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Effect of dexmedetomidine on haemodynamic parameters in patients undergoing laparoscopic surgeries

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Abstract
Background: Pnuemoperitoneum created during laparoscopic surgeries cause adverse haemodynamic changes. Many drugs are used to blunt these effects. Dexmeditomidine is a highly selective alpha2 agonist, causes sympatholysis, analgesia and also has cardiovascular stabilizing property. Hence the present study is an attempt to study the effects of dexmeditomidine in attenuating these adverse haemodynamic effects.
Methodology: A total of 60 patients were divided into two groups. Group D patients recieved dexmeditomidine at a rate of 0.2µg/kg/hour or 0.04ml/kg/hr and Group S patients recieved 0.9% Normal Saline at the same rate. Infusion was started 5 mins before induction. Heart rate, blood pressure, mean arterial pressure were monitored.
Result: In group D haemodynamic stress response was significantly attenuated when compared to group S. Results were statistically significant.
Conclusion: Dexmedetomidine, a highly selective alpha-2 agonist, when infused at a low dose of 0.2µg/kg/hour has stable hemodynamics during laparoscopic surgery.

Keywords: Haemodynamics, laparoscopic surgery, pnuemoperitoneum, dexmeditomidine

1. Introduction
Phillipe Mouret, in 1987, introduced laparoscopic cholecystectomy as a minimally invasive alternative to open surgeries [1-3]. Since then laparoscopic surgeries are being performed widely, mainly because the less trauma to tissues is associated with shorter healing time compared to open surgery. Nevertheless, this type of surgery is not immune to complications like deep venous thrombosis [4, 5] abdominal wall hematoma (2.0%), umbilical hernia [Jiang X]. Its advantages include reduced pain due to smaller incisions, less haemorrhage and shorter recovery time. Though it offers many advantages, it also causes considerable stress hormone responses (cortisol, epinephrine, norepiniephrine), especially when pneumoperitoneum is concurrently used [6], but less than the open surgeries [7]. Pneumoperitoneum is produced by using carbon dioxide during laparoscopic surgery. Both pneumoperitoneum and carbon dioxide cause adverse cardiovascular effects in terms of elevated arterial pressure, increased systemic and pulmonary vascular resistance and reduced cardiac output by increasing plasma levels of norepinephrine, epinephrine [8] in addition to the reverse Trendelenburg position used for surgeries.
Many drugs have been used to counteract these effects during laparoscopic surgeries. In a randomized trial, investigators found clonidine to be better than magnesium sulphate [9] and Pregabalin [10], in blunting the hemodynamic responses to laparoscopic procedures. Other drugs like nicardipine [11] and nitroglycerin [12] were also tried to abate cardiovascular responses to pneumoperitonium.
Alpha-2 agonists are currently used as sedatives and as well as adjuvants to anaesthesia. Dexmedetomidine has a unique property of reducing sympathetic outflow associated with laparoscopic procedures with added sedative property and an opioid sparing action. It is more selective and safer than its predecessor clonidine [13]**.** These properties of dexmedetomidine help the anaesthetist to reduce the use anti-hypertensive drugs to avoid possible drug interactions due to polypharmacy.
Therefore this study was designed to study the effects of Dexmedetomidine on hemodynamic parameters during laparoscopic surgeries.

2. Materials and Method

The Institutional ethics committee approval was taken before starting the study. Written informed consent was obtained from the patients before starting the study. A total of sixty patients were included in this study and they were allocated to two groups of thirty patients each for this prospective randomized controlled study. The randomization was done by computer generated randomization charts.

2.1 Inclusion Criteria

- Patients willing to consent
- Age of patients: 18-60 years; Either gender; Weight: 50 to 70 kg
- Patients under American Society of Anaesthesiologist (ASA) Physical status grade I & II
- Undergoing laparoscopic surgery i.e. Laparoscopic Cholecystectomy (LC), Laparoscopic Appendicectomy (LA)

2.2 Exclusion Criteria

- Patients who are not willing to consent
- Extremes of age
- Uncontrolled systemic diseases
- Allergy to drug
- History of alcohol or drug abuse

All patients underwent a detailed pre anaesthetic check-up before surgery and all the routine and specific investigations were noted. The patients were electively kept nil per oral for 6 hours before surgery and prior to operation patients were explained about the procedure. After the patient was shifted to the theatre, standard monitors like ECG, NIBP, and pulse oximeter were applied and patient's baseline parameters like pulse, blood pressure, respiratory rate, oxygen saturation were recorded. Two intravenous lines were secured in all the patients and intravenous fluid was started.

2.3 Technique of Anaesthesia

The patients were divided into two groups.

