The role of dexmedetomidine infusion on intraoperative desflurane and fentanyl requirement in spine surgery: a double-blinded, randomized, controlled trial

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Introduction Dexmedetomidine is a potent selective agonist of α2 adrenoceptor having sedative, amnestic, sympatholytic, and pain-relieving properties without producing significant respiratory depression and promotes hemodynamic stability when used as an adjuvant during general anesthesia.

Aim The objective of this study was to evaluate the effect of dexmedetomidine infusion on desflurane consumption, intraoperative fentanyl requirement, and hemodynamic changes.

Patients and methods Sixty patients of American Society of Anesthesiologists I and II enlisted for elective spine surgery were randomly classified into two groups: group D dexmedetomidine group received preoperative intravenous dexmedetomidine 0.5 μg/kg over 10 min followed by 0.25 μg/kg/h (1 ml, 100 μg diluted with normal saline in 20 ml syringe) intraoperative infusion till the end of surgery and group P, the placebo group received a similar volume of normal saline. Desflurane consumption and intraoperative fentanyl requirement were recorded as well as intraoperative hemodynamic changes.

Results Desflurane consumption and intraoperative fentanyl requirement were significantly lower in group D ($P<0.001$) as well as there was a significant decrease in heart rate and mean arterial blood pressure ($P<0.05$) in D group

Conclusion Dexmedetomidine infusion resulted in significant reduction of desflurane consumption and intraoperative fentanyl requirement with significant decrease in heart rate and mean arterial blood pressure.

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Keywords: desflurane, dexmedetomidine, fentanyl, spine surgery

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Introduction

Spine surgery presents a number of challenges to the anesthetist. The surgeon prefers the patient to be conscious and able to respond to command immediately after anesthesia for early neurological assessment [1]. The use of desflurane as inhalation anesthesia provides fast-track anesthesia, as it is characterized by very low solubility in water with a low blood gas partition coefficient; it undergoes minimal metabolism (0.02%) and eliminated via the lung and therefore, it has faster onset and faster offset of anesthesia with adequate intraoperative hemodynamic stability [2–4]. The use of alternative analgesics is needed to improve the anesthetic management and to reduce the requirement of inhalational anesthesia and opioids [5]. Hence, ultra-short-acting anesthetics are recommended; α2 adrenergic receptor agonist can be a good choice [6,7]. Dexmedetomidine is an active pharmacological D-isomer of medetomidine. It is a potent selective agonist of α2 adrenoceptor compared with clonidine having sedative, amnestic sympatholytic, and pain-relieving properties [5,8] without producing significant respiratory depression and promotes hemodynamic stability when used as an adjuvant during general anesthesia [9]. Thus, we hypothesized that the use of dexmedetomidine infusion can decrease intraoperative desflurane and fentanyl consumption and maintain hemodynamic stability. The primary outcome of the present study was to study the effect of dexmedetomidine infusion on desflurane and fentanyl consumption intraoperatively, while the secondary outcome was to study its effect on intraoperative hemodynamic changes.

Patients and methods

This study is an interventional, randomized, prospective, double-blinded, controlled study that was performed at Al-Zahraa University Hospital in the period from January 2018 till May 2018, after obtaining ethics committee approval and patient informed written consent. Sixty patients aged from 21 to 40 years under the American Society of Anesthesiologists (ASA) status I and II of either sex enlisted for selective spine surgeries were recruited into

