

**COMPARING THE EFFECTS OF INTRAVENOUS CLONIDINE VS INTRAVENOUS
DEXMEDATOMIDINE ON PERIOPERATIVE HEMODYNAMICS IN PATIENTS
UNDERGOING LUMBAR SPINE SURGERIES*****Dr. Jyoti Petkar, Dr. Prakash Audichya, Dr. Sameer Goyal and Dr. Virendra Sharma**

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ABSTRACT

Background: Alpha 2 agonists are commonly used as premedication in major surgeries under general anaesthesia and are useful in maintaining intraoperative haemodynamics. There are very few studies comparing of the two alpha2 agonists clonidine and dexmedetomidine. **Methods:** Sixty patients aged between 18 to 60 years with ASA status I and II, were included in this prospective, double blinded randomized control study. Patients were randomized into 2 group, Group C-Clonidine group and Group D- Dexmedetomidinegroup using computer generated random numbers. Group C patients received Inj. Clonidine 2 mcg/kg diluted in 10 ml distilled water intravenously and Group D patients received Inj. Dexmedetomidine 1mcg/kg diluted in 10 ml distilled water slow i.v over 10 min. Baseline, intra-operative and post-operative haemodynamics were noted. Post-op seation score and intra-operative blood loss was noted. **Results:** HR and MAP after induction and after intubation and 2, 4, 6 min post intubation, there was minimal changes seen in Group D as compared to Group C. Post-op sedation score was lower in Group D(0.07 ± 0.06) as compared to group C (1.91 ± 0.03) as observed in post-op recovery room. **Conclusion:** Dexmedetomidine is more effective than clonidine in attenuating hemodynamic response during laryngoscopy and maintaining intraoperative and post-operative hemodynamics with minimal post-operative sedation and can be effectively used in spine surgeries operated under general anaesthesia.

KEYWORDS: Dexmedetomidine, haemodynamics, anaesthesia.**INTRODUCTION**

Spine surgeries are commonly performed under general anaesthesia in prone position.^[1] Spine surgeries are sometimes associated with major blood loss which may also increase transfusion requirement.^[2,3] Laryngoscopy and endotracheal intubation activate sympathetic nervous system, inducing tachycardia and hypertension.^[4] Controlling this post-intubation pressor response plays a major role in modern anaesthesia. Also maintaining stable hemodynamics^[5] throughout surgery is a major goal to prevent blood loss and improve surgical field.^[6,7] Various techniques are used for controlled hypotension during spine surgeries.

Clonidine and Dexmedetomidine are two pharmacologically related alpha agonists^[8] and has been used in anaesthesia^[9] for many years to provide sedation, anxiolysis, analgesia and controlled hypotension. Dexmedetomidine has 8 times greater affinity for alpha-2 receptors than clonidine.^[10] Alpha 2 agonists decrease norepinephrine release and inhibit sympathetic activity^[11] which decrease heart rate (HR) and blood pressure (BP).

There are very few studies^[12] which have compared the two alpha 2 agonists for blunting intubation response under general anaesthesia. We conducted this study to compare the effect of two alpha 2 agonists clonidine and dexmedetomidine on laryngoscopy and intubation response, intraoperative hemodynamics and post-operative sedation in patients undergoing spine surgeries under general anaesthesia.

OBJECTIVES

Primary goal of our study is to compare the

1. Hemodynamics during laryngoscopy and intubation
2. Intraoperative and post-operative hemodynamics

Secondary goal

1. post-operative sedation score
2. Intraoperative blood loss

MATERIALS AND MEDHODS

Sixty patients aged between 18 to 60 years with ASA status I and II, were included in this prospective, double blinded randomized control study. Ethical committee approval was taken. Written informed consent was taken for inclusion in the study. Patients were randomized into

2 group, Group C-Clonidine group and Group D-Dexmedetomidine group using computer generated random numbers. Patients aged 18 to 60 years with ASA PS-I and II and posted for elective lumbar laminectomy and discectomy 1 or 2 level were included in the study. Exclusion criteria were patients with history of seizure or intracranial hypertension, contraindication for spinal anesthesia (such as patients refusal, coagulopathy, infection at site of needling, hypovolemia), severe spinal stenosis, patients with significant coronary artery disease or ischemic heart disease, chronic obstructive pulmonary disease, renal failure, hepatic dysfunction, morbid obesity, moderate to severe anemia, uncontrolled diabetes and uncontrolled hypertension, patients not willing to enroll in the study.

