

Tolerability of Bowel Preparation and Colonoscopy in IBD Patients: Results From a Prospective, Single-Center, Case–Control Study

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Background: Endoscopy plays a fundamental role in the management of patients with inflammatory bowel disease (IBD). The aim of this study was to prospectively evaluate the tolerability and efficacy of bowel preparation and colonoscopy in ulcerative colitis (UC) and Crohn's disease (CD) patients compared to subjects participating in a colorectal cancer population screening program.

Methods: Consecutive enrolment of CD and UC patients and screening subjects (SS) undergoing colonoscopy. Bowel preparation was done by split dose of 2 L PEG-ELS + simethicone. We recorded endoscopic, clinical, and demographic features; cleanliness rating using the Boston Bowel Preparation Scale (BBPS); and sedation doses. Bowel-preparation tolerability, discomfort, and pain during colonoscopy were assessed using a Visual Analogue Scale from 0 to 100 mm.

Results: Sixty-three UC (mean age 49.9 ± 14.9 years), 63 CD (mean age 44.0 ± 14.0 years), and 63 SS (mean age 59.9 ± 6.3 years) patients were enrolled. Bowel preparation was similarly tolerated in UC, CD, and SS ($P = 0.397$). A complete colonoscopy was similarly performed in UC (59/63, 93.7%), CD (58/63, 92.1%), and SS (60/63, 95.2%) ($P = 0.364$). The BBPS did not show significant differences between UC (6.2 ± 1.6), CD (6.1 ± 1.3), and SS (6.2 ± 1.4) ($P = 0.824$). The need to increase sedation doses was significantly higher in CD (24/63, 38.1%) and UC (16/63, 25.4%) than in SS (4/63, 6.3%) ($P < 0.0001$).

Conclusions: Bowel preparation is equally tolerated and efficacious in IBD patients and in healthy SS. In IBD, higher sedation doses are needed to guarantee an equally tolerated colonoscopy.

Lay Summary

Bowel preparation, done by split dose of 2 L, was equally tolerated and efficacious in Crohn's disease and ulcerative colitis patients and in healthy subjects undergoing colonoscopy. In IBD patients, higher sedation doses are needed to guarantee an equally tolerated colonoscopy.

Key Words: Crohn's disease, ulcerative colitis, endoscopy, sedation, bowel preparation

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Data Availability: The data that support the findings of this study are not public; they are available from the corresponding author, upon reasonable request.

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INTRODUCTION

Endoscopy plays a fundamental role in the management of patients with inflammatory bowel disease (IBD). Ileocolonoscopy with biopsies is essential for IBD diagnosis, colorectal cancer (CCR) surveillance and evaluation of endoscopic activity, postsurgical recurrence of Crohn's disease (CD), and endoscopic response to treatment.^{1,2} In particular, mucosal healing (MH) represents a treatment goal since it is associated with prolonged remission times, lower complication rates, and reduced hospitalization and surgery.^{3,4}

Considering the multiple indications for colonoscopy and an incidence peak that occurs at a young age, IBD patients will undergo a high number of endoscopic procedures during their lifetime. Endoscopy is perceived as useful by IBD patients but, mainly because of bowel preparation, is among the less-appreciated procedures.^{5,6} Poor tolerability of intestinal preparations represents the main factor in patients failing to adhere to recommended surveillance in long-standing IBD.⁷

Adequate bowel cleanliness is fundamental for a high-quality colonoscopy⁸ and even more so in IBD patients, especially in case of surveillance for dysplasia.⁹

IBD patients experience more pain and discomfort than subjects undergoing colonoscopy for other indications.^{6, 10} Moreover, IBD patients are young, with high levels of preprocedural anxiety and have already undergone a high number of previous colonoscopies: these characteristics are known risk factors for intolerance to colonoscopy.¹¹⁻¹³

However, despite the relevance of these multiple aspects connected to colonoscopy in patients with IBD, there is only a small amount of low-quality available data.¹⁴

The aims of this prospective study were to evaluate the acceptability and the adequacy of bowel preparation and the tolerability of colonoscopy in patients with a diagnosis of ulcerative colitis (UC) or CD and in subjects undergoing screening colonoscopies for colorectal cancer prevention.

