Effect of Intravenous use of Dexmedetomidine on Anesthetic Requirements in Patients Undergoing Elective Spine Surgery: A Double Blinded Randomized Controlled Trail

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Abstract

Background and Aims: Intravenous (IV) dexmedetomidine, a highly selective α₂ agonist approved by the FDA 1999, has been extensively used for providing sedation and analgesia in intensive care units. Dexmedetomidine has been demonstrated to reduce requirements of anesthetic agents. There are only a few studies are available regarding the intraoperative use of dexmedetomidine on anesthetic requirements in elective spine surgery patients have been done to date. We conducted this randomized, prospective, double-blinded study to evaluate the effects of intraoperative use of dexmedetomidine on anesthetic requirements in patients undergoing elective spine surgery.

Materials and Methods: A total of 60 patients, American Society of Anesthesiologists physical Status I and II, undergoing elective spine surgery, were randomly assigned to two groups. Group D (n = 30) received a loading does of dexmedetomidine 1 µg/kg IV before induction of anesthesia, followed by continuous infusion at a rate of 0.4 µg/kg/h throughout the operation. Group P (n = 30) received same volume of bolus and infusion of 0.9% saline. Anesthesia was induced and maintained with fentanyl citrate, propofol, 0.5% isoflurane, and atracurium. Heart rate, peripheral oxygen saturation mean arterial blood pressure, train of four counts of the patients were recorded intraoperatively. Induction time, recovery time and consumption of propofol as well as fentanyl citrate were also recorded.

Results: In Group D, requirement of propofol (P < 0.0001) and requirement of fentanyl (P < 0.0001) were significantly reduced.

Conclusion: The use of dexmedetomidine infusions significantly reduced the consumption of propofol and fentanyl citrate with better maintenance of hemodynamics, less post-operative pain score.

Key words: Dexmedetomidine, Fentanyl, Propofol, Train of four

INTRODUCTION

Dexmedetomidine is a highly selective α₂ agonist (α₂/α₁ activity 1620:1 u) and a safe adjuvant in diverse clinical applications.¹ It has antinociceptive, analgesic, opioid sparing and sedative properties² but has been approved by FDA in 1999 for clinical properties only for ICU sedation for short-term period less than 24 h.³ It use has also expanded to various surgical specialties including cardiac surgical, pediatric surgical, and neurosurgical practices. Its use has been found to be reduce the needs for opioids and anesthetics intraoperatively.⁴ It possesses analgesic properties and many other advantageous influences, but also lacks respiratory depression⁵ that makes it useful adjuvant in many diverse clinical applications.

Both hypnotic and supraspinal analgesic effects of dexmedetomidine are mediated by nonadrenergic neurons (via hyperpolarization). It causes inhibition of norepinephrine release and suppression of firing in the locus cereleus⁶ which lead onto release of mediators and neurotransmitters that in turn decrease the secretion of...
histamine and provide hypnosis very similar to normal sleep without evidence of depression of ventilation.7

Spine surgeries under general anesthesia are associated with hemodynamic changes in the form of increased systemic vascular resistance leads to hypertension, forcing anesthesiologist to increase the depth of anesthesia and even require use of vasodilators to control hypertension. Dexmedetomidine is the new α₂ agonist, 8 times more affinity for α₂ receptors is known to decrease the plasma catecholamines levels and suppressing the release of catecholamines also.69 The aim of the study is to assess the efficacy and safety of intravenous (IV) dexmedetomidine on anesthetic requirements and hemodynamic changes in patients undergoing elective spine surgeries.

MATERIALS AND METHODS

After approved by the Institutional and Ethical Committee, this study was conducted in 60 American Society of Anesthesiologists (ASA) I and II patients undergoing elective spine surgeries under general anesthesia and all patients are explained about the procedure and written informed consent was obtained in the age group of 30-60 years. The patients and investigators recording the data in the operating room were blinded to the treatment with either placebo or dexmedetomidine, but the anesthesiologist was aware of the treatment condition.

Patients with liver, renal, cardiac disorders, and ASA Grade III and IV are excluded from this study. Pre-operative evaluation was done with history, clinical examination, height, weight, and basic biochemical investigations such as blood sugar, urea and creatinine, electrocardiogram (ECG), chest X-ray, complete hemogram, coagulation profile, blood grouping and typing was done properly. After pre-anesthetic checkup, written, valid informed consent was taken from patients posted for spine surgery under general anesthesia. Patients were randomized to receive either placebo with normal saline (Group P, n = 30) or dexmedetomidine (Group D, n = 30) using closed cover technique. Dexmedetomidine infusion was prepared in normal saline in the concentration of 2 μg/ml. Two IV lines were secured, one for routine fluids and other exclusively for dexmedetomidine.

