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A PROSPECTIVE STUDY ON THE HAEMODYNAMIC STRESS RESPONSES TO SURGERIES AND THE INTRA-OPERATIVE AND POST-OPERATIVE EFFECTS OF DEXMEDETOMIDINE

[1]Sachin Kumar Gupta, [1]Shrikanta, [2]Ali Raza, [2]Divyansh Gaur, [1]Shah Raj Jayantilal
[1]Senior Resident, Department of Anaesthesiology, Deen Dayal Upadhyay Hospital, India
[2]Secondary DNB, Department of Anaesthesiology, Deen Dayal Upadhyay Hospital, India

Abstract

Background

The surgical stress response triggers neuroendocrine and hemodynamic variations that can compromise patient outcomes. Dexmedetomidine, an alpha-2 adrenoceptor agonist, offers sedation, analgesia, and hemodynamic stability without respiratory depression.

Methods

This prospective study was carried out at Deen Dayal Upadhyay Hospital over six months and included 100 adult patients (ASA I/II) undergoing elective surgeries lasting over one hour. Patients were categorized into two groups: one receiving dexmedetomidine and the other a saline placebo. Hemodynamic parameters, anesthetic and analgesic requirements, and postoperative pain scores were monitored.

Results

Dexmedetomidine significantly stabilized heart rate, with a reduction from 78.0 ± 4.1 bpm in the placebo group to 69.0 ± 3.5 bpm before induction ($p = 0.0001$). Mean arterial pressure (MAP) was lower in the dexmedetomidine group after intubation (96.5 ± 2.0 mm Hg vs. 105.4 ± 3.2 mm Hg, $p = 0.0001$) and during surgery, with values of 84.3 ± 2.2 mm Hg compared to 89.8 ± 2.5 mm Hg ($p = 0.0001$). Additionally, patients in the dexmedetomidine group required significantly less propofol (93.5 ± 3.1 mg vs. 110.8 ± 7.5 mg, $p = 0.0001$) and reported lower postoperative pain scores at 60 minutes (0.5 ± 0.3 vs. 1.2 ± 0.4, $p = 0.0001$).

Conclusion

Dexmedetomidine is effective as an anesthetic adjunct, enhancing hemodynamic stability and postoperative analgesia while reducing anesthetic and opioid requirements.

Recommendation

We recommend researchers to do additional studies with a substantial sample size, incorporating invasive blood pressure measurement and multicenter randomized controlled trials.

Keywords: *Dexmedetomidine, Hemodynamic Stability, Anesthetic Adjunct, Postoperative Analgesia, Surgical Stress Response.*
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Corresponding Author: Shah Raj Jayantilal
Email: *rjshah.121@gmail.com*
Senior Resident, Department of Anaesthesiology, Deen Dayal Upadhyay Hospital, India.

Introduction

The physiological response to injury or trauma triggers significant hormonal and metabolic changes. During surgery, this response is marked by heightened activity in the endocrine system and the activation of the immune and sympathetic nervous systems [1]. Various strategies have been implemented to reduce the neuroendocrine, cardiovascular, and inflammatory reactions associated with surgical interventions, aiming to preserve organ function and improve clinical outcomes [2]. Techniques such as tracheal intubation, extubation, laryngoscopy, and minimally invasive laparoscopic procedures often stimulate the sympathetic nervous system. For instance, the pneumoperitoneum and carbon dioxide insufflation used in laparoscopic surgery increase plasma levels of norepinephrine, epinephrine, and renin activity [3]. These changes result in heightened systemic and pulmonary vascular resistance, elevated blood pressure, and decreased cardiac output. Moreover, the reverse Trendelenburg position frequently adopted during surgery further reduces cardiac output, raising the risk of ischemia, a potentially life-threatening complication [4].
To control sympathetic activation and achieve hemodynamic stability, a variety of pharmacological

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agents are utilized, including opioids, beta-adrenergic blockers, benzodiazepines, calcium channel inhibitors, and vasodilators [5]. Among these, alpha-2 adrenergic receptor agonists have gained increasing prominence. The earliest alpha-2 agonists, developed in the early 1960s, were associated with sedation and severe cardiovascular depression, leading to the introduction of clonidine in 1966. Since then, clonidine has been used to manage hypertension and conditions such as alcohol and drug withdrawal, myocardial ischemia, pain, and spinal anesthesia [6].

