Original Article

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Comparison of the Sedative Effect and Recovery Time of Dexmedetomidine and Fentanyl during Elective Colonoscopy

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ABSTRACT

BACKGROUND AND OBJECTIVE: Various medications such as propofol or midazolam are used with or without fentanyl as sedatives for colonoscopy. Dextroduromedine is a new sedative that activates the alpha-2 adrenergic receptor in the brain and the spinal cord with sedative, analgesic and sympatholytic effects. The aim of this study was to compare the sedative effect and recovery time of dexmedetomidine and fentanyl during elective colonoscopy.

METHODS: In this double – blind clinical trial, 80 colonoscopy candidates aged 20-70 years old were randomly divided into two equal groups. 1 mcg/kg dexmedetomidine was administered to the intervention group and 0.5 mcg / kg fentanyl was administered to the control group before the start of the colonoscopy. Propofol (20 mg) was administered as bolus dose if needed during colonoscopy. The sedation rate was recorded based on Ramsay standard and mean bolus dose of propofol during colonoscopy. Recovery time and pain were recorded based on Visual Analog Scale (VAS) before discharge.

FINDINGS: The two groups did not have a significant difference in terms of age, gender and sedation rate. The mean bolus dose of propofol in the fentanyl group was 72±14 and in the dexmedetomidine group was 7±0.24 mg (p=0.000). The recovery time in the fentanyl group was 4.38±2.38 minutes and in the dexmedetomidine group was 2.63±1.22 minutes (p=0.000). The pain after colonoscopy was 2.30±0.69 in the fentanyl group and 1.98±0.7 in the dexmedetomidine group (p=0.039).

CONCLUSION: The results of this study showed that the combination of dexmedetomidine and propofol are more suitable for colonoscopy compared to the combination of fentanyl and propofol due to shorter recovery time.

KEY WORDS: *Propofol, Dexmedetomidine, Fentanyl, Colonoscopy, Sedation.*

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Introduction

Colonoscopy is used for diagnostic and therapeutic purposes (polypectomy, determining the location of the lesion, removal of foreign bodies, decompression of sigmoid volvulus and bleeding control) (1–3). In order to select the appropriate colonoscopy method for each patient, the need for sedation and its risks should be assessed. In moderate sedation, no intervention is needed to keep the airway open during sedation without anesthesia (4–6).

Deep sedation reduces the level of consciousness such a way that it is not easy to wake up the patient but he/she responds to repeated or painful stimulation (1, 5, 7). Before sedation, patients should not have oral fluids for 2 hours and should not have food for 6 to 8 hours (1, 5, 7). Midazolam has sedative, hypnotic and anti-anxiety effects, but it is not analgesic. Short-acting opioids, such as fentanyl, alone or in combination with sedatives, are used for sedation and analgesia in procedures (1, 5). Fentanyl is often used in combination with midazolam for sedation in procedures. One of its important complications is respiratory depression, which is exacerbated by simultaneous administration of the sedatives, and the possibility of the need for airway intervention is increased. Risk factors for these complications include old age, underlying disease (particularly pulmonary disease), dementia, anemia, obesity and emergency endoscopy (1, 5). Propofol is the most common intravenous anesthesia that has clinical use. The onset of hypnosis after a dose of 2.5 mg / kg is fast and the maximum effect is seen within 90 to 100 seconds. The subhypnotic dose causes sedation and amnesia. Propofol also has anti-nausea / vomiting properties. Respiratory arrest occurs after the injection of the anesthetic induction dose of propofol (1, 5, 8, 9).

Dexmedetomidine is a new sedative that induces sedative, analgesic, and sympatholytic effects by activating the alpha-2 adrenergic receptors in the brain and the spinal cord. Its pharmacological properties may reduce the need for another drug for sedation (1). Its analgesic effects are due to the agonist effects of the alpha-2 adrenergic receptor on the posterior horn of spinal cord (7,12,13).

