



# Dexmedetomidine versus Propofol in Combination with Fentanyl for Sedation-Analgesia in Colonoscopy Procedures: A Randomized Prospective Study

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## ABSTRACT

### BACKGROUND

Colonoscopy is an uncomfortable and short procedure needing brief sedation with fast emergence.

### METHODS

This research is going to measure intravenous dexmedetomidine against propofol-fentanyl combination in terms of sedation-analgesia and hemodynamic changes in non-obligatory colonoscopy procedures. 70 colonoscopy candidates aged between 20 to 70 years were enrolled in this study while separated into two random equal-sized groups (P stands for propofol- & D stands for dexmedetomidine groups). All patients were premedicated with 0.03 mg/kg midazolam and 1 µ/kg fentanyl, 10 minutes and 5 minutes before the colonoscopy process, respectively. 0.5-1 mg/kg propofol for the P group and 1 µ/kg dexmedetomidine for the D group were infused in one minute before the initiation of the procedure following by normal saline as maintenance liquid and boluses of 25-50 µg fentanyl as needed.

### RESULTS

These variables were entered into a datasheet: hemodynamic changes, sedation-analgesia level throughout the procedure, and patients' and physicians' contentment. The mean arterial pressure changes were similar and insignificant in the two groups (82.44±12.34 vs. 87.63±22.45  $p=0.2$ ). The D group had lower heart rates in comparison with the P group (72.51±16.7 vs. 81.56±15.71  $p=0.001$ ). The P group was deeply to moderately sedated and required a significantly lower doses of fentanyl rescue treatment (71.02±25.63 vs. 91.45±38.62 µg  $p=0.003$ ). The P group was associated with a high incidence of apnea and was significantly superior to the D group in the matter of satisfaction (43% against 77%).

### CONCLUSION

Colonoscopists' contentment rates were identical in both groups. Propofol infusion is more satisfactory yet having more respiratory depression possibility in comparison with dexmedetomidine infusion in colonoscopy candidates.

### KEYWORDS:

Colonoscopy; Contentment; Dexmedetomidine; Propofol; Sedation-analgesia

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## INTRODUCTION

Pliable colonoscopy is a widely applied procedure for either screening-diagnostic or therapeutic purposes. Considering the patients' discomfort and nervousness being added to the painful nature of the procedure, using sedation-analgesia drugs through the procedure seems inevitable. Many anesthetic drugs such as midazolam, propofol, and/or alfentanil or pethidine combinations,  $\alpha$ -agonists, and neuroleptics are frequently administered for this matter.<sup>1,2,3</sup>

Conscious sedation-analgesia is aimed to comfort the patients with minimal adverse effects, and the ideal method is the one with fast induction and emergence, which preserves respiration and hemodynamics stability. Several regimens of drugs are being used at this time for this purpose.<sup>4,5</sup>

Small doses of propofol infusing alongside slight amounts of opioid and ketamine make the epitome of sedation-analgesia with the least possible adverse respiratory and hemodynamic effects.<sup>6</sup> Dexmedetomidine is a relatively selective  $\alpha_2$  adrenoceptor agonist that has a sedative-analgesic, anxiolytic, and sympatholytic action.<sup>7</sup> And has been employed for sedation in a variety of non-intubating procedures like colonoscopy, awake carotid endarterectomy, shockwave lithotripsy, and vitreoretinal surgery.<sup>8</sup> Sympatholytic effects of dexmedetomidine may be responsible for distressing side effects, marked hemodynamic instability, and longsome recovery in some studies like a colonoscopy.<sup>9</sup> This study was done to illustrate that dexmedetomidine, combined with fentanyl, is risk-free and operational in providing safe sedation for colonoscopy. We compared its impacts on analgesia-sedation and hemodynamic alterations with propofol/fentanyl. And also examined its impact on the colonoscopists' and patients' contentment.

## MATERIALS AND METHODS

Permitted by the Ethics Board Committee of Tehran University of Medical Sciences (TUMS) with ethical approval number: 1396.2762 and also approved by IRCT (Iranian Registry of Clinical Trials) registration number of IRCT20170805035510N4, this interventional, randomized clinical trial was carried out on 70 non-emergent (between 20 to 70 years of age) applicants for a pliable

colonoscopy under conscious-sedation and analgesia from march 28, 2018 to February 31, 2019.

