Dexmedetomidine Versus Ketamine Combined With Fentanyl for Sedation-Analgesia in Colonoscopy Procedures: A Randomized Prospective Study

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Abstract- Colonoscopy is a painful, embarrassing and short-term procedure that needs temporary sedation and rapid recovery. The aim of this study was to compare the sedation and analgesia effect and hemodynamic changes due to bolus intravenous injection of dexmedetomidine and ketamine during elective colonoscopy. This clinical trial was conducted on 70 patients aged 20-70 years, candidates for elective colonoscopy, who randomly divided into two equal groups. For all patients 0.03 mg/kg midazolam 10 min before procedure was injected. Fentanyl 1 μ/kg was administrated in both groups 5 min before procedure, and one min before colonoscopy. K group received 0.5 mg/kg ketamine and D group received 1 μ/kg dexmedetomidine. Then, the normal saline infusion was used as maintenance. Fentanyl 25-50 μg was prescribed as the rescue dose if needed during the procedure. Hemodynamic changes, sedation level during procedure, patients and colonoscopists satisfaction were recorded in recovery. The mean heart rate and mean blood pressure was significantly less in the dexmedetomidine group than in the ketamine group. All of the patients in the ketamine group were deep to moderately sedated during colonoscopy, and the amount of fentanyl required in this group is much less than dexmedetomidine group (68.02±25.63 vs 91.45±38.62 μg *P*-0.003). In terms of satisfaction, only 42% of patients in the dexmedetomidine group were completely satisfied with colonoscopy, while 65% of Ketamine group had complete satisfaction with colonoscopy (*P*=0.001). The level of colonoscopist satisfaction during colonoscopy was similar in both group, and complete satisfaction was 43%. In patients undergoing colonoscopy, IV bolus injection of dexmedetomidine in comparison with ketamine provides less patients satisfactory and low level of sedation with supplemental multiple doses of fentanyl during the procedure.

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Introduction

Flexible colonoscopy is one of the most common invasive outpatient procedures throughout the world as a screening, diagnostic, and therapeutic tool. The pain and anxiety which are frequently associated with colonoscopy may lead to either patient refusal or elevated sedative drug administration. Many anesthetic drugs such as midazolam, propofol, and/or alfentanil or pethidine combinations, α-agonists, and neuroleptics are commonly used for sedation (1,2,3).

The goals of conscious sedation with analgesia are to reduce pain and anxiety, maximize amnesia, minimal adverse effects, and stable cardiovascular and respiratory conditions. Today the number of patients that need colonoscopy has been increased; therefore, the ideal agents must have a rapid onset and short recovery. At present, usually various doses of different drug combinations are used to achieve most of these desired effects (4,5).

Low doses of ketamine makes analgesia with minimal effect on the central respiratory drive while stable hemodynamics is maintained. The combination of ketamine and propofol induces quality sedation, minimizes adverse effects, and provides a stable hemodynamic and respiratory profile in procedural sedation (6).

Dexmedetomidine is a relatively selective α2 adrenoceptor agonist that has a sedative, anxiolytic, analgesic, and sympatholytic activity (7).

It has been used for sedation in much non-intubated procedures such as colonoscopy, awake carotid

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endarterectomy, shockwave lithotripsy, vitreoretinal surgery (8). Sympatholytic effect of dexmedetomidine may cause distressing side effects, pronounced hemodynamic instability, and prolonged recovery in some study such as colonoscopy (9).

This study was designed to demonstrate that dexmedetomidine in combination with fentanyl is safe and efficacious in providing sedation for colonoscopy. We compared its effects on analgesia/sedation and hemodynamic changes with ketamine/fentanyl. We also examined its impact on the colonoscopist and patient's satisfaction.

Materials and Methods

After being approved by the Ethical Board Committee of Anaesthesiology Department of Tehran University of Medical Sciences (TUMS), this interventional, randomized clinical trial, was conducted on 70 elective patients (20-70-year-old) candidates for a flexible colonoscopy under conscious sedation and analgesia from June 28, 2018 to febrary31, 2019.