In Group D
Loading dose of dexmedetomidine infusion 1 μg/kg over 15 min followed by maintenance infusion at a rate of 0.4 μg/kg/h.

In Group P
Normal saline instead of dexmedetomidine was given in the same volume (ml) and rate (ml/h).

Patients were pre-medicated with glycopyrrolate 4 mg/kg, midazolam 0.04 μg/kg, metoclopramide 10 mg and ranitidine 50 mg. Baseline monitors like ECG, pulse oximetry, noninvasive blood pressure (BP) are attached to the patient and baseline values of heart rate (HR), peripheral oxygen saturation, and BP were noted. In all the patients, anesthesia was induced with fentanyl 1.5 μg/kg, propofol 2 mg/kg till the loss of verbal response and succinylcholine 1.5 mg/kg intravenously to facilitate intubation. Vasopressor response to laryngoscopy and intubation was documented by HR and BP. Anesthesia was maintained with O₂ and N₂O and inhalational anesthetic isoflurane 0.5% with an initial dose of atracurium 0.5 mg/kg followed by 0.15 mg/kg based on train of four neuromuscular response. In both Groups, anesthetic requirement was gauged by hemodynamics (HR and BP showed 20% increase from baseline) and whenever required, anesthesia was deepened by fentanyl 0.5 μg/kg and propofol top up of 20 mg intravenously.

Intraoperatively, HR and BP were monitored and documented at the time of pre-induction, after the loading dose of dexmedetomidine, induction of anesthesia, during laryngoscopy and intubation, then every 5 min till the end of surgery, during extubation and postoperatively. The total duration of anesthesia and surgery were recorded. At the end of the surgery, injection diclofenac sodium 75 mg intramuscularly given for post-operative analgesia for all patients. Any side effects such as hypotension, bradycardia, and respiratory depression were noted. In the post-anesthesia care unit, subjective patient pain scores were obtained with a scale of 0-10 (numerical scale of pain with 0 = No pain and 10 = worst pain) and HR and BP were recorded by recovery nurse blinded to the treatment procedure. The total amount of propofol and fentanyl used were also calculated. The profile of recovery after anesthesia was compared between the groups and the incidence of post-operative nausea and vomiting (PONV) was recorded.

Statistical Analysis
Data were expressed as means and standard deviation. Repeated measures by ANOVA and Student’s t-test were used for each parameter for within and between group comparisons. Pain score and incidence of side effects were compared using Wilcoxon signed rank test, and the P < 0.05 was considered significant.

RESULTS
A total of 60 patients were studied and no dropouts occurred. Patient demographic data were shown in Table 1. There was no difference in age, weight, height, sex, ASA physical status, and duration of the procedure between the two groups. The duration of the procedure was expressed
in minutes (mean ± SD) in Group D was 157 ± 29 min and Group P was 155 ± 27 min.

During intraoperative period, HR was significantly decreased in the dexmedetomidine Group D (73.56 ± 4.60) compared with the placebo Group P (93.94 ± 10.6) (Table 2, Figure 1). \( P = 0.0001 \) statistically significant in Group D compared to Group P. A mean arterial pressure also was significantly decreased in dexmedetomidine Group D (89.06 ± 3.13 mmHg) compared with placebo Group P (104.8 ± 11.9 mmHg), \( P = 0.0002 \) (<0.05) statistically significant (Table 3, Figure 2).

The total amount of propofol required to maintain the duration of anesthesia was significantly lower in the dexmedetomidine Group D (144 ± 31 mg) compared with the placebo Group P (216 ± 45 mg), \( P = 0.002 \) (<0.05) statistically significant. The total amount of intraoperative fentanyl required to maintain the hemodynamics was significantly lower in the dexmedetomidine Group D (109.4 ± 14.6 µg) compared with the placebo Group P (162.2 ± 21.2 µg), \( P = 0.003 \) (<0.05) statistically significant (Table 4, Figure 3).

During recovery, the time taken for onset of spontaneous respiration in Group D (3.3 ± 0.4 min), Group P (4.6 ± 1 min) \( P = 0.0001 \) and the time taken for responding to verbal commands in Group D (3.5 ± 0.6 min), Group P (4.2 ± 1.2 min) \( P = 0.02 \) (<0.05) statistically significant in Group D. The time taken for safe extubation in Group D (5.1 ± 0.7 min) and Group P (7.5 ± 1.3 min) \( P = 0.0001 \) statistically significant in Group D. (Table 5).

