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## A comparative study to know the effects of dexmedetomidine on hemodynamics in patients undergoing laparoscopic surgeries under general anaesthesia

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### Abstract

**Introduction:** Dexmedetomidine is a highly selective  $\alpha_2$  agonist with sedative, sympatholytic and analgesic properties making it an ideal anesthetic adjuvant. The aim of this study was to evaluate the effect of dexmedetomidine infusion on hemodynamic response to critical incidences such as laryngoscopy, endotracheal intubation, creation of pneumoperitoneum and extubation in patients undergoing elective laparoscopic surgeries.

**Methods:** Sixty patients of American Society of Anesthesiologists (ASA) physical grades I and II undergoing elective laparoscopic surgeries were randomly allocated into two groups of 30 patients each. Group NS patients received normal saline, group D received loading dexmedetomidine infusion at 1 mcg/kg for 15 min before induction, followed by maintenance infusion at a rate of 0.3mcg/kg/hr, continued till the end of surgery. Heart rate and mean arterial pressure (MAP) were noted preoperative, after bolus drug administration, 1 min after induction, 1 min after intubation, and after pneumoperitoneum at 15 min interval till the end of pneumoperitoneum and postoperative period. SPSS 17.0 version software was used for statistical analysis.

**Results:** In group NS, significant hemodynamic stress response was seen following laryngoscopy, tracheal intubation, creation of pneumoperitoneum and extubation. In group D, the hemodynamic response at all times was attenuated significantly.

**Conclusion:** Dexmedetomidine effectively attenuates hemodynamic stress response during laparoscopic surgery and thus is an efficient pre-anaesthetic medication and intraoperative adjunct.

**Keywords:** Dexmedetomidine, Hemodynamics, Laparoscopic surgery

### Introduction

Nowadays laparoscopic surgery is the first choice for surgical management of various indications, especially with the well-trained laparoscopic surgeon. The benefits of minimal access techniques include less pain, early mobilization, shorter hospital stay, and better cosmetic results, which have further increased its applications<sup>[1, 2]</sup>. During general anaesthesia, laryngoscopy, tracheal intubation and extubation are the critical events provoking transient but marked sympatho-adrenal response manifesting by hypertension and tachycardia. In addition, in laparoscopic surgery, CO<sub>2</sub> is routinely used to create pneumoperitoneum, which causes increased plasma level of catecholamine and vasopressin.

Elevation of intra-abdominal pressure with raised diaphragm causes various adverse effects on the cardiovascular system such as decreased cardiac output, elevated arterial pressure, and increased systemic and pulmonary vascular resistance leading to hypertension and tachycardia<sup>[3, 4]</sup>. Severe increases in arterial pressure can be a risk factor in patients with pre-existing hypertension, ischaemic heart disease, or increased intracranial pressure. Opioids, alpha-2-adrenergic agonists, beta-blocking agents, or vasodilators are often used to avoid circulatory response to pneumo-peritoneum<sup>[5]</sup>.

Dexmedetomidine is an alpha-2-adrenergic agonist; it has properties of analgesia, sympatholytic effect, and sedation without respiratory depression. It decreases opioid requirements and stress response to surgery ensuring a stable hemodynamic state. Its distribution half-life is around six min, so it can be used to attenuate the stress response to laryngoscopy<sup>[8-10]</sup>. The aim of this study was to evaluate the effect of dexmedetomidine on hemodynamic response to critical incidences such as laryngoscopy, endotracheal chickenpox

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creation of pneumoperitoneum and extubation in patients undergoing laparoscopic surgeries.

### Materials and Methods

After obtaining approval from the Institutional Ethics Committee and written informed consent from the patients, 60 ASA grade I and II patients, aged 18-45 years of either sex, undergoing elective laparoscopic surgeries were randomly assigned to two different groups, 30 each using a computer-generated random table.

Group NS received saline infusion during procedure, group D received infusion of dexmedetomidine 0.3 µg/kg/hr. Patients with uncontrolled hypertension, morbid obesity, allergic to α<sub>2</sub> adrenergic agonist or antagonist, and severe hepatic, renal, endocrine and cardiac dysfunction and pregnant or breast-feeding patients were excluded from the study. Infusion was prepared separately for each group by a separate person.

To prepare the infusion, dexmedetomidine 1 mL containing 100 µg of the drug was withdrawn in a 10-mL syringe and was diluted up to 10 mL with normal saline resulting in the final concentration of 10 mcg/mL. Dexmedetomidine or normal saline infusion was given through a syringe infusion pump. Targeted infusion rate was delivered, depending on the weight and allotted group of the patient. All the patients underwent thorough pre-anesthetic evaluation on the day prior to surgery. Basic laboratory investigations were conducted including hemogram, urine analysis, chest X-ray, electrocardiogram, blood sugar, serum creatinine, blood urea, serum electrolytes and coagulation profile. Patients were reassured to alleviate their anxiety.