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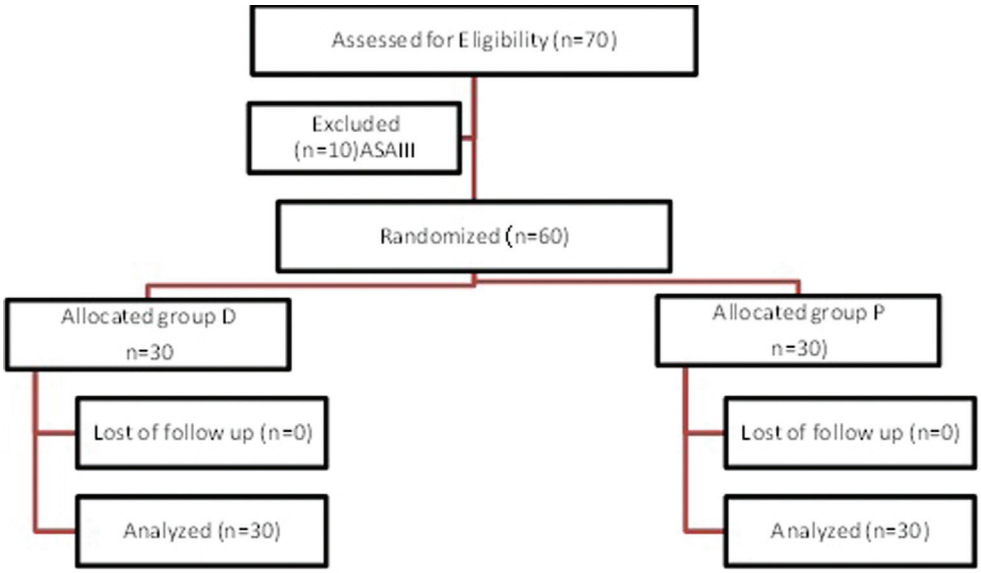
Figure 1



Flowchart of the study.

the study. Patients with cardiovascular, psychiatric, and respiratory disorders were excluded.

Randomization was performed using computer-generated random numbers and sealed opaque envelope technique that the patients were alienated to one of the two groups: group D (the dexmedetomidine group) and group P (the placebo group). Each group contained 30 patients. A CONSORT flow diagram displaying the number of participants who were randomly assigned, excluded, and analyzed is shown in Fig. 1.

Monitoring was achieved by continuous ECG, pulse oximetry, noninvasive blood pressure, and end-tidal CO_2. All patients received 3–5 min preoxygenation. Group D received intravenous dexmedetomidine at a dose of 0.5 μg/kg over 10 min using a syringe pump prior to anesthesia induction (1 ml; 100 μg dexmedetomidine diluted with saline in 20 ml/syringe), while group P received a similar volume of normal saline over 10 min using identical syringe pump; both infusions were set by an anesthetist not involved in the study. Anesthetic infusion was obtained via intravenous fentanyl (1 μg/kg) followed by propofol (1 mg/kg) sleeping dose. Then atracurium 0.5 mg/kg was given to facilitate endotracheal intubation. Fluid regimen consisted of Ringer's solution given at a rate of 6–8 ml/kg/h infusion throughout the procedure. Fresh gas flow was 2 l/min. A mixture of 60% O_2/40% air was administered through a closed system while ventilation was controlled to keep end-tidal CO_2 at 30–35 mmHg. Patients in both groups received desflurane at a concentration of 6% and then adjusted to keep the anesthetic level guided by BIS from 40 to 50. A maintenance dose of dexmedetomidine 0.25 μg/kg/h was infused to group D. At 10–20 min before the end of the procedure, the infusion was stopped. A top-up dose of atracurium 0.1 mg/kg was repeated every 30 min guided by nerve stimulator and any rise in heart rate (HR) and mean arterial blood pressure (MABP) exceeding 20% of the preoperative level in spite of adequate anesthetic level was treated with fentanyl 0.5 μg/kg, while any decrease of MABP or HR exceeding 20% was treated by intravenous ephedrine 5 mg or atropine 0.5 mg, respectively. At the end of the procedure, desflurane was discontinued. Neostigmine 0.05 mg/kg and atropine 0.2 mg/kg were given to reverse residual neuromuscular blockade for extubation and transfer to the recovery room. Assessment parameters were demographic data such as age, weight, height, sex, ASA, duration of surgery, HR and MABP preoperative baseline and after intubation and then every 10 min in the first 30 min and then every 15 min till the end of surgery. Total intraoperative fentanyl requirements were also recorded.