The study was a double blinded, prospective, randomized control study. For the study to have a power of 90% with an alpha-error of <0.05, a minimum of 28 patients were registered in each group. To compensate for the dropouts, we took 30 patients in each group.

Patients were taken in the operating room and routine monitoring done, HR, SpO₂, NIBP, ECG. Patients were started with i.v fluid ringer lactate. Study drug was prepared by the incharge nurse according to the group allotted. Drug was given by the anaesthesiologist incharge of the case who was blinded as to which group the patient belonged. Group C patients received Inj. Clonidine 2 mcg/kg diluted in 10 ml distilled water intravenously and Group D patients received Inj. Dexmedetomidine 1mcg/kg diluted in 10 ml distilled water slow i.v over 10 min. All the vital parameters were noted and patient followed up till discharge from recovery room by the same anaesthesiologist.

Premedication was given with Inj. Glycopyrolate 0.2 mg i.v, Inj, Ondan 4 mg i.v and Inj Fentanyl 100mcg i.v. Patient was induced with Inj. Propofol 2mg/kg i.v followed by Inj. Succinylscoline 1.5 mg/kg i.v. Intubation was done with appropriate sized endotracheal tube with direct laryngoscopy. Maintenance was done with Inj. Atracurium 25 mg i.v loading and 5 mg every 15 min i.v. and Sevoflurane 1 vol % and oxygen: nitrous oxide 50:50. Baseline vitals(T0) were noted and vitals noted at 1, 2,3,5,15 min noted and every 15 min thereafter till patient was shifted to recovery room. Patients were properly placed onto a prone position, arms resting on the arm boards while they were flexed 90 degrees at elbow. For prevention of pressure on nose and globe of the eyes, the faces placed on a smooth brace and operated by the same team of orthopedician.

Intraoperative blood loss was measured using the sponge count and amount of blood in the suction apparatus and amount of irrigating fluid. Patient was reversed with Inj. Neostigmine 2.5 mg iv and Inj. Glycopyrolate 0.4 mg i.v.

Patient was extubated and post-op sedation score was measured.

Heart rate <50 /min was considered as bradycardia and treated with Inj. Atropine 0.6 mg i.v and hypotension (MBP< 60 mm Hg) was treated with Inj. Mephenteramine 6mg i.v.

Post-operative sedation score was measured using a 4-point sedation score.^[13]

Grade 0- Awake, Grade 1- Drowsy, Grade 2- Sleeping but arousable on verbal commands, Grade 3- sleeping but arousable on tactile stimulation.

Continuous data were presented as mean± SD and categorical data were presented as percentage within the group. The mean values of both groups were compared using Student t-test and later by Pearsons Chi-square test. P-value <0.05 was considered statistically significant. All statistical analysis were done using SPSS version 16.

RESULTS

Sixty patients were studied in 2 groups with thirty patients in each group. Group C was clonidine group and Group D was dexmedetomidine group.

Age, Sex, Weight, ASA status and duration of surgery was comparable between the groups and no statistically significant difference was found (Table 1).

Hemodynamics were compared pre-op, during laryngoscopy and intubation, intra-operative and post-operatively between both groups. (Table 2 and Table 3).

HR was compared between the two groups, it was found that HR after induction and after intubation and 2, 4, 6 min post intubation, there was minimal changes seen in Group D as compared to Group C. The HR was lower than the baseline in both Groups, at 8 min post-intubation, throughout the intraoperative and postoperative period.

MAP was compared between both the groups. It was found that, MAP was lower than the baseline value after induction and after intubation and 2,4,6 min post-intubation in Group D as compared to Group C. However, MAP was comparable in both the groups and maintained lower than the baseline value at 8 min, intra and post-operative period.

Post-op sedation score was lower in Group D(0.07±0.06) as compared to group C (1.91±0.03) as observed in post-op recovery room.

Complications – one patient in Group D and 2 patients in group C had episode of bradycardia and was treated with Inj. Atropine 0.6 mg i.v.

Demographic Characteristic: (Table 1).

		Group D	Group C
Age(years)		47.60±7.75	51.50±9.60
Sex n(%)	M	19	22
	F	11	8
Weight(kg) (mean± SD)		62.11± 5.44	64.22± 7.4
ASA(no.of patients)	I	16	15
	II	4	5

Group D: Haemodynamic Variations (Table 2).