Group D: Inj. Dexmedetomidine 0.2μg/kg/hour

Group S: 0.9% Normal Saline at the same rate

Dexmedetomidine 200μg (2ml) was added to 0.9% normal saline (38ml) to make a total volume of 40ml (resulting concentration 5μg/ml) and was used at a rate of 0.04ml/kg/hr. Infusion of study drug or saline was started 5 minutes before induction.

All patients were pre-oxygenated with 100% oxygen for 5 min using Bain's circuit.

2.3.1 Premedication: Inj. Ondansetron 0.15 mg/kg
Inj. Glycopyrrolate 0.004 mg/kg
Inj. Fentanyl 2 μg/kg

2.3.2 Induction and intubation: All patients were induced 5 minutes after starting the infusion of the study drug. Patients were induced using Inj. Propofol 2.5 mg/kg. Endotracheal intubation was facilitated using Inj. Succinylcholine 2 mg/kg and intubation done using an appropriate tube. Positive pressure ventilation was started. $EtCO_2$ monitoring was started.

2.3.3 Maintenance: Anaesthesia was maintained using oxygen, nitrous oxide, inhalational agent (Isoflurane) and intermittent doses of Inj. Vecuronium.

2.3.4 Monitoring: Pulse rate, blood pressure, oxygen saturation and $EtCO_2$ values were noted after starting infusion of drug, after induction and intubation, and at regular intervals throughout the surgery.

Carbon dioxide insufflation was done to create pneumoperitoneum. The intra-abdominal pressure was maintained between 14 - 16 mmHg throughout the surgery. Intraoperative hypertension was managed using Inj. Nitroglycerine and hypotension was managed using intravenous fluids and Inj. Ephedrine. At the end of pneumoperitoneum, infusion of study drug was stopped and port site instillation was done with 40 ml of Inj. Bupivacaine (0.25%).

2.3.5 Reversal and Extubation: All patients were reversed using Inj. Glycopyrrolate 0.008 mg/kg and Inj. Neostigmine 0.05 mg/kg. After thorough oral and endotracheal suction patients were extubated after they satisfied the criteria for extubation.

All patients were then shifted to the post-operative room and observed for 3 hours. Any post-operative complications were noted and treated accordingly.

3. Statistical Analsis

Data was entered and analyzed in Microsoft Excel 2010 sheet. Descriptive statistics such as mean, median, standard deviation were employed to summarize the quantitative data such as age, BMI, Mean Arterial Pressure (MAP) etc. Independent sample't' test was used for comparison of various parameters between the two groups. A statistical significance of 0.05 was considered.

4. Results

We studied 60 patients undergoing LC and LA surgery. After studying 60 cases, the observations and results were summarized in tabulated form. The patients were divided into two groups with 30 patients in each group (n=30).

Table 1: Demographic data

Variables	Group D	Group S
Age (in years)* Mean ±SD	45.0333±10.12	37.8000±11.65
Gender Ratio (M:F)*	7:23	6:24
Weight (Kg)* Mean ±SD	53.3±5.14	51.9±4.31

Table 1 shows the distribution of patients according age, gender and weight; *p>0.05

In Group D, 23 (76%) and 07 (24%) patients underwent LC and LA respectively. Similarly in Group S, 18 (60%) and 12 (40%) patients underwent LC and LA respectively. The following were the observations from the study.

Table 2: Comparison of mean pulse rate at different time points with baseline value (Mean±SD)

	Group D	Group S
Baseline	93.47±15.32	89.13±11.75
After Infusion	92.30±12.42	91.2±12.43
After Induction	96.83±10.18	94.83±12.76
After Intubation	95.6±9.23	99.80±11.42*
After Pneumoperitoneum		
15 min	88.53±10.45	96.13±12.05*
30 min	86.17±9.98*	96.47±9.53*
45 min	85.72±11.37*	95.12±10.53*
60 min	83.36±8.48*	90.15±8.83

*$p<0.05$

Table 3: Comparison of mean Systolic Blood Pressure (SBP) at different time points with baseline value (Mean ± SD)

	GROUP D	GROUP S
Baseline	132.57±12.04	131.33±14.34
After Infusion	126.5±12.04*	135.20±12.11
After Induction	121.47±14.69*	137.53±10.67
After Intubation	123.4±14.58*	143.97±9.27*
After Pneumoperitoneum		
15 min	121.60±14.11*	143.27±15.01*
30 min	121.73±13.61*	143.57±15.79*
45 min	122.64±11.69*	139.04±13.55*
60 min	119.89±12.06*	139.05±16.75*

*$p<0.05$; This table shows the changes in mean systolic blood pressure at various time periods with respect to the mean baseline value in both the groups.