Pain scores at 1 h for Group D (3 ± 0.4), Group P (6 ± 0.8), \( P = 0.0001 \) and 2 h for Group D (2 ± 0.3), Group P (5 ± 0.9), \( P = 0.0001 \) were statistically significant (Table 6, Figure 4).

There was no difference in the incidence of PONV between both groups (Table 7). Incidence of PONV data was presented as number percentage 96.66% for D Group (dexmedetomidine) and 93.33% for P Group (placebo).

**DISCUSSION**

The effect of dexmedetomidine like analgesia, sedation, anxiolysis sympatholysis, and blunting of exaggerated hemodynamic response is being extensively studied and is mainly mediated by the activation of \( \alpha_2 \) receptors located in the post-synaptic terminals in the central neuronal system which caused the decreased neuronal activity and augmentation of vagal activity.\(^{10-12}\)

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**Table 1: Demographic profile**

<table>
<thead>
<tr>
<th>Demographic profile</th>
<th>Group P Normal saline</th>
<th>Group D Dexmedetomidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49±8</td>
<td>50±6</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>(18/12)</td>
<td>(28/3)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>68±12</td>
<td>67±11</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165±8</td>
<td>167±10</td>
</tr>
<tr>
<td>ASA (physical status)</td>
<td>I (24) II (6)</td>
<td>I (26) II (4)</td>
</tr>
<tr>
<td>Duration of the procedure (minutes)</td>
<td>155±27</td>
<td>157±29</td>
</tr>
</tbody>
</table>

**Table 2: Comparison of HR between both Groups P and D (mean value)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Group D</th>
<th>Group P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base line</td>
<td>85.13</td>
<td>81.8</td>
</tr>
<tr>
<td>After drug injection</td>
<td>65.87</td>
<td>79.83</td>
</tr>
<tr>
<td>After induction</td>
<td>73.27</td>
<td>86.7</td>
</tr>
<tr>
<td>1 min after intubation</td>
<td>76.4</td>
<td>113.97</td>
</tr>
<tr>
<td>3 min after intubation</td>
<td>74.4</td>
<td>108</td>
</tr>
<tr>
<td>5 min after intubation</td>
<td>72.5</td>
<td>100.73</td>
</tr>
<tr>
<td>10 min after intubation</td>
<td>71.07</td>
<td>91.93</td>
</tr>
<tr>
<td>15 min after intubation</td>
<td>70.83</td>
<td>87.42</td>
</tr>
<tr>
<td>30 min</td>
<td>70.6</td>
<td>86.2</td>
</tr>
<tr>
<td>60 min</td>
<td>70.4</td>
<td>86.6</td>
</tr>
<tr>
<td>Extubation</td>
<td>78.2</td>
<td>106.4</td>
</tr>
<tr>
<td>1 h</td>
<td>74.2</td>
<td>95.4</td>
</tr>
<tr>
<td>2 h</td>
<td>73.5</td>
<td>96.3</td>
</tr>
</tbody>
</table>

\( \text{HR: Heart rate} \)
The patient received dexmedetomidine showed better control of intraoperative and post-operative mean BP and HR. In the post-operative period, it decrease the pain scores and showed better recovery profile compared with placebo. Opioids can be associated with potentially pronounced respiratory depressant effects but the ability of dexmedetomidine to decrease anesthetic requirements, better control of HR and BP and provide analgesia without respiratory depression.

Bajwa et al. Attenuation of pressor response with dexmedetomidine showed the mean dose of fentanyl and isoflurane were also decreased significantly (less than 50%) and mean recovery time was shorter by the administration of dexmedetomidine.

When infused at rates of 0.4 μg/kg/h dexmedetomidine produced clinically effective sedation and reduced the analgesic requirements of ventilated ICU patients. There was no clinically apparent respiratory depression after cessation of assisted ventilation, while at the same time dexmedetomidine maintained a high degree of patient arousability.

Our Study Showed

Better recovery profile in the dexmedetomidine-treated patients compared with placebo which can be explained by the fewer amounts of intraoperative fentanyl and propofol required to maintain anesthesia in this group of patients. Because a primary effect of dexmedetomidine is
to decrease sympathetic activity, it was expected that the \( \alpha_2 \) adrenergic agonist would be effective in controlling intraoperative BP.\(^{18}\)

**CONCLUSION**

The intraoperative infusion of dexmedetomidine may be better option for elective spine surgeries as it decreased the total amount of propofol and fentanyl required to maintain anesthesia, and better control of intraoperative and postoperative hemodynamics decreased post-operative pain level and less incidence of PONV. It also reduced the risk of narcotic induced post-operative respiratory depression and hypoxemia in spine surgeries.

**REFERENCES**


*Source of Support: Nil, Conflict of Interest: None declared.*