

# Effects of Intravenous Dexmedetomidine Premedication on Hemodynamics Changes during Laparoscopic Cholecystectomy

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**Abstract:** *Dexmedetomidine is known to prevent haemodynamic responses by decreasing the peripheral sympathetic discharge. This study aims to find out the effect of I.V. Dexmedetomidine premedication on hemodynamic changes during laryngoscopy, intubation and during pneumoperitoneum for laparoscopic cholecystectomies. **Methodology:** We compared Dexmedetomidine along with placebo to know that at which point of time during anesthesia patient will be benefitted most with dexmedetomidine. And for this purpose a randomised control study was done in a total 60 ASA I/2 patients. **Results:** Patients who received dexmedetomidine Group D showed significant fall in HR, SBP, DBP and MABP post induction, laryngoscopy, intubation, at the time of pneumoperitoneum, in the intraoperative and post operative period as compared to Group S. **Conclusion:** Intravenous Dexmedetomidine 1mcg/kg may be accepted as an effective premedication to attenuate the hemodynamic response to laryngoscopy and intubation as well as intra operative and post operative period.*

**Keywords:** dexmedetomidine, laryngoscopy, hemodynamics, pneumoperitoneum, laparoscopic

## 1. Introduction

Laparoscopic cholecystectomy is now the “gold standard” for cholecystectomy because of its documented advantages over open cholecystectomy like - minimal pain, small incision, better cosmesis, less post operative ileus, reduced morbidity, early ambulation, economic benefits - shorter hospital stay, early return to work and normal activities. It is now commonly accepted that pneumoperitoneum which is the prerequisite for laparoscopic surgery causes intraoperative adverse cardiovascular effects<sup>1,2</sup>. Carbondioxide pneumoperitoneum induces significant haemodynamic changes. Both mechanical (Increased intraabdominal pressure) and neurohumoral factors contribute to the haemodynamic changes induced by carbon dioxide pneumoperitoneum.<sup>2</sup>

Laryngoscopy and endotracheal intubation is known to cause a stress response which results in haemodynamic fluctuations. These haemodynamic changes are an increase (or sometimes decrease) in heart rate, systolic, diastolic and mean arterial blood pressures, and myocardial oxygen demand along with cardiac rhythm disturbances<sup>3</sup>. Numerous pharmacological trials have been made to attenuate these pressor responses in patients. Among the many agents used are nitroglycerine<sup>7</sup>, lidocaine hydrochloride<sup>7,8</sup>, esmolol<sup>7,8</sup>, fentanyl citrate<sup>8</sup>, magnesium sulphate<sup>29</sup>, and calcium channel blockers<sup>9,12</sup>. Nerve blocks and topical applications of local anaesthetics, have also been used to attenuate the pressor response. Most recently, selective  $\alpha_2$  adrenoceptor agonists (clonidine hydrochloride, dexmedetomidine hydrochloride) have been used for their sympatholytic properties. Most of the drugs used to attenuate the response to laryngoscopy and intubation may cause other unacceptable side effects like prolonged sedation, nausea and vomiting, dysrhythmias and hypotension. Still others require invasive blood pressure monitoring.

Dexmedetomidine<sup>9,13-15</sup>, d-enantiomer of medetomidine belongs to imidazole subclass of  $\alpha_2$ receptor agonists, similar to clonidine and shows high specificity for  $\alpha_2$  receptor ( $\alpha_2:\alpha_1 = 1600:1$ ). It was introduced in clinical practice in united states in 1999 and approved by FDA only as short term (<24hrs) sedative for mechanically ventilated adult ICU patients. It is now being used off label outside of the ICU in various settings, including sedation and adjunct analgesia in the operating room, sedation in diagnostic and procedure units, and for other applications such as withdrawal/detoxification amelioration in adult and paediatric patients. It improves perioperative haemodynamics (attenuates blood pressure and heart rate responses to surgical stimulation) and sympathoadrenal stability. It also induces sedation, decreases anaesthetic requirements and decreases vasoconstriction and shivering thresholds. Many studies were done in assessing the clinical efficacy of Dexmedetomidine, and it has shown that dexmedetomidine decreases peripheral sympathetic discharge attenuates the increase in systemic vascular resistance. Dexmedetomidine improves intraoperative and postoperative hemodynamic stability by stabilizing the changes in arterial pressure, heart rate and cardiac output. Dexmedetomidine has also been found to be an effective agent for the inhibition of perioperative shivering which can adversely increase the metabolic rate and cardiac work and may also disrupt surgical repair or result in wound dehiscence. Dexmedetomidine increases gastrointestinal motility by decreasing sympathetic outflow and increasing para sympathetic outflow from the central nervous system. Episodes of postoperative nausea and vomiting has been found to be less in patients receiving dexmedetomidine as compared to placebo. Although many workers have reported the antiemetic property of dexmedetomidine, the mechanism by which it acts warrants further investigation. So dexmedetomidine also affords an added advantage of reduction in postoperative complications such as nausea,