All the patients were kept fasting overnight. On arrival at the operation theater, patient's pulse oximeter, noninvasive blood pressure monitor and three lead ECG monitoring were done. Intravenous access was secured with 18 G cannula. All patients received inj. *Glycopyrrolate* 0.2 mg intravenously, inj. *Ondansetron* 4 mg intravenously and inj. *Midazolam* 1 mg. Group NS patients received normal saline, group D patients received loading dexmedetomidine infusion at 1 mcg/kg for 15 min before induction, followed by maintenance infusion at a rate of 0.3 mcg/kg/hr continued till the end of surgery.

Patients were induced after 15 min of infusion of study drug with *Fentanyl* 1 mcg/kg intravenously and *Propofol* 2 mg/kg, given 20 mg every 5 sec. Endotracheal intubation was facilitated by muscle relaxant *Succinylcholine* 1.5 mg/kg. Anesthesia was maintained with O<sub>2</sub> in N<sub>2</sub>O (50:50), intermittent bolus dose of fentanyl citrate 0.5 µg/kg and vecuronium 0.02 mg/kg. CO<sub>2</sub> insufflation into the peritoneal cavity (at a rate of 2 L/min) was done to create pneumoperitoneum. Intra-abdominal pressure was maintained at 14 mmHg throughout the laparoscopic procedure. The patients were mechanically ventilated to keep ETCO<sub>2</sub> between 35 and 40 mmHg.

At the end of the operation, the infusion of study medication was stopped. Residual neuromuscular block was reversed by appropriate dose of *Neostigmine* and *Glycopyrrolate* and tracheal extubation was performed. Heart rate and mean arterial pressure were monitored preoperative, after bolus

drug administration, 1 min after induction, 1 min after intubation, and after pneumoperitoneum at 15 min interval till the end of pneumoperitoneum and postoperative period. Mean arterial pressure was maintained within ± 25% of baseline. Hypotension (MAP < 25% of baseline on two consecutive readings within 2-3 min) treated with fluid bolus and ephedrine 3 mg intravenous boluses. Infusion of study medication was discontinued if hypotension persisted for >2 min. Upon return of MAP to ± 25% of baseline, the study medication was resumed at 50% of initial infusion rate. Hypertension (MAP > 25% of baseline on two consecutive readings within 2-3min) and/or tachycardia (HR > 25% of baseline for >2min) treated with *Metoprolol* 1 mg intravenous boluses. Bradycardia (HR < 45 for more than 2 min) treated with *Atropine* 0.5 mg intravenous boluses. Results were presented as mean ± standard deviation. SPSS 17.0 version software was used for statistical analysis. Chi-square test was used for non-parametric data (age, sex, weight and duration of surgery). Heart rate and mean arterial pressure were compared within the group against baseline values using paired t-test. ANOVA test was used for three group comparisons of continuous variables. If ANOVA was found significant, Tuckey post-hoc test was used for comparing two groups. P value < 0.05 was considered significant and highly significant if < 0.001.

### Results

All the three groups under study were comparable to each other in reference to the baseline PR. In group NS, after starting the infusion there was no significant change in PR but increased highly significantly above preoperative value infusion level after intubation and extubation (p < 0.001) and significantly after pneumoperitoneum (P < 0.05). In group D, after starting the infusion, the PR decreased highly significantly below the preoperative value. No further significant changes were observed immediately after induction. After intubation and extubation, the PR increased significantly above the preoperative value in group D, though this increase was less compared to increase in group NS (P < 0.05). Unlike these changes in Dex 0.3 group, PR in Dex 0.6 group remained below preoperative value after intubation and extubation (P < 0.05 when compared with Dex 0.3). Pneumoperitoneum did not result in a significant effect in both the Dex groups.

**Table 1:** Changes in heart rate

	Group D	Group NS	P value
Preoperative	80.0± 6.0	78.5±8.5	P >0.05
Preinduction after bolus		94.5±11.5	P <0.05
Post intubation	82.0±9.0	93.0± 14.5	P <0.05
1minute after intubation	81±12.0	92.5±16.5	P <0.05
After pneumoperitonium	80.5±13.5	96.5±18.5	P <0.05
15minutes	85.5±10.0	102.5±18.0	P <0.05
30minutes	88.5±10.5	100.0±15.0	P <0.05
45 minutes	90.0±9.5	101.5±16.5	P <0.05
60minutes	95.5±10.0	102±16.0	P >0.05
End of pneumoperitonium	97.5±9.0	98.5±12.0	P >0.05
Post-operative			
1 hour	82.5±10.5	99.5±15.0	P <0.05

