Dexmedetomidine and fentanyl combination versus dexmedetomidine and pethidine as sedatives during colonoscopy

Ahmed M.M. El-Garhy[a], Khaled S.S. Makboul[b]

Background and aim Endoscopy procedures are generally performed under sedation, which ranging from minimal sedation to deep sedation. Conscious sedation during colonoscopic procedures provides a high level of patient and physician satisfaction. An ideal sedative agent should allow rapid modification of the sedation level by modifying the dose and should not have any adverse effects. Because such an ideal sedative agent does not exist, the combination use of dexmedetomidine with opioids (fentanyl or pethidine) may have the advantages over the use of a single agent. The goal of this study was to assess the effect of dexmedetomidine in combination with fentanyl or pethidine as a sedative for outpatient colonoscopy on hemodynamics, level and onset of sedation, analgesia, and degree of satisfaction of the colonoscopist and patients.

Patients and methods A total of 60 colonoscopy patients between 21 and 60 years of age were included in the study. The patients scheduled for elective outpatient colonoscopy (with conscious sedation) were randomized into two groups: group 1 'DF group' (N=30): dexmedetomidine 1 μ/kg/h infusion by syringe pump along with 1 μ/kg fentanyl was administered before the start of colonoscopy as a single shot, and Group 2 'DP group' (N=30): dexmedetomidine 1 μ/kg/h infusion by syringe pump along with 1 mg/kg pethidine was administered before the start of colonoscopy as a single shot. The assessment includes heart rate (HR, beats/min), mean arterial blood pressure (MAP, mmHg), oxygen saturation at baseline and every 5 min, onset and level of sedation by Ramsay Sedation Score (RSS) after administration of the drugs, Numeric Pain Rating Scale at the end of colonoscopy, and the degree of satisfaction of the patients and the colonoscopist.

Results The average value of the 6 h measurements in fentanyl group was 75.6±0.91 beats/min; whereas in pethidine group was 92.2±0.67 beats/min, with highly significant statistical difference (P<0.001), whereas there were nonsignificant differences regarding MAP and oxygen saturation. There was a highly significant decrease in the onset of sedation and increase in RSS and Numeric Pain Rating Scale in fentanyl group compared with pethidine group (P<0.01 for all). Moreover, there were nonsignificant differences regarding the degree of satisfaction for the colonoscopist and the patient (P>0.05). Multiple regression analysis shows that the increase in baseline HR had an independent effect on increasing onset of sedation (P<0.0001). Moreover, the fentanyl usage and the decrease in baseline HR had an independent effect on increasing RSS (P<0.01).

Conclusion Patients who underwent colonoscopy and received dexmedetomidine-fentanyl regimen showed better hemodynamics (decreased HR, normal MAP, and oxygen saturation measurements), along with rapid onset of sedation and satisfied RSS compared with patients who received dexmedetomidine–pethidine regimen. In contrast, pethidine group showed better analgesia than fentanyl group. Both groups showed comparable satisfaction results in the colonoscopist and patients.

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Departments of, [a]Anesthesia, [b]Internal Medicine, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Correspondence to Ahmed M.M. El-Garhy, MD of anaesthesia and icu, Department of Anesthesia, Faculty of Medicine, Al-Azhar University, Cairo, 12512, Egypt. Tel: 01099668540, 01110888332, 0237710636; e-mail: elgarhy_79@yahoo.com

