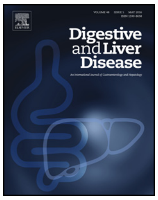
Digestive and Liver Disease 48 (2016) 592–600

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld



Alimentary Tract

Burden of disease and patient-reported outcomes in patients with moderate to severe ulcerative colitis in the last 12 months – Multicenter European cohort study

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ARTICLE INFO

Article history:
Received 30 September 2015
Accepted 18 January 2016
Available online 29 January 2016

Keywords:
Control of disease
Health related quality of life
Inflammatory bowel disease
Unmet needs

ABSTRACT

Background: Treatment of ulcerative colitis (UC) is aimed at maintaining corticosteroid-free remission and improving quality of life (QoL).
Aim: Assess patients' perception of disease burden and unmet clinical needs in moderate/severe UC patients.
Methods: Adults surgery-free conventionally treated patients with Mayo score ≥6 were enrolled in an observational, cross-sectional, retrospective study in 11 European countries. Disease control was defined as Mayo score ≤2 with no sub-score >1. No corticosteroid was used the previous two months. Unmet clinical needs were defined as: non-controlled disease, self-perception of 'moderate'/'severe' disease, and dissatisfaction with treatments. Disease burden on QoL and work productivity were assessed (EuroQol-5D-5L, Short Inflammatory Bowel Disease Questionnaire (SIBDQ) and Work Productivity and Activity Impairment (WPAI) in UC questionnaire).
Results: UC patients ($n = 253$) with mean Mayo score at enrolment of 4.9, 44.3% of patients had Mayo score ≥6. Main treatment was 5-ASA (75%). Overall, 25% met the composite endpoint for unmet clinical needs.

Mean (SD) questionnaire scores were: EQ-5D-5L-VAS, 71 (19.1), EQ-5D-5L utility, 0.77 (0.19), SIBDQ, 4.8 (1.3), and WPAI, 26% (32%).
Conclusions: Patients with moderate/severe UC in the last 12 months treated with conventional therapies felt that their disease was not controlled and 25% reported unmet clinical needs. QoL and work productivity were seriously impaired.

1. Introduction

Ulcerative colitis (UC) is a lifelong inflammatory colonic disease that runs a relapsing-remitting or chronically active course [1,2]. The incidence of UC in northern Europe is estimated to be 24.3/100,000 person-years [3]. Moderate to severe UC is

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http://dx.doi.org/10.1016/j.dld.2016.01.011

associated with increased morbidity, exerts a profound impact on patients' health related quality of life (HRQoL), and is associated with severe impairment of patients' social and professional activities, and higher rates of sick leave and unemployment compared to the general population [4–7]. As there is no definitive therapy, the goals are to induce and maintain remission without corticosteroids; this prevents complications and disability, maintains a good HRQoL, and relieves the burden of disease on healthcare resources by reducing the need for hospitalizations and surgeries, which are the main drivers of increased direct costs [8–10].

Despite the heavy burden of UC on patients and their families, few studies have assessed patients' experiences and opinions [11,12], and to date no study has been conducted to identify unmet clinical and therapeutic needs from the patient perspective. Furthermore, there is no data available evaluating the correlation between patient self-perceived disease severity and clinical variables.

This study was conducted in surgery-free patients with moderate to severe UC within the last 12 months treated with conventional therapies, and describes clinical characteristics, treatment patterns and the impact of disease burden on patients' HRQoL, daily activities and work productivity, as well as to explore unmet clinical needs.

2. Methods

2.1. Study design

The study was designed as an observational, multinational, multi-center, retrospective chart review including a cross-sectional collection of patient reported outcomes (PROs) and perceived disease severity. The maximum retrospective review period was 24 months.

The study was carried out in 39 centers from 11 European countries: Belgium, France, Germany, Greece, Italy, Spain, Sweden, Switzerland, The Netherlands, Turkey, and the United Kingdom, under the International Conference of Harmonization ethical standards, and was notified to or approved by the Ethics Committees of participating centers in accordance with local and national regulations.