Desflurane consumption (ml/min)=flow (l/min)×concentration×molecular weight/100×24×density.

As gram molecular weight/100×24×density is constant for each inhalation agent, the constant of desflurane=0.0477 (the molecular weight of desflurane is 168 and the density is 1.465 g/ml), and desflurane consumption (ml/h)=flow×concentration×0.477×60.

Table 1 Demographic data and surgical time

	Group D (*N*=30) (mean±SD)	Group P (*N*=30) (mean±SD)	Test value	*P* value
Age (years)	33.25±7.67	32.85±9.12	–0.184[a]	0.855
Weight (kg)	142.58±8.57	138.65±7.43	–1.898[a]	0.063
Height (cm)	170.36±6.54	173.68±7.52	1.825[a]	0.073
Sex [*n* (%)]				
Males	10 (33.3)	12 (40.0)	0.287*	0.592
Females	20 (66.7)	18 (60.0)		
ASA [*n* (%)]				
I	20 (66.7)	18 (60.0)	0.287*	0.592
II	10 (33.3)	12 (40.0)		
Duration of surgery (min)	88±20	85±15	–0.657[a]	0.514

ASA, American Society of Anesthesiologists. [a]Independent *t* test. *P* value more than 0.05: nonsignificant (NS). *means non significant.

Table 2 Intraoperative consumption of desflurane and fentanyl

	Group D (*N*=30) (mean±SD)	Group P (*N*=30) (mean ±SD)	Test value[a]	*P* value
Desflurane (ml/h)	24.56±1.85	30.12±1.62	12.384	<0.001
Fentanyl (μg)	160±13.07	200.6±26.41	7.547	<0.001

[a]Independent *t* test. *P* value less than 0.01: highly significant (HS).

Table 3 Preoperative and intraoperative changes in mean arterial blood pressure (mmHg)

	Group D (*N*=30) (mean ±SD)	Group P (*N*=30) (mean ±SD)	Test value	*P* value	Significance
Baseline preoperative	90.0 ±5.0	89.0 ±4.0	0.855	0.395	NS
After intubation	80.0 ±5.0	84.0 ±3.0	3.757	0.001	HS
After 10 min	78.0 ±3.0	80.0 ±4.0	2.191	0.032	S
After 20 min	78.0 ±1.0	81.0 ±3.0	5.196	<0.001	HS
After 30 min	79.0 ±4.0	81.0 ±4.0	1.936	0.058	NS
After 45 min	79.0 ±2.0	82.0 ±2.0	5.09	<0.001	HS
After 60 min	80.0 ±5.0	82.0 ±4.0	1.711	0.093	NS
After 75 min	81.0 ±2.0	83.0 ±5.0	2.034	0.046	S
After extubation	81.0 ±5.0	84.0 ±5.0	2.324	0.023	S

χ^2 test: independent *t* test. *P* value more than 0.05: nonsignificant (NS). *P* value less than 0.05: significant (S). *P* value less than 0.01: highly significant (HS).

Sample size

The sample size was calculated using graph pad instant statistics version 3. Based on previous studies, dexmedetomidine infusion was expected to reduce desflurane consumption by 26% and intraoperative fentanyl by 23%. The calculated sample size was 26 patients for each group, with the level of significance being 0.05 and the power being 90%. So, 30 patients were randomized into each group to ensure reliable results.

Statistical analysis

Data were collected, revised, coded, and entered to the Statistical Package for Social Sciences (IBM SPSS) released 2015 for Windows, version 23.0 (IBM Corporation, Armonk, New York, USA). The qualitative data were presented as numbers and percentages while quantitative data were presented as mean, SDs, and ranges when their distribution was found parametric. The comparison between two groups regarding qualitative data were done by using the χ^2 test, while the comparison between two groups regarding quantitative data were done by using the independent *t* test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *P* value was considered significant at the level of less than 0.05.

Results

As regards demographic data (age, weight, height, sex, and ASA status) as well as duration of surgery and anesthesia, they were comparable in both groups (Table 1).