METHODS

Population

We consecutively enrolled patients with UC or CD and subjects undergoing colonoscopy at the Rho Hospital Gastroenterology Unit between August 2017 and August 2019. As controls, we enrolled screening subjects (SS) who underwent colonoscopy as part of the regional CCR screening program.

For the IBD patients, we considered data on diagnosis, extension/localization of disease according to the Montreal classification,¹⁵ clinical activity (according to partial Mayo score for UC¹⁶ and Harvey-Bradshaw Index for CD¹⁷), previous surgery for IBD, and ongoing therapy. This information was already included in the clinic notes for each patient by the respective gastroenterologists.

Procedure

All patients enrolled received the same split-dose low-volume bowel preparation (2 L polyethylene glycol + simethicone + electrolytes).

All endoscopic examinations were performed by the same experienced endoscopist with the same model of colonoscope, using a combination of intravenous midazolam and fentanyl at a starting dose of 3 mg and 50 µg, respectively.

We used specifically designed questionnaires to collect data on the tolerability of the bowel preparation and endoscopic procedure; they were administered by a blinded endoscopy nurse. Within 1 hour before the procedure, subjects were asked to fill in a questionnaire to evaluate bowel preparation tolerability; immediately after the procedure, when woken up, they were asked to complete the questionnaire to assess the tolerability of the endoscopic procedure. Bowel preparation tolerability, abdominal pain, and discomfort experienced during colonoscopy, and overall endoscopic procedure tolerability

was measured using a Visual Analogue Scale (VAS) from 0 to 100 mm. VAS was recorded by the same endoscopy nurse trained by a single education module, to provide objective, consistent evaluation across all CD/UC/SS subjects.

For each colonoscopy, we recorded indication, examination completion (defined as terminal ileum intubation), disease activity, using a Mayo endoscopic score for UC¹⁶ and Simple Endoscopic Score for Crohn's Disease (SES-CD) for CD,¹⁸ adjustment to sedation dose, and the amount of additional midazolam and fentanyl. Quality of bowel preparation was assessed by Boston Bowel Preparation Scale (BBPS)¹⁹: adequate if BBPS BP6, with a minimum of 2 for each segment. Well-tolerated bowel preparation and endoscopic procedure were defined by a VAS > 70 mm.

Statistical Analysis

Supposing that patients with UC and CD have a poor tolerability of bowel preparation and endoscopic examination and considering a statistical test power of 80%, a probability of 0.05 for type I error and assuming a 2-tailed test, we calculated a sample size of 63 subjects for each group to find a difference of about 15% in tolerability (primary outcome of tolerability of bowel preparation and endoscopic procedure using VAS: 70 ± 15 mm vs 60 ± 15).

We reported arithmetic mean and standard deviation as continuous variables and absolute frequency and percentage as discrete variables. Comparisons between groups (UC, CD, and SS) were made using the analysis of variance and Tukey's range test for quantitative variables and the chi-square test for qualitative variables. All tests have to be considered as 2 tailed with statistical significance set at 0.05.

Ethical Considerations

The study was approved by the local ethics committee and then has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

RESULTS

We enrolled 189 patients: 63 with UC (26 women, mean age 49.9 ± 14.9 years), 63 with CD (29 women, mean age 44.0 ± 14.0 years), and 63 subjects undergoing screening colonoscopy (32 women, mean age 59.9 ± 6.3 years). The demographic and clinical features of the enrolled populations are shown in [Table 1](#). Indications to colonoscopy in IBD patients were the following: disease flare in 38/63 CD (60.3%) and 29/63 (46.0%), assessment of MH in 22/63 CD (34.9%) and in 8/63 UC (12.7%), and surveillance in 3/63 CD (4.8%) and in 26/63 UC (41.3%). Endoscopic and clinical activity of IBD patients is shown in [Table 2](#).

