

Assessment of pain between sedated and unsedated colonoscopy: Double-blind randomized clinical trial

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Background: Colonoscopy plays a vital role for the diagnosis and treatment of colonic diseases but can be associated with anxiety and discomfort or pain. We tested whether unsedated colonoscopy impacts quality indicators and investigated predictors of pain during colonoscopy. **Materials and Methods:** This randomized controlled trial was performed on candidates for elective colonoscopy at AL Zahra Hospital, Isfahan at 2018–2019. Balanced block randomization was used to allocate 275 cases into two groups. At finally, 124 patients in case and 122 patients in control group enrolled in analysis. Patients in the sedation group received midazolam with/out pethidine before colonoscopy. Pain intensity in rectal examination (PIREX), preprocedural anxiety, pain intensity during colonoscopy, hemodynamics, duration of colonoscopy, polyp detection rate, cecal intubation rate, bloating within 24 h after colonoscopy, and willingness to repeat colonoscopy were assessed and compared between two groups. **Results:** Compared to the group with sedation, cecal intubation time was shorter and bloating was less frequent (7% vs. 16%, $P = 0.02$) in the unsedated group. There was no difference between the two groups regarding polyp detection rate, cecal detection rate, and willingness to repeat colonoscopy. Pain during rectal examination was significantly associated with pain during colonoscopy ($P < 0.001$, 95% confidence interval; 0.5–1.3). **Conclusion:** The assessment of pain intensity during rectal examination may help to identify patients who can benefit from sedation during colonoscopy. Colonoscopy with sedation does not seem to have a negative impact on colonoscopy quality indicators, and may even reduce cecal intubation time and bloating following procedure.

Key words: Analgesia, colonoscopy, endoscopy, sedation

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INTRODUCTION

Colonoscopy is used for diagnostic and therapeutic indications.^[1] Despite all the new inventions, colonoscopy is still the best way for diagnosing gastrointestinal bleeding and its pivotal role for treating colorectal polyps and cancer screening is proven.^[2,3] Colonoscopy can reduce mortality of patients with colonic cancer by 50%.^[4] Colonoscopy is usually operated with sedations. Different medications are used for sedation during colonoscopy including

midazolam, pethidine, and propofol,^[5] with propofol having shorter recovery time.^[6] However, sedation has some risks and disadvantages such as hypotension, respiratory depression, drug allergy and needs time to recovery.^[7-11] Furthermore, colonoscopy without sedation can have some important advantages such as reducing load of colorectal cancer screening and it is beneficial to lower the overall cost to patients and health-care facilities.^[5] Due to the complications of sedation and its extra costs, whether it is acceptable to do colonoscopy without sedation is yet under debate. Also, factors that can predict pain during

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unsedated colonoscopy is not fully investigated which can provide information on candidate for unsedated colonoscopy. Limited studies have examined effects of sedation on quality of colonoscopy. For instance, study by Iqbal *et al.* showed that sedation does not affect polyp detection rate or complete performance of colonoscopy.^[12] Some studies have examined the factors that are related to pain during unsedated colonoscopy and found that nervousness is related to pain during unsedated colonoscopy.^[13] We tested whether unsedated colonoscopy impacts quality indicators and investigated predictors of pain during colonoscopy. Therefore, the aim of this study was to determine the effect of sedation in elective colonoscopy on quality indicators, including polyp detection rate, cecal intubation rate, cecal intubation time, rate of complications during unsedated colonoscopy and to compare willingness to colonoscopy with the same manner between sedated and unsedated group, also to assess the factors that are related to pain during unsedated colonoscopy including age, sex, body mass index, pain in rectal exam, previous abdominal surgery, indications for colonoscopy and level of anxiety.

MATERIALS AND METHODS

Participants and study settings

This randomized controlled trial was performed in the endoscopy unit of AL Zahra Hospital, Isfahan (Iran) from September 2018 to September 2019. Patients were checked with regards to the inclusion and exclusion criteria by a physician a day before colonoscopy. Eligibility criteria for colonoscopy were, age of above 18 years, indications for elective colonoscopy (e.g., constipation, rectorrhagia, abdominal pain, diarrhea, or screening surveillance for colon cancer), and willingness to participate. Patients with the following conditions were not included in the study: Poor preparation of colon, severe colitis, history of colorectal surgery, hypersensitivity to sedative drugs, cardiovascular or pulmonary instability and colon tumors or colon stenosis that interfere with completion of colonoscopy. The study was approved by the Ethics Committee of the Isfahan University of Medical Sciences (IR.MUI.MED.REC.1397.247) and registered in the Iranian Registry of Clinical Trials (IRCT20190105042246N1). Informed consent was obtained from all patients after full explanation of the study aims and protocols. Primary outcome was pain relief.

