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## Comparative Analysis of Intravenous Clonidine and Dexmedetomidine for Hemodynamic Stability and Intraoperative Bleeding in Lumbar Spine Surgeries

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**Abstract.** Lumbar spine surgeries are complex procedures often associated with challenges in maintaining hemodynamic stability and controlling intraoperative bleeding, which are crucial for optimizing patient outcomes. Clonidine and dexmedetomidine both are  $\alpha_2$ -adrenergic agonists with sedative and analgesic properties, known for their potential to attenuate sympathetic responses and stabilize hemodynamics. However, their comparative efficacy in lumbar spine surgeries remains underexplored.

**Methodology.** This study was carried out in 40 patients, ASA grade 1 and 2, undergoing lumbar spinal instrumentation requiring laminectomy. The patients were randomly allocated into two groups (20 each) using the computer generated random number table. Group C received 2  $\mu\text{g}/\text{kg}$  of clonidine diluted in 10 ml of normal saline, given slowly intravenous infusion over 10 min before induction of general anaesthesia. Group D received 1  $\mu\text{g}/\text{kg}$  of dexmedetomidine diluted in 10 ml normal saline, given slow intravenous infusion over 10 minutes before induction of general anaesthesia.

Heart rate, systolic, diastolic, and mean arterial pressure were monitored before intubation as the baseline and after intubation, 15, 30, and 60 minutes after starting the surgery, and after extubation. The amount of intraoperative blood loss was estimated based on the volume of blood in the suction bottle and the number of the blood-soaked gauze pads (20 mL for a completely blood-soaked gauze and 50 mL for a completely blood-soaked long gauze).

**Observation.** No statistically significant difference was found on comparing the two drugs in terms of Baseline characteristics, Mean Arterial Pressure and the amount of blood loss. However Dexmedetomidine group had a higher reduction in Heart Rate as compared to the Clonidine Group.

**Conclusion.** In conclusion, both the  $\alpha_2$  agonist drugs; intravenous clonidine and dexmedetomidine represent valuable options for achieving stable hemodynamics as well as decreases the intraoperative surgical bleeding in lumbar spine surgeries. Total opioid requirements for intraoperative and rescue analgesia in postoperative period were decreased in both the groups.

**Keywords.** Clonidine, Dexmedetomidine, Spine Surgery, Alpha 2 Agonists

## CONFLICTS OF INTEREST Nil

## ACKNOWLEDGEMENT Nil

### Introduction

Lumbar spine surgeries often necessitate meticulous management of hemodynamic stability due to the physiological stressors associated with the procedure. Anesthetic agents that can attenuate sympathetic responses and maintain cardiovascular stability are crucial in optimizing perioperative outcomes. One way to prevent hemodynamic instability and reduce intraoperative blood loss is to use  $\alpha_2$  agonist drugs such as clonidine and dexmedetomidine. The administration of these drugs either orally before the surgery or intravenously during the surgery has proven to be useful in maintaining hemodynamic stability and reduce blood loss<sup>1-3</sup>.

They provide a blood-free surgical field and hence better visibility to the surgeon, reduces the chances of iatrogenic injury and lessens the surgical time. They also reduce the need of blood transfusions and associated complications.

The  $\alpha_2$  agonist drugs are sympatholytic and affect the central receptors to reduce peripheral norepinephrine release by the stimulation of prejunctional inhibitory  $\alpha_2$  adrenoceptors. They also have a sedative effect produced by binding to post synaptic  $\alpha_2$  receptors in Locus ceruleus. Sleep produced by these agents resemble "normal sleep" as they predominantly affect the endogenous, non rapid eye movement sleep promoting pathways whereas midazolam acts by activating GABA receptors which can cause clouding of consciousness and agitation on arousal. Our comparative analysis aims to evaluate and contrast the efficacy, practical considerations of clonidine and dexmedetomidine in this clinical context.

### Methodology

This randomized, double-blinded clinical trial was carried out in 40 patients of age group 18–65 years of either sex, with an American Society of Anesthesiologists (ASA) physical status 1 and 2 and undergoing lumbar spinal instrumentation requiring laminectomy (minimum one level and maximum three levels), after they provided informed written consent.