Bowel preparation tolerability, measured by VAS, was similar in UC (70.5 ± 18.1 mm), CD (73.1 ± 12.9 mm), and SS

TABLE 1. Demographic and Clinical Features of IBD Population

	CD (n = 63)	UC (n = 63)	SS (n = 63)	P
Women, n (%)	29 (46.0)	26 (41.3)	32 (50.8)	0.563
Mean age \pm SD, years	44.0 \pm 14.0	49.9 \pm 14.9	59.9 \pm 6.3	<0.0001*
Previous abdominal surgery [†] , n (%)	25 (39.7)	2 (3.2)	3 (4.8)	<0.0001
Previous colonoscopies > 3 [‡]	36 (57.1)	34 (54.0)	5 (7.9)	<0.0001
Location				
L1	29 (46.0%)	—	—	—
L2	15 (23.8%)	—	—	—
L3	19 (30.2%)	—	—	—
Perianal	7 (11.1%)	—	—	—
Extension				
E1	—	7 (11.1%)	—	—
E2	—	33 (52.4%)	—	—
E3	—	23 (36.5%)	—	—
Therapies				
Mesalamine	12 (19.0%)	55 (87.3%)	—	—
Thiopurines	11 (17.5%)	9 (14.3%)	—	—
Biologics	23 (36.5%)	14 (22.2%)	—	—
Low-bioavailability steroids	2 (3.2%)	2 (3.2%)	—	—
Systemic steroids	6 (9.5%)	3 (4.8%)	—	—
Topical therapy	1 (1.6%)	14 (22.2%)	—	—

*UC versus CD $P < 0.05$, UC versus SS $P < 0.01$, CD versus SS $P < 0.01$.

[†]in CD: 18 ileo-caecal resection, 3 ileal resection, 2 fistulectomy, 1 ileo-caecal resection + right ovariectomy, 1 ileal resection + prostatectomy; in UC: 1 cystectomy + prostatectomy, 1 nephrectomy; and in SS: 2 hysterectomy, 1 hysteroneussiectiony.

[‡]3 is the median value in CD and UC populations.

TABLE 2. Endoscopic and Clinical Activity of IBD Population

	CD (n = 63)	UC (n = 63)
Clinical activity*		
Remission	44 (69.8%)	32 (50.8%)
Mild	9 (14.3%)	23 (36.5%)
Moderate	10 (15.9%)	7 (11.1%)
Severe	0 (0.0%)	1 (1.6%)
Endoscopic activity [†]		
Remission	24 (38.1%)	23 (36.5%)
Mild	17 (27.0%)	7 (11.1%)
Moderate	17 (27.0%)	18 (28.6)
Severe	5 (7.9%)	15 (23.8%)

*According to partial Mayo score for Ulcerative Colitis¹⁵ and Harvey-Bradshaw Index¹⁶ for Crohn's disease.

[†]According to Mayo score for Ulcerative Colitis¹⁷ and SES-CD for Crohn's disease.¹⁸

(71.9 \pm 13.4 mm) ($P = 0.397$; [Figure 1](#)). With regard to symptoms (headache, insomnia, nausea/vomiting, bloating/abdominal distension, abdominal pain, unpleasant taste in mouth, and feeling of fullness), no statistical difference was observed between UC, CD, and SS groups ([Supplementary Table 1](#)).

No difference was observed in bowel preparation quality between UC (mean BBPS \pm SD 6.2 \pm 1.6), CD (6.1 \pm 1.3), and SS (6.2 \pm 1.4) ($P = 0.940$). Likewise, bowel preparation was adequate with similar rates between UC (53/59, 89.8%), CD (50/58, 86.2%), and SS (55/60, 91.7%) groups ($P = 0.623$; [Figure 2](#)).

Colonoscopy was completed with similar rates between UC (59/63, 93.7%), CD (58/63, 92.1%), and SS (60/63, 95.2%) ($P = 0.766$). We observed a statistical difference between the groups in the number of procedures where an adjusted sedation dose was required: 24/63 (38.1%) in CD, 16/63 (25.4%) in UC, and 4/63 (6.3%) in SS ($P < 0.0001$), with no significant difference between UC and CD ([Figure 2](#)).

The mean dosage of midazolam and fentanyl was statistically different between the 3 groups: 3.43 \pm 0.67 mg and 58.73 \pm 19.13 mcg, respectively in CD patients, 3.31 \pm 0.64 mg and 57.94 \pm 18.42 mcg in UC patients, and 3.06 \pm 0.30 mg and 51.59 \pm 8.84 mcg in SS ([Figure 3](#); overall $P = 0.001$ and $P = 0.027$, respectively), with no statistical difference between UC and CD groups ([Figure 3](#)).