Sample size

Determining the sample size according to power 80% and the first type error of 0.05% was determined using the sample size formula equal to 100 people in each group. Sampling was performed sequentially and taking into account the inclusion criteria.

Randomization

Eligible patients were enrolled into the study consecutively and were randomized to the sedation and nonsedation group. Balanced block randomization method with quadruple blocks was used for random allocation.^[14] The production of blocks was done using Excel software.

Blindness

Double-blind study was performed. Participants and the interviewers did not know the type of drug injected.

Intervention

Patients consumed 210 g powder of polyethylene glycol in 3 L of water (Pidrolax, Sepidaj Co, Tehran, Iran) 1 day before colonoscopy, and 140 g powder of polyethylene glycol in 2 L of water at the day of procedure with the time between last dose and colonoscopy set at 2 h. Colonoscopy was done by a Gastroenterologist with experience of more 10,000 colonoscopies. Midazolam in 2.5-mg increments (Caspian Tamim Co., Tehran, Iran) with or without pethidine 25-mg increments (Caspian Tamin Co., Tehran, Iran) was given in the sedated group 5 min before the procedure. Normal saline was given in the unsedated group as a placebo. In the event of extreme discomfort, experienced frequently during the procedure, sedatives were given also to patients in the unsedated group during the procedure.

Assessments

Demographic information including age, sex, body mass index (BMI), reasons of colonoscopy, and history of surgery were taken from patients. Rectal examination was performed before colonoscopy and intensity of pain felt during rectal examination was recorded based on a verbal scale of one to five (PIREX score), where 0 means no pain and 5 means a severe and unbearable pain. Level of patient's anxiety was recorded 15 min before colonoscopy using a verbal scale from 0 (not at all) to 3 (very much). Quality of bowel preparation was determined using Boston bowel preparation scale and rated from 0 to 9.^[15] Colonoscopy quality criteria including polyp detection rate, cecal intubation rate, and cecal intubation time were recorded.^[16] Patient's pain was recorded during colonoscopy, only in unsedated group, using a verbal scale of 0 (no pain) to 4 (severe). Bloating was documented by calling patients until 24 h after colonoscopy. During colonoscopy, patients were monitored for blood pressure and oxygen saturation. Complications including bowel perforation, drug reaction, and bleeding were documented.

Statistical analysis

The sample size was calculated based on comparison of two independent proportions ($n = [Z\alpha + Z\beta] 2 \times [P1(1 - P1) + P2(1 - P2)]/[P1 - P2]^2$). Data analysis was done using SPSS for windows version 21.0 (IBM SPSS Statistics [IBM Corp, Armonk, NY, USA]). Data distribution was checked for normality.

Continuous variables are presented as mean (standard deviation) and were compared between the two groups using Independent sample *t*-test or Mann–Whitney *U*-test for ordinal variables. Categorical nominal variables are presented as number (%) and were compared between the two groups using Chi-square test. Ordinal logistic regression was used to determine the associations between pain during colonoscopy and independent variables including age, gender, BMI, preprocedural anxiety, and pain intensity during rectal examination. A $P < 0.05$ was considered significant in all analysis. Known confounding variables including age, sex, BMI, history of abdominal surgery, pain during examination, and individual anxiety were matched in two groups. No missing data were found.

