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Effect of dexmedetomidine on propofol requirement during elective spine surgery in adolescents

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ABSTRACT

Background: Total intravenous anesthesia with propofol and a synthetic opioid is a frequently chosen anesthetic technique for posterior spinal fusion. **Aims and Objectives:** The aim of this study is to evaluate the effect of dexmedetomidine on propofol requirement for induction and maintenance of desired depth of anesthesia. **Materials and Methods:** We carried our study on 80 patients aged 20–60 years, scheduled for elective spinal surgeries under general anesthesia. The patients were divided randomly into two Groups D and P of 40 each. Patients of Group D received an initial loading dose of dexmedetomidine at 1 μg/kg over 10 min, started 15 min before induction of anesthesia followed by an infusion at a rate of 0.2 μg/kg/h. Patients of Group P received the same volume of 0.9% normal saline solution as placebo. **Results:** Mean induction dose of propofol was found to be significantly lesser in Group D (63.68 ± 11.368 mg) when compared with Group P (118 ± 17.042 mg). Mean maintenance dose of propofol in Group D was 148.55 ± 42.08 mg and that in Group P was 398.24 ± 64.62 mg. The total requirement of propofol and mean requirement in Group D (215.24 ± 43.652 mg) was lesser than the requirement in Group P (521.29 ± 71.098 mg). **Conclusion:** Administration of dexmedetomidine significantly reduces the requirement of propofol while maintaining desired depth of anesthesia without any significant complication.

Key words: Dexmedetomidine, intubation, propofol, spine surgery

INTRODUCTION

The pressor response, which is part of a huge spectrum of stress response, results from the increase in sympathetic and sympathoadrenal activity, as evidenced by increased plasma catecholamines concentrations in patients undergoing surgery under general anesthesia.[1]

Various drug regimens and techniques have been used from time to time for attenuating the stress response to laryngoscopy and intubation, including opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers, and vasodilators. The dose of opioids required for effective attenuation of stress response is fairly high, and numerous drugs have been used as adjuncts in decreasing the dose of opioids with a varied level of success but are not absolutely free from side-effects.[1,2]

Alpha-2 agonists like clonidine have been used extensively in the past for attenuation of sympathoadrenal stimulation caused by tracheal intubation and surgery. Dexmedetomidine is the new alpha-2 agonist having 8 times more affinity for alpha-2 adrenoceptors as compared with clonidine, which has shown only partial agonist activity and is known to decrease the plasma catecholamines levels and suppressing the release of catecholamines also.[3-5]

Propofol is an intravenous (IV) sedative/hypnotic agent that is extensively used for the induction and maintenance of anesthesia and for sedation in the Intensive Care Units. Due to its rapid induction and recovery characteristics and anti-emetic properties, propofol is commonly incorporated into the anesthetic regimen for outpatient surgeries.[6]

Adequate depth of anesthesia is essential for maintaining intraoperative hemodynamic stability and prevention of recall afterward. Total IV anesthesia with propofol and a synthetic opioid is a frequently chosen anesthetic technique for posterior spinal fusion. Despite its utility, adverse effects may occur with high or prolonged propofol dosing regimens including delayed awakening. Various studies shown that dexmedetomidine decreases the requirement of thiopentone and volatile anesthetic agents in perioperative period. There is a paucity of clinical trials regarding the effect of dexmedetomidine on the requirement of propofol in maintaining adequate depth of anesthesia with stable hemodynamic status perioperatively during the spine surgery.[7,8]

The present study was designed as randomized, double-blinded, manner to evaluate the effect of dexmedetomidine on propofol requirement for induction and maintenance of desired depth of anesthesia on the basis of targeted bispectral index (BIS) value in spine surgery on prone patients under general anesthesia.

MATERIALS AND METHODS

We carried our study on 80 patients of the American Society of Anesthesiologists (ASA) physical status I and II, aged 20–60 years, scheduled for elective spinal surgeries under general anesthesia.

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The study period was between January 2016 and May 2017 and was carried out after obtaining the institutional ethical committee approval. Consent was obtained from all the patients. Initially, 100 patients were enrolled in the study. 20 patients were excluded as they did not meet the inclusion criteria. 80 patients were divided randomly into two groups of 40 each [Figure 1]. We followed the methodology used by Sen *et al.*[8]

A pharmacologist of the institution not involved in this study prepared injectable solution of either dexmedetomidine (study solution) or 0.9% saline (control solution). The investigator also remained blind regarding the content of these solutions prepared for the patients.