The abdominal discomfort and pain experienced during colonoscopy were similar in patients with UC (34.1 \pm 22.8 mm and 26.9 \pm 24.5 mm, respectively), CD (37.1 \pm 21.8 mm and 28.4 \pm 22.5 mm), and SS (36.9 \pm 20.3 mm and 30.1 \pm 22.3 mm) ($P = 0.530$ and $P = 0.866$, respectively; [Figure 1](#)).

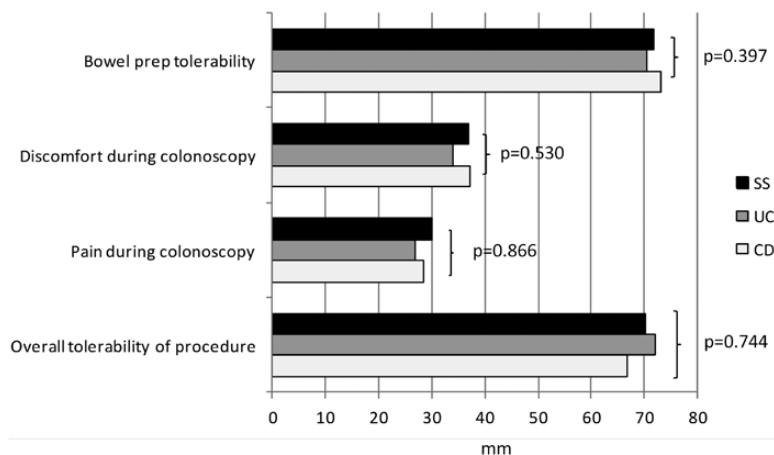
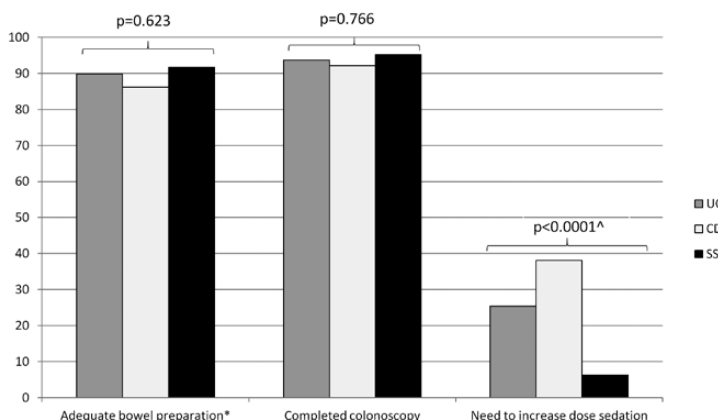


FIGURE 1. Feeling about bowel preparation and colonoscopy assessed by VAS (for bowel preparation tolerability and overall procedure tolerability: from 0 mm [the worst] to 100 mm [the best]; for discomfort and pain during colonoscopy: from 0 mm [none] to 100 [the maximum]).



*Adequate preparation defined as Boston Bowel Preparation Scale ≥ 6 , with each value ≥ 2

^UC vs. SS $p < 0.0007$; CD vs. SS $p < 0.0001$; UC vs. CD $p = 0.180$

FIGURE 2. Quality parameters of colonoscopy.

Overall procedure tolerability (bowel preparation + endoscopic examination) was comparable in patients with UC (72.1 ± 22.2 mm), CD (66.8 ± 23.1 mm), and SS (70.2 ± 19.7 mm) ($P = 0.744$; Figure 1).

No significant associations were found between tolerability of bowel preparation and colonoscopy and clinical and demographic features: sex, disease activity (clinical and endoscopic), previous number of colonoscopies, indications, and previous surgery.

DISCUSSION

Our findings clearly and unequivocally demonstrate that patients with UC and CD do not show statistical differences in terms of tolerability and efficacy of bowel preparation in comparison with healthy subjects. Colonoscopy completion rates and

overall procedure tolerability are similar between UC, CD, and control group. However, it is essential to highlight that in IBD patients, especially those with CD, higher doses of midazolam and fentanyl are needed compared to the control population.