The average intraoperative consumption of desflurane and fentanyl were highly significantly less in group D versus group P ($P<0.001$) (Table 2).

In group D, MABP values were highly significantly decreased versus the placebo group, ($P<0.001$) after intubation, after 20 min, and after 45 min. But after 10 min, after 75 min, and after extubation it was significantly decreased ($P<0.05$), while at 30 min and 60 min, there were no significant decrease in MABP in group D versus group P (Table 3).

As regards HR, the dexmedetomidine group showed a highly significant decrease versus the placebo group throughout the procedure ($P<0.001$) (Table 4 and Fig. 2)

Disscussion

The current study estimated the impact of dexmedetomidine infusion on consumption of desflurane and intraoperative fentanyl as well as hemodynamics during spine surgery Our study showed that the average consumption of desflurane was highly significantly lower in group D compared with group P. Similar results were obtained by the study that used dexmedetomidine as a preanesthetic medication followed by infusion during laparoscopic sleeve gastrectomy with significant reduction in desflurane consumption [10]. Another study showed that intravenous administration of dexmedetomidine at a dose of 1 μg/kg before induction of anesthesia, followed by intraoperative infusion of 0.5 μg/kg/h resulted in statistically significant reduction in desflurane consumption by 27% [5]. In agreement with our results there was another that study used other inhalation anesthesia that showed a significant reduction of end-tidal sevoflurane by 23.8% up to 64% when using dexmedetomidine in children undergoing ambulatory surgery [11]. The high percentage may be due to the different age group, type, and time of surgery. Other results have shown 28% reduction in sevoflurane consumption when using dexmedetomidine adjuvant during abdominal surgery [12] .Another study showed a significant decrease in end-tidal isoflurane ($P<0.05$), when used dexmedetomidine infusion as an adjuvant to general anesthesia for laparoscopic surgeries [13], while another study reported marked decrease in isoflurane consumption by 32% when used dexmedetomidine infusion at a dose of 1 μg/kg/h loading dose followed by 0.05 μg/kg/h maintenance dose for elective surgeries of more than 3 h [14]. This difference may be due to the different inhalation agent, duration of surgery, or variable drug doses.

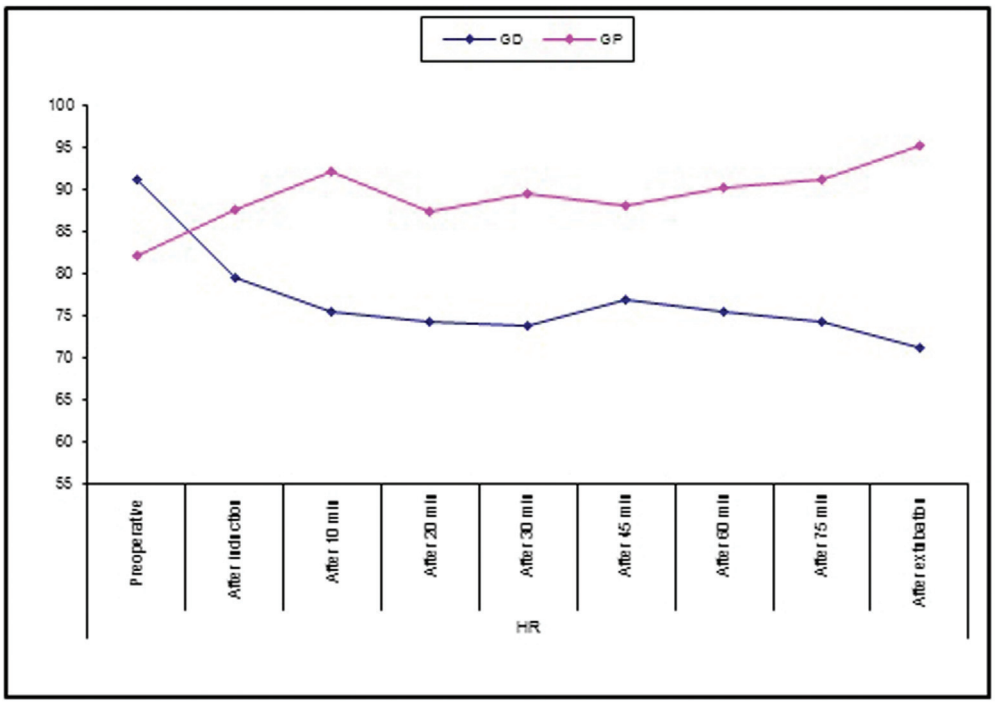
Table 4 Preoperative and intraoperative changes in heart rate (beats/min)