The half-life of dexmedetomidine is 2 to 3 hours. Unlike other sedative factors, a patients that is anesthetized by dexmedetomidine returns to previous consciousness level by stimulation, and it causes less respiratory depression compared to other sedatives. Dexmedetomidine does not have additive effect when combined with propofol and does not exacerbate respiratory depression caused by propofol (7, 11-14). Assessment of depth of anesthesia in out – of – operating room procedures is performed based on Ramsay sedation scale (15). Aldrete's scoring system is used to determine the recovery time (16).

For sedation and analgesia during colonoscopy, propofol and fentanyl are used. The use of these drugs is associated with complications such as hypotension, respiratory depression, and bradycardia. Nowadays, other analgesic drugs can be used instead of fentanyl to prevent hypotension, respiratory depression, and loss of arterial oxygen saturation (10-12). Dexmedetomidine is a new sedative drug used for sedation during procedures. Considering the complications of fentanyl, including respiratory depression and the risk of apnea in combination with propofol, and lower respiratory complications caused by dexmedetomidine, this study was conducted to compare the hypnotic effects and recovery time of dexmedetomidine and fentanyl during elective colonoscopy.

Table 1. The hypnotic rate based on Ramsay sedation scale

Clinical Grading	Patient characteristics
1	awake, anxious or restless, or both
2	Is awake and cooperates
3	Is awake but just responds to the request
4	asleep, fast response to stimuli like loud noise
5	asleep, partial response to stimuli such as loud noise
6	asleep, does not give any response to stimuli

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Table 2. Recovery scoring based on Aldrete's scoring system

Patient characteristics	Clinical Parameters		
	zero	One	Two
Activity level, ability to move limbs	No limbs	Both limbs	All four limbs
Respiration	Apnea	Dyspnea, shallow breathing, breathing restrictions	The ability to breathe deeply and cough easily
Blood pressure	More than 50 mm Hg higher or lower than pre-anesthetic status	More than 20-50 mm Hg higher or lower than pre-anesthetic status	More than 20 mm Hg higher or lower than pre-anesthetic status
Level of consciousness	No response	Wake up by calling the patient	Totally awake
Oxygen saturation levels	Less than 90% with supplemental oxygen	The need for supplemental oxygen to help preserve saturation by more than 90%	More than 90% in room air breathing

Methods

This randomized clinical trial was approved by the Ethics Committee of the Babol University of Medical Sciences registered on the Clinical trials database (IRCT: 201602297752 N6). The study was performed on 80 ASA Class I and II patients who referred to the endoscopy department of Ayatollah Rouhani Hospital in Babol for elective colonoscopy from October 2016 until August 2017. Patients aged 20-70 years old and ASA Class I and II were included in the study and patients with cardiovascular disease, liver disease, kidney disease, neuropsychiatric disorders, drug addiction, bradycardia, hypotension and lack of cooperation were excluded.

Sample size with 95% confidence level and 80% power and assuming Q1 = Q2 = 0.6 in terms of Ramsay sedation scale to find 0.5 units of difference in the two groups was estimated 23 people for each group. To increase the test power, 40 samples were considered for each group. Patients were randomly divided into two equal groups through systematic (convenience) sampling. In the intervention group, 1 mcg / kg dexmedetomidine was administered 10 min before the start of colonoscopy and then 0.5 mcg / kg / hr during colonoscopy, while fentanyl group received 0.5 mcg / kg three min before the start of colonoscopy. If necessary, 20 mg propofol was administered as bolus dose during the procedure. The syringes were coded by an anesthetist who was not involved with the process of sedation and assessment of the patient. Patients, anesthetist, colonoscopist, and patient assessor (anesthesiologist assistant) were unaware of the drug regimen. Sedation rates based on the Ramsay sedation scale (Table 1) and the mean bolus dose of propofol were recorded from the start of the colonoscopy (minute 0) and every five minutes until recovery. Recovery time (score of 9 or greater based on Aldrete's scoring system) (Table 2) and pain after colonoscopy were recorded based on visual analogue scales (VAS) before discharge (15, 16). Nausea, vomiting, hypotension (BP below 80% from baseline), bradycardia (heart rate below 50 BPM) and delayed discharge (below 2 hours) were recorded. Data were analyzed using SPSS V.22, Chi-Square and t-test, while $p<0.05$ was considered significant.