Inclusion Criteria

The following criteria were included in the study:

1. Patients undergoing elective spinal surgeries under general anesthesia,
2. Patients above 20 years of age.

Exclusion Criteria

The following criteria were excluded from the study:

1. Patients' refusal,
2. Patients above 60 years,
3. Patients with a higher degree A-V block, obstructive sleep apnea, and morbid obesity,
4. Patients on the chronic opioid analgesic, tricyclic antidepressant, clonidine, mono amine oxidase-inhibitor therapy.

Infusion of the study or control solution was started for patients of Group D or Group P, respectively, initially at a rate of 1.5 ml/kg/h over 10 min (i.e., loading dose of dexmedetomidine at 1 μg/kg over 10 min), followed by infusion of 0.05 ml/kg/h (i.e., maintenance of dexmedetomidine at a rate of 0.2 μg/kg/h) according to the study protocol.

Injection fentanyl 2 μg/kg body weight was given IV 3 min before induction. Induction of anesthesia was started in all patients by injection propofol, slow IV, until loss of response to verbal command. Anesthesia was maintained with nitrous oxide 66% in oxygen and injection propofol as a continuous infusion through a separate syringe pump. Propofol was started initially at 5 mg/kg/h and then adjusted to maintain a BIS value in the range of 40–60, and its requirement was observed and recorded in each patient.

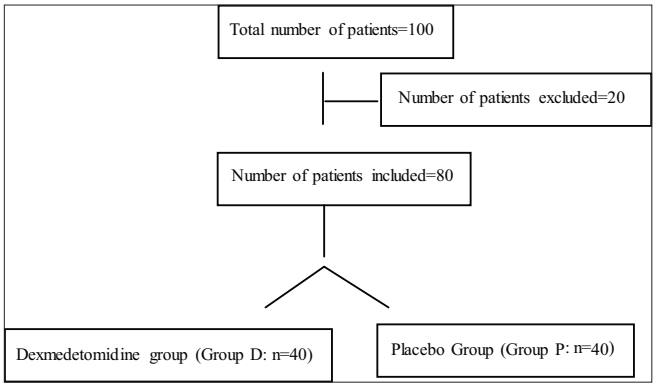

Figure 1: Flow diagram showing patient selection and randomization

Comparison of mean arterial pressure and heart rate (MAP and HR) was done in two groups - baseline (before receiving study/control solution - MAP1 and HR1), at pre-induction (after completion of study/control solution - MAP2 and HR2), at induction (1 min after administration of induction agent - MAPi and HRi), after intubation (1 min after laryngoscopy and intubation - MAPi2 and HRi2), at skin incision (1 min after giving skin incision - MAPs and HRs), and during the intraoperative period at 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, and 120 min and after 1 min of extubation.

The depth of anesthesia was monitored with BIS™ monitoring (Aspect Medical Systems, Inc.). Additional boluses of injection propofol 20 mg IV were administered whenever BIS value approaching toward target higher value of 60. Injection fentanyl IV was administered intermittently to maintain MAP and HR within 20% of their pre-induction values. Patients were observed throughout the surgeries for any significant bradycardia. Categorical data (e.g., sex distribution and ASA physical status) were analyzed using the Pearson's Chi-square-test with Yate's correction. Parametrical numerical data between groups were analyzed using the Student's t-test. Within group, variables at different time points were analyzed using the Friedman's analysis of variance followed by Wilcoxon's matched-pairs signed-rank test for *post hoc* analysis. A $P < 0.05$ was considered to be statistically significant.

RESULTS

Demographic data such as age, sex, body weight, and ASA physical status in both the groups (Groups P and D) were comparable. There was a significant difference ($P = 0.0476$) in the mean duration of surgery and insignificant difference ($P = 0.925$) among the sites of spinal surgery performed between the groups [Table 1].

Mean induction dose of propofol was found to be significantly lesser in Group D (63.68 ± 11.368 mg) when compared with Group P (118 ± 17.042 mg).