HR (mmHg)	Group D (*N*=30) (mean±SD)	Group P (*N*=30) (mean±SD)	Test value	*P* value
Before dexmedetomidine infusion	91.3±7.3	82.2±6.5	−5.099	<0.001
After induction	79.5±6.8	87.6±6.5	4.716	<0.001
After 10 min	75.4±5.6	92.1±6.5	10.661	<0.001
After 20 min	74.2±4.8	87.3±5.9	9.434	<0.001
After 30 min	73.9±6.2	89.5±4.8	10.897	<0.001
After 45 min	76.8±4.4	88.2±6.7	7.790	<0.001
After 60 min	75.4±2.5	90.2±5.6	13.218	<0.001
After 75 min	74.2±3.8	91.2±2.2	21.206	<0.001
After extubation	71.1±0.5	95.3±3.9	33.711	<0.001

HR, heart rate. *P* value less than 0.01: highly significant (HS).

In this study, intraoperative fentanyl consumption was significantly lower in the dexmedetomidine group compared with the placebo group. Similar results were reported with a reduction in fentanyl consumption when used dexmedetomidine infusion as an anesthetic adjuvant for cerebellopontine angle

Figure 2



Preoperative and intraoperative changes in heart rate (b/m).

surgeries [15]. Another study has reported that fewer patients needed intraoperative fentanyl on using dexmedetomidine combined with isoflurane versus the placebo group [13]. Another study augmented this result when different doses of dexmedetomidine intravenous infusion was used during laparoscopic bariatric surgery, and the fentanyl requirement was seen to be reduced [16]. Yet another study showed that the use of dexmedetomidine during laparoscopic sleeve gastrectomy reduces fentanyl requirement [10].

As regards hemodynamic, our result showed significant reduction in MABP and HR in the dexmedetomidine group compared with placebo group. Similarly, the results of the study showed that preoperative administration of a single dose of dexmedetomidine resulted in blunted hemodynamic responses during laryngoscopy. Furthermore, dexmedetomidine decreased blood pressure and HR as well as the recovery time after the operation [17]. Another study used varying infusion doses (0.4–0.5 μg/kg/h) of dexmedetomidine in parturients for elective cesarean delivery, resulting in lower HR and MABP [18]. Another study showed that the use of dexmedetomidine during laparoscopic sleeve gastrectomy maintains hemodynamic stability due to attenuation of stress response and the potent suppressive effect of dexmedetomidine on the sympathetic nervous system, with decreased risk of respiratory depression in the postoperative care unit [10]. In contrast to our study, a study used 1 μg/kg dexmedetomidine in laparoscopic cholecystectomy and reported minimal change in BP after pneumoperitoneum [19], as laparoscopic surgery is commonly associated with tachycardia and hypertension resulting from the sympathomimetic effect of absorbed carbon dioxide after insufflation. The results of an another study was different from the results of the present study, as they detected a significant increase in hemodynamic parameters after intubation, with no significant difference between the control and dexmedetomidine groups [20]. This may be due to the use of dexmedetomidine infusion without a loading dose.The limitation of this study is the small sample size and the limited age group, and therefore we need further studies in different age groups with different doses of dexmedetomidine and different coanalgesics.

Conclusion

Preoperative intravenous dexmedetomidine infusion resulted in a significant reduction of desflurane consumption and intraoperative fentanyl requirement with significant decrease in HR and MABP in spine surgeries.

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Conflicts of interest
None declared.

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