Dexmedetomidine, a short-acting and highly selective alpha-2 adrenergic receptor agonist, has emerged as a powerful agent with significant physiological effects even at plasma concentrations below 1.0 ng/ml. It suppresses sympathetic activity, mitigates neuroendocrine and hemodynamic stress responses to anesthesia and surgery, decreases the requirement for anesthetics and opioids, and provides sedation and analgesia without impairing psychomotor performance. These properties make it particularly effective in preventing and managing perioperative myocardial ischemia [7]. Its unique profile allows its application throughout the perioperative phase, including as premedication, as an adjunct to general and regional anesthesia, and for postoperative sedation and pain control. Unlike benzodiazepines, dexmedetomidine provides these benefits without causing respiratory depression, making it a safe and effective choice for patients who are extubated or breathing spontaneously, especially in intensive care settings before, during, and after extubation [8, 9].

This investigation aims to examine the intraoperative and postoperative hemodynamic stress responses in patients receiving dexmedetomidine as an anesthetic adjunct.

Methods

Study Design

This prospective study was conducted in the Anaesthesiology department of Deen Dayal Upadhyay Hospital over six months.

Inclusion and exclusion criteria

The study included 100 adult patients aged 18–60 years, classified under ASA (American Society of Anesthesiologists) physical status I or II, and scheduled for elective surgeries requiring general anesthesia lasting more than one hour. Patients below 18 years of age, pregnant women, and those with specific comorbidities such as morbid obesity, chronic pulmonary diseases, endocrine disorders, autoimmune conditions, and Raynaud's disease were excluded from the study. These criteria ensured a homogenous study population and minimized confounding variables.

Study Groups and Categorization

Participants were randomly divided into two groups of 50 each to compare the effects of Dexmedetomidine and placebo:

- **Group I (Placebo):** Normal saline solution as a control.
- **Group II (Dexmedetomidine):** Administered Dexmedetomidine hydrochloride at a concentration of 100 µg/ml.

In Group II, a loading dose of Dexmedetomidine (1 µg/kg) was administered intravenously over 10 minutes, followed by a continuous maintenance infusion of 0.5 µg/kg/hour. The same protocol was applied to Group I using a saline solution as the placebo. Random categorization ensured unbiased allocation and comparability between the two groups.

Preoperative Preparation

To ensure uniform preoperative sedation, all participants were administered oral Alprazolam (0.5 mg) the night before surgery. This step aimed to reduce preoperative anxiety and optimize conditions for anesthesia induction.

Anesthetic Protocol

Anesthesia was induced in all patients using a standardized protocol. A sleep dose of Propofol was administered to initiate sedation, followed by Succinylcholine (1.5 mg/kg) to facilitate endotracheal intubation. After partial recovery of muscle power, Vecuronium (0.08 mg/kg) was given to maintain muscle relaxation. This uniform induction technique ensured consistency in the anesthetic management of all patients across both groups.

Monitoring and Data Collection

- **Preoperative Monitoring:** Baseline recordings of mean arterial pressure (MAP) and heart rate (HR) were taken 30 minutes prior to the induction of anesthesia to establish reference values.
- **Intraoperative Monitoring:** MAP and HR measurements were recorded every 15 minutes during surgery to evaluate hemodynamic stability. These parameters were continuously monitored and documented for six hours postoperatively to assess recovery trends.
- **During Induction and Intubation:** Data collection was intensified during the induction phase, with MAP and HR recorded every two minutes. Monitoring continued for 10 minutes following tracheal intubation to capture immediate stress responses.

Postoperative Pain Assessment

Postoperative pain intensity was assessed using the Visual Analogue Scale (VAS), a reliable and widely accepted

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tool for pain evaluation. Patients were closely monitored, and the need for additional postoperative analgesia was determined based on their VAS scores. This ensured appropriate pain management while facilitating comparisons between the two study groups in terms of analgesic requirements.

Statistical Analysis

Statistical analysis was performed using descriptive statistics for baseline data using the SPSS software. The comparison between groups was done using the Student's t-test, with a p-value of <0.05 considered statistically significant.

Ethical Considerations

Informed consent was taken from all participants.