RESULTS

From initially 300 enrolled patients, 246 participants completed the trial in two groups: colonoscopy with sedation ($n = 124$) and colonoscopy without sedation ($n = 122$) [Figure 1]. Patients in the two studied groups were similar regarding their demographic characteristics [Table 1, $P > 0.05$]. There was no significant difference between the two groups regarding history of abdominal pain, or pain in rectal examination and level of anxiety before colonoscopy ($P > 0.05$). Outcomes of the colonoscopy procedure in the two studied groups are presented in Table 2. Mean of cecal intubation time was significantly longer in the sedated group than unsedated group ($P = 0.016$). Bloating was reported more frequently in the sedated group than unsedated ($P = 0.033$). There was no significant difference regarding other variables including polyp detection rate, cecal intubation rate, and willingness to repeat the colonoscopy between sedated and unsedated groups [Table 2]. The association between pain during colonoscopy and independent variables in unsedated group showed significant association between pain during rectal examination and pain during colonoscopy ($P < 0.001$, wald = 19.4, 95% confidence interval; 0.5–1.3).

Complications

There was a no colon perforation or bleeding in both groups. Transient hypoxemia due to midazolam was noted in one participant in the sedated group.

DISCUSSION

In our study, there were not any significant differences between sedated group and unsedated group in regard to cecal intubation rate and polyp detection rate as two indicators of quality criteria for colonoscopy.

In study by Aljebreen *et al.*, cecal intubation rate between two group was comparable, though in that study sedated group and unsedated group were not match in terms of male to female ratio and anxiety level.^[9] Furthermore, in study by Bannert *et al.*, two groups did not have any statistically significance difference in regards to polyp detection rate.^[11] In our study, cecal intubation time in unsedated group was shorter than sedated group and justification of this could be the possibility of changing position in unsedated group that facilitates the procedure as study by Zhao *et al.* proven that changing position of patients to supine can decrease cecal intubation time.^[16] In our study, based on multi variant analyzes pain intensity during unsedated colonoscopy didn't have any correlation with patient's gender, BMI, anxiety level, and age. Pain in rectal examination was related to pain during colonoscopy in unsedated group. Based on our investigation, this relation was not investigated in previous studies hitherto. Pain during colonoscopy could be due to different anatomic variations and angulation of bowel that can cause looping of colonoscopy or it can be due to lower level of pain threshold. We can determine pain threshold in patients with intra rectal balloon and also, rectal examination can mimic intra rectal balloon and determines pain threshold, hence it can predict severity of pain during colonoscopy maneuvers or insufflation. In the study by Daza *et al.* same as our study, pain intensity during unsedated colonoscopy did not have any correlation with history of abdominal surgery and age.^[13] In study by Holme *et al.*, women's pain intensity during unsedated colonoscopy was higher. Furthermore, pain during unsedated colonoscopy was related to female gender.^[17] However, in these two studies several endoscopists were involved in the research but in our study colonoscopy was performed by one endoscopist and this difference can be due to inter observer variation in their studies or it can be due to lower sample size that

