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Evaluating the Effect of Intravenous Clonidine and Dexmedetomidine on Haemodynamic Stress Response during Pneumoperitoneum in Laparoscopic Abdominal Surgeries

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Original Research Article

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Abstract: Laparoscopic surgeries are superior over open surgical procedures and former has now become the gold standard for cholecystectomy. Though laparoscopic procedures are more beneficial and have less complications rate but they are not free from all the complications. Pneumoperitoneum created during laparoscopic procedure by insufflattion of gases and its duration leads to blood pressure and heart rate changes. Many pharmacological agents are used to subside effect of pneumoperitoneum. Clonidine and dexmedetomidine are selective α- 2 agonists used for the same purpose. This randomized control study was conducted on 60 patients of ASA grade 1 and 2 after taking ethics committee approval. Group CL (n=30) clonidine is infused during the surgery and in group D (n=30) dexmedetomidine is infused during the surgery is infused. Diastolic and systolic blood pressure, mean arterial blood pressure and heart rate were measured throughout the procedure till 30 minutes after the procedure. Sedation score was also measured after the surgery. Effect of intubation and laryngoscopy induced stress response, creation of pneumoperitoneum, reversal of pneumoperitoneum and extubation was seen over heart rate, SBP, DBP and MAP in both the groups but was significantly less in the dexmedetomidine group(D) compared to the clonidine(CL) group showing better stability of the hemodynamic vitals in the patients given dexmedetomidine intraoperatively ($P<0.05$). Dexmedetomidine and clonidine both suppresses pneumoperitoneum induced hemodynamic instabilities in patients undergoing laparoscopic cholecystectomy under general anaesthesia but dexmedetomidine is better than clonidine.
Keywords: Blood pressure, Clonidine, Dexmedetomidine, General anaesthesia, Heart rate, Sedation.

INTRODUCTION

Laparoscopic surgeries are gold standard for gall bladder and other abdominal procedures as it more benefits and less complications when compared with the open surgical procedure [1-3]. But laparoscopic abdominal procedures are also not free from disadvantages as occur during the duration of pneumoperitoneum (PNP) [4, 5] made by gases mainly carbon dioxide (mainly $CO2$) insufflations and patient positioning [6, 7].

Pneumoperitoneum leads to decreased cardiac output, increased arterial pressures, increased systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) [8, 9] and it also decreases FRC [10] and thoracopulmonary compliance [11].

For maintaining the hemodynamic stability during period of pneumoperitoneum, various medicinal methods have been adopted since time like, beta blockers [12], Ca channel blocker, vasodilators [13], lidocaine [14], adrenoreceptor blockers [15], opioids [16], pregabalin [17], magnesium sulfate [18], and remifentanil [19].

Clonidine and dexmedetomidine are selective and potent specific α- 2 agonists [20]. α-2 agonist produces diverse responses including analgesia, anxiolysis, sedation and sympatholysis [21].

They attenuates the haemodynamic response to tracheal intubation, decrease plasma catecholamine and norepineprine concentration and thus maintain blood pressure and heart rate [22] and also decreases perioperative requirements of inhaled anaesthetics during anaesthesia [23]. Dexmedetomidine is seven to ten times more selective for α -2 receptors compared to clonidine and has shorter duration of action (6-10 hr Vs 2-3 hr) [24].

Hence this study is designed to compare the beneficial effect of the two α- 2 agonists namely clonidine and dexmedetomidine in maintaining the perioperative haemodynamic parameters such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR) during pneumoperitoneum in laparoscopic abdominal surgeries and to identify a better drug in attenuating these haemodynamic responses.

MATERIALS & METHODS

After obtaining approval from the ethics committee and well written informed consent from the patients, study was carried out on 90 patients of ASA grade I and II, aged 20-50 years, undergoing laparoscopic cholecystectomy lasting 1-3 hours requiring general anaesthesia with endotracheal intubation at J.A Group of Hospitals of G.R. Medical College, Gwalior (M.P), India. Patients were allocated randomly using envelope technique in two groups of 30 each. In group CL, intravenous clonidine was given and in group D, intravenous dexmedetomidine was given.

