms of prednisolone, the number of courses of systemic steroid therapy during the year, the duration and dose of systemic steroid therapy during the year, escalation of the dose of corticosteroids).

Statistical Processing

Statistical analysis was carried out using the StatTech v.2.8.4. program.

Quantitative indicators were evaluated for compliance with the normal distribution using the Shapiro-Wilk and Kolmogorov-Smirnov criteria. Indicators of descriptive statistics included: number of cases (n), mean (M), standard deviation (SD), 95% coincidence interval limits (95% CI), median (Me), lower and upper quartiles (Q1–Q3). Absolute values with percentages were used to describe categorical data. To compare groups by quantitative indicator, Student's t-test, Tukey's test, Mann-Whitney's U-test, Kraskel-Wallis' test, and Dann's test with Holme's correction were used. The comparison of percentages in the analysis of multipole conjugacy tables was performed using Pearson's χ^2 criterion. The search for significant differences was carried out, the critical value of the level of which (p) was assumed to be 0.05. To assess the diagnostic significance of quantitative signs in predicting a certain outcome, the method of analysis of ROC curves was used. The separating value of the quantitative feature at the cut-off point was determined by the highest value of Youden's index.

Table 3. *Regression analysis to identify predictors and risk factors for steroid resistance*

Indicators	SR is present (*n* = 56)	SR is absent (*n* = 114)	HR	95% CI	*p*
Males, abs. (%)	32 (57.1%)	74 (64.9%)	0.721	0.375–1.387	0.327
Females, abs. ((%)	24 (42.9%)	40 (35.1%)	1.387	0.721–2.670	0.327
Age of patient, years, Me (Q1–Q3)	36 (30.00–44.00)	37 (32.00–47.75)	0.993	0.966–1.019	0.585
Disease debut age, Me (Q1–Q3)	27 (22.75–35.25)	28.5 (22.25–41.75)	0.995	0.969–1.021	0.689
Heredity, abs. (%)	2 (4.1%)	6 (5.8%)	0.688	0.134–3.540	0.654
Smoker status, abs. (%)	5 (11.4%)	18 (20.5%)	0.499	0.172–1.446	0.2
Lesion extent, abs. (%) – Left-sided – Total	 8 (14.3%) 48 (85.7%)	 18 (15.8%) 96 (84.2%)	 0.889 1.125	 0.361–2.190 0.457–2.773	 0.798 0.798
Acute course, abs.(%)	10 (17.9%)	13 (11.4%)	1.698	0.690–4.133	0.251
Extra-intestinal manifestations, abs. (%)	9 (16.1%)	25 (21.9%)	0.682	0.294–1.579	0.371
Starting dose of prednisolone < 60 mg, abs. (%)	9 (18.8%)	33 (30.3%)	0.531	0.231–1.221	0.136
Total number of GCS courses, Me (Q1-Q3)	2 (1–3)	2 (1–3)	0.928	0.780–1.105	0.401
2 ⩾ GCS courses per year, abs. (%)	17 (30.4%)	42 (36.8%)	0.747	0.377–1.483	0.405
Prednisolone administration < 1 mg/kg, abs. (%)	10 (18.2%)	45 (39.5%)	0.502	0.227–1.107	0.088
Prednisolone administration > 2 mg/kg, abs. (%)	6 (10.9%)	10 (8.8%)	1.273	0.438–3.702	0.657
The course of GCS < 4 weeks, abs. (%)	25 (45.5%)	16 (16.8%)	4.114	1.933–8.758	**< 0.001**
The course of GCS > 12 weeks, abs. (%)	5 (9.1%)	20 (17.5%)	0.470	0.166–1.327	0.154
Escalation of the dose of GCS, abs. (%)	20 (35.7%)	26 (22.8%)	1.880	0.933–3.789	0.077
Administration of topical GCS (budesonide MMX), abs. (%)	5 (8.9%)	21 (18.4%)	0.434	0.154–1.220	0.114
Mayo Index, points, Me (Q1-Q3)	10 (9–11)	9 (8–10)	1.717	1.339–2.201	**< 0.001**

RESULTS

According to data obtained, the incidence of SD among 762 patients receiving systemic steroid therapy was 33.9% (259/762), and SR– 22.04% (168/762). When comparing the groups by gender, lesion extent and body weight, they were homogenous (Table 1). Among patients with SD and SR, younger people prevailed compared to the control group ($p = 0.03$). Chronic continuous course of the disease was characteristic for patients with SD ($p = 0.005$), and acute disease was significantly more common in patients with SR and in the control group ($p = 0.029$). When comparing the groups, depending on previous therapy, it was revealed that 5-ASA were significantly more often used in patients of the control group ($p = 0.045$), immunosuppressants — in patients with SD ($p < 0.001$), and patients with SR were significantly more often without specific therapy ($p = 0.04$), which occurred mainly in the acute disease.