The exclusion criteria included patients with study drug allergy, hypertension, diabetes, epilepsy, pregnancy, coagulation disorders, ischemic heart disease, history of  $\beta$ -blockers or calcium channel blockers intake,

drug or alcohol abuse, and the operating time of over 150 minutes. Patients with other injuries (chest, abdominal, head, long bones, etc.) were also excluded.

The patients were randomly allocated into two groups (20 each) using the computer generated random number table. Group C received 2  $\mu\text{g}/\text{kg}$  of clonidine diluted in 10 ml of normal saline, given slowly intravenous infusion over 10 min before induction of general anaesthesia. Group D received 1  $\mu\text{g}/\text{kg}$  of dexmedetomidine diluted in 10 ml normal saline, given slow intravenous infusion over 10 minutes before induction of general anaesthesia.

All patients were monitored with standard multi-parameter monitors (ECG monitoring, pulse oximetry, heart rate, saturation and noninvasive blood pressure monitoring). Ringer lactate solution was started using a peripheral 20 gauge IV line. Baseline cardio-respiratory hemodynamic parameters like systolic, diastolic and mean blood pressure, heart rate, SpO<sub>2</sub> were noted. Pre-medication with intravenous ondansetron 4 mg, glycopyrrolate 0.2 mg and fentanyl 2  $\mu\text{g}/\text{kg}$  was given. Then the study drug was given diluted in 10 ml of normal saline over 10 minutes in both the groups, just before induction. After preoxygenation, general anaesthesia was induced with propofol 2 mg/kg (till the loss of eye-lash reflex), endotracheal intubation was then facilitated by giving intubating dose of vecuronium bromide 0.1 mg/kg intravenously. Anaesthesia was maintained with oxygen and nitrous oxide (in ratio of 33:66) and with sevoflurane. Muscle relaxation was maintained by vecuronium bromide 0.02 mg/kg intermittently thereafter. Intraoperative fluid and blood transfusion was done as per standard protocol.

Heart rate, systolic, diastolic, and mean arterial pressure were monitored before intubation as the baseline and after intubation, 15, 30, and 60 minutes after starting the surgery, and after extubation.

At the end of surgery, residual neuromuscular block was reversed by neostigmine in dose of 0.05 mg/kg and glycopyrrolate in dose of 0.2 mg per mg of neostigmine intravenously. Patients were extubated after complete reversal of neuromuscular blockade and restoration of spontaneous respiration and patients were then transferred to recovery room.

The amount of intraoperative blood loss was estimated based on the volume of blood in the suction bottle and the number of the blood-soaked gauze pads (20 mL for a completely blood-soaked gauze and 50 mL for a completely blood-soaked long gauze). Recording of the vital signs and the amount of blood loss in each patient was

done by an assistant anesthesiologist who was unaware of the study groups.

## Analysis

The data are reported based as means  $\pm$  standard deviation. The significance level was set at  $P < 0.05$ . In order to compare the obtained data between the groups, the normal distribution of data was studied using the analysis of variance (ANOVA) and chi-square tests. All statistical analyses were performed using SPSS software (version 19).

## Observations

A total of 40 patients who underwent Lumbar Spine Surgery were included in the study divided into groups of 20 each Group C — Clonidine group and Group D — Dexmedetomidine group.

Both the groups were comparable in terms of demographic characteristics like age, gender, weight and ASA Grading. The Table is annexed as Annexure 1.

The changes in heart rate, systolic, diastolic, and mean arterial blood pressure in both the groups were compared. Dexmedetomidine group had a greater reduction in Heart rate as compared to the Clonidine group ( $p$  value  $< 0.05$ ) but was comparable in terms of changes in Mean Arterial pressure to the Clonidine Group ( $p$  value  $> 0.05$ ). Table 2 and Table 3 show the comparison between the two groups in terms of these parameters.

**Table 1. Showing the Demographic Data and ASA Grading Which was Comparable in Both the Groups**

Demographic Data	Group C	Group D
Age(years)	36.1 $\pm$ 7.2	37.4 $\pm$ 28.1
Male : Female	12 : 8	11 : 9
Weight (kg)	67.4 $\pm$ 5.3	68.3 $\pm$ 5.8
ASA Grading, I : II	15 : 5	14 : 6

While there was no statistical significant difference in baseline characters in the two groups, Heart rates were significantly lower in the Dexmedetomidine group as compared to the Clonidine Group.