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Introduction

Colonoscopy is an important diagnostic and therapeutic procedure and usually regarded as an invasive procedure that cannot be tolerated by most patients without sedation. Endoscopy procedures are generally performed under sedation, which ranges from minimal sedation to deep sedation. The term 'conscious sedation' is used for sedation for therapeutic or diagnostic procedures, which corresponds to moderate level of sedation that enables the patient to respond to verbal and tactile stimulation and preserve cardiovascular and respiratory systems. Conscious sedation during colonoscopic procedures provides a high level of patient safety and physician satisfaction [1,2]. An ideal sedative agent should allow for rapid modification of the sedation level by modifying the dose and should not have any adverse effects. It should have rapid onset and short duration of action without cumulative effects. The metabolites of the drugs used for sedation should be inactivated at the end of procedure so that hospitalization is not prolonged [3,4]. An ideal sedative agent does not exist; therefore, the combination of dexmedetomidine with opioids (fentanyl or pethidine) may have the advantages over the use of a single agent [4–6]. The

aim of this study is to assess the effect of dexmedetomidine in combination with fentanyl and pethidine as a sedative for outpatient colonoscopy on hemodynamics, level and onset of sedation, pain, and satisfaction of the colonoscopist and the patients. Fentanyl is an opioid, which is often used for anesthesia and analgesia. During anesthesia, it is often used along with a hypnotic agent like propofol. It is also administered in combination with a benzodiazepine, such as midazolam, to produce sedation for procedural sedation, for example, colonoscopy, cardiac catheterization, and dental surgery, or in emergency rooms [7]. Pethidine (meperidine) is a synthetic opioid for pain medication of the phenylpiperidine class [8].

Aim

The primary outcome of the study is to assess onset and level of sedation during colonoscopy by adding dexmedetomidine to pethidine or fentanyl, and the secondary outcome of the study is to assess changes in hemodynamics after procedural analgesia and degree of satisfaction for the patient and the colonoscopist.

Patients and methods

Patients

This prospective randomized comparative double-blind clinical study was done in Al-Azhar University Hospital (Al-Hussein) from September 2017 to March 2018, following the local ethics committee approval and informed written consent from the patients.

A total of 60 colonoscopy patients between 21 and 60 years of age, with American Society of Anesthesiologists status I and II, were included in the study.

Exclusion criteria were as follows:

(1) Patients with airway problems.
(2) History of sleep apnea.
(3) Neuropsychiatric disorders.
(4) American Society of Anesthesiologists status III and IV (chronic cardiac, respiratory, and renal disorders).

The patients scheduled for elective outpatient colonoscopy with conscious sedation were randomized into two equal groups according to the given drug.

(1) Group 1 'DF group' (*N*=30): dexmedetomidine 1 μ/kg/h infusion by syringe pump and 1 μ/kg fentanyl administered before the start of colonoscopy as a single shot.
(2) Group 2 'DP group' (*N*=30): dexmedetomidine 1 μ/kg/h infusion by syringe pump and 1 mg/kg pethidine administered before the start of colonoscopy as a single shot.

Methods

Procedure

(1) On arrival in the endoscopy unit, an intravenous line was inserted and secured, and all patients were monitored for heart rate (HR, beats/min), noninvasive arterial blood pressure (per mmHg), ECG, and oxygen saturation as baseline values by GE Datex-Ohmeda monitor (GE health care, newyork, USA). Oxygen at the rate of 3 l/min was administered by nasal cannula. A syringe pump (Fresenius Kabi, Homburg, germany) containing 100 μg dexmedetomidine in 50 ml normal saline, with each ml containing 2 μg of dexmedetomidine, ready for infusion, along with 100 μg of fentanyl in 10 ml normal saline given in a dose of 1 μ/kg or 100 mg pethidine in 10 ml normal saline, given in a dose of 1 mg/kg given as a single shot, was given before the start of colonoscopy.
(2) All colonoscopic procedures were conducted by the same endoscopist, whereas the drugs were administered by the same anesthesiologist throughout the study.