Volume 8 Issue 9, September 2019

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vomiting and shivering. These characteristics of dexmedetomidine suggests that it can be useful in the anaesthetic management of patients undergoing Laparoscopic Cholecystectomy.

## 2. Literature Survey

Laryngoscopy and endotracheal intubation are known to be associated with a sympathoadrenal response, manifesting as tachycardia and hypertension<sup>5</sup>. This is associated with an increase in the levels of circulating norepinephrine. These circulatory and endocrine changes have already been described by Prys-Roberts<sup>5</sup> (1971). More recently,  $\alpha_2$  adrenergic receptor agonists are being increasingly used to attenuate the pressor response to laryngoscopy and intubation<sup>16</sup>.

Dexmedetomidine hydrochloride, a novel clonidine-like agent, is a highly selective and specific  $\alpha_2$  adrenergic receptor agonist. It has clinically significant effects on the sympathoadrenal and haemodynamic responses induced by anaesthesia and surgery. Apart from its sympatholytic effects, it also has sedative, anxiolytic and analgesic properties. It decreases the incidence of postoperative nausea and vomiting, and shivering. It also decreases the requirements of anaesthetic agents perioperatively. These unique properties render it a suitable agent for premedication, as an anaesthetic adjunct and as a postoperative sedative and analgesia<sup>9,17</sup>.

Kallio *et al*<sup>15</sup> (1989) administered 5 different doses of dexmedetomidine intravenously to 5 patients over 30 seconds, and reported a decrease in heart rate and blood pressure, accompanied by reduction in circulating norepinephrine levels (upto 92 %). A biphasic blood pressure response was observed after the highest two doses. The increase in blood pressure was accompanied by a concomitant sharp, transient bradycardia.

Aantaa *et al*<sup>19</sup> (1991) compared intramuscular dexmedetomidine (1  $\mu\text{g}/\text{kg}$ ) administered 1 hour prior to surgery, with intravenous midazolam as premedication for minor gynaecological surgery. Administration of dexmedetomidine was associated with moderate reductions in arterial blood pressure (15-20 %), heart rate (10-15 %), and plasma concentrations of norepinephrine at the time of laryngoscopy and intubation.

Aho *et al*<sup>18</sup> (1992) also studied the effects of intramuscularly administered dexmedetomidine in three different concentrations (0.6, 1.2, and 2.4  $\mu\text{g}/\text{kg}$  intramuscularly) administered 45 – 60 minutes prior to induction. They reported that arterial blood pressure and heart rate increased after endotracheal intubation in all three groups, but the least rise in Mean Arterial Pressure was seen in the 2.4  $\mu\text{g}/\text{kg}$  dexmedetomidine group.

Bloor *et al*<sup>14</sup> (1992) examined the haemodynamic effects of four doses of dexmedetomidine, administered intravenously over 2 minutes. Lower doses resulted in a monophasic reduction in Mean Arterial Blood Pressure (MABP), while the two largest doses resulted in a biphasic response along with a baroreceptor mediated decrease in heart rate. They

also reported that dexmedetomidine reduced plasma norepinephrine levels at all doses, for more than 4 hours.

Keniya *et al*<sup>16</sup> (2011) used an induction dose of dexmedetomidine (1  $\mu\text{g}/\text{kg}$ ) given intravenously over 10 minutes, followed by an infusion (0.2 – 0.7  $\mu\text{g}/\text{kg}$ ). They reported a dose dependent decrease in the haemodynamic response to tracheal intubation after induction of anaesthesia.

