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Study of Adding Pheniramine to Midazolam on Sedation during Colonoscopy in Tanta University Hospital: A Comparative Study

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ABSTRACT

Background: The whole big bowel may be seen inspected during a colonoscopy. The gold standard for the early identification of polyps and colorectal cancer, it is safe and reliable. The most often used drugs for moderate sedation are midazolam and fentanyl, which are benzodiazepines or mixtures of benzodiazepines and opioids.

Objective: The aim of the current study was to assess the safety and viability of midazolam with that of midazolam/pheniramine in sedation of patients undergoing colonoscopy.

Patients and methods: This clinical trial was carried out on 90 patients indicated for colonoscopy. Patients were randomized into 2 equal groups: ***Group A*** was sedated using midazolam (Dormicum) 5mg given slowly intravenously over one minute, and ***Group B*** was sedated using phinarimine 25mg (Avil) ampule given slowly intravenously 5 minutes before the procedure, then midazolam 5mg given slowly intravenously over one minute.

Results: There was a significant delay in time for initiation of sedation, and procedure time in ***Group A***. But there was a significant delay in the post-procedure time and recovery time in ***Group B***. There was a significant increase in satisfaction scale, endoscopist's satisfaction in patients of *Group B.*

Conclusion: Use of intravenous pheniramine maleate given before initiation of midazolam is superior to using midazolam alone in the decrease of preprocedural's anxiety, quality improvement for moderate sedation during colonoscopy, high satisfaction score for the patients, high tolerance to the procedure and higher endoscopes' satisfaction during the procedure.

Keywords: Pheniramine, Midazolam, Sedation, Colonoscopy.

INTRODUCTION

The whole big bowel may be seen inspected during a colonoscopy. The gold standard for the early identification of polyps and colorectal cancer, it is safe and effective. It is also advised for a number of reasons [1].

Indications of colonoscopy: 1) Colorectal cancer screening, assessment, and follow-up, screening in individuals with average risk, assessment, and removal of polyps, present or prior bowel resection for colon cancer, and family history of cancer. 2) Management of ulcerative colitis or Crohn's disease, follow-up treatment for individuals with these conditions, and management of patients with these conditions. 3) Locating the location of bleeding, identifying acute bleeding sites, and treating them with endoscopic therapy that includes epinephrine injection, electro-cauterization, argon plasma coagulation (APC), band therapy, and/or clips. 4) Colon decompression. In cases of sigmoid volvulus and for the treatment of individuals with Ogilvie syndrome, colonoscopy/sigmoidoscopy can be utilised to decompress the colon [1].

As it is a painful invasive procedure, the use of sedation is necessary [2].

Sedation is intended to reduce discomfort and anxiety in the patient and to induce amnesia, which creates the ideal conditions for a thorough examination of the patient and the endoscopist [3]. A benzodiazepine or a benzodiazepine and opioid combination is often used to induce moderate sedation, with midazolam and fentanyl being the most frequently used drugs [4].

However, some patients cannot get enough sedation with the typical benzodiazepine and opioid combination; in these cases, the addition of diphenhydramine is advised by current recommendations since it "may allow adequate and safe sedation to be achieved". Furthermore, a number of studies have demonstrated that administering intravenous diphenhydramine hydrochloride prior to the administration of midazolam significantly improves the level of mild sedation experienced during colonoscopy procedures while reducing sedative-related problems [5].

Therefore, we aimed in this study to assess the safety and viability of midazolam alone that is usually used in most centres in Egypt with midazolam/pheniramine combination for conscious sedation of patients undergoing colonoscopy.

PATIENTS AND METHODS

This clinical trial was carried out on 90 patients indicated for colonoscopy, at the Tropical Medicine Department, Tanta University Hospital from October 2020 to September 2021.

Patients having allergies to study medicines, neuropsychiatric disorders, advanced cardiac or respiratory conditions, alcohol or drug addiction, and severe bleeding were excluded from the study.

Patients were randomized into 2 equal groups: ***Group A*** was sedated using midazolam (Dormicum) 5mg given slowly intravenously over one minute, and *Group B* was sedated using phinarimine 25mg (Avil) ampule given slowly intravenously 5 minutes before the procedure, then midazolam 5mg given slowly intravenously over one minute.

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All patients were subjected to history taking, physical examination and laboratory investigations [CBC, LVP, RFT, and colonoscopy].

Colonoscopy:

Intravenous line was inserted. All subjects were examined while conscious under light sedation.

The patients removed their clothes and wore a disposable gown and special pantaloons. The patients lied on left lateral position. Digital rectal examination was done and the lubricated colonoscope tip was gently slided over the fingertip. All cases were examined by an experienced endoscopist using Olympus GIF-PCF 180AL colonoscope.