	HR	MBP
baseline	98.5±6.2	80.44±5.67
Pre-Induction	88.54±7.3	74.67± 6.45
1 min post-intubation	90.54±5.3	70.45±8.32
2-min post-intubation	86.20±7.3	72.54±4.46
3-min post-intubation	88.1± 4.4	68.34±6.52
4-min post-intubation	80.52± 6.33	74.56±4.45
5-min post-intubation	78.44±3.54	75.21±3.56
15 min	70.55± 6.48	70.87±5.67
30 min	66.3± 7.23	65.54±3.56
45 min	69.88±4.33	68.52±4.67
60 min	60.55±4.67	66.84±5.6
75 min	58.55±3.45	67.89±4.76
90 min	60.50± 5.54	62.63±4.67

Group C: Haemodynamic Variations (Table 3).

	HR	MBP
baseline	102±6.78	82.54±5.45
Pre-Induction	94.46±6.78	84.36±6.3
1 min post-intubation	100.47±4.67	86.26± 5.83
2-min post-intubation	98.78±6.56	87.44±4.52
3-min post-intubation	102.5± 4.67	82.92± 3.57
4-min post-intubation	99.34±3.47	84.75±7.45
5-min post-intubation	95.53±4.56	83.83±6.43
15 min	90.57±5.67	80.73±6.35
30 min	85.48±4.68	78.68± 6.97
45 min	78.75±5.67	75.53±2.54
60 min	82.65± 4.27	74.68±5.36
75 min	75.54± 3.63	75.73±5.37
90 min	72.54±5.34	76.64±6.45

DISCUSSION

Alpha-2 agonists are the established drugs for attenuating the hemodynamic response to laryngoscopy and intubation. There have been several studies which have proved that clonidine and dexmedetomidine have been used as premedication and helpful in attenuating laryngoscopic response. But there were very few studies which have compared these two alpha-2 agonists as premedication in suppressing laryngoscopic and intubation response and its effects on hemodynamics in intra and post-operative period. This study was done to fill the gap.

It was observed that HR and MBP was lower than the baseline and was maintained in Group D as compared to Group C during intubation and immediately post-

intubation and 2,4 6 min post-intubation. Group C patients had increase in HR and MAP during intubation and 2,4 and 6 min post-intubation. However at 8 min and thereafter the HR was maintained lower than the baseline value and was stable throughout the surgery. This must be due to the fact that Dexmedetomidine had earlier onset of action of 5 min as compared to clonidine which has the onset of action of 10 min. Arindam *et al*^[4] also observed similar results and concluded that Dexmedetomidine was a promising choice and effective in attenuation of hemodynamic response to tracheal intubation.

Carabine *et al*^[14] demonstrated that 0.625 and 1.25 mcg/kg clonidine IV 15 min prior to induction of anaesthesia attenuates the pressor response to

laryngoscopy and intubation. In our study we gave infusion 10 min prior to intubation in a dose of 2mcg/kg. Arindam *et al*^[4] demonstrated that SPB, DBP and MAP in dexmedetomidine group remained close to the baseline as compared to clonidine and placebo group which was due to higher efficacy of dexmedetomidine. It was also observed that the changes in all parameters in dexmedetomidine group were consistent and did not show a steep rise or fall at any time interval. Stimulation of medullary alpha-2 adrenoreceptors decrease sympathetic tone and increases vagal activity.

Post-operative sedation was compared between both groups. It was observed that, patients in Group D had early recovery and less sedated as compared to patients in Group C. It is due to the fact that dexmedetomidine has a property of conscious sedation due to short duration of action 2 to 2.5 hrs as compared to clonidine which has duration of action is 5 to 7 hrs. Therefore clonidine causes more sedation and also delay in recovery from anaesthesia. Sedation is mediated by alpha-2b receptors, whereas alpha-2a receptors mediate analgesia and hypotensive effects.

Many factors affect intraoperative blood loss in spine surgery. Prone position is associated with increase intra-abdominal pressure leading to increase pressure in paravertebral plexus leading to increase blood loss. Other factors include increased body weight and number of spinal segments involved. Blood loss was compared in both the groups. It was observed that blood loss was comparable in both groups. Zahra *et al*^[2] observed that clonidine is effective in decreasing blood loss in spine surgeries as compared to placebo. Ramamani mariappan *et al*^[12] also observed that both oral clonidine and intraoperative dexmedetomidine were effective in decreasing blood loss in spine surgeries.

