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RESEARCH ARTICLE
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COMPARISON OF EFFECT OF LOW DOSE DEXMEDETOMIDINE INFUSION (0.2 VS 0.4 MCG/KG/HR) ON HEMODYNAMIC STRESS RESPONSE IN PATIENTS UNDERGOING LAPROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANESTHESIA AT TERTIARY CARE HOSPITAL KARACHI

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ABSTRACT

Background: Dexmedetomidine, an α2-adrenergic receptor agonist, has gained prominence for its hemodynamic stabilizing properties in anesthesia. Its dose-dependent effects on reducing stress responses during laparoscopic surgeries remain underexplored.

Objective: To compare the effects of low-dose dexmedetomidine infusion at 0.2 mcg/kg/h versus 0.4 mcg/kg/h on the hemodynamic stress response in patients undergoing laparoscopic cholecystectomy under general anesthesia.

Study Design and Setting: This randomized controlled trial was conducted from November 2020 to March 2021 at the Department of Anesthesiology, Civil Hospital Karachi.

Methodology: A total of 182 patients (91 per group) of ASA status ≤2, aged 20–60 years, were randomly assigned to receive dexmedetomidine infusions at 0.2 mcg/kg/h (Group A) or 0.4 mcg/kg/h (Group B). Hemodynamic parameters, including pulse rate (PR) and mean arterial pressure (MAP), were recorded at predefined intervals.

Results: Group B demonstrated significantly lower pulse rates and mean arterial pressures compared to Group A at all measured time points. For example, at 1 minute post-intubation, the

pulse rate was 96.57 ± 3.52 in Group A versus 86.98 ± 1.06 in Group B (p = 0.001). Similarly, MAP was 101.1 ± 9.54 mmHg in Group A versus 94.69 ± 1.58 mmHg in Group B (p = 0.001). These differences persisted post-stratification for variables such as age, gender, BMI, and surgical duration.

Conclusion: A dexmedetomidine infusion at 0.4 mcg/kg/h is more effective in attenuating the hemodynamic stress response during laparoscopic cholecystectomy compared to 0.2 mcg/kg/h, with statistically significant reductions in pulse rate and mean arterial pressure.

Keywords: Anesthesia, Dexmedetomidine, Hemodynamic Response, Laparoscopic Cholecystectomy.

INTRODUCTION

Laparoscopic cholecystectomy is the gold standard for removing symptomatic gallbladders due to advantages like reduced post-operative pain, shorter hospital stays, and faster recovery.[1] Symptoms of symptomatic cholelithiasis often include right upper quadrant pain, fever, vomiting, and sometimes perforation.[2] However, like any surgery, laparoscopic cholecystectomy induces a stress response from surgery and anesthesia.[3] Intraoperative hemodynamic changes may result from intra-abdominal carbon dioxide (CO_2) insufflation and kidney handling, leading to renin release.[4] Stress responses involve various endocrinal, immunological, and hematological effects.[5]

Several drugs, including alpha-2 adrenergic agonists, high doses of opioids, and β-blockers, have been explored to reduce these stress responses during laparoscopic surgery.[6-7] Alpha-2 agonists can decrease sympatho-adrenal and cardiovascular reactions to surgical stimuli by inhibiting the sympathetic nervous system.[8] Activation of alpha-2 adrenoceptors leads to sympatholysis, reduced renin release, and decreased insulin secretion.[9] Clonidine, a centrally acting partial alpha-2 agonist (220:1 α2:α1), has been employed to lower stress responses.[10-11] Dexmedetomidine is a selective and potent α2-adrenergic agonist.[12] Its α2/α1 selectivity is 1600 times greater than that of clonidine.[13-14] Recently, there has been increased interest in using α2 agonists in anesthesia for their anxiolytic, sedative, sympatholytic, and analgesic-sparing properties.[15] Therefore, our rationale was to find out the changes in hemodynamic responses to two different infusions of dexmedetomidine, so that local statistics with knowledge as which dose is superior to another and recommend that as first choice of treatment. To compare the hemodynamic stress response in low dose dexmedetomidine infusion (0.2 vs 0.4 mcg/kg/h) in patients undergoing laparoscopic cholecystectomy under general anesthesia at Tertiary Care Hospital, Karachi

