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Topical therapy is underused in patients with ulcerative colitis☆

F. Seibold[a,f,*], N. Fournier[b], C. Beglinger[c], C. Mottet[d], V. Pittet[b], G. Rogler[e], and the Swiss IBD cohort study group

[a] *Gastroenterologie, Spital Netz Bern Tiefenau, Bern, Switzerland*
[b] *Institute of Social & Preventive Medicine, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland*
[c] *Gastroenterologie, Universitätsspital Basel, Basel, Switzerland*
[d] *Gastroenterologie, Hôpital neuchâtelois, Neuchâtel, Switzerland*
[e] *Gastroenterologie und Hepatologie, Universitätsspital Zürich, Zürich, Switzerland*
[f] *Inselspital University of Bern, Gastroenterology Bern, Switzerland*

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Abstract

The availability of new topical preparations for the treatment of left sided ulcerative colitis offers a therapy optimization for many patients. Rectal application of steroids and 5-aminosalicylic acid (5-ASA) is associated with fewer side effects and has a higher therapeutic efficacy in left-sided colitis as compared to a systemic therapy. Therefore, we were interested in the use of topical therapy in patients with ulcerative colitis. The key question was whether topical treatment is more frequently used than oral therapy in patients with proctitis and left sided colitis. Data of 800 patients of the Swiss IBD cohort study were analyzed.

Sixteen percent of patients of the cohort had proctitis, 21% proctosigmoiditis and 41% pancolitis. Topical therapy with 5-ASA or corticosteroids was given in 26% of patients with proctitis, a combined systemic and topical treatment was given in 13%, whereas systemic treatment with 5-ASA without topical treatment was given in 29%. Proportion of topical drug use decreased with respect to disease extension from 39% for proctitis to 13.1% for pancolitis (P = 0.001). Patients with severe colitis received a significantly higher dose of topical 5-ASA than patients in remission.

Abbreviation: SIBDCS, Swiss Inflammatory Bowel Disease Cohort study.

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* Corresponding author at: Gastroenterologie, Spital Netz Bern Tiefenau, Tiefenaustrasse 112, 3004 Bern, Switzerland. Tel.: +41 31 308 89 40; fax: +41 31 308 89 43.
E-mail address: frank.seibold@spitalnetzbern.ch (F. Seibold).

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Side effects of topical or systemic 5-ASA or budesonide treatment were less frequently seen compared to other medications. Topical treatment was frequently stopped over time. The quality of life was the same in patients with limited disease compared to patients with pancolitis.
Topical treatment in proctitis patients was underused in Switzerland. Since topical treatment is safe and effective it should be used to a larger extend.

1. Introduction

Ulcerative colitis (UC) is a chronic relapsing inflammatory disorder of the colon and besides Crohn's disease (CD) one of the two major forms of inflammatory bowel disease (IBD). Its incidence in Europe is estimated to be around 5 to 25 new patients per 100,000 inhabitants per year. The etiology of UC remains unclear and subsequently medical therapies are not available that may completely cure the disease. The clinical presentation of UC is characterized by abdominal pain, diarrhea with or without hematochezia and mucosal ulcerations. UC is limited to the mucosa of the large intestine. It always involves the rectum and shows variable extension to the left side or entire colon. 70% of the UC patients in population based studies exhibit only a proctitis/procto-sigmoiditis or left sided colitis. Only 30% will have extended disease.[1] This may be different in a cohort such as the Swiss IBD cohort study (SIBDCS, 28) which includes 2/3 of hospital treated patients having more severe of extensive disease.

In addition to the varying extent of the disease there is a wide variation in the severity of UC. Clinically mild disease is associated with less than four bowel movements per day, with or without bloody stools but without systemic manifestations. Blood tests in patients with mild disease are usually normal. Moderate disease has been defined as more than four bowel movements per day with minor systemic manifestations. Severe disease description is attributed to patients with more than six bowel movements a day, fecal blood loss and systemic signs of inflammation. Classifications for disease severity show minor differences, however, the criteria for the discrimination of mild, moderate and severe disease remain more or less the same.

The basic treatment in mild to moderate UC is 5-aminosalicylic acid (5-ASA; mesalazine or mesalamine) irrespective of the disease localization. However, in patients with proctitis or left sided colitis topical application of 5-ASA as suppository, enema or foam preparation is more effective as compared to systemic treatment.[2] Topically administrated steroids are superior to placebo in this situation, however, inferior if compared to topical 5-ASA.[3,4] Therefore the treatment of choice in mild to moderate left-sided colitis is 5-ASA foams or enemas.[5] During acute flares of the disease enemas are frequently less well tolerated due to their volume of up to 100 ml than suppositories.[6] As usually the rectum is affected by the most severe inflammation while containing the highest number of sensory nerves it is easily understandable that high volume enemas cause discomfort and urgency. Foam preparations are usually better tolerated and accepted by patients with acute flares of left sided colitis.[7] Mesalazin suppositories seem to be well tolerated in patients with proctitis and recommended by the ECCO guidelines as first line treatment.[8]

Compliance and patient acceptance are essential for the success of a rectal therapy.[9–12] In general patients well accept to perform topical therapy if explained properly.[13,14] It is not the case that a topical therapy per se is associated with lower adherence and compliance. Only in very severe disease application of topical therapy may cause pain and discomfort. Therefore, topical therapy may be paused during severe disease flares.

As mentioned foam preparations are better tolerated as compared to enemas.[15–18] 5-ASA foam preparations have a similar distribution pattern as compared to enemas.[19] 5-ASA suppositories in a dosage of 1 g/day are the preferred therapy of mild to moderate proctitis.[10] A meta-analysis of 11 studies showed a median remission rate of 67% for rectal 5-ASA (as compared with 7 to 11% for placebo.[5] A study by Eliakim and co-workers with a low volume rectal 5-ASA foam preparation showed remission rates of 78% in patients with mainly proctitis.[20]

Topical steroids should be used for patients that are intolerant to 5-ASA. However, an additive therapy of topical 5-ASA and steroid may also be beneficial.[21]

In moderate active distal colitis topical 5-ASA therapy in combination with oral 5-ASA therapy has proven to be highly effective (88% response after 6 weeks).[22] A meta-analysis of 33 studies showed that topical 5-ASA is more effective as compared to topical conventional steroids or budesonide.[15,3,23] Remission also can be maintained by topical treatment of at least two years duration.[9–11,24,25] For maintenance 3 g of 5-ASA total per week is recommended. A topical therapy in distal UC has several advantages. The majority of patients have a distal disease type.[24,26] Thus a topical therapy should be applied in the majority of patients with UC as the success rate is higher as compared to oral therapy and side effects are fewer. However, there are reports of an underuse of topical therapies despite guideline recommendations.[27]

Given the above mentioned facts we expected a more frequent use of topical 5-ASA use compared to systemic treatment in patients with proctitis.

The aim of this study was to investigate the use of topical and systemic therapies in patients with ulcerative colitis of the SIBDCS.

2. Methods

Data of the Swiss Inflammatory Bowel Disease Cohort study (SIBDCS) were used to perform this study. The cohort goals and methodology are described elsewhere.[28] The aim of the present study was the characterization of the use of topical versus oral therapies in UC patients within IBD patients included in the SIBDCS. We first performed a descriptive