The fact that UC and CD patients satisfactorily tolerate a split-dose low-volume PEG preparation confirms previous observations about better tolerability of low-volume bowel preparations in patients with IBD.^{20,21} Moreover, we found that no demographic and clinical features of IBD patients are associated with a lower efficacy of bowel preparation. This finding rebuts previous observations who indicated disease activity and surgical intestinal resections as factors associated with poor bowel preparation.^{22,23}

The need of higher sedation doses in IBD patients is consistent with other results from previous studies^{6,24} and was not associated with any demographic and clinical features.

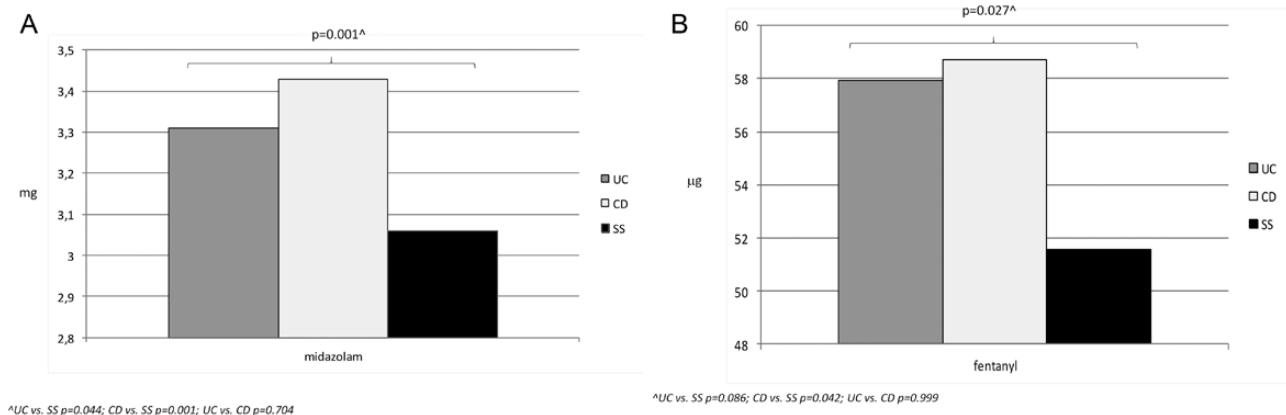


FIGURE 3. Mean total doses of midazolam (a) and fentanyl (b) during colonoscopy.

Patients with IBD will undergo many endoscopies during their lifetime. Furthermore, UC and CD are chronic diseases characterized, even during remission, by intestinal symptoms, a need for surgery, and strong emotional impact. All these factors contribute to the idea that the overall tolerability of endoscopic procedures in IBD patients is inferior with respect to the general population. This may apply both to bowel preparation (in terms of tolerability and efficacy) and to endoscopic examination (in terms of completion rates and tolerability).

However, although highly relevant, there are very little data on these issues in the literature and, when available, they come mostly from retrospective studies, in which the type of bowel preparation, the outcomes and evaluation methods are not always clearly defined, or do not specifically refer to this group of patients.¹⁴ Moreover, these studies include patients with diagnosis of IBD, without distinguishing between UC and CD that are actually 2 distinct diseases in terms of clinical course, anatomical involvement, and need for surgery.

The limitations of this study are the choice of SS as control population, which did not allow for balanced groups in terms of age, and being a referral center for IBDs which may limit the generalizability of our findings to different clinical contexts. While the assessment questionnaires used in the study are not standardized and validated tools, they were specifically designed in order to obtain solid data. Moreover, we cannot exclude that retrograde and anterograde amnesia caused by procedural sedation could have been impaired the actual perceptions of subjects undergoing colonoscopy. The strengths of this study are the prospective case-control design, the distinction between UC and CD, and all endoscopic examinations carried out by the same endoscopist.

In conclusion, a split-dose low-volume PEG + simethicone bowel preparation is a valid option for patients with UC and CD who need to undergo colonoscopy for any indication. Using higher initial doses of sedation in patients with IBD can be necessary in order to obtain colonoscopy

completion rates and overall procedure tolerability similar to those of the general population.

Future studies could also assess tolerability, safety, and efficacy in IBD patients of the new very low-volume colon preparations, such as NER1006.²⁵ Indeed, they may further improve the acceptability of colonoscopy and then the adherence to endoscopic indications, a critical issue in this peculiar setting.⁷

SUPPLEMENTARY MATERIAL

Supplementary data are available at *Crohn's & Colitis 360* online.

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