There was no statistically significant difference in the two groups at different intervals of surgery in terms of changes in Mean arterial Pressure.

**Table 2. Shows the difference in Heart rates in the Two Groups as per the Time Intervals of Surgery**

Heart Rate	Group C	Group D	P value
Baseline	82 $\pm$ 7.4	83.68 $\pm$ 7.62	$> 0.05$
After intubation	87 $\pm$ 6.82	81.25 $\pm$ 7.2	$< 0.05$
15 minutes after starting surgery	76.8 $\pm$ 5.92	70.2 $\pm$ 5.4	$< 0.05$
30 minutes after starting surgery	74.6 $\pm$ 6.74	69 $\pm$ 5.4	$< 0.05$
60 minutes after starting surgery	75.25 $\pm$ 5.84	69.2 $\pm$ 5.25	$< 0.05$
After extubation	81.5 $\pm$ 7.12	76.4 $\pm$ 7.2	$< 0.05$

**Table 3. Shows the difference in Mean Arterial Pressure in the Two Groups as per the Time Intervals of Surgery**

MAP	Group C	Group D	P value
Baseline	92.6 $\pm$ 7.42	94.55 $\pm$ 8.06	$> 0.05$
After intubation	85.85 $\pm$ 8.83	81.25 $\pm$ 7.87	$> 0.05$
15 minutes after starting surgery	74.75 $\pm$ 9.10	76.50 $\pm$ 7.85	$> 0.05$
30 minutes after starting surgery	72.45 $\pm$ 5.07	73.80 $\pm$ 6.84	$> 0.05$
60 minutes after starting surgery	71.70 $\pm$ 6.49	69.15 $\pm$ 6.66	$> 0.05$
After extubation	85.60 $\pm$ 6.68	79.10 $\pm$ 8.93	$> 0.05$

The amount of intraoperative bleeding was not significantly different between the two groups. Intraoperative blood loss in patients who received Clonidine (Group C) was 240  $\pm$  58 ml and Dexmedetomidine (Group D) was 262  $\pm$  62 ml ( $P > 0.05$ ).

## Discussion

It is well known that the hemodynamic responses that occurs during laryngoscopy and intubation in the form of elevated blood pressure, tachycardia, coughing reflex, increased intracranial, and increased intraocular pressure are mainly due to the stimulation of the sympathetic drive; which corresponds to adverse outcome in terms

of morbidity and mortality associated with the procedure. Hence blunting of these responses is one of the important responsibility of an Anesthesiologist. Alpha 2 Agonists have become a weapon in the armamentarium of an Anesthetist to mitigate this challenge as well as to provide opioid free analgesia.

Previously also several studies have investigated the efficacy of clonidine and dexmedetomidine in maintaining hemodynamic stability during lumbar spine surgeries<sup>4-7</sup>.

While both agents have demonstrated effectiveness in blunting sympathetic responses and attenuating intraoperative blood pressure fluctuations, Dexmedetomidine is found to be more potent in reduction of Heart rate and more so after 3–5 minutes of administration of the drug<sup>8</sup>. Our study also found a similar result and Dexmedetomidine group was found to have a higher reduction in Heart rate as compared to the Clonidine group but no significant difference was found in Mean Arterial pressure.

This difference is probably attributed to the difference in pharmacokinetics in the two drugs. Clonidine and dexmedetomidine are both  $\alpha_2$  agonists that vary in terms of affinity for different types of  $\alpha_2$  receptors. Clonidine has a specificity of 220:1 ( $\alpha_2:\alpha_1$  receptors), whereas dexmedetomidine of 1620:1. Dexmedetomidine is a pharmacologically active dose of medetomidine, a total agonist of the  $\alpha_2$  adrenergic receptor. Clonidine is used to decrease the systemic blood pressure through central brain stem adrenergic stimulation, Low dose dexmedetomidine acts on both central and peripheral receptors and does not cause an initial increase in heart rate as seen with Clonidine. However this action changes on giving a high dosage/bolus of Drug and a paradoxical increase in Heart rate due to activation of peripheral  $\alpha_1$  post-junctional adrenergic receptors, hence the importance of correct dosing<sup>9</sup>.