Results

The demographic characteristics of the study participants were well-matched between the two groups. The average age was 36 years in the placebo group and 34 years in the dexmedetomidine group. The gender distribution was comparable, with slightly more females in both groups (Group I: 23 males, 27 females; Group II: 20 males, 30 females). The mean body weight was also similar between the groups, with 56 kg in the placebo group and 57 kg in the dexmedetomidine group, ensuring baseline comparability (Table 1).

Table 1: Characteristics of the two cohorts:

Variable	Placebo group	Dexmedetomidine group
Age (yrs, mean)	36	34
Gender (M/F)	23/27	20/30
Weight (kg, mean)	56	57

The heart rate comparison revealed significant differences between the groups at several time points. Baseline values were similar (p = 0.071), but before induction, the dexmedetomidine group showed a marked reduction in heart rate compared to the placebo group (69.0 ± 3.5 vs. 78.0 ± 4.1, p = 0.0001). After intubation and during surgery, the dexmedetomidine group maintained lower heart rates, particularly at 15 and 30 minutes (p = 0.025 and 0.037, respectively). In the PACU, significant differences persisted at 1, 60, and 180 minutes, with the dexmedetomidine group consistently exhibiting lower heart rates (p = 0.0001). These findings indicate that dexmedetomidine effectively stabilized heart rates during and after surgery compared to the placebo (Table 2).

Table 2: Evaluation of the heart rate in beats per minute in both groups:

Timing	Placebo group	Dexmedetomidine group	p-value
Baseline	76.5 ± 3.5	77.0 ± 2.2	0.071
Before Induction	78.0 ± 4.1	69.0 ± 3.5	0.0001*
After Intubation	85.0 ± 4.8	78.5 ± 2.8	0.0001*
During Surgery			
15 minutes	77.0 ± 1.2	76.0 ± 3.2	0.025*
30 minutes	77.5 ± 3.2	76.3 ± 3.1	0.037*
45 minutes	76.5 ± 2.0	76.8 ± 3.0	0.290
60 minutes	76.2 ± 1.5	76.7 ± 3.2	0.180
In PACU			
1 minute	87.0 ± 3.1	75.0 ± 2.0	0.0001*
60 minutes	77.5 ± 3.0	69.0 ± 1.2	0.0001*
180 minutes	76.0 ± 1.5	69.5 ± 1.8	0.0001*

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360 minutes	76.8 ± 2.6	76.3 ± 3.9	0.420

The examination of MAP between the two groups reveals significant differences at specific time points. After intubation, the dexomedetomidine group demonstrated significantly lower MAP (p = 0.0001) compared to the placebo group, indicating better hemodynamic stability. During surgery, the dexomedetomidine group maintained consistently lower MAP values, particularly at 75, 90, and 120 minutes, with all differences being statistically significant (p = 0.0001). Similarly, in the PACU, the dexmedetomidine group exhibited lower MAP, reflecting the sustained effects of Dexmedetomidine in managing blood pressure postoperatively (Table 3).

Table 3: Mean Arterial Blood Pressure (mm Hg) Comparison placebo and Dexmedetomidine group:

Timing (minutes)	Placebo group	Dexmedetomidine group	p-value
Baseline	88.2 ± 2.1	87.8 ± 2.5	0.081
Before Induction	88.5 ± 2.3	87.3 ± 2.8	0.292
After Intubation	105.4 ± 3.2	96.5 ± 2.0	0.0001*
During Surgery	89.8 ± 2.5	84.3 ± 2.2	0.0001*
In PACU	87.1 ± 2.1	85.2 ± 1.8	0.0001*

The anesthetic and analgesic requirements differed markedly between the groups. dexomedetomidine group required significantly lower doses of propofol (93.5 ± 3.1 mg vs. 110.8 ± 7.5 mg) and fentanyl (82.7 ± 3.0 µg vs. 106.2 ± 8.9 µg) compared to the placebo group (p = 0.0001 for both). This highlights the role of Dexmedetomidine in reducing the need for additional sedatives and opioids during surgery (Table 4).

Table 4: Propofol and Fentanyl Requirements

Parameter	Placebo group	Dexmedetomidine group	p-value
Sleep Dose of Propofol (mg)	110.8 ± 7.5	93.5 ± 3.1	0.0001*
Intraoperative Fentanyl (µg)	106.2 ± 8.9	82.7 ± 3.0	0.0001*

Postoperative pain scores, as measured by the VAS, were consistently lower in the dexomedetomidine cohort. At 60 and 120 minutes, the dexomedetomidine group reported significantly reduced pain scores (p = 0.0001 and p = 0.028, respectively). This trend continued through 180 and 240 minutes, with substantial differences in favor of the dexomedetomidine group (p = 0.0001 and p = 0.003, respectively). While differences at 300 and 360 minutes were not statistically significant, the overall trend suggests better pain management in the Dexmedetomidine group (Table 5).