**Table 2:** Changes in mean arterial pressure

	<b>Group D</b>	<b>Group NS</b>	<b>P value</b>
Preoperative	104.5±14.5	104.0±14.0	P >0.05
Preinduction after bolus	88.5±13.5	94.5±11.5	P <0.05
Post intubation	82.0±9.0	93.0± 14.5	P <0.05
1minute after intubation	81±12.0	92.5±16.5	P <0.05
After pneumoperitonium	80.5±13.5	96.5±18.5	P <0.05
15minutes	85.5±10.0	102.5±18.0	P <0.05
30minutes	88.5±10.5	100.0±15.0	P <0.05
45 minutes	90.0±9.5	101.5±16.5	P <0.05
60minutes	95.5±10.0	102±16.0	P >0.05
End of pneumoperitoneum	97.5±9.0	98.5±12.0	P >0.05
Post-operative			
1 hour	82.5±10.5	99.5±15.0	P <0.05

## Discussion

Dexmedetomidine is a highly selective alpha 2 adrenergic agonist with sedative, anxiolytic, and analgesic, sympatholytic and antihypertensive effects [1]. Dex, alpha 2 adrenoreceptor agonist shows a biphasic, dose dependent, blood pressure effect. At low dose the dominant action is a reduction in sympathetic tone mediated by reduction of norepinephrine release at the neuroeffector junction and inhibition of neurotransmission in sympathetic nerves. The net effect of dex is a significant reduction in circulating catecholamines with a slight decrease in blood pressure and moderate reduction in heart rate.

When dex is administered as a continuous infusion, is associated with an expected and stable hemodynamic response. With continuous infusion for 24 hr, distribution half life of 6 min, elimination half life of 2 hrs, availability of antagonistic agent Atipamezole, makedex an ideal drug for continuous infusion in the ICU, operation theatre and other areas<sup>5</sup>. When labour epidural analgesia could not work, in such cases intravenous dexmedetomidine infusion with systemic opioids has been successfully used [6, 7].

At higher doses of dex produce hypertensive action caused by activation of alpha 2 adrenoreceptor located on vascular smooth muscle cells. Therefore rapid injection of dex is not advised. Dex produces analgesia effect by an action on alpha receptor within the locus ceruleus and the spinal cord. Dex is eight times more specific for alpha 2 receptors than clonidine (alpha2 alpha 1 ratio for dex is 1620:1 and that for clonidine is 220:1)<sup>8</sup> When combined with alfentanil. Dex enhances analgesia without causing further respiratory depression.

Few studies have reported use of Dexmedetomidine upto 7 days and case studies have reported use beyond 3 weeks, without any side effects. Low and high dose of Dexmedetomidine is reported to cause a 55% and 45% decrease in Isoflurane MAC respectively [4, 9].

In our study, we observed that group D(Dexmedetomidine + fentanyl) provided more hemo stability-interoperatively as compare to group NS ( NS + Fentanyl). In addition to that, Dexmedetomidine reduced the requirement of fentanyl. Similar findings studied by B. Tufango [10]. Author used intra operative Dexmedetomidine infusion (0.2 – 0.8µg/Kg/hr) which decrease fentanyl requirement. Research showed that Intraoperative Dex infusion is helpful in alleviation of post-operative shivering, nausea and vomiting in gynaec laparoscopic surgery. We found that Group D provided better pressure attenuation response during direct laryngoscopy and intubation as compare to group NS (Pvalue<0.05) FerdiMenda<sup>16</sup> *et al.*, hypothesized

that in fast track CABG, Fentanyl 5 µg/Kg and IV dex infusion started before endotracheal intubation provided attenuation response to intubation without hemodynamic compromise.

However, sixty minutes after pneumoperitoneum, there is no significant difference in either of Group. (P value>0.05) Its use is associated with a decrease in heart rate and blood pressure both in animals and humans<sup>22</sup>. After discontinuation of dex, rapid recovery was found in in Group D as compare to Group NS (Pvalue<0.05). Hassan *et al.* studied same findings in morbidly obese patients. <sup>12</sup> According to Staffan Wahlander, Dex reduces the rescue analgesia requirement in Post-operative thoracic patients along with low dose epidural bupivacaine (0.125%). <sup>23</sup> The activation of α2adrenoceptors, imidazoline-preferring receptors, or both in the ventrolateral medulla and especially in the solitarius nucleus tract by dexmedetomidine causes bradycardia. In our study, 4 patients had episode of bradycardia, treated with inj. Atropine 0.5 mg. similar findings have been made bycarollo DS and Lawrence CJ. The novel therapeutic uses of this a2-AR agonist can be put safely into practice after thorough evaluation by Randomized Controlled Trials.

## Conclusion

The present study concluded that dexmedetomidine infusion in dose of 0.3µg/kg/h, after the loading dose of dexmedetomidine (1µg/kg), appeared to be significantly effective for attenuating the hemodynamic changes during laryngoscopy, tracheal intubation and pneumoperitoneum during laparoscopic surgeries.

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