Vega<sup>19</sup> *et al* (2009) reported that nasally administered dexmedetomidine is the safe route to control hemodynamics and lower analgesic requirement during immediate post operative period in patients undergoing laproscopic cholecystectomy.

Bhattacharjee DP<sup>18</sup> *et al* (2010) reported that dexmedetomidine reduces elevation in mean arterial BP and heart rate during and after pneumoperitoneum in laproscopic cholecystectomy and thereby improving perioperative hemodynamic stability during surgery.

## 3. Methods

**Place:** Department of Anaesthesiology, Mallya Hospital, Bangalore, after obtaining institutional ethics committee approval in all consented patients. **Inclusion criteria:** ASA I/II patients, either sex, 18-60 yr undergoing laparoscopic cholecystectomy under GA, lasting upto 90 min **Exclusion criteria:** Cardiac disorders, CVA, Asthma/COPD, Renal or Hepatic insufficiency, anticipated difficult airway, pregnant, lactating or nursing mothers, patients on  $\beta$  blockers, clonidine, antipsychotics, etc, BMI > 30 kg/m<sup>2</sup> BSA, hypersensitivity to drugs. Randomisation to one of the two groups: **Group D** (n=30): Dexmedetomidine (1.0  $\mu\text{g}/\text{kg}$ ) in 10 ml NS, slowly IV over 2 min, 10 min prior to induction. **Group S** (n = 30): Saline, 10 ml of NS, slowly IV over 2 min, 10 min prior to induction. All patients were Premedicated Inj fentanyl 1mcg/kg i.v, Induced with Inj Thiopentone (3-5 mg/kg) till loss of eyelash reflex. After checking mask ventilation Muscle relaxation was achieved with Inj suxamethonium 1.5mg/kg for intubation. After that all were Maintained with: 40% O<sub>2</sub> in 60% N<sub>2</sub>O and Isoflurane with intermittent top-ups of Inj vecuronium i.v. Monitoring: SBP, DBP, Mean BP, HR, SpO<sub>2</sub>, ETCO<sub>2</sub> before and after premedication, at induction, intubation and 3 min after intubation, every 5 min till the end of pneumoperitoneum, and post-operatively. PONV and sedation were also noted post-op.

### Statistics

Sample technique:

Reference values considered from previous studies and details are given below :-

Mean pulse rate of Control group  $\bar{X}_1 = 83.6$

Mean pulse rate of study group  $\bar{X}_2 = 64.28$

Mean difference  $\bar{X}_1 - \bar{X}_2 = 19.32$

Standard deviation (SD) = 21.15

Power of study (1- $\beta$ ) = 0.90

According to previous study: Barkha Bindu, Surender Pasupuleti, Upender P Gowd, Venkateshwarlu Gorre,

Radha R Murthy , M Bhanu Laxmi. A double blind, randomized, controlled trial to study the effect of dexmedetomidine on haemodynamic and recovery responses during tracheal extubation. *J Anaesthesiol Clin Pharmacol* 2013 ; 29 :162-7<sup>24</sup>.

Sample size is 27 per group so I selected 30 per group

d) Data collection technique and tools.

All patients data collected as a measurement of hemodynamic parameters and recorded by standard multi parameter monitoring (Datex –ohmeda Cardiacap 5, Made in Finland) was attached having Heart Rate (HR), Non-Invasive Blood Pressure (NIBP), continuous surface ECG, Pulse Oximetry (SpO<sub>2</sub>), End Tidal Carbon Dioxide (ETCO<sub>2</sub>), was attached to all patients.

e) Data analysis and statistical test used:

**Null Hypothesis:** There is no significant difference in the mean value between two groups i.e.  $\mu_1 = \mu_2$

**Alternate Hypothesis:** There is a significant difference in the mean value between two groups i.e.  $\mu_1 \neq \mu_2$