Mean maintenance dose of propofol in Group D was 148.55 ± 42.08 mg and that in Group P was 398.24 ± 64.62 mg.

The total requirement of propofol and mean requirement in Group D (215.24 ± 43.652 mg) was lesser than the requirement in Group P (521.29 ± 71.098 mg) [Table 2].

MAP and HR were significantly decreased in Group D after administration of loading dose of dexmedetomidine, i.e., MAP2

Table 1: Demographic characteristics of the patients in two groups

Parameter	Group D	Group P	*P*
Age (years)	45.13±9.86	41.68±10.49	0.1337 (NS)
Male: Female	27:13	27:13	1.000 (NS)
Weight (kg)	67.35±10.16	65.98±9.05	0.5261 (NS)
ASA 1:ASA 2	23:17	25:15	0.5785 (NS)
Duration of surgery (min)	139.35±10.41	134.68±10.34	0.0476 (Sig)*
Site (cervical: dorsal: lumbar)	8:9:23	8:8:24	0.925 (NS)

ASA: American society of anesthesiologists, NS: Non-significant, *Sig: Significant

Table 2: Induction, maintenance, and total dose of propofol requirement characteristics in two groups

Time	Group	Mean (mg)	Standard deviation	Standard error of mean	Confidence interval at 95%	
					Upper	Lower
Induction	*P*	118	17.042	2.694	21.88253	13.96014
	D	63.68	11.368	1.797	14.59692	9.31222
Maintenance	*P*	398.24	64.62	10.21	82.9744	52.9342
	D	148.55	42.08	6.65	54.0322	34.4703
Total	*P*	521.29	71.098	11.24158	91.29236	58.24070
	D	215.24	43.652	6.901	56.05072	35.75801

and HR2 in Group D were significantly lower when compared with MAP1 ($P < 0.001$). Whereas, the above two parameters in Group P were not different statistically.

Pre-induction value of MAP and HR was compared with MAP and HR after induction, laryngoscopy, and intubation and skin incision in the same group with Wilcoxon signed-rank test. In both groups, MAP and HR declined significantly after induction with propofol.

MAP and HR after laryngoscopy and intubation and after skin incision rose in both groups, but the rise was more in Group P [Figures 2 and 3].

For comparison of intraoperative hemodynamics, in both groups, MAP and HR at 10–120 min at 10 min interval and after extubation were compared individually with MAP2 and HR2, respectively (i.e., pre-induction value of MAP and HR), with Wilcoxon signed-rank test. In both groups, although they were found to be different statistically at various points of times, they were considered clinically insignificant [Figures 4 and 5].

None of the patients in both groups developed significant bradycardia and significant hypotension that required treatment any time during the study period.

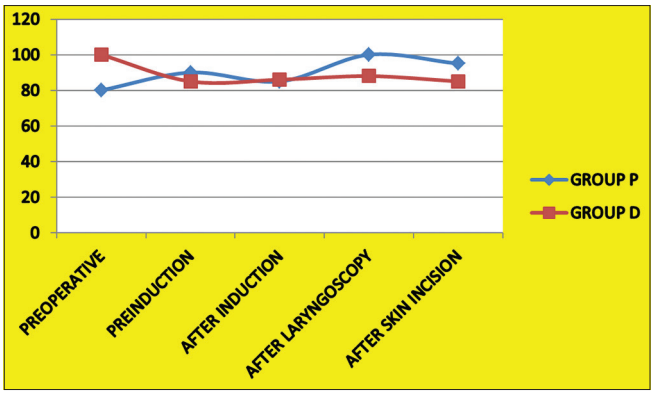

Figure 2: Comparison of hemodynamic parameter (mean arterial pressure) at various points of time (pre-operative, pre-induction 1 min after induction, 1 min after laryngoscopy and intubation, and after skin incision)