METHODOLOGY

This randomized controlled trial was conducted after the approval of institutional review board, from November, 2020 to March, 2021 at the Department of Anesthesiology, Surgical ICU and Pain Management, Civil Hospital Karachi. A total of 182 patients (91 in each group) who were equals to or less than ASA status 2, were undergoing laparoscopic cholecystectomy, and were aged between 20 – 60 years were included. Patients were excluded from the study for several reasons: those who did not provide consent, individuals with a history of type II diabetes mellitus and hypertension, and those who had previously experienced a myocardial infarction. Additionally, patients with a history of taking β-blockers, α-blockers, or calcium channel blockers were excluded, as were individuals with anemia requiring blood transfusion (Hb < 10 g/dL). Other exclusion criteria included a history of thromboembolic disorders, stroke, renal impairment, chronic obstructive pulmonary disease (COPD), asthma, chronic liver disease, hypothyroidism, and congestive heart failure (CHF).

Demographic data was collected from each patient, who were randomly assigned into two groups: Group A received dexmedetomidine infusion at 0.2 mcg/kg/h, and Group B at 0.4 mcg/kg/h. Laparoscopic cholecystectomy was performed by an experienced surgeon, while an uninvolved

anesthesiologist prepared the solutions. Loading doses were calculated, diluted in 10 ml, and infused over 10 minutes using an INFUSA® 101-P syringe pump, maintaining blinding for the researcher.
On the operating table, baseline vital signs—pulse rate (PR), mean arterial pressure (MAP), and oxygen saturation—were recorded. A wide-bore intravenous cannula was placed for fluids and the infusion. All patients received premedication (glycopyrrolate 5 mcg/kg IM and tramadol 1.0 mg/kg IM) 45 minutes before induction, along with ranitidine (50 mg IV) and ondansetron (4 mg IV) at induction. Pre-oxygenation occurred 15 minutes after starting the infusion.
Induction involved propofol (2 mg/kg IV) and succinylcholine (1.5 mg/kg IV) for intubation. Anesthesia was maintained with O2:N2O (50:50), isoflurane, and atracurium, with intra-abdominal pressure kept between 12 and 14 mmHg. Mechanical ventilation maintained EtCO2 between 35 and 45 mmHg. Vital signs were monitored at key intervals during the procedure. Drug infusion was stopped at the end of surgery, followed by conventional reversal and extubation. Height and weight were measured to calculate BMI. Quantitative (age, height, weight, hemodynamic stress response, duration of surgery) and qualitative variables (gender, smoking status, BMI, socioeconomic status) were documented.
Data was analyzed using SPSS Version 20. Means and standard deviations were calculated for quantitative variables, including age, height, weight, hemodynamic stress responses (pulse rate and mean arterial pressure), and duration of surgery. Frequencies and percentages were determined for qualitative variables such as gender, smoking status, BMI, and socioeconomic status. An unpaired t-test compared mean differences in hemodynamic stress responses between the two groups. Effect modifiers were controlled by stratifying data based on age, gender, smoking status, BMI, socioeconomic status, and duration of surgery. Post-stratification, independent t-tests were conducted, with a p-value of ≤ 0.05 considered statistically significant.

RESULTS

In our study involving 91 patients, demographic analysis revealed that Group A had a mean age of 47.25 years (SD ±7.91), while Group B had a mean age of 48.71 years (SD ±8.01). The age distribution showed that 35.2% of Group A and 26.4% of Group B were in the 20-40-year range, whereas 64.8% of Group A and 73.6% of Group B were aged 41-60 years. Gender distribution indicated that 34.1% of Group A were male compared to 26.4% in Group B. Additionally, Group A had a higher average weight (121.84 kg, SD ±23.02) compared to Group B (110.84 kg, SD ±28.57). Despite these differences in demographic factors, no statistically significant differences were found among age, gender, or weight between the groups as shown in Table 1

Table-1: Descriptive statistics in dexmedetomidine group (91) versus group b (91) n=182

Variable	Mean	Standard Deviation	Min-Max
Age Group A (Years)	47.25	±7.91	24-60
Age Group B (Years)	48.71	±8.01	24-60
Duration Of Surgery Group A (Hours)	1.25	±1.84	1-3
Duration Of Surgery Group B (Hours)	1.77	±1.60	1-3
Height Group A (Cm)	145.41	±11.47	120-180
Height Group B (Cm)	138.04	±14.51	120-180
Weight Group A (Kg)	121.84	±23.02	52-154
Weight Group B (Kg)	110.84	±28.57	52-154

On the physiological front, mean pulse rates at various points during the procedure demonstrated significant differences between the groups, with Group A consistently showing higher pulse rates, particularly after intubation (96.57 vs. 86.98, p=0.001) and after extubation (91.04 vs. 83.31, p=0.001) as shown in Table 2.