The exclusion criteria were patients with heart failure, liver failure, chronic use of drugs such as benzodiazepines, neuroleptics, and anticonvulsants , hypersensitivity reactions to drugs used in the study; those undergoing abdominal laparotomy; body mass index above 35 kg m−2 and psychiatric patients. All patients who were candidates for flexible colonoscopy are explained about the intervention then an informed writing concern was taken from them.

Patients who fulfilled the inclusion criteria ASA I, II age 20-65 yr, were randomly allocated into two groups. A computer-generated randomization list was used to assign patients to one of two study groups. Dexmedetomidine (D) and ketamine (K) groups consisted of 70 patients each.

The syringes were coded by an anesthetic nurse who was not involved in the process of sedation and patient evaluation. Syringes containing drugs were selected similarly in terms of volume. The patients, anesthetists, colonoscopists, and patient assessors (anesthetist's assistant) were blind to the drug regimen. All patients were monitored with pulse oximetry, continuous ECG, and noninvasive blood pressure assessed every 3 min and recorded.

Thereafter, an i.v. line was inserted, and a crystalloid solution like normal saline was started.

All patients received supplemental O_2 4-6 l/min through face mask throughout the procedure and premedication 0.03 mg/kg midazolam for all patients 10 min before the procedure was injected.

Fentanyl 1 μ /kg was administrated in both groups 5 min before procedure, and one min before colonoscopy K group received 0.5 mg/kg ketamine and D group received 1 μ/kg dexmedetomidine.

The sedation level was evaluated using the Observer Assessment of Alertness/Sedation (OAA/S) Scale every 3 min during the procedure and in recovery as 1=complete quiet/unconscious, 2=deep sedated, 3=moderate sedated, 4=light sedated and 5 not sedated. We inject fentanyl 25-50 μg in cases of sedation level more than 3 during the procedure.

In the recovery room, the degree of satisfaction of the patients and colonoscopy specialist were recorded as follows: 1=Not at all satisfied, 2=low, 3=medium, 4=high, 5=very high.

Any complications such as nausea, vomiting, change in systolic, diastolic, and heart rate greater or lower than 30% of initial value apnea more than 30 seconds was also recorded.

Statistical analysis

In order to describe and compare the qualitative data of the study, frequency (percent) was used, and for quantitative variables, the mean (standard deviation) was used. Categorical variables were expressed as frequencies and percentages. X^2 -Test and Fisher's exact test were used to examine the relationship between categorical variables. To investigate the relationship between the intervention and qualitative outcomes we used chi-square analysis.

Results

Seventy patients were enrolled in the study, 45 in each group. The median age of patients was 51.5±10.8 year (23-69 yr). Demographic variables of patients are depicted in table 1.

The range of hemodynamic changes during procedure was less in dexmedetomidine group. Generally, the mean of mean arterial pressure was lower in dexmedetomidine compared to ketamine group (86.44±12.34 vs,100.83±22.45 P=0.001). In terms of heart rate, the dexmedetomidine group also had lower heart rate during procedure (72.51±16.7 vs 90.56±15.71 P=0.001). The trend of Spa02 changes remained similar through the colonoscopy in two groups (P.0.5).

Table 1. Characteristics of included patients and the procedures

Variables	Group D	Group K	*P*
Age (mean±sd)	52.8±12.2	53.5±12.7	0.24
Sex (Male/Female)	16/19	20/15	0.13
Mean Duration Procedure, min,	9.4±2.9	8.7±2.8	0.139
Mean Duration Recovery ,min	12.3±2.9	13±1.9	0.12

All of the patients in the ketamine group were deep to moderate sedated during colonoscopy, and the amount of fentanyl required in this group was much less than dexmedetomidine group (68.02±25.63 vs 91.45±38.62 µg *P*-0.003). Ten percent of patients in dexmedetomidine group had light sedation, and thus they needed more fentanyl during procedure.