Regression analysis was carried out to identify predictors and risk factors for SD and SR.

Reliable risk factors for the SD (Table 2), according to our data, are: the age of the patient < 52 years, the age of the disease onset < 30 years, the starting dose of prednisolone < 60 mg, the total number of courses of systemic steroid therapy ⩾ 2 during life, as well as the administration of ⩾ 2 courses of systemic steroid therapy during year, Mayo index < 10 points. The threshold values of the indicators were obtained by sequentially constructing the ROC curve at the cut-off point, which

Table 4. *Regression analysis to identify laboratory predictors and risk factors for steroid dependence and steroid resistance*

Indicator	SD (*n* = 56)	SR (*n* = 56)	Control (*n* = 58)	*p*
Erythrocytes, × 10^{12}/l	4.42 ± 0.76	3.98 ± 0.77	4.33 ± 0.60	**0.012**
Hemoglobin, g/l	111.92 ± 24.92	108.19 ± 23.71	116.87 ± 22.91	0.197
Platelets, × 10^9/l	339.00 (275.20–416.50)	382.00 (303.00–507.65)	378.50 (298.35–450.93)	0.164
Leukocytes, × 10^9/l	9.00 (6.84–12.50)	9.26 (6.83–12.50)	9.90 (7.51–12.80)	0.636
Rod-shaped neutrophils, × 10^9/l	0.18 (0.10–0.41)	0.19 (0.08–0.40)	0.23 (0.11–0.36)	0.859
Segmented neutrophils, × 10^9/l	5.66 (4.22–9.14)	6.50 (4.73–9.15)	6.73 (4.56–8.63)	0.532
Lymphocytes, × 10^9/l	1.73 (1.18–2.38)	1.41 (1.12–2.04)	1.97 (1.34–2.55)	0.182
Monocytes, × 10^9/l	0.60 (0.42–0.69)	0.47 (0.34–0.80)	0.65 (0.36–0.91)	0.718
ESR, mm/hour	22.00 (11.50–32.00)	23.00 (14.00–43.00)	23.00 (14.00–32.00)	0.463
Total protein, g/l	65.43 ± 7.96	63.25 ± 7.53	65.61 ± 7.17	0.243
Albumin, g/l	37.00 (34.00–40.00)	34.00 (30.00–36.00)	36.00 (32.00–41.00)	**0.005**
Globulins, g/l	30.44 ± 5.99	30.83 ± 4.68	29.28 ± 6.13	0.607
Albumin/globulinratio	1.24 (0.98–1.39)	1.11 (0.95–1.26)	1.25 (1.06–1.48)	0.133
CRP, mg/l	11.75 (4.83–31.98)	51.30 (11.60–89.00)	14.90 (5.00–40.30)	**0.014**
Fibrinogen, g/l	3.10 (2.70–4.00)	3.81 (3.25–4.60)	3.5 (3.00–4.10)	**0.019**

corresponded to the highest value of Youden's index. Prescribing prednisolone at a dose of < 1 mg/kg and duration of over 12 weeks significantly influenced the SD development. It was also found that the escalation of the dose of GCS in the anamnesis demonstrates significance in the SD formation.

During the multivariate analysis, the following predictors and risk factors for the SD were identified:

- age of onset < 30 years (COR = 0.960, 95% CI = 0.931–0.990, *p* = 0.010, AOR = 0.960, 95% CI = 0.928–0.993, *p* = 0.019);
- starting dose of prednisolone < 60 mg (COR = 2.924, 95% CI = 1.387–6.160, *p* = 0.005, AOR = 2.369, 95% CI = 1.030–5.441, *p* = 0.042);
- administration of ⩾ 2 courses of GCS during the year (COR = 3.663, 95% CI = 1.790–7.493, *p* < 0.001 AOR = 2.988, 95% CI = 1.349–6.619, *p* = 0.007);
- Mayo index < 10 points (COR = 0.645, 95% CI = 0.517–0.804, *p* < 0.001 AOR = 0.631, 95% CI = 0.492–0.809, *p* < 0.001).