Results

Overall, 90 patients were included in the study. However, six patients were excluded due to lack of readiness and four patients were excluded from the study due to age conditions. The mean age of the fentanyl group was 48.88±13.84 years and the mean age of the dexmedetomidine group was 49.20±13.98 years, and the two groups were not different in this regard. Twenty four patients (60%) in the fentanyl group and 21 patients (52.5%) in dexmedetomidine group were male,

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and the two groups were not significantly different. The duration of the colonoscopy was 7.82±3.13 minutes in the dexmedetomidine group, and 7.8±3.09 minutes in the fentanyl group, and there was no significant difference. Nine patients in dexmedetomidine group (an average of 7±0.24 mg) and 40 patients in fentanyl group (an average of 72±0.14 mg) received bolus dose of propofol (p=0.000). In terms of sedation rate, there was no significant difference between the dexmedetomidine and fentanyl groups (Figure 1). The recovery time in the fentanyl group was 4.38±2.38 minutes and in the dexmedetomidine group was 2.63±1.22 minutes (p=0.000). The pain after colonoscopy (VAS) was 2.30±0.69 in the fentanyl group and 1.98±0.70 in the dexmedetomidine group (p = 0.039). Fifteen patients in the dexmedetomidine group and three patients in the fentanyl group suffered from bradycardia, but only one patient in the dexmedetomidine group suffered from severe bradycardia (below 40) and hypotension, which improved with treatment (Table 3).

Table 3. Comparison of side effects of drugs in the two groups

Group / Drug side effect	Fentanyl	Dexmedetomidine	P-value
Number of hypotension cases (%)	0 (0)	3 (7.5)	0.241
The number of bradycardia (%)	3 (7.5)	15 (37.5)	0.000
Number of nausea and vomiting (%)	2 (5)	5 (7.5)	0.432
Bradypnea (%)	17 (42.5)	3 (7.5)	0.001

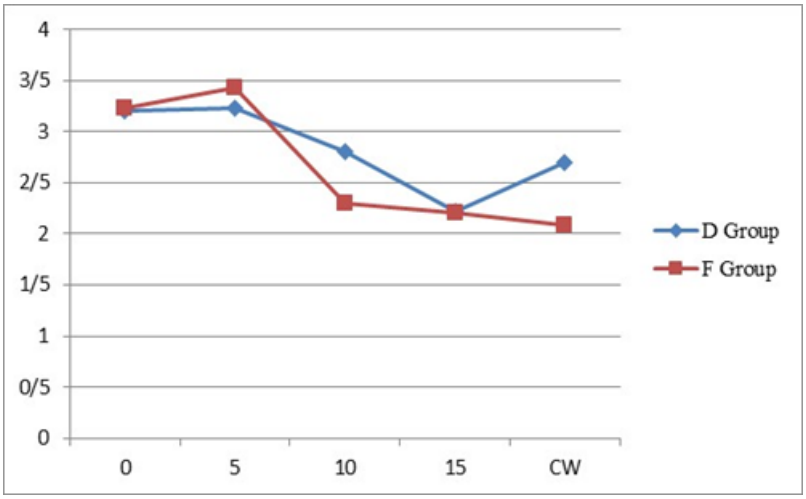

Figure 1. The mean sedation rate based on Ramsay sedation scale in the two groups
CW: colonoscopy withdrawal, D: dexmedetomidine, F: fentanyl