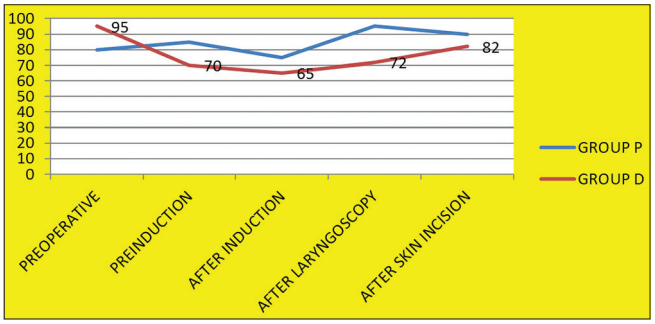

Figure 3: Comparison of hemodynamic parameter (heart rate) at various points of time (pre-operative, pre-induction, 1 min after induction, 1 min after laryngoscopy and intubation, and at skin incision)

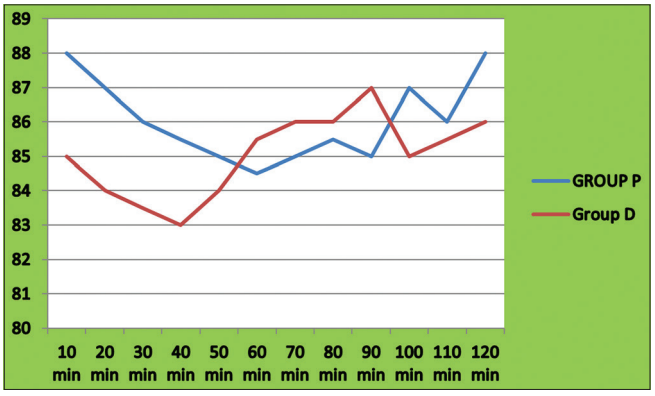

Figure 4: Comparison of mean arterial pressure in intraoperative period

DISCUSSION

Achieving adequate depth of anesthesia during surgical procedures is desirable. Spinal anesthesia is a unique technique to provide sensory and motor blockade in the large part of the body with a lesser amount of drug. The challenge to the anesthetist is to provide optimal surgical conditions while ensuring adequate oxygenation to the brain and spinal cord and facilitating the use of intraoperative spinal cord monitoring techniques if appropriate. Moreover, a prone position for spine surgery itself requires maintenance of adequate depth of anesthesia to avoid hemodynamic and airway-related complications.[8-10]

Propofol (2,6-diisopropylphenol) is becoming the IV anesthetic of choice nowadays. It is extensively metabolized, with most of the administered dose appearing in the urine as glucuronide conjugates. Favorable operating conditions and rapid recovery are claimed as the main advantages in using propofol, whereas disadvantages include a relatively high incidence of apnea and blood pressure reductions. Hence, the idea was to use propofol with another adjuvant having sedative properties that could reduce the requirement of propofol.[6,8]

Dexmedetomidine, a highly selective α 2 adrenergic agonist, has evolved as a panacea for various applications and procedures in the perioperative and critical care settings. It is also emerging as

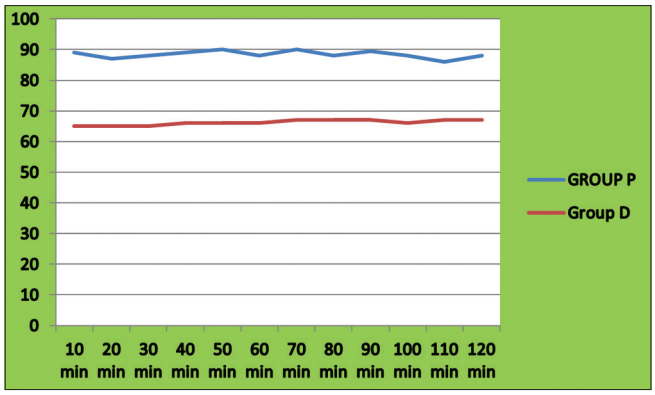

Figure 5: Comparison of heart rate in intraoperative period

a valuable adjunct to regional anesthesia and analgesia, where gradually evolving studies can build the evidence for its safe use in central neuraxial blocks. It is being used as both sedative analgesic and anxiolytic agent, thus found to reduce anesthetic drug requirements in the intraoperative period.[11,12]

Sympatholysis is the hallmark feature of central neuraxial blockade, and dexmedetomidine has been shown to decrease MAP and HR by reducing norepinephrine release. They had also shown to decrease BIS value in the intraoperative period when used as an adjuvant with other drugs given as continuous IV infusion.[13]