The exclusion criteria were the patients suffering from liver or heart failure and also those with longtime consumption of drugs like benzodiazepines, neuroleptics, and anticonvulsants. Those with an allergy to drugs used in the investigation, those undergoing laparotomy surgeries, those with body mass index (BMI) above 35 kg/m<sup>2</sup>, and mentally ill patients were excluded either. All candidates were thoroughly informed, and written consents were obtained from them prior to the study.

Patients who met the inclusion criteria ASA I & II, aged 20-65 years old, were anyhow divided into two groups. A computer-based randomization list was used to assign patients to each one of the two study groups. Dexmedetomidine (D) and propofol (P) groups consisted of 35 subjects each.

The syringes were labeled by a colleague who did not participate in sedating and assessment of the patients. Drug syringes of analogous capacity were chosen and were unbeknown to all the staff (the patients, anesthetists, colonoscopists, and the patients' examiner). All patients were kept under standard monitoring conditions, including SPO<sub>2</sub>, uninterrupted electrocardiography, and Non Invasive Blood Pressure (NIBP) (checked on 3 minutes intervals), and all the data were collected precisely.

Afterward, an intravenous line was fixed, and a balanced solution such as sodium chloride 0.9% was initiated. All the patients received supplemental O<sub>2</sub> of 4-6 lit/minute by face-mask during the procedure and were injected 0.03 mg/kg midazolam 10 minutes prior to the procedure. Both groups received fentanyl 1  $\mu$ /kg five minutes prior to the procedure. The propofol (P) group was administered 0.5-1 mg/kg of propofol, and the dexmedetomidine (D) group, received 1  $\mu$ /kg of dexmedetomidine one minute prior to the procedure, respectively. The level of sedation was estimated using the Observer Assessment of Alertness/Sedation (OAA/S) Scale at 3-minute intervals during the procedure and also in the recovery room as regards; 1=complete quiet/unconscious, 2=deeply sedated, 3=moderately sedated, 4=lightly sedated, and 5=not sedated. Intermittent administration of fentanyl (25- 50  $\mu$ g) was used whenever the sedation level reached grade three or above. Patients' pain intensity was measured by

the VAS (visual analog scale) method during the procedure. In the recovery room, the estimation of satisfaction stage for both the patients and the colonoscopy specialists were elicited based on the following categorization: 1=no satisfaction, 2=low satisfaction, 3=medium satisfaction, 4=high satisfaction, and 5=full satisfaction.

Adverse outcomes such as nausea, vomiting, significant alterations in systolic blood pressure (BP) & diastolic BP, heart rate (HR) swings more than 30% of the primary rate, and apnea episodes lasting more than 30 seconds were meticulously recorded.

### Statistical Analysis

To demonstrate the qualitative-information of the investigation, frequency analysis (by percentage) was employed, and for the quantitative data, the mean (standard deviation) was used. Variables and values were declared in the form of frequencies and percentages. Then  $X^2$  test and Fisher's exact test were used to determine the interrelationships and their significance level. To investigate the interaction between the intervention and the qualitative outcomes, Chi-square analysis ( $X^2$  test) was applied.

## RESULTS

70 patients were entered in this study and divided into two equal-sized groups randomly. The average age of the patients was  $51.5 \pm 10.8$  years (between 23 to 69 years old). Table 1 contains the demographic information of the study.

Hemodynamic alterations magnitude during the procedure were similar between the two groups, as well as the average of mean arterial pressure (MAP) alterations in the D group in comparison with the P group ( $82.44 \pm 12.34$  vs.  $87.63 \pm 22.45$   $p=0.2$ ).

On the subject of heart rate, the D group showed lower quantities during the procedure ( $72.51 \pm 16.7$  vs.  $81.56 \pm 15.71$   $p=0.001$ ). Desaturation episodes happened more in the P group compared with the D group; therefore three patients in the P group required bag-mask ventilation assistance during the procedure ( $p=0.001$ ).

Deep to moderate sedation level was observed in all the subjects in the propofol group during the procedure, and the quantity of fentanyl cumulative dosage, which was used in these patients, was far less than the other

**Table 1: Characteristics of included patients and the procedures**

Variables	Group D	Group P	P
Age (mean±sd)	55.8±12.2	57.5±12.7	0.24
Sex (Male/female)	15/20	18/17	0.13
Mean duration procedure, min,	9.5±2.9	8.7±2.8	0.139
Mean duration	12.3±2.9	13±1.9	0.12

group ( $71.02 \pm 25.63$  vs.  $91.45 \pm 38.62$   $\mu\text{g}$ ,  $p=0.003$ ). In the D group we faced with 9% prevalence of light sedation status; therefore more boluses of fentanyl necessarily were injected during the procedure in this group. According to pain estimation results, considering the VAS score below 4, 48% of the patients in the D group and 41% of the patients in the P group had average pain severity score (VAS score) below 4 ( $p=0.5$ ).