Discussion

In this study, there was no significant difference in the sedation rate between dexmedetomidine group and fentanyl group. The recovery time was shorter in the dexmedetomidine group. In the study of Cariffiths et al., patients were divided into two groups of dexmedetomidine (D) and propofol (P). Sedation was done in propofol group with 1.5 mg/kg (119 patients) and then with 0.5 mg/kg if necessary, and it was done with 1 mcg/kg (112 patients) in the dexmedetomidine group. Hypotension occurred in 65.8% of the patients in dexmedetomidine group and 41.4% of the patients in propofol group. Loss of arterial oxygen saturation occurred in 10 patients (4.7%) in the propofol group, while only one patient in the dexmedetomidine group suffered from this problem. The results of this study showed that both dexmedetomidine and propofol can provide acceptable sedation. Propofol decreases arterial blood oxygen and dexmedetomidine increases

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hypertension in patients (15). Although the method of this study was slightly different from our study, the results were similar to our study. In our study, nine patients in dexmedetomidine group (an average of 7±0.24 mg) and 40 patients in fentanyl group (an average of 72±0.14 mg) received bolus dose of propofol. The bolus dose of propofol and recovery time were lower in the dexmedetomidine group, but there was no significant difference between the two groups in terms of mean sedation rate. The main reason for this difference was the administration of more propofol in the fentanyl group.

In the study of Nishizawa et al., the level of GAG and body movements during endoscopy, as well as the rate of hypotension, hypoxia and bradycardia were different in the two groups (17). In our study, contrary to this study, the loss of arterial oxygen saturation was lower in the dexmedetomidine group. In the study of Oshima et al., body movements and respiratory depression were lower during endoscopy in the dexmedetomidine group. There was no difference in hypotension and bradycardia in the two groups (18). Although pentazocine was used instead of fentanyl in this study, the results were similar to our study. The only difference was the bradycardia complication, which was more common in the dexmedetomidine group in our study.

In a study, Choi et al. assessed the quality of sedation and the hemodynamic effects of dexmedetomidine, fentanyl and remifentanil during surgery, and found that the sedation rate was lower in the dexmedetomidine group (19). The hemodynamic and respiratory complications were similar to our study. Ji et al. investigated the effects of dexmedetomidine and propofol on the depth of anesthesia in colonoscopy. They divided the patients into two groups of dexmedetomidine and propofol. Similar to our study, propofol was administered in both groups in case of body movements. The recovery time, the loss of oxygen saturation and the required dose were lower in the dexmedetomidine group (20). Although the procedure and the evaluated variables were similar to the study, the adjuvant drug in our study was propofol, whose hypnotic effects disappear quickly, but in the study of Ji et al., fentanyl was added to dexmedetomidine. Although adding fentanyl does not increase respiratory complications, it exacerbates bradycardia.

The results of most studies on the sedative effects of dexmedetomidine show that the hypnotic effect of dexmedetomidine during colonoscopy is acceptable compared with other drugs. The recovery time in the dexmedetomidine group was shorted than fentanyl (21 – 23). The prevalence of bradycardia was more common in dexmedetomidine group than the fentanyl group. The frequency of nausea and vomiting was five cases in the dexmedetomidine group and two cases in the fentanyl group. The lower incidence of vomiting can be attributed to the lower consumption of propofol in the dexmedetomidine group.

One of the limitations of this study is that dexmedetomidine requires more time than fentanyl to reach its maximum effect. Therefore, it can delay the colonoscopy. There was no difference in the sedation rate in the dexmedetomidine group compared with the fentanyl group, but the use of propofol in the fentanyl group was much higher. The recovery time was lower in the dexmedetomidine group. The combination of dexmedetomidine and propofol is more appropriate than fentanyl and propofol for colonoscopy. Due to less respiratory complications of dexmedetomidine, this drug is recommended for sedation in other procedures, such as fiberoptic bronchoscopy.

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