Few of recently done studies have found the definite role of dexmedetomidine in reducing dose requirement of propofol for induction and during maintenance of anesthesia. The studies were done using mainly motor, sensory, or autonomic responses for monitoring depth of anesthesia.[9,15-18]

We preferred BIS monitoring to sensory or motor responses as it is a standard and food and drug administration approved monitor for depth of anesthesia in perioperative period and also more convenient for personnel and the institutional operating theater setup.[8,9,14]

Bashir *et al.* observed that mean requirement of propofol for induction of anesthesia was reduced to 50.6% in patients who received dexmedetomidine as compared to patients on placebo.[15]

Samel *et al.* found that dexmedetomidine significantly reduces heart rate, systolic, diastolic, and mean arterial blood pressure values as compared to when only propofol was used and reduces the requirement of propofol while maintaining stable hemodynamics. They suggested that dexmedetomidine effectively attenuates hemodynamic stress response during laparoscopic cholecystectomy with a reduction in requirement of concomitantly administered propofol.[16]

Le Guen *et al.* found that dexmedetomidine administration significantly reduced the requirement for propofol during anesthetic induction and reduced propofol use during maintenance of anesthesia. Dexmedetomidine also delayed post-operative analgesic use. They suggested that dexmedetomidine is a useful adjuvant that reduces anesthetic requirement and provides post-operative analgesia.[17]

Ergenoglu *et al.* found that total propofol consumption, propofol dose required for targeted sedation levels according to observer's assessment of alertness and sedation scores and bispectral index levels, and recovery times were significantly lower in Group D ($P < 0.001$). According to them, dexmedetomidine premedication lowers intraoperative propofol consumption to maintain targeted level of sedation. Therefore, low-dose dexmedetomidine premedication in addition to propofol infusion might be an alternative in geriatric patients with end-stage renal disease for sedation.[18]

In our study, the demographic features in both the groups were comparable. This is in accordance with the studies of Sen *et al.*, Bashir *et al.*, and Samel *et al.*[8,15,16] However, we found a significant difference ($P = 0.0476$) among the groups regarding the mean duration of surgery.

We also found that the mean induction dose of propofol and mean dose requirement for maintenance were significantly lower in Group D patients when compared with Group P patients. Total mean requirement of propofol, in Group D patients, was also found to be lower than the requirement in Group P patients, which was also remained significant. Our findings are similar to the studies of Sen *et al.*, Bashir *et al.*, Samel *et al.*, Le Guen *et al.*, and Ergenoglu *et al.*[8,15-18]

However, one recent study where the depth of anesthesia was measured with responses to stimuli in children for short surgical procedures had found that dose-response curve for propofol was not altered with the concomitant use of dexmedetomidine.[19]

Most of the previous studies that had found the positive adjuvant effect of dexmedetomidine did not consider hemodynamic status in their observations. Here, in our study, although not a primary outcome measurement, hemodynamic changes during direct laryngoscopy aided intubation and following skin incision were found to be much higher in patients of Group P than Group D, which suggests a significant role of dexmedetomidine in preventing hemodynamic response to laryngoscopy as corroborated to the previous study.[1]

However, intraoperative hemodynamic parameters were found to be similar in both groups. Although some data of intragroup variables were found to be statistically significant, no clinical correlation in terms of treatment of adversities was faced in any point of time during study periods of these patients. Our findings are similar to the studies of Sen *et al.*, Bashir *et al.*, and Samel *et al.*[8,15,16]

Dexmedetomidine is a good anesthetic adjuvant that decreases the requirement of anesthetics; however, its use is limited because the drug is somewhat costly (1 ampoule containing 200 μg of drug costs 600 rupees).[15]

Our study had some limitations like BIS being the only mode of measuring the depth of anesthesia for the patients. Use of N_2O might confound the interpretation of BIS. A single kind of procedure at single spinal level would become more appropriate for comparison of data rather than all spinal surgeries. Hence, we suggest future studies on a larger sample with more parameters.

CONCLUSION

Administration of dexmedetomidine significantly reduces the requirement of propofol while maintaining desired depth of anesthesia without any significant complication. Thus, dexmedetomidine could be an important part of the armamentarium of the anesthesiologist that can be used in the efforts to achieve good control of the hemodynamics of the patient undergoing spine surgeries.

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