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Intravenous corticosteroids in moderately active ulcerative colitis refractory to oral corticosteroids

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Abstract

Background: Oral corticosteroids remain the mainstay of treatment for moderately active ulcerative colitis (UC). In patients who fail to respond to oral corticosteroids, attempting the intravenous route before starting rescue therapies is an alternative, although no evidence supports this strategy.
Aim: To evaluate clinical outcomes after a course of intravenous corticosteroids for moderate attacks of UC according to the failed oral corticosteroids or not.
Methods: All episodes of active UC admitted to three university hospitals between January 2005 and December 2011 were identified and retrospectively reviewed. Only moderately active episodes treated with intravenous corticosteroids were included. Treatment outcome was compared between episodes which failed to outpatient oral corticosteroids for the index flare and those directly treated by intravenous corticosteroids.
Results: 110 episodes were included, 45% of which failed to outpatient oral corticosteroids (median dose 60 mg/day [IQR 50–60], median length of course 10 days [IQR 7–17]). Initial response (defined as mild severity or inactive disease at day 7 after starting intravenous corticosteroids, without rescue therapy) was achieved in 75%, with no between-group differences (78% vs. 75%). After a median follow-up of 12 months (IQR 4–24), 35% of the initial responders developed steroid-dependency and up to 13% required colectomy. Unsuccessful response to oral corticosteroids was the only factor associated with steroid-dependency in the long term (P = 0.001).

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Conclusions: Intravenous corticosteroids are efficient for inducing remission in moderately active UC unresponsive to oral corticosteroids, but almost half of these patients develop early steroid-dependency. Alternative therapeutic strategies should be assessed in this clinical setting.

1. Introduction

Ulcerative colitis (UC) is a chronic inflammatory condition of the colon that usually follows a relapsing–remitting course [1]. Within 5 years of diagnosis, most patients will have experienced several relapses regardless of disease extent, as reported in the recent population-based studies assessing the natural history of the disease [2]. Medical therapy of acute UC flares depends mainly on their severity. Thus, mild flares are usually managed with oral and/or topical aminosalicylates, whereas intravenous corticosteroids (CSs) remain as the first-line therapy for severe attacks [3]. To optimize clinical outcomes in these patients, response to any treatment should be assessed in a timely manner; in this sense, it is widely accepted that response to aminosalicylates should be evaluated in 2 to 4 weeks, whereas response to intravenous CS in severe attacks should be assessed in 3 to 5 days [4].

The approach to moderate flares is not so clear. Although oral aminosalicylates are also considered as the treatment of choice in this clinical setting [3], many patients use these agents for maintenance treatment, and dose escalation in this situation has been poorly evaluated. An accepted alternative in these patients and in those not responding to oral aminosalicylates is oral CS therapy [3]. The use of oral CS in moderately active UC is supported by the early British trials [5–7], carried out in small samples and more than 60 years ago. We now know that almost half of UC patients will require at least one course of CS in their lives (mainly for moderate flares), and that this has not changed in the last six decades [2]. We also know that CS requirements do not depend on the time from disease diagnosis or disease extent, and that the yearly proportion of patients treated with CS remains stable over time in a given UC cohort [8]. Unlike in mild and severe flares, there is no established timing for the assessment of response to oral CS [4], although prospective data suggest that it can be predicted as simply and early as in severe flares [9].

Despite the widespread use of oral CS in clinical practice, few RCTs including conventional oral CS for the treatment of moderately active UC have been performed [10,11]. These trials reported clinical remission rates of 60–65% after 4 weeks of treatment. Therefore, an appreciable proportion of patients treated with oral CS will require "rescue" therapy, a clinical scenario where no specific RCTs have been done to date. Current recommendations advise initiation of anti-TNF agents, although tacrolimus or intravenous CSs are also considered potential alternatives to colectomy [3]. The aim of our study was to evaluate the utility of intravenous CS in patients who failed to respond to oral CS for a moderate flare of UC.

2. Materials and methods

Between January 2005 and December 2011, all patients admitted for UC flares who received intravenous corticosteroids (CSs) were identified from the electronic records of three referral university hospitals. Patients were only included in the study if they had moderately active UC according to the Montreal classification of severity [12] at the time intravenous CSs were started, and patients with ulcerative proctitis were excluded. Episodes of patients with more than one episode were only included if they did not meet steroid-dependency criteria (defined by a clinical relapse during corticosteroid therapy or within the first 3 months after corticosteroid discontinuation). Patients were grouped according to whether they had received oral prednisone for the same flare before admission. For IV therapy, methyl-prednisolone at a dose of 1 mg/kg/day was used in the three centres. In the case of clinical response, CS tapering was started at discharge and the dose was reduced by 10 mg weekly until reaching 20 mg, and by 5 mg weekly thereafter until complete withdrawal.

Relevant information regarding several variables was collected, including epidemiological (sex, age, smoking habits, family history of IBD), clinical (time from UC diagnosis to index flare, previous CS courses, UC extent, failed oral CS for the index flare, extraintestinal manifestations, steroid dependency criteria, and/or colectomy during follow-up), biological (C-reactive protein at baseline, 3, and 7 days, duration of follow-up), and treatment (previous maintenance therapy, disease severity at day 3 and 7 of intravenous CS, need for rescue therapy during the index flare, CS-related major side effects [new onset or worsening of pre-existing arterial hypertension, hyperglycaemia requiring insulin therapy, or infections]) parameters. For the purposes of this study, we arbitrarily defined initial efficacy as mild activity or inactive disease according to the Montreal severity score, with no need for rescue treatment at day 7 after starting intravenous CS. Patients were followed up until colectomy, death, or date of data collection (September 2012), and the occurrence of steroid-dependency criteria or colectomy during follow-up was also recorded.

For each episode, every outcome was addressed until the end of follow-up, death or the occurrence of a new flare requiring corticosteroids.

The study was approved by the Institutional Review Board of the coordinating centre (Hospital Universitari Germans Trias i Pujol).

All statistical analyses were performed using SPSS12.0 for Windows (SPSS Inc., Chicago, IL, USA). Data are expressed as median and interquartile range (IQR) or absolute and relative frequencies. Chi-square was used to compare dichotomous variables. For continuous variables, Student's *t*-test was used provided that values showed a normal distribution and variances were homogenous. Otherwise, Mann–Whitney U-test was used. Predictive factors of initial efficacy, colectomy, and steroid-dependency were initially univariately screened with the above-mentioned tests. Those variables achieving a P-value ≤ 0.1, as well as those believed to be clinically meaningful, were included in