The attendant kept track of the patients' vital signs while measuring their arterial blood pressure, heart rate, oxygen saturation, and level of drowsiness using the Ramsay sedation scale (RSS) at time zero, one minute following the onset of sedation, and then every five minutes after that. Also, we monitored the patient during and after colonoscopy and recorded any side effects through a patient-controlled technique.

The beginning of the sedation, the insertion of the colonoscope, the removal of the colonoscope, the recovery period, and the time of discharge were all noted. Five intervals were calculated from these five events: time to sedation (from the start of sedation to the insertion of the colonoscope), procedure time (from the insertion to the removal of the colonoscope), postprocedure time (from the removal of the colonoscope to the time of discharge), procedure room time (from the start of sedation to the time of recovery), and post-anaesthesia care unit time (from the recovery time to the time of discharge).

The endoscopist was asked to rate his level of satisfaction on a scale of 1 to 10 immediately following the operation (1= Not satisfied and 10= Very satisfied). Patients were asked to rate their satisfaction with sedation and analgesia on a scale of 1 to 10 (1= not pleased and 10= very satisfied) just before being discharged. So, on this study we compared between the two groups as regard sedation used to assess the safety and viability of midazolam with that of midazolam/pheniramine in sedation of patients undergoing colonoscopy on Tanta university hospitals to clarify whether this combination increase the satisfaction of both the patient and the endoscopist during and after colonoscopy or not and would it affect the safety of the procedure.

Ethical approval:

Tanta Medical Ethics Committee of the Tanta Faculty of Medicine gave its approval to this study. All participants gave written consent after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

SPSS v27, software for statistical analysis, was used. Histograms and the Shapiro-Wilks test were employed to confirm the normality of the data distribution. The unpaired student t-test was used to analyse quantitative parametric data that was presented as mean and standard deviation (SD). The interquartile range (IQR) and median of quantitative non-parametric data were examined using the Mann Whitney test. When suitable, qualitative variables were analysed using Fisher's exact test or Chi-square test, and results were given as a frequency and percentage (%). Statistical significance was determined using a two-tailed P value of 0.05.

RESULTS

There was no significant difference between the studied patients as regard sex, age and blood picture before and after procedure (**Table 1**).

Table (1): Demographic data and CBC in the studied groups.

Variable		Group A (n = 45)	Group B (n = 45)	P Value
Sex	Male	22 (48.9%)	24 (53.3%)	0.673
	Female	23 (51.1%)	21 (46.7%)	
Age (years)		39.96 ± 13.58	36.20 ± 12.94	0.183
Hgb (g/dL)	Pre	10.92 ± 1.71	10.39 ± 1.92	0.171
	Post	11.25 ± 1.40	10.90 ± 1.53	0.259
p_1		<0.001*	<0.001*	---
PLT (×10³/µl)	Pre	245.89 ± 60.13	238.36 ± 56.88	0.364
	Post	247.73 ± 61.38	238.53 ± 58.12	0.313
WBCs (×10³/µl)	Pre	6.95 ± 1.61	7.18 ± 1.74	0.731
	Post	6.95 ± 1.59	7.18 ± 1.67	0.731

P: P value for comparing between the studied groups, p1: p value for comparing between Pre and Post in each group, *: significant P value.

There was a significant delay in time for initiation of sedation, and procedure time in ***Group A***. However, there was a significant delay in the post-procedure time and recovery time in ***Group B*** (**Table 2**).

Table (2): Comparison between the two studied groups according to time intervals during and after the procedure

Variable	Group A (n = 45)	Group B (n = 45)	P-value
Time for initiation of sedation	3.69 ± 1.0	3.04 ± 0.74	0.001*
Procedure time	30.87 ± 4.57	27.98 ± 5.66	0.009*
Post procedure time	28.29 ± 5.65	36.73 ± 4.59	<0.001*
Recovery time	64.87 ± 6.94	73.09 ± 5.74	<0.001*
Post anesthesia care unit time (PACU) (min)	30.82 ± 1.57	30.53 ± 2.72	0.539

Table 3 shows comparison between the two studied groups according to colonoscopy indications.

Table (3): Comparison between the two studied groups according to colonoscopy indications

Colonoscopy indication	Group A (n = 45)	Group B (n = 45)
Abdominal pain	4 (8.9%)	17 (37.8%)
Recurrent Diarrhea	6 (13.3%)	5 (11.1%)
Chronic diarrhea	0 (0.0%)	4 (8.9%)
Post hemi-colectomy	1 (2.2%)	1 (2.2%)
Constipation	6 (13.3%)	6 (13.3%)
Alternating bowel habit	1 (2.2%)	0 (0.0%)
Anal fissure	4 (8.9%)	0 (0.0%)
Anemia	7 (15.6%)	0 (0.0%)
Bleeding per rectum	6 (13.3%)	6 (13.3%)
Crohn's follow up	1 (2.2%)	1 (2.2%)
Post ileostomy	4 (8.9%)	0 (0.0%)
Ulcerative colitis FU	5 (11.1%)	5 (11.1%)

Data are presented as frequency (%).