It was revealed that gender, the lesion extent, heredity, smoking status, extra-intestinal manifestations, the administration of topical GCS in the anamnesis are not associated with the SD.

When assessing the risk of SR(Table3), we have found significance with Mayo's index of ⩾ 10 points. The threshold value of the indicator was obtained by constructing the ROC curve at the cut-off point, which corresponded to the highest value of Youden's index. It was revealed that the duration of systemic steroid therapy was < 4 weeks. It is a risk factor for the SR development. However, this is due to the fact that 48.2% (*n* = 27) of patients with SR were operated on, and therefore the therapy of GCS was terminated prematurely.

Other clinical and demographic factors, as well as the schemes of systemic steroid therapy, did not significantly affect the SR development.

In the regression analysis of laboratory parameters (Table 4) it was found that the level of albumin, as well as the level of inflammatory markers (CRP and fibrinogen) significantly affect the SR development.

Using the construction of ROC curves, threshold values of laboratory parameters were identified:

albumin (< 37.1 g/l), CRP (⩾ 47.1 mg/l), fibrinogen (⩾ 3.4 g/l).

During the multivariate analysis, the following predictors and risk factors for the SR were identified:

– Mayo's index ⩾ 10 points (COR = 3.391, 95% CI = 1.556–7.389, p = 0.002 AOR = 2.573, 95% CI = 1.094–6.050, p = 0.030);
– albumin < 37.1 g/l (COR = 5.320, 95% CI = 1.904–14.865, p = 0.001 AOR = 4.571, 95% CI = 1.567–13.330, p = 0.005);
– CRP ⩾ 47.1 mg/l (COR = 4.014, 95% CI = 1.800–8.953, p = 0.001 AOR = 2.641, 95% CI = 1.102–6.328, p = 0.029).

DISCUSSION

Predictors of aggressive UC and risk of colectomy are actively discussed by Russian and foreign authors [5,20–24]. In our work, we did not aim to evaluate the predictors of colectomy in UC, focusing on the predictors and risk factors for SD and SR.

The data we obtained on the risks of SD at the onset of the disease at the age of < 30 years correlate with the results of Reinisch W., who demonstrated that the age of ⩽ 40 years at the time of diagnosis is associated with a more severe disease and short periods of remission [20].

Inadequate courses of systemic steroid therapy significantly affect the SD development. The Russian clinical guidelines for the diagnosis and treatment of UC [5] strictly regulate the doses of prednisolone and the duration of courses of systemic steroid therapy. In case of UC recurrence, requiring repeated administration of GCS for a year or less, it is recommended to prescribe immunosuppressants (azathioprine or mercaptopurine) simultaneously with GCS. According to our data, conducting ⩾ 2 courses of GCS during the year with high reliability affects the SD development, which confirms the need for immunosuppressive therapy during the second course of GCS during the year. In case of UC exacerbation after two or more courses of systemic GCS carried out during the year, it is necessary to consider the administration of biological or targeted therapy. The initial administration of low doses of prednisolone (< 60 mg), as well as the subsequent escalation of the dose, contribute to the SD formation, and therefore it is advisable to recommend hospitalization to patients not only with a severe attack of UC, but also with a moderate attack to a hospital for the administration of an adequate dose of prednisolone in accordance with clinical recommendations.

Laboratory indicators (albumin and CRP levels), as well as the clinical and endoscopic Mayo's index can be routinely used in clinical practice to assess the risk of SR, allowing the doctor to be wary of the ineffectiveness of steroid therapy from the first days of treatment. It is advisable for this category of patients from the first days of admission to do a specific tests (Diaskin's — test, quantiferon test, T-SPOT) to exclude tuberculosis infection in order to timely prescribe genetically engineered biological and targeted therapy for the SR development.

CONCLUSION

In the era of personalized medicine, it is rational to predict an individual response to GCS. Predictors of a high risk of SD and SR in patients with ulcerative colitis have been identified, which can be used in clinical work. In this category of patients, it is advisable to consider the early administration of genetically engineered biological and targeted therapy, avoiding repeated use of GCS.

AUTHORS CONTRIBUTION

Concept and design of the study: *Irina A. Tishaeva, Oleg V. Knyazev*
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