While many studies have found both Clonidine and Dexmedetomidine as an effective agents to reduce intraoperative Blood loss, some studies have found Clonidine to be better among the two<sup>10</sup>, to reduce intra operative bleeding. However, our study did not find any statistically significant difference between the two drugs.

### Practical Considerations

Practical considerations, including dosing regimens, timing of administration, and intraoperative monitoring, are essential when selecting between clonidine and dexmedetomidine for lumbar spine surgeries. Factors

such as patient characteristics, surgical complexity, and concurrent medications should be carefully evaluated to optimize perioperative management and minimize the risk of adverse event.

### Conclusion

In conclusion, both the alpha agonist drugs; intravenous clonidine and dexmedetomidine represent valuable options for achieving stable hemodynamics as well as decreases the intraoperative surgical bleeding in lumbar spine surgeries. Dexmedetomidine can effectively attenuate the pressor responses during intubation, provides better Heart rate stability throughout the surgical duration, and arousable sedation without respiratory depression with a smooth emergence. Total opioid requirements for intraoperative and rescue analgesia in postoperative period were decreased in both the groups.

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### Порівняльний аналіз внутрішньовенного введення клонідину та дексмедетомідину для стабілізації гемодинаміки й інтраопераційної кровотечі при оперативних втручаннях на поперековому відділі хребта

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**Вступ.** Операції на поперековому відділі хребта є складними процедурами, які часто супроводжуються труднощами в підтримці гемодинамічної стабільності та контролю інтраопераційної кровотечі, що є важливими для оптимізації результатів лікування пацієнтів. Клонідин та дексмедетомідин є  $\alpha_2$ -адренергічними агоністами із седативними та анагетичними властивостями, відомі своєю здатністю послаблювати симпатичні реакції та стабілізувати гемодинаміку. Однак їх порівняльна ефективність при оперативних втручаннях на поперековому відділі хребта залишається недостатньо дослідженою.

**Методи.** Дослідження було проведено за участю 40 пацієнтів, ступенів 1 та 2 за шкалою ASA, яким виконували інструментальну фіксацію поперекового відділу хребта з необхідністю ламінектомії. Пацієнти були випадковим чином розподілені на дві групи (по 20 у кожній) за допомогою комп'ютерної таблиці випадкових чисел. Група С отримувала 2 мкг/кг клонідину, розведеного у 10 мл фізіологічного розчину, повільною внутрішньовенною інфузією протягом 10 хвилин перед індукцією загальної анестезії. Група D отримувала 1 мкг/кг дексмедетомідину, розведеного у 10 мл фізіологічного розчину, повільною внутрішньовенною інфузією протягом 10 хвилин перед індукцією загальної анестезії.

Частота серцевих скорочень, систолічний, діастолічний та середній артеріальний тиск контролювалися перед інтубацією як початкові значення, а також після інтубації, через 15, 30 і 60 хвилин після початку операції та після екстубації. Обсяг інтраопераційної крововтрати оцінювався на основі об'єму крові в аспіраційній ємності та кількості просочених кров'ю ватно-марлевих тампонів (20 мл для повністю просоченого кров'ю ватно-марлевого тампона та 50 мл для повністю просоченого кров'ю довгого ватно-марлевого тампона).

**Результати.** Не було виявлено статистично значущої різниці при порівнянні двох препаратів за базовими характеристиками, середнім артеріальним тиском та кількістю крововтрати. Проте у групі дексмедетомідину спостерігалось більше зниження частоти серцевих скорочень порівняно з групою клонідину.

**Висновок.** На завершення, обидва препарати –  $\alpha_2$ -агоністи і внутрішньовенне введення клонідину та дексмедетомідину є цінними опціями для досягнення стабільної гемодинаміки, а також зменшення інтраопераційної кровотечі при оперативних втручаннях на поперековому відділі хребта. Загалом потреба в опіоїдах для інтраопераційної та екстреної аналгезії в післяопераційному періоді була знижена в обох групах.

**Ключові слова.** клонідин, дексмедетомідин, операції на хребті,  $\alpha_2$ -агоністи