There was a significant increase in satisfaction scale, Endoscopist's satisfaction in patients of ***Group B*** (**Table 4**).

Table (4): Comparison between the two studied groups according to satisfaction scale, endoscopist's satisfaction and Colonoscopy results

Variable		Group A (n = 45)	Group B (n = 45)	P-value
Satisfaction scale	4	1 (2.2%)	0 (0.0%)	<0.001*
	5	12 (26.7%)	2 (4.4%)	
	6	17 (37.8%)	4 (8.9%)	
	7	7 (15.6%)	15 (33.3%)	
	8	7 (15.6%)	21 (46.7%)	
	9	1 (2.2%)	3 (6.7%)	
Endoscopist's satisfaction	7	15 (33.3%)	1 (2.2%)	<0.001*
	8	27 (60%)	35 (77.8%)	
	9	3 (6.7%)	9 (20%)	
Colonoscopy results				
Unremarkable		16 (35.5%)	18 (40%)	
Picture of ulcerative colitis		11 (24.4%)	15 (33.3%)	
Hemorrhoid's		7 (15.5%)	4 (8.89%)	
Healthy blind loop multiple biopsies for histopathology		5 (11.1%)	2 (4.44%)	
Cancer colon		3 (6.67%)	1 (2.2%)	
Colonic polyps		2 (4.4%)	3 (6.6%)	
Stenotic fistulizing ulcer		1 (2.2%)	2 (4.4%)	

DISCUSSION

The primary goals of employing sedation during a colonoscopy are to enhance the examination's quality and increase the patient's comfort level [6]. When necessary, midazolam can be successfully reversed by a nurse working under the endoscopist's supervision [7]. The present study was comparing the safety and viability of midazolam with that of midazolam/pheniramine in sedation of patients undergoing colonoscopy. We designed this study as a prospective observational cohort study which was carried out on 90 patients indicated for colonoscopy. They were collected from Tropical Medicine Department, Tanta University Hospital. Both groups were matching as regards age and sex, as well as pre-procedure routine lab investigations including CBC, liver enzymes, bilirubin, INR, and serum albumen. Indications of colonoscopy in our cases were abdominal pain, chronic diarrhea, constipation, follow up after hemicolectomy, alternating bowel habits, bleeding per rectum, and follow up of cases with IBD. Cases with abdominal pain were significantly more in group II, but all other indications had non-significant difference.

Another study carried on patients from Nile Delta revealed that the most common indications for colonscopy was abdominal pain undiagnosed after laboratory and imaging studies(63% of cases), while 50% of cases presented with bleeding per rectum, 48% of cases presented with diarrhea, 30% with constipation, 27% of cases presented with weight loss, 22% of cases presented with iron deficiency anemia, 8% of cases presented with fever, and 4% of cases mass lesions that were palpable or suspected on CT were present [8].

Adding pheniramine to midazolam was found to decrease the procedural pain score significantly. Another study was conducted on 500 colonoscopies using midazolam bolus alone showed that moderate or severe pain appeared in 28% of the cases [9]. The difference in outcome of this study and our study could be due to a small sample size in our study. The sedation related complication s or adverse effects like hypertension, hypoxia and cardiorespiratory events as apnea, arrhythmia or need of reversal agents did not occur in both groups. On the other hand, **El shahawy and El-Fayoumy**[5] reported some complications as hypoxia (18.8%) and hypotension (9.4%) in colonscopy with diphenhydramine. According to the need of analgesia there was a significant difference between both groups the group of midazolam alone (67%) needed more analgesia than group midazolam with pheniramine (9%). the patient satisfaction rating scale. past colonoscopy experiences, discomfort during the operation, an acceptable amount of sleep throughout the process, and perception of sedation at the present colonoscopy compared to past colonoscopies are the four factors that predict patient satisfaction [10].

In our study midazolam with pheniramine showed better results than group of midazolam alone, this result is similar to results of study which evaluated influence of starting a mild sedative procedure for a colonoscopy with midazolam and pethidine before adding diphenhydramine [5]. Endoscopist satisfaction is influenced by a number of independent variables, including healthcare provider conduct, patient empowerment, and collaborative decision-making [11]. In our study, there was a significant increase in endoscopist's satisfaction with adding pheniramine to midazolam.

CONCLUSIONS

Use of intravenous pheniramine maleate given before initiation of midazolam is superior to using midazolam alone in the decrease of preprocedural's anxiety, quality improvement for moderate sedation during colonoscopy, high satisfaction score for the patients, high tolerance to the procedure and higher endoscopes' satisfaction during the procedure.

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