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The effect of third-party reporting on adoption of evidence-based mesalazine regimens in ulcerative colitis: An observational study

Wolfgang Kruis [a,*], Ludger Leifeld [a], Julia Morgenstern [a], Roland Pfützer [a], Birgitta Reimers [b], Sabine Ceplis-Kastner [b]
the CARE study group [1]

[a] *Evangelisches Krankenhaus Kalk, Innere Medizin, Köln, Germany*
[b] *Ferring Arzneimittel GmbH, Kiel, Germany*

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Abstract

Background and aims: The optimal mesalazine dosing strategy for ulcerative colitis (UC) continues to evolve. The current study aimed to explore whether documenting drug use could prompt changes in prescribing habits.
Methods: In a multicenter, prospective, observational study, outpatients with active or quiescent UC were enrolled if they were receiving, or were planned to receive, sustained release mesalazine microgranules (Pentasa®). Clinical and prescribing data were collected at study entry, after 2 and 8 weeks. Physician-reported influences on prescribing decisions were recorded at study entry.
Results: 360 patients were analyzed (203 active UC, 157 remission). Prior to study entry, the range of oral mesalazine doses was 0.50–6.00 g/day in active UC patients, and 0.50–4.00 g/day for patients in remission. These changed to 1.50–5.00 g/day and 1.00–4.00 g/day, respectively, at study entry with little change thereafter. Use of a single daily mesalazine dose increased from 16.7% to 58.0% of active cases during the study, and from 5.9% to 46.8% in remission cases. Gastroenterologists reported that their basis for prescription decision-making was most frequently medical experience (80.8%), followed by guidelines (67.2%), further education or colleagues' recommendations (50.0%) and current study results (20.0%).

Abbreviations ECCO, European Crohn's and Colitis Organisation; UC, ulcerative colitis; UC-DAI, Ulcerative Colitic Disease Activity Index.

* Corresponding author at: Evangelisches Krankenhaus Kalk, Buchforststrasse 2, D-51103, Cologne, Germany. Tel.: +49 221 8289 5289; fax: +49 221 8289 5291.
E-mail address: kruis@evkk.de (W. Kruis).

[1] See Appendix A.

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Conclusion: In this analysis of mesalazine dosing in routine clinical practice, there was an improvement in adherence to European Crohn's and Colitis Organisation (ECCO) guidelines and in use of once-daily dosing, consistent with recent trial results, following documentation of dosing regimens. Written reporting of drug dosing schedules should be considered fundamental for chronic, complex diseases such as UC.

1. Introduction

Ulcerative colitis (UC) is a chronic condition that necessitates extensive medical care and long-term medication. Although treatment guidelines for UC exist,[1–3] evidence regarding the extent to which these guidelines are applied in clinical practice is mixed.[4,5]

Treatment of UC with the aminosalicylate mesalazine is a long-established practice, but the optimal dosing strategy for its use has continued to evolve. The recent European Crohn's and Colitis Organisation (ECCO) consensus on the management of UC recommended that active left-sided UC of mild to moderate severity should first be treated with a combination of oral and topical mesalazine at a minimum dose of 2.00 g/day, which is considered more effective than topical or oral treatment alone.[3] The ECCO consensus recommended mesalazine suppositories (1.00 g/day) with oral mesalazine or steroids for mild-to-moderately active proctitis, and a combination oral mesalazine (>2.00 g/day) with topical mesalazine for mild-to-moderate active extensive UC. For patients in remission, the consensus advises a minimum mesalazine dose of 1.00 g/day for oral therapy or 3.0 g/week for rectal therapy.[3] In terms of dosing frequency, use of once-daily dosing of mesalazine has been explored with the aim of improving adherence and thus avoiding impaired therapeutic efficacy. A series of controlled trials in active UC[6–9] and quiescent UC[10–16] has demonstrated that once-daily dosing of mesalazine offers at least equivalent efficacy and safety to conventional multiple dosing regimens.[17] The systemic pharmacokinetic and pharmacodynamic characteristics of mesalazine are less relevant than for other drugs since it acts topically i.e. through luminal contact between mesalazine and the mucosal cell. A model comparing the intestinal concentrations of mesalazine after single and multiple dosing under different physiological conditions found that the predicted maximum and average concentrations in the total colon and in individual colonic segments differed by less than 10% between dosing regimens.[18] Importantly, once-daily mesalazine does not accumulate in plasma over time during ongoing treatment.[19] Thus, the clinical imperative for once-daily dosing is not contraindicated by pharmacokinetic or pharmacodynamic findings. Shortly prior to the current study, or during it, three randomized trials[8,9,20] and several review articles[21–25] were published supporting the use of once-daily mesalazine versus multiple daily doses in UC.

In the current study, the pattern of mesalazine prescribing in active and quiescent UC was selected as the basis for assessing a strategy to improve adherence to guidelines and introduction of evidence-based treatment into daily clinical practice. Mesalazine prescribing was documented over an eight-week observation period for each patient to determine how the drug was being prescribed routinely compared to recent guidelines and trial results, and to explore whether the simple process of documenting drug use could prompt changes in prescribing habits.

2. Methods

2.1. Study design and conduct

CARE (Ulcerative **C**olitis—**A**cute therapy and **RE**mission maintenance) was a multicenter, prospective, observational study of outpatients at 107 private gastroenterology practices in Germany undertaken between October 2007 and May 2008. The primary objective was to describe prescription behavior for mesalazine in outpatients with active UC or UC in remission within routine clinical practice. The secondary objective was to investigate whether basis recording of prescriptions could influence prescribing habits.

The study was reviewed by the German Federal Institute for Medicine and Medicinal Products (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM: 22-A-12510-24302/97) and conducted as an observational study according to relevant national guidelines (§ 67 Abs 6 AMG Arzneimittelgesetz). The ethics committee of the Landesärztekammer Schleswig-Holstein decided that no further ethical evaluation was necessary. Patients provided written informed consent.

2.2. Patients

All patients older than 18 years with a confirmed diagnosis of active UC or UC in remission based on typical clinical, endoscopical and histological findings were eligible for inclusion if they were currently receiving, or were planned to receive, treatment with sustained release mesalazine microgranules (Pentasa®, Ferring Arzneimittel GmbH, Kiel, Germany). Candidates were excluded if they had known intolerability to mesalazine or if full communication with the patient was not possible.

2.3. Evaluation

All patients were followed for 8 weeks. At study entry, the following data were recorded: patient demographics, date of first symptoms and first diagnosis of UC, current status (acute/remission), details of current acute flare-up (start date, type and dose of medication during remission prior to current flare-up) or current remission period (start data, type and dose of medication at start of remission), date of last endoscopy and findings (location of UC), abbreviated