Table-2: Pulse rate in dexmedetomidine group a (91) versus group B (91) (n=182)

Pulse rate (beats/min)	Dexmedetomidine group A	Dexmedetomidine group B	p value
At 15 min after starting infusion	81.94±1.26	80.21±0.78	0.001
At 1 min after induction	82.16±1.40	80.16±0.68	0.001
At 1 min after intubation	96.57±3.52	86.98±1.06	0.001
At 1 min after creation of pneumoperitoneum	82.08±1.40	76.35±2.87	0.001
At 1 min after release of pneumoperitoneum	75.04±1.03	74.93±1.01	0.001
At 1 min after extubation	91.04±1.54	83.31±1.46	0.001

Similarly, mean arterial pressures were significantly higher in Group A at all measured intervals, indicating notable differences in hemodynamic responses ($p<0.01$) as shown in Table 3

Table 3: Mean Arterial Pressure in Dexmedetomidine Group A (91) Versus Group B (91) (n=182)

MAP (mmhg)	Dexmedetomidine Group A	Dexmedetomidine Group B	P Value
at 15 min after starting infusion	94.79±1.62	92.86±1.77	0.001
at 1 min after induction	88.75±1.76	88.84±1.92	0.001
at 1 min after intubation	101.1±9.54	94.69±1.58	0.001
at 1 min after creation of pneumoperitoneum	93.85±1.71	88.75±1.76	0.001
at 1 min after release of pneumoperitoneum	92.21±6.57	88.03±2.06	0.001
at 1 min after extubation	104.7±3.22	96.25±2.22	0.001

Stratification analyses for age, gender, surgical duration, BMI, smoking status, and socioeconomic status consistently reinforced these findings, highlighting statistically significant differences in both pulse rates and arterial pressures between the two groups.

DISCUSSION

Dexmedetomidine is a highly selective α2 adrenergic agonist that exerts its effects through three receptor subtypes (α2A, α2B, α2C) located in the brain and spinal cord. Its pharmacological properties include sedation, anxiolysis, analgesia, and sympatholysis, which can lead to hypotension and bradycardia. Specifically, α2A receptor activation in the brain stem reduces norepinephrine release, resulting in decreased heart rate and blood pressure, while α2A and α2C receptor stimulation in the locus ceruleus contributes to sedation. In the spinal cord, these receptors diminish pain transmission by reducing substance P release. Given these effects, dexmedetomidine has been

studied for its impact on hemodynamic responses during laparoscopic surgeries, typically administered via infusion with or without a bolus. While infusion rates from 0.1 to 10 mcg/kg/h have been explored, higher doses have been associated with adverse cardiac effects. Notably, a biphasic blood pressure response occurs with bolus doses, initially causing hypertension followed by hypotension, particularly in younger, healthier patients.

In our study of 182 patients, Group A had a mean age of 47.25 years (SD ±7.91) and Group B 48.71 years (SD ±8.01). The respective mean pulse rates at 1-minute post-intubation were 96.57 (SD ±3.52) for Group A and 86.98 (SD ±1.06) for Group B, with mean arterial pressures of 101.1 (SD ±9.54) and 94.69 (SD ±1.58). Significant differences in heart rate and arterial pressure were observed between the groups, particularly following intubation and extubation ($p<0.001$). Additional studies support dexmedetomidine's efficacy in maintaining hemodynamic stability and reducing intraoperative stress responses. For instance, a study involving ASA physical grades I and II patients undergoing laparoscopic cholecystectomy noted significantly attenuated hemodynamic responses in dexmedetomidine groups compared to controls, with a notable opioid-sparing effect[16, 17, 18, 19, 20]. Overall, our findings reinforce dexmedetomidine's role in enhancing hemodynamic stability during laparoscopic procedures while minimizing analgesic requirements, highlighting its potential as an effective anesthetic adjuvant.

CONCLUSION:

Low dose infusion of dexmedetomidine at the rate of 0.4 mcg/kg/h without any bolus dose serves as a very useful anesthesia adjuvant to control hemodynamic stress response to intubation, pneumoperitoneum and extubation in patients undergoing laparoscopic cholecystectomy. It also provides lighter sedation and reduces the post-operative analgesic requirements without any significant adverse effects.

CONFLICT OF INTEREST:

The authors have no conflict of interest.

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