With regard to satisfaction as an important clinical parameter, 43% of the patients' satisfaction in the D group versus 77% of the patients' satisfaction in the P group was noticeable and of the significant value ( $p=0.001$ ).

Colonoscopists' satisfaction recordings during the procedures displayed equality in both groups, with a complete satisfaction prevalence of 41%.

## DISCUSSION

Colonoscopy is a standard technique for diagnosis, screening, treatment, and follow-up purposes in many colorectal diseases. It is usually a painful and unpleasant procedure. So it demands a proper sedation-analgesia drug combination for utmost pain-free patients' cooperation while avoiding adverse outcomes. This investigation has demonstrated the superiority of propofol-fentanyl drug regimen over dexmedetomidine-fentanyl in desirable qualities such as sedation depth and patients' satisfaction during colonoscopy. Dexmedetomidine is usually administered in the ICU to put the patients under light to moderate sedation state.<sup>10</sup> It is applicable to induce light sedation during procedures like colonoscopy as well.<sup>11</sup> Dexmedetomidine can be used as an additive to other tranquilizers, for instance, midazolam, fentanyl, and propofol, to improve anxiolysis and keeping the hemody-

dynamic stability by reducing the need of tranquilizers.<sup>12</sup>

The study of Wu and colleagues was conducted on 60 patients in two equal groups to compare dexmedetomidine and midazolam used for endoscopy. Parameters like SPO<sub>2</sub>, HR, MAP, patients' satisfaction estimation, and pain severity index were evaluated in this study. Not to mention, fentanyl boluses were used for both groups besides the primary drugs. The outcomes demonstrated a decline in pain scores and improvement of SPO<sub>2</sub> values in the dexmedetomidine group.<sup>13</sup>

In the study of Amri and co-workers, dexmedetomidine 1 µg/kg was administered 10 minutes prior to the procedure, followed by 0.5 µg/kg/hour maintenance infusion. The control group was received fentanyl 0.5 µg/kg 3 minutes prior to the procedure, and boluses of 20 mg propofol were injected afterward if necessary. They eventually declined pain scores and improved hemodynamic steadiness in the dexmedetomidine group versus the propofol group.<sup>14</sup>

In several studies, unlike our investigation, intravenous infusion of dexmedetomidine was started after a loading dose injection.

The procedure time length in our research was under 10 minutes, and we just injected the loading dose of dexmedetomidine alone; thinking of its pharmacokinetic properties, it has a fast distribution half-life of about six minutes and a short-term span of action.<sup>15</sup>

Patients' satisfaction in the dexmedetomidine group was lower than in the propofol group due to unpleasant colonoscopic pain, so these patients received more fentanyl.

With regard to hemodynamic alterations, outcomes of our research were similar to other studies, expressing that the dexmedetomidine group showed a lower HR than the propofol group. Dexmedetomidine is a potent, selective α<sub>2</sub>-adrenergic agonist, and it inspires sedation by declining the noradrenergic neurons' activity in the locus ceruleus located in the brainstem, escalating the possibility of bradycardia and hypotension in combination with fentanyl.<sup>16</sup>

Jalowiecki and colleagues have found that administering dexmedetomidine alone is not applicable for conscious sedation in outpatient colonoscopy because repetitive fentanyl injection is needed throughout the

procedure.<sup>9</sup>

Propofol, joint with opioids or ketamine, is considered risk-free in colonoscopy with little hemodynamic derangements and superior patients' satisfaction.<sup>17,18,19</sup> Propofol usage in this research approves this discovery that intravenous bolus injections of propofol-fentanyl regimen can improve patients' satisfaction instead of dexmedetomidine regimen throughout the colonoscopy.

Sedation-analgesia level achieved by propofol-fentanyl administration while maintaining the hemodynamic indices caused more satisfaction and fewer pain-scores rather than the dexmedetomidine group, although, in the dexmedetomidine group, desaturation episodes were infrequent and needed no invasive intervention by the anesthetist.

#### ETHICAL APPROVAL

There is nothing to be declared.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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