Exclusion Criteria were**:** ASA grade III and above, BMI >30, patients undergoing Laparoscopic to open surgery conversion intraoperatively, pneumoperitoneum duration >90 minutes, known history of allergy or sensitivity or any other reaction to study drug, patients with cardiopulmonary and respiratory disorders, patients with hypertension on treatment with beta-Blocker, Methyl-dopa, MAO inhibitors, tricyclic antidepressant, patients with psychiatric illness, patients with renal and hepatic dysfunction, pregnant and lactating females.

Consent

Details of procedure were explained to all the patients during preanaesthetic assessment and an informed and written consent was obtained.

Patients' grouping

90 patients of ASA grade I & II of either sex scheduled for abdominal surgeries under general anaesthesia were divided into 2 groups (n=30 each) randomly using envelope technique as below:

Group CL (n=30)	Clonidine 1.5µg/kg in 50ml normal saline over a period of 10 minutes after induction and before PNP, followed by a continuous infusion at the rate of 2 µg/kg/hr.
Group D (n=30)	Dexmedetomidine 1µg/kg in 50ml normal saline over a period of 10 minutes after induction and before PNP, followed by a continuous infusion at the rate of 0.2 µg/kg/hr.

Preparation of the patient

Upon arrival of the patient in the operation room, intravenous access with 18G cannula was established and 500 mL of crystalloid infusion was started. All the baseline vital parameters (HR, SBP, DBP, MAP), electrocardiography using three lead ECG were monitored. Oxygen saturation (SPO2) was monitored by using pulse oximeter. End tidal Carbon dioxide was monitored intraoperatively and kept between 25 and 30 mmHg.

Anaesthesia procedure and recording

Drugs were administered by a person who was not involved in the study to avoid bias. Patients were preoxygenated with 100% oxygen at appropriate flow for 3 minutes by facemask. After premedication with i.v. Inj Pentazocine 0.5mg/kg, general anaesthesia was induced with i.v. Inj Thiopentone Sodium 5 mg/kg body weight. Endotracheal intubation was facilitated with i.v. Inj. Succinylcholine 1.5 mg/kg body weight and IPPV was done for 60 seconds with 100% oxygen.

Laryngoscopy was done with laryngoscope having Macintosh blade and tracheal intubation done with appropriate size of cuffed endotracheal tube. Cuff was inflated and bilateral equal air entry was checked and then tube was fixed.

General anaesthesia was maintained with nitrous oxide & oxygen (67:33) and Isoflurane (0.5-1%) with Bain's anaesthetic circuit. Loading and intermittent dosage of non-depolarizing muscle relaxant, IV Atracurium Besylate 0.5mg/kg body weight initially followed by increment doses at 0.1mg/kg was used to maintain general anaesthesia under controlled ventilation throughout the surgical procedure. After intubation, the infusion of Clonidine (1.5µg/kg) in 50 mL normal saline or Dexmedetomidine (1 µg/kg) in 50 mL normal saline was started 10 min before induction of pneumoperitoneum. This was followed by a continuous infusion clonidine at a rate of 2 µg/kg/hr or dexmedetomidine at the rate of 0.2 µg/kg/hr according to the study group.

During study period haemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded at 0 minute (B), D_0, D_{10}, BPN, APN, APN_{10}, APN_{20}, APN_{30}, APN_{40}, APN_{50}, APN_{60}, APN_{90},RPN, AR, AR_{15}, AR_{30}, intervals. PNP - Pneumoperitoneum, B- Basal value (0 minute), D_0- Before study drug,

D_{10} - After study drug, BPN-Before pneumoperitoneum, APN- After pneumoperitoneum, RPN- Release of pneumoperitoneum, AR- After reversal.

All the study drugs were stopped once surgical procedure was over and pneumoperitoneum was released.

After surgery, patients were reversed with Inj. Glycopyrrolate 0.005mg/kg and Neostigmine 0.08mg /kg intravenously. After extubation patients were observed for recovery time defined as time to vocalize after extubation.

Side effects and complications

Patients were closely observed for bradycardia / tachycardia (± 20% of basal value), hypotension / hypertension (± 20% of basal value), bradyarrythmia & desaturation (<85%) during intra and postoperative period. During postoperative period along with above, nausea, vomiting, respiratory depression, sedation and shivering were also recorded if occurred. Any complication if occurred was treated with appropriate medications.

Statistical Analysis