In terms of satisfaction, only 42% of patients in the Dexmedetomidine group were completely satisfied with colonoscopy, while 65% of Ketamine group had complete satisfaction with colonoscopy (*P*=0.001).

The level of colonoscopist satisfaction during colonoscopy was similar in both group, and complete satisfaction was 43%. The incidence of nausea and vomiting in both groups was 7%.

Discussion

Colonoscopy is a standard method for diagnosis, screening, treatment, and follow-up for many colorectal diseases. Colonoscopy is often a painful and embarrassing method. It requires a suitable drug to maximize patient comfort with sufficient sedation, good cooperation, and minimal side effects.

The results of our study showed that ketamine in combination with fentanyl had a more sedative and satisfaction compared to dexmedetomidine and fentanyl in patients undergoing colonoscopy.

Dexmedetomidine is most often used in the intensive care setting for light to moderate sedation (10).

It can also be used for procedural sedation, such as during colonoscopy (11). Dexmedetomidine can be used as an adjunct with other sedatives like midazolam, fentanyl, and propofol to enhance sedation and help maintain hemodynamic stability by decreasing the requirement of other sedatives (12).

The study of Wu *et al*., was conducted on 60 patients in two equal groups to compare dexmedetomidine and midazolam in endoscopy. Variables included were peripheral oxygen saturation, heart rate, mean arterial pressure, and pain intensity procedure. The level of patient satisfaction was also evaluated. Of course, Fentanyl was added to both groups along with the main drug. The results showed that in the dexmedetomidine group, there was a lower pain score and higher peripheral oxygen saturation (13).

In the study of Amri *et al*., dexmedetomidine 1 µg/kg was given 10 minutes before starting the colonoscopy and then, 0.5 µg/kg/hour during colonoscopy was prescribed. In the control group, fentanyl 0.5 µg/kg was prescribed three minutes before starting the colonoscopy, and propofol 20 mg was prescribed as the rescue dose if needed during the procedure. They concluded that pain score is lower in the dexmedetomidine group than in the fentanyl group and dexmedetomidine is able to better control hemodynamic changes (14).

In many of these studies intravenous infusion of dexmedetomidine is initiated with a loading dose followed by a maintenance infusion that is different from our method.

The duration of the colonoscopy in our study was less than ten minutes, and we only injected the loading dose of dexmedetomidine, which in terms of its pharmacokinetic it has a rapid distribution half-life of approximately 6 minutes and short duration of action (15). The main reason for the administration of a higher dose of fentanyl in the dexmedetomidine group was a feeling of discomfort during colonoscopy. For this reason, patients' satisfaction declined during the colonoscopy in the dexmedetomidine group.

In terms of hemodynamic changes, the results of our study were similar to other studies; this means that patients in the dexmedetomidine group have a lower heart rate and lower blood pressure than the ketamine group. Dexmedetomidine is a highly selective α2-adrenergic agonist, and it induces sedation by decreasing activity of noradrenergic neurons in the locus ceruleus in the brain stem, which can increase the risk of bradycardia and hypotension with fentanyl (16).

In the study of Jalowiecki *et al*., sole use of dexmedetomidine has limited utility for conscious

sedation during outpatient colonoscopy because their patients needed multiple doses of fentanyl during the procedure (9).

Ketamine in combination with midazolam, propofol was used as a safe method in colonoscopy with low hemodynamic instability and more patient satisfaction (17-18-19). The use of ketamine in the present study confirms this finding that IV bolus injection of ketamine-fentanyl can lead to more patients' satisfaction than dexmedetomidine during colonoscopy.

In conclusion, in patients undergoing colonoscopy dexmedetomidine compared to ketamine provides a less satisfactory level of sedation with supplemental multiple doses of fentanyl during the procedure.

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