Table 5: Postoperative Visual Analogue Score (VAS)

Timing	Placebo group	Dexmedetomidine group	p-value
60 min	1.2 ± 0.4	0.5 ± 0.3	0.0001
120 min	2.3 ± 0.5	1.3 ± 0.4	0.028
180 min	3.4 ± 0.6	2.3 ± 0.5	0.0001
240 min	4.2 ± 0.5	3.5 ± 0.5	0.003
300 min	4.7 ± 0.8	4.3 ± 0.6	0.051
360 min	5.7 ± 0.7	4.6 ± 0.7	0.063

Discussion

Dexmedetomidine, a fat-soluble compound derived from imidazole, has a binding strength to alpha-2 receptors that is nearly 100 times higher than that of clonidine [10]. Its hemodynamic effects stem from central sympatholytic actions and peripheral vasoconstrictive properties, both of which are dose-dependent [13-15]. Dexmedetomidine lowers serum norepinephrine levels by activating receptors in the medullary vasomotor center, reducing norepinephrine turnover and suppressing central sympathetic outflow. This mechanism effectively blunts the hemodynamic responses to stimuli like intubation and extubation without significant adverse effects.

Surgical procedures, including endotracheal intubation and anesthesia, induce considerable stress and are associated with physiological disturbances such as increased catecholamine release, elevated heart rate, and higher blood pressure [11]. These responses are particularly pronounced in patients with preexisting conditions like hypertension or coronary artery disease, putting them at heightened risk for perioperative complications such as myocardial ischemia or postoperative infarction [12]. Dexmedetomidine, by mitigating these stress-related effects, has been shown to stabilize hemodynamic parameters, including heart rate and arterial pressure, during surgery.

In this study, the perioperative administration of dexmedetomidine resulted in a significant reduction in heart rate and blood pressure compared to baseline values, supporting its role in minimizing sympathetic activation during surgery. Findings from prior research highlight that stressors such as laryngoscopy, pneumoperitoneum, and extubation lead to marked increases in heart rate and arterial pressure in patients receiving no active treatment [16, 17]. Conversely, those given dexmedetomidine maintained stable hemodynamics, with no reports of bradycardia.

The drug's ability to dampen the neuroendocrine response has been associated with a 15-20% reduction in arterial pressure and a 10-15% decrease in heart rate [18,19]. Furthermore, dexmedetomidine has been noted to reduce the requirement for opioids during and after surgery, enhancing postoperative recovery by minimizing the need for additional analgesics [20,21]. Compared to other anesthetic adjuncts, it consistently provides superior hemodynamic control, making it a valuable agent in surgical settings.

Conclusion

This study demonstrates that Dexmedetomidine effectively reduces the stress response during surgery by stabilizing heart rate and arterial blood pressure. The drug's sympatholytic effects lead to a significant reduction in hemodynamic fluctuations during critical perioperative events, such as intubation, surgery, and extubation, compared to the control group. Furthermore, Dexmedetomidine's ability to reduce opioid requirements due to its hemodynamic stability suggests its potential as an advantageous perioperative adjuvant, promoting smoother recovery and reducing the risk of cardiovascular complications in high-risk patients.

Limitations

The limitations of this study include the small sample population who were included in this study. Furthermore, the lack of a comparison group also poses a limitation to this study's findings.

Recommendation

We recommend that researchers do additional studies with a substantial sample size, incorporating invasive blood pressure measurement and multicenter randomized controlled trials.

Acknowledgement

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Data Availability

Data is available upon request.

Author contributions

All authors contributed to the design of the research. SRJ and AR collected and analyzed the data. S and SKG wrote the manuscript. DG and SRJ edited the paper. All authors read and approved the paper.

List of abbreviations:

MAP- Mean arterial pressure
ASA- American Society of Anesthesiologists
HR- Heart rate
VAS- Visual Analogue Scale

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No funding was received.

Conflict of interest

The authors have no conflicting interests to declare.

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