Table 1: Characteristics of the patients in the two studied groups

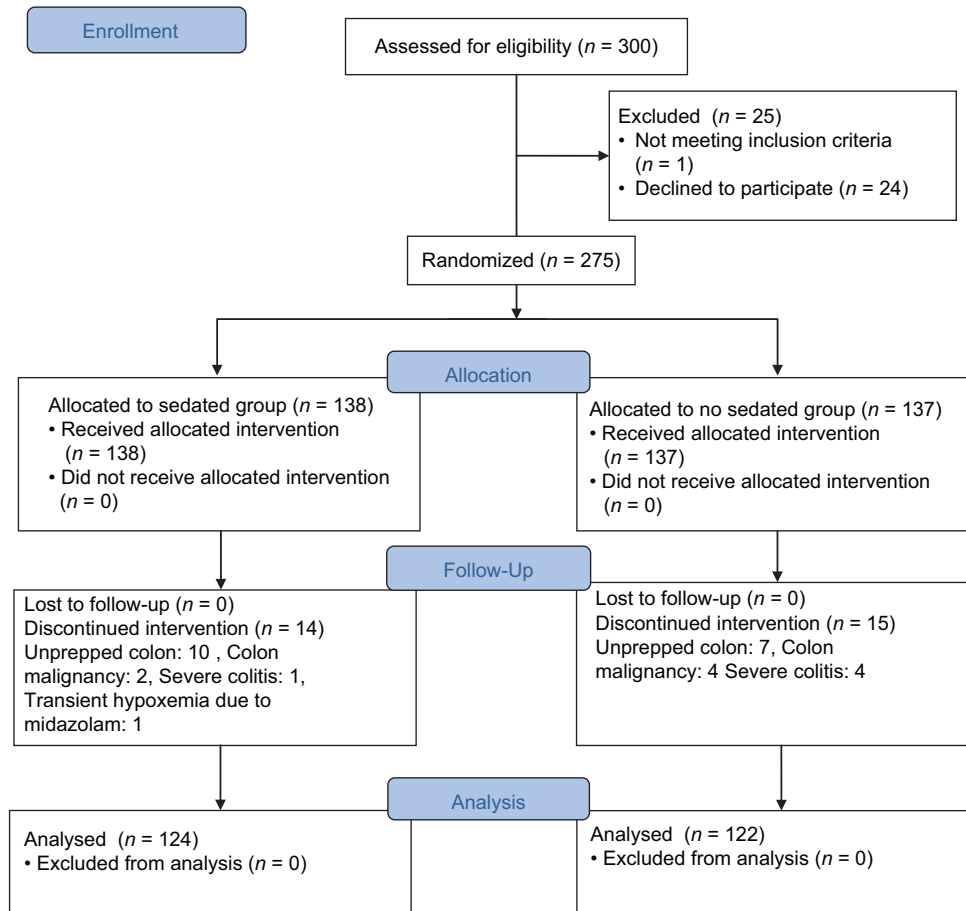
Variables	Sedation (n=124)	No sedation (n=122)	P
Age (years); mean±SD	50.5±12.1	49.2±13.6	0.43*
Male, n (%)	52 (41.9)	54 (44.3)	0.71†
BMI (kg/m ²); mean±SD	25.2±3.7	25.1±3.6	0.91*
History of abdominal surgery, n (%)	5 (4.0)	4 (3.3)	0.75†
Pain in rectal examination ^a ; mean±SD	1 (1, 2)	1 (0, 2)	0.060‡
Anxiety precolonoscopy ^b ; mean±SD	1 (0, 2)	1 (0, 2)	0.62‡
BBSP score; Mean±SD	7.8±0.9	7.7±0.8	0.28‡

*Independent sample *t*-test, †Chi-square test, ‡Mann–Whitney *U*-test. ^aNo pain (0) to unbearable pain (5), ^bNo anxiety (0) to severe anxiety (4). SD=Standard deviation; BMI=Body mass index; BBSP=Boston Bowel Preparation Scale

Table 2: Outcomes of the colonoscopy procedure in the two studied groups

	Sedation (n=124)	No sedation (n=122)	P
Polyp detection rate, n (%)	30 (24.2)	37 (30.3)	0.28*
Cecal intubation rate, n (%)	122 (98)	122 (99)	0.50*
Time of cecal intubation, minute; mean±SD	11.4±1.7	10.7±2.2	0.016†
Willing to repeat colonoscopy, n (%)	95 (77)	85 (69)	0.21*
Bloating, n (%)	20 (16)	9 (7)	0.033*

*Chi-square test. †Mann-Whitney U-test. SD=Standard deviation

**Figure 1:** Patients flow diagram

was used in our research. In unsedated group bloating after colonoscopy was less than sedated group. One potential interpretation is less insufflation due to the possibility of changing position or reporting pain during colonoscopy in unsedated patients. We did not find statistically significant difference for willingness to repeat colonoscopy with the same manner between sedated and unsedated patients. In study by Ma *et al.*, 88% of patients who underwent colonoscopy without sedation accepted to repeat free sedated colonoscopy for the second time.^[18] It means in this type of colonoscopy when is performed appropriately, patients will almost never experience a bad feeling. We had several limitations in this study; First Colonoscopy was performed by an experienced person and if it is done with less experienced hand, results could be different.

Second for insufflation we used air instead of CO₂, if we used CO₂ insufflation, rate of bloating after procedure in both groups could be different. Moreover, third although in our study lower pain threshold was considered to be the reason of pain during colonoscopy but we did not check the relations between irritable bowel syndrome and pain during colonoscopy.

CONCLUSION

Colonoscopy without sedation does not have any significant effect on polyp detection rate and cecal intubation rate but cecal intubation time in unsedated patients was shorter and bloating after procedure in unsedated group was less than sedated group. Furthermore, we acknowledged that

pain during colonoscopy can be predicted with pain during rectal examination.

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Conflicts of interest

There are no conflicts of interest.

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