Table 4: Comparison of mean Diastolic Blood Pressure (DBP) at different time points with baseline values (Mean ± SD)

	Group D	Group S
Baseline	78.70±10.48	78.93±8.52
After Infusion	81.30±8.08	83.70±7.52*
After Induction	79.13±11.69	90.67±9.01*
After Intubation	78.73±9.52	90.90±5.09*
After Pneumoperitonium		
15 min	80.47±13.20	88.87±6.82*
30 min	80.67±11.89	90.17±6.06*
45 min	82.00±9.59	86.28±5.55*
60 min	81.00±9.35	88.05±6.77*

*$p<0.05$

This table shows the changes in mean diastolic blood pressure at various time periods with respect to the mean baseline value in both the groups.

Table 5: Comparison of Mean Arterial Pressure (MAP) at different time points with baseline values (Mean ± SD)

	GROUP D	GROUP S
Baseline	98.50±10.97	97.60±10.80
After Infusion	96.90±8.76	101.67±8.99*
After Induction	94.07±12.95	107.83±7.76*
After Intubation	94.57±11.66	110.17±6.24*
15 min	94.43±14.08	108.63±9.44*
30 min	96.36±12.78	109.57±9.18*
45 min	97.16±10.40	105.76±6.38*
60 min	96.05±9.80	106.65±9.88*

*$p<0.05$

5. Discussion

Laparoscopic surgeries have become a common practice in the modern era and are now being preferred over open surgeries in many instances. But they are not without risks. Though there is no difference between laparoscopic surgeries and open surgeries in terms of complications and operative time [14], the former offers various advantages like less pain due to smaller incisions, less hemorrhage and a shorter recovery time. Peritoneal insufflation induces alterations of hemodynamics, characterized by decrease in cardiac output, elevations of arterial pressure, and increase in systemic and pulmonary vascular resistances [15-17]. Hemodynamic changes are accentuated in high-risk cardiac patients. The α_2 agonist, Dexmedetomidine, is known to decrease central sympathetic outflow and modifies intraoperative cardiovascular and endocrine responses favorably to laryngoscopy and surgical stimuli. The reduction in tachycardia, hypertension, sympathetic activity and consequently total body oxygen consumption may be of benefit in patients at risk of developing inadequate cardiac output or myocardial ischemia.

5.1 Pulse Rate

The findings in our study were similar to one study [18], where they found that Dexmedetomidine infusion attenuated the hemodynamic changes during laparoscopic surgeries.
Another study [19] investigated the effects of two different doses of Dexmedetomidine (0.3 and 0.6µg/kg) premedication administered intravenously as a single bolus dose. They found that the tachycardia and blood pressure in the higher dose group was significantly less than that of lower dose group, suggesting a bi-phasic response. The bi-phasic response was evident in another study(20). During our study the response to laryngoscopy and intubation presented no hemodynamic in-stability.
The haemodynamic parameters were comparable to our results, when short laparoscopic diagnostic procedures in gynaecology were carried out with premedication of intramuscular Dexmedetomidine at different doses (0.6, 1.2, 2.4µg/kg) [21]. Though the authors reported a frequent sinus bradycardia at higher doses of Dexmedetomidine premedication, we did not encounter any such adverse drug reaction in our study, since we used a less dose compared to above study. Thus future studies with evaluating different doses can help set a range of dose under which excessive deterioration of hemodynamic parameters can be curtailed.

5.2 Systolic Blood Pressure

We anticipated a rise in SBP during laryngoscopy, intubation and as a result of pneumoperitonium. The rise in SBP was promptly blunted by premedication with dexmedetomidine, which was statistically significant. Reduction in SBP was also seen during intra-operative period. Though decrease in SBP is similar to that seen during laryngoscopy and intubation but reduction was more with esmolol and fentanyl [22]. Nevertheless the SBP provided by dexmedetomedine is more desirable and avoids hypotension.

5.3 Mean Arterial Pressure

The results from our study showed a sympatholytic response of decrease in MAP at the dose mentioned above. A 13% reduction of MAP from the baseline was observed by Ebert *et al.* [20] at lower plasma concentrations of dexmedetomidine but a paradoxical rise of about 12% from the baseline was reported at higher concentrations (>1.9 nanograms/l). This indicates the need for cautious maintenance of dexmedetomidine within its therapeutic window to avoid counterproductive hypertension, especially due to pneumoperitonium, which produces a cardiovascular stress. The meta-analysis shows similar results in terms of decreased hemodynamic parameters with dexmedetomidine [23].

6. Conclusion

Dexmedetomidine, a relatively newer highly selective alpha-2 agonist, when infused at a dose of 0.2µg/kg/hour has stable hemodynamics during laparoscopic surgery.

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