Investigators were physicians involved in the management and treatment of UC (gastroenterologists, internists or GPs). Patients who consecutively attended a routine office visit and met the study selection criteria were included.

After giving written informed consent, patients completed a set of questionnaires to measure HRQoL, work productivity, treatment satisfaction and patient's perceived disease activity. Demographics and clinical data were collected at inclusion and retrospectively for a period of 12 months from the patients' medical charts. Healthcare resources, such as physician and/or emergency room visits, as well as corticosteroid prescription, were retrospectively collected for up to 24 months, if available.

2.2. Study population

Enrolled patients were ≥18 years and diagnosed with moderate to severe UC (Mayo score ≥6) at inclusion or within the previous 12 months. Core study data from medical charts had to be available at least for the previous 12 months and patients had to be able to self-complete study questionnaires. Patients were excluded if ever received biologic therapies, had any change in UC treatment medications within the 2 weeks prior to inclusion, had previous colectomy or ileo-anal J-pouch reconstruction, were pregnant or breast-feeding and participating in a clinical trial within the last 3 months of inclusion.

2.3. Study measures

Disease remission was defined as total Mayo score ≤2, with no individual sub-score >1 [13]. For patients with no endoscopy available, remission was defined as a partial Mayo score ≤2, with no individual sub-score >1. Patients in remission not receiving corticosteroids during the previous two months were defined as controlled. The Mayo scores range from 0 (best) to 12 (worst) and a score ≥6 indicates moderate to severe UC.

PROs were collected using four validated questionnaires: EQ-5D-5L [14,15], Short Inflammatory Bowel Disease Questionnaire (SIBDQ) [9], Treatment Satisfaction Questionnaire for Medication (TSQM) [16] and the Work Productivity and Activity Impairment in Ulcerative Colitis (WPAI:UC). The EQ-5D-5L questionnaire [14] is a generic questionnaire that measures HRQoL using a descriptive system with five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) with five choices of answer each, and a visual analogue scale (VAS) ranging from 0 (worst) to 100 (best) [15].

The SIBDQ is a validated tool for grading HRQoL of patients with inflammatory bowel diseases [9], with scores ranging from 10 (poor HRQoL) to 70 (optimum HRQoL); it was used to assess patients' HRQOL over the previous two weeks.

The TSQM [16] assesses patient's satisfaction with medication, providing scores on four scales (side effects, effectiveness, convenience and global satisfaction). In this study only items related to the effectiveness score were calculated, because effectiveness of treatment was perceived as the key for the study objectives and to avoid overloading patients with too many questionnaires. The composite score was transformed to obtain a score ranging from 0 to 100 (higher scores representing higher satisfaction).

The WPAI:UC questionnaire [17] contains six questions and assesses the impact of UC on work and daily activities during the past seven days. WPAI scores range from 0% to 100% with higher numerical values indicating greater impairment and less productivity.

Patient's perceived disease activity was collected using a set of ad-hoc questions specially designed.

Patients were asked to select perceived disease activity at inclusion as:

- Normal or in remission
- Mild (symptoms are present but not bothersome)
- Moderate (symptoms are bothersome)
- Severe (symptoms interfere with normal activities)

Patients' unmet clinical needs were measured by a composite endpoint defined by the presence of all three of the following criteria: uncontrolled disease, self-perception of 'moderate' or 'severe' disease activity, and dissatisfaction with current treatments (defined as 'TSQM effectiveness composite score' lower than the median values obtained for study patients).

2.4. Statistical analysis

All evaluable patients included in the study were considered for the analysis. Analyses were primarily performed using descriptive statistics. Continuous variables were described in terms of number of patients with valid/missing observations, mean, standard deviation (SD), median, minimum and maximum. Categorical variables were described by frequencies and 95% confidence intervals (CI) and related percentages per class level.

Sociodemographics, clinical variables and HRQoL were reported by disease control. HRQoL and productivity loss were stratified in terms of patients' perception of disease activity. An $\alpha = 0.05$ was applied in statistical tests. Continuous variables were assessed