**Level of Significance:**  $\alpha = 0.05$

**Statistical test used:** t- test/Mann-Whitney test (Based on data following normality)

**Decision Criterion:** We compare the P-Value with the level of significance. If  $P < 0.05$ , we reject the null hypothesis and accept the alternate hypothesis. If  $P \geq 0.05$ , we accept the null hypothesis

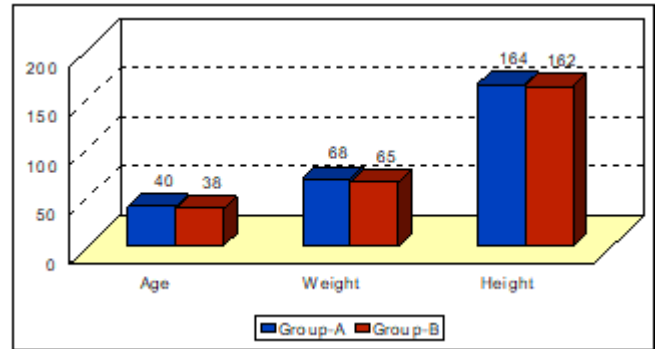
## 4. Results

Demographic profile was similar in both the groups.

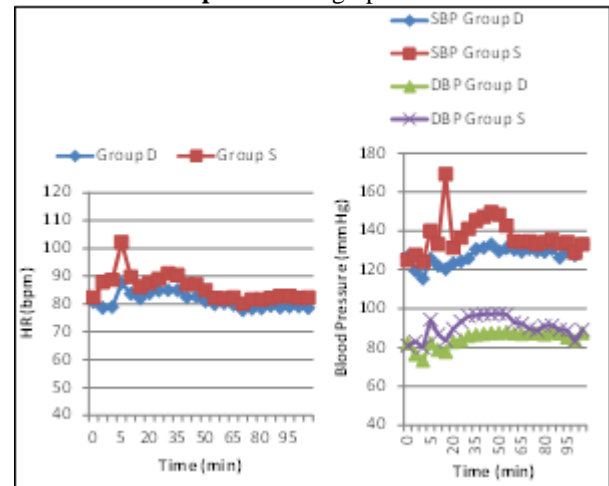
**Heart rate:** A fall in HR after the infusion of study drug was noted at T0 and T1. Increase in HR in both groups at T2, Tp more in group S than in group D.

**Blood pressure:** A fall in SBP and DBP at T2 in group D than group S. At Tp, there was a rise in SBP and DBP in both the

- 1) At T1, there was a statistically significant fall in DBP in both the groups (more in Group D,  $p = 0.002$ ). At T2, there was a statistically significant rise in DBP in Group S ( $p < 0.001$ ).
- 2) At T0, MAP decreased significantly in Group D compared to Group S ( $p = 0.001$ ). Both groups showed a statistically significant fall in MAP at T1 and T2 ( $p = 0.001$ ).
- 3) Perioperative complications like hypertension, hypotension, bradycardia and PONV was comparable in both groups ( $p > 0.05$ ).



Graph 1: Demographic Data



## 5. Discussion

- 1) At T0 and T1, a statistically significant fall in HR was seen, more in Group D than in Group S ( $p < 0.001$ ) (also seen by Aho *et al.*)<sup>20</sup>
- 2) The rise in SBP at T2 in Group S was greater than in Group D  $p = 0.004$  (similar to Ebert *et al.*)<sup>10</sup>.
- 3) The rise in SBP post pneumoperitoneum was significantly less in Group D than Group S ( $p = 0.041, 0.004, 0.007$ ) as seen by Dhrujotji P bhattarjee *et al.*<sup>18</sup>
- 4) The incidence of post operative nausea vomiting (PONV) in group D was 20% in comparison with 43.33% of group S and is not significant ( $p$  value  $> 0.05$ ). Also seen by Massad *et al.*<sup>23</sup>

## 6. Conclusion

IV dexmedetomidine (1  $\mu\text{g}/\text{kg}$ ) is effective in attenuating the haemodynamic response to laryngoscopy and intubation and provides good intra-operative and post operative haemodynamic stability both during and after pneumoperitoneum in laparoscopic cholecystectomies

## 7. Future Scope

We can now use different loading doses or lower loading doses for the same purpose in larger number of patients to minimise the side effects.

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