CONCLUSION

Dexmedetomidine is more effective than clonidine in attenuating hemodynamic response during laryngoscopy and maintaining intraoperative and post-operative hemodynamics with minimal post-operative sedation and can be effectively used in spine surgeries operated under general anaesthesia.

REFERENCES

1. Robert WA Nowicki. Anaesthesia for Major Spinal Surgery. *BJA Education*. 2014; 14(4): 147-152.
2. Zahra Taghipour Anvari, Nader Afshar-Fereydouniyan, Farnad Imani *et al.* Effect of Clonidine Premedication on Blood Loss in Spine Surgery. *Anesthesiology and Pain Medicine*, 2012; 1(4): 252-256.
3. Szpalski M, Gunzburg R, Sztern B. An overview of blood-sparing techniques used in spine surgery during the perioperative period. *Eur Spine J*. 2004; 13(Suppl 1): S18-27.
4. Arindam Sarkar, R. K. Tripathi, Sanjay Choubey *et al.* Comparison of effects of intravenous clonidine and dexmedetomidine for blunting pressor response during laryngoscopy and tracheal intubation: A randomized control study. *Anesth Essays Res*. 2014 Sep-Dec; 8(3): 361-366.
5. M.T. Taittonen, O.A. Kirvela, R. Aanta *et al.* Effect of clonidine and Dexmedetomidine premedication on perioperative oxygen consumption and haemodynamic state. *British Journal of Anaesthesia*. 1997; 78: 400-406.
6. Rohini V Bhat Pai, Santhoshi Badiger¹, Roopa Sachidananda² *et al.* Comparison of surgical conditions following premedication with oral clonidine versus oral diazepam for endoscopic sinus surgery: A randomized, double-blinded study. *Journal of Anaesthesiology Clinical Pharmacology*. April-June 2016; 32(2): 250-56.
7. Amrinder Singh, Ruchi Gupta, Tripath Bindra A Study to Evaluate the Effectiveness of Clonidine vs Atenolol in Providing Optimal Surgical Field in Nasal Surgeries under General Anaesthesia. *Anesthesia & Clinical Research*. 2014; 5(3).
8. Hoffman BB, Lefkowitz RJ, Taylor P. Neurotransmission: The autonomic and somatic motor nervous systems. In: Hardman JG, Limbird LE, Goodman GA, editors. *Goodman and Gilman's the Pharmacological Basis of Therapeutics*. 10th ed. New York, NY: McGraw Hill Professional; 2001; 137-82.
9. Maze M, Tranquilli W. Alpha-2 adrenoreceptor agonists: defining the role in clinical anaesthesia. *Anesthesiology*, 1991; 74: 581-605.
10. Coursin DB, Coursin DB, Maccioli GA. Dexmedetomidine. *Curr Opin Crit Care*. 2001; 7: 221-6.
11. Bustillo MA, Lazar RM, Finck AD, Fitzsimmons B, Berman MF, Pile-Spellman J, *et al.* Dexmedetomidine may impair cognitive testing during endovascular embolization of cerebral arteriovenous malformations: A retrospective case report series. *J Neurosurg Anesthesiol*. 2002; 14: 209-12.
12. Ramamani Mariappan, Hari Narayana Prabhu A, Balaji Kuppaswamy. Comparing the Effects of Oral Clonidine Premedication With Intraoperative Dexmedetomidine Infusion on Anesthetic Requirement and Recovery From Anaesthesia in Patients Undergoing Major Spine Surgery. *Journal of neurosurgical anaesthesiology*, July 2013; 26(3).
13. Santvana Kohli, Manpreet Kaur, Sangeeta Sahoo *et al.* Brachial Plexus Block: Comparison of two different doses of clonidine added to bupivacaine. *Journal of Anaesthesiology Clinical Pharmacology*, Oct-Dec 2013; 29: 491-95.
14. Carabine UA, Allen RW, Moore J. Partial attenuation of the pressor response to endotracheal intubation. A comparison of the effects of intravenous clonidine and fentanyl. *Eur J Anaesthesiol*. 1992; 9: 325-9.