After the administration of drugs in both groups, each patient was evaluated for the following:

(1) Hemodynamics:
  (a) HR (beats/min).
  (b) Mean arterial pressure (MAP, mmHg).
  (c) Oxygen saturation.
  (d) All vital data were recorded at baseline, and 5, 10, 15, 20, and 25 min after starting of sedation.
(2) Onset of sedation (min):
  (a) Time from the start of drug administration till Ramsey's Sedation Score (RSS) 4 [9].
(3) Level of sedation (RSS): from 1 to 6 [9]:
  (a) Anxious or restless – 1.
  (b) Co-operative, oriented –.2
  (c) Responding to commands – 3.
  (d) Brisk response to stimulus – 4.
  (e) Sluggish response to stimulus – 5.
  (f) No response to stimulus – 6.
  Level of sedation measured from the start of drug administration and every 5 min till RSS 4.
(4) Postprocedural analgesia:
  (a) Evaluated pain by Numeric Pain Rating Scale (NPRS) (from 1 to 10), measured at the end of colonoscopy when RSS reaches 1.

(5) Degree of satisfaction: for colonoscopist:
   (a) Good.
   (b) Mild.
   (c) Moderate.
   (d) Unsatisfied.
(6) Degree of satisfaction: for patient:
   (a) Comfortable.
   (b) Uncomfortable.
   (c) Intensely uncomfortable.

Patients were transferred to the recovery room when vital signs were within normal limits.

Statistical analysis

Data entry, processing, and statistical analysis was carried out using MedCalc, version 15.8 (MedCalc, Ostend, Belgium). Tests of significance (Mann–Whitney's U, χ^2, factorial analysis of variance tests, Spearman's correlation coefficient, and multiple regression analysis) were used. Data were presented, and suitable analysis was done according to the type of data (parametric and nonparametric) obtained for each variable. P values less than 0.05 (5%) was considered to be statistically significant.

Results

In this study, 60 colonoscopy patients between 21 and 60 years of age were included in the study. Regarding (Table 1) describing basic clinical and demographic data, it was found that the mean age of all colonoscopy patients was 40.33±9.27 years, where in fentanyl group was 38.33±12.16 years, whereas in pethidine group was 42.33±4.32 years. The mean BMI in fentanyl group was 20.17±5.9, whereas in pethidine group was 21.38±6.84. The mean colonoscopy duration in fentanyl group was 26.02±3.16 min, whereas in pethidine group was 27.53±4.89 min. Regarding sex, most patients were males (65%) and 35% were females. In fentanyl group, 66.7% were males and 33.3% were females, whereas in pethidine group, 63.3% were males and 36.7% were females, as shown in Table 1.

Table 1 Demographic data

Variables	Fentanyl group (N=30) (mean±SD)	Pethidine group (N=30) (mean±SD)
Age (years)	38.33±12.16	42.33±4.32
BMI	20.17±5.9	21.38±6.84
Duration of colonoscopy	26.02±3.16	27.53±4.89
Sex [n (%)]		
Female	10 (33.3)	11 (36.7)
Male	20 (66.7)	19 (63.3)

Regarding primary outcome (onset of sedation and level of sedation), follow-up period revealed the following:

(1) There was a highly significant decrease in onset time of sedation in fentanyl group compared with pethidine group, with highly significant statistical difference (P<0.01). The median value of onset of sedation in fentanyl group was 7 min, whereas in pethidine group was 11.5 min, with highly significant statistical difference (P<0.001), as shown in Table 2.
(2) There was a highly significant increase in RSS in fentanyl group compared with pethidine group of patients, with highly significant statistical difference (P<0.01). The median value of RSS in fentanyl group was 4.5, whereas in pethidine group was 2.5, with highly significant statistical difference (P<0.001), as shown in Table 2.
(3) Regarding secondary outcome (pain score), follow-up period revealed the following:
   There was a highly significant increase in NPRS in fentanyl group compared with pethidine group, with highly significant statistical difference (P<0.01). The median value of NPRS in fentanyl group was 3.5, whereas in pethidine group was 2.5, with highly significant statistical difference (P<0.001), as shown in Table 3.

Regarding satisfaction data, comparative studies regarding satisfaction data during our follow-up period revealed the following:

There was a nonsignificant difference regarding the degree of satisfaction of the colonoscopist and the patient (P>0.05), as shown in Table 4.

Comparative studies between fentanyl and pethidine group of patients during follow-up period revealed the following:

(1) Regarding HR, the average value of the six time measurements of HR, with all measurements at 5 min interval, in fentanyl group was 75.6±0.91,

Table 2 Comparison between fentanyl and pethidine groups as regards sedation data

Variables	Fentanyl group (N=30) [median (IQR]	Pethidine group (N=30)[median (IQR]	P value (Mann–Whitney U-test)
Onset of sedation (min)	7 (7–7.5)	11.5 (10–12)	<0.001**
Level of sedation (RSS)	4.5 (4–5)	2.5 (2–3)	<0.001**

IQR, interquartile range; RSS, Ramsay Sedation Score.

Table 3 Comparison between fentanyl and pethidine groups regarding pain score

Variables	Fentanyl group (*N*=30) [median (IQR]	Pethidine group (*N*=30)[median (IQR]	*P* value (Mann–Whitney *U*-test)
Pain (NPRS)	3.5 (3–4)	2.5 (2–3)	<0.001**

IQR, interquartile range; NPRS, Numeric Pain Rating Scale.

whereas in pethidine group was 92.2±0.67, with highly significant statistical difference ($P<0.001$). Fentanyl group showed a steady decrease in HR compared with pethidine group, which showed a marked decrease during the serial vital measurements, as shown in Fig. 1.

(2) Regarding MAP, the average value of the six MAP measurements in fentanyl group was 96.15±7.73 mmHg, whereas in pethidine group was 96.09 ±8.44 mmHg, with nonsignificant statistical difference ($P>0.05$). Fentanyl and pethidine groups showed comparable decrease in MAP during the serial vital measurements, as shown in Fig. 2.

(3) Regarding oxygen saturation, the average value of the six oxygen saturation measurements in fentanyl group was 99.32±0.44, whereas in pethidine group was 99.37±0.41, with nonsignificant statistical difference ($P>0.05$). Fentanyl and pethidine groups showed comparable levels in oxygen saturation during the serial vital measurements, as shown in Fig. 3.

Correlation studies regarding sedation outcomes revealed the following:

(1) Multiple regression analysis shows that after applying (forward method) and entering some predictor variables, the increase in baseline HR had an independent effect on increasing onset of sedation, with significant statistical difference ($P<0.0001$), as shown in Table 5.

(2) Multiple regression analysis shows that after applying (forward method) and entering some predictor variables, the increase in age and fentanyl usage and the decrease in baseline HR had an independent effect on increasing RSS, with a significant statistical difference ($P<0.01$, respectively), as shown in Table 5.

Discussion

Colonoscopy is an important diagnostic and therapeutic procedure and is usually regarded as an invasive procedure that cannot be tolerated by most patients without sedation [1].

Table 4 Comparison between fentanyl and pethidine groups regarding satisfaction data

Variable	Fentanyl group (*N*=30) [*n* (%)]	Pethidine group (*N*=30) [*n* (%)]	*P* value (χ^2-test)
Satisfaction (colonoscopist)			
Good	17 (56.7)	14 (46.7)	0.605
Mild	6 (20)	8 (26.6)	
Moderate	7 (23.3)	8 (26.6)	
Unsatisfied	0 (0)	0 (0)	
Satisfaction (patients)			
Comfortable	17 (56.7)	19 (63.3)	0.792
Uncomfortable	13 (43.3)	11 (36.7)	
Intensely uncomfortable	0 (0)	0 (0)	

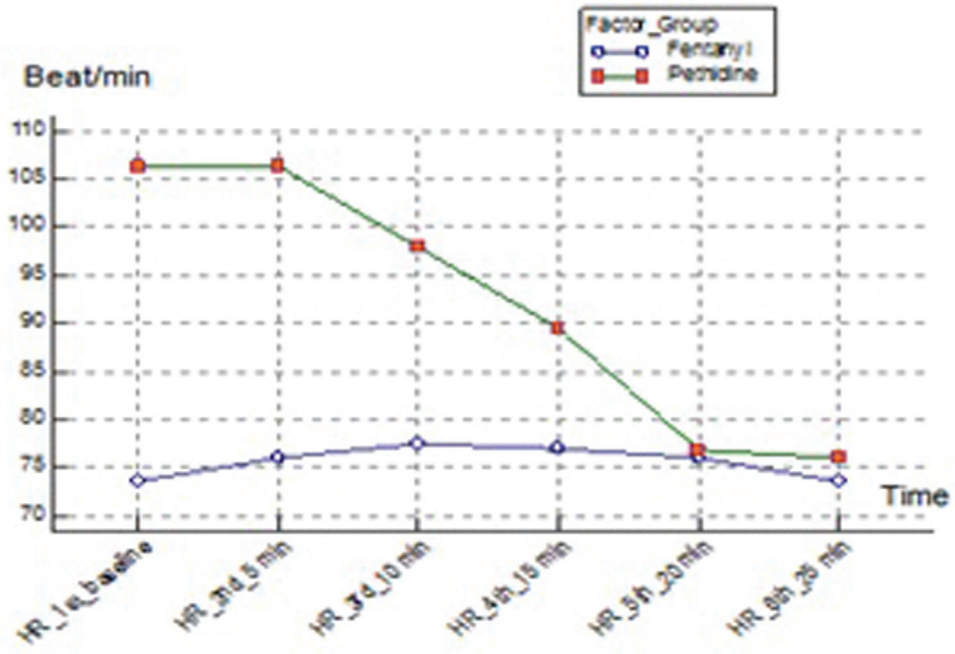
The fentanyl and pethidine groups were further analyzed and compared according to the serial vital measurements (baseline, 5, 10, 15, 20, and 25 min after start of sedation).

Regarding sedation data, a comparative study between the two groups revealed a highly significant decrease in onset of sedation in fentanyl group compared with pethidine group of patients, with a highly significant statistical difference ($P<0.01$). The median value of onset of sedation in fentanyl group was 7 min, whereas in pethidine group was 11.5 min, with a highly significant statistical difference ($P<0.001$). These results came in agreement with amornyotin [10], who reported that fentanyl has a rapid onset, short duration of action, lack of direct of myocardial depressant effects, and absence of histamine release. The onset of action is 30–60 s, peak effect is 5–15 min, and duration of action is 30–45 min. Intravenous fentanyl can be easily and rapidly titrated for painful procedures. The combination of fentanyl and midazolam is a popular regimen, with a safety profile when both drugs are carefully titrated.

A comparative study between the two groups also revealed a highly significant increase in RSS in fentanyl group compared with pethidine group of patients, with a highly significant statistical difference ($P<0.01$). The median value of RSS in fentanyl group was 4.5, whereas in pethidine group was 2.5, with a highly significant statistical difference ($P<0.001$). These results came in agreement with Dere *et al.* [11].

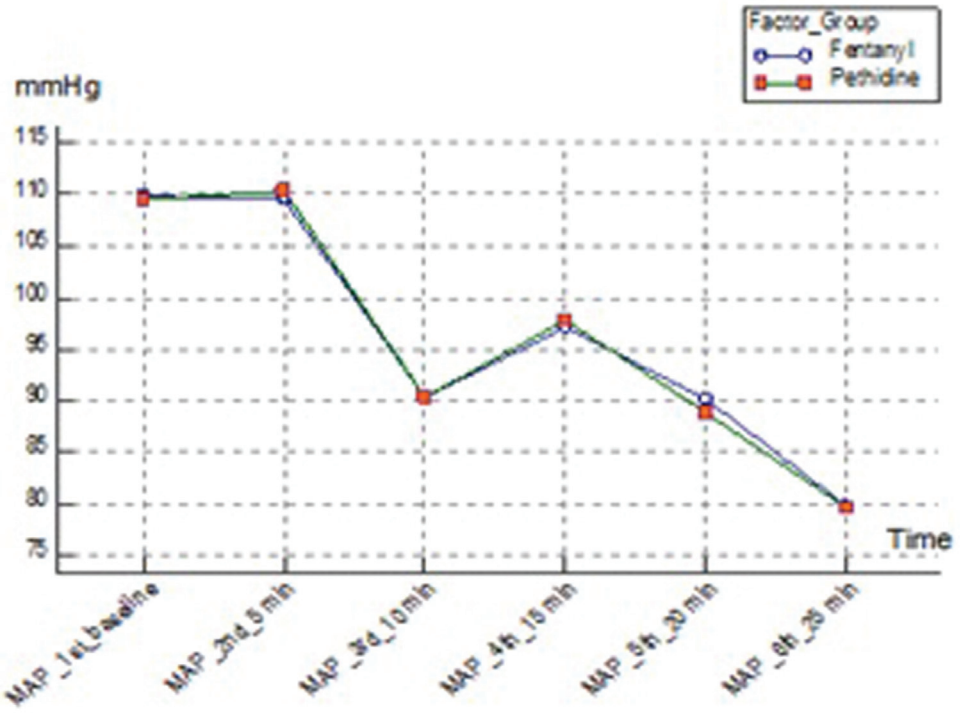
A comparative study between the two groups also revealed a highly significant increase in NPRS in fentanyl group compared with pethidine group, with a highly significant statistical difference ($P<0.01$). The median value of NPRS in fentanyl group was 3.5, whereas in pethidine group was 2.5, with a highly

Figure 1



Comparison between the two groups of patients regarding serial heart rate (HR) measurements.

Figure 2



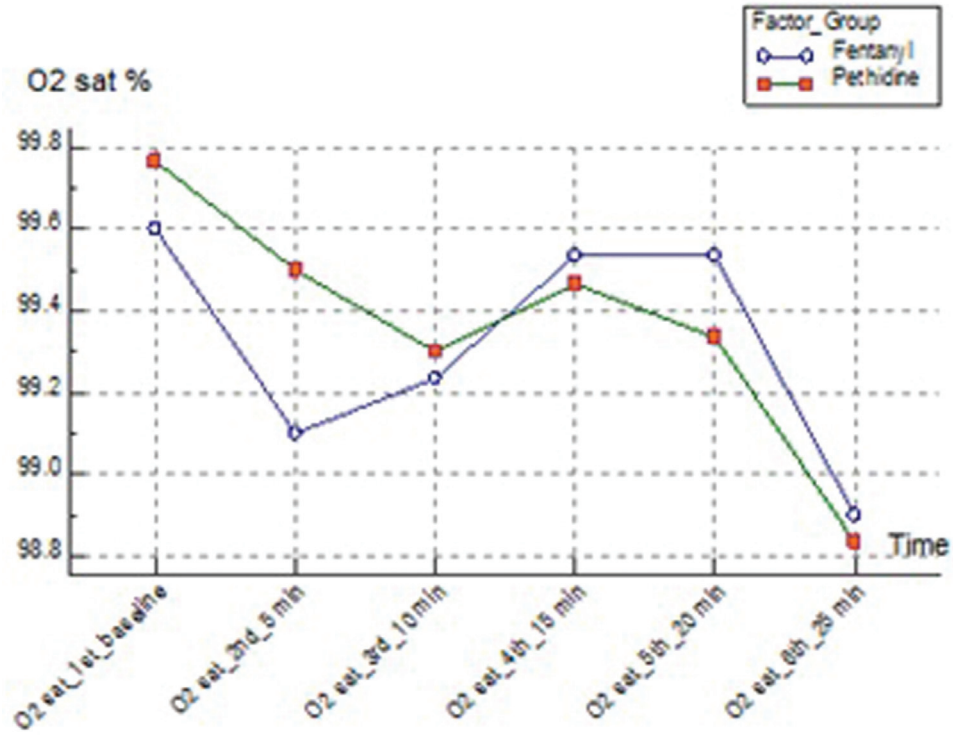
Comparison between the two groups of patients regarding six time measurements of mean arterial pressure (MAP); all the time of the procedures had 5-min interval.

significant statistical difference ($P<0.001$). These results came in agreement with Dere *et al.* [11].

Multiple regression analysis showed that after applying (forward method) and entering some predictor variables the increase in baseline HR had an independent effect on increasing onset of sedation, with a significant statistical difference ($P<0.0001$). These results came in agreement with Ozel *et al.* [12].

Multiple regression analysis also showed that after applying (forward method) and entering some

Figure 3



Comparison between the two groups of patients regarding serial oxygen saturation measurements.

Table 5 Multiple regression model for the factors affecting level of sedation (Ramsay Sedation Score) using forward method

Predictor factors	β	SE	*P*
Constant	3.0242		
Age	0.03460	0.002483	<0.0001**
Type of sedation (fentanyl)	4.0026	0.1613	<0.0001**
Baseline HR	–0.05649	0.004833	<0.0001**
Baseline MAP	–	–	–
Baseline oxygen saturation	–	–	–

–, excluded from the model if $P>0.1$; β, regression coefficient; HR, heart rate; MAP, mean arterial pressure.

predictor variables, the increase in age and fentanyl usage and the decrease in baseline HR had an independent effect on increasing RSS, with a significant statistical difference ($P<0.01$ for all). These results came in agreement with Ozel *et al.* [12].

Regarding satisfaction data, a comparative study between the two groups revealed nonsignificant difference regarding the degree of satisfaction for the colonoscopist and the patient ($P>0.05$). These results came in agreement with Obara *et al.* [13].

Comparative studies revealed that the average value of the 6 h measurements in fentanyl group was 75.6±0.91, whereas in pethidine group was 92.2±0.67, with a highly significant statistical difference ($P<0.001$). The average value of the six MAP measurements in fentanyl group was 96.15 ±7.73 mmHg, whereas in pethidine group was 96.09±8.44 mmHg, with a nonsignificant statistical difference ($P>0.05$). The average value of the six oxygen saturation measurements in fentanyl group was 99.32±0.44, whereas in pethidine group was 99.37±0.41, with a nonsignificant statistical difference ($P>0.05$). These results came in agreement with Ozel *et al.* [12] and came in disagreement with Dere *et al.* [11], who stated that HR, MAP, and oxygen saturation were significantly lower when compared with pethidine group [11,12].The two groups showed marked increase in HR in pethidine group compared with fentanyl group and a marked decrease during the serial vital measurements. In contrast, fentanyl group showed a steady HR during serial vital measurements. These results came in agreement with Ozel *et al.* [12].

Both groups showed comparable decrease in MAP during the serial vital measurements. These results came in agreement with Ozel *et al.* [12] and came in disagreement with Dere *et al.* [11].

Both groups showed comparable levels in oxygen saturation during the serial vital measurements. These results came in agreement with Ozel *et al.* [12].

Conclusion

Colonoscopy patients who received dexmedetomidine-fentanyl regimen showed better vital state (decreased HR, normal MAP, and oxygen saturation measurements), along with rapid onset of sedation and satisfactory RSS, compared with patients who received dexmedetomidine–pethidine regimen. In contrast, pethidine group showed better analgesia than fentanyl group. Both groups showed comparable satisfaction results regarding the colonoscopist and the patient.

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Nil.

Conflicts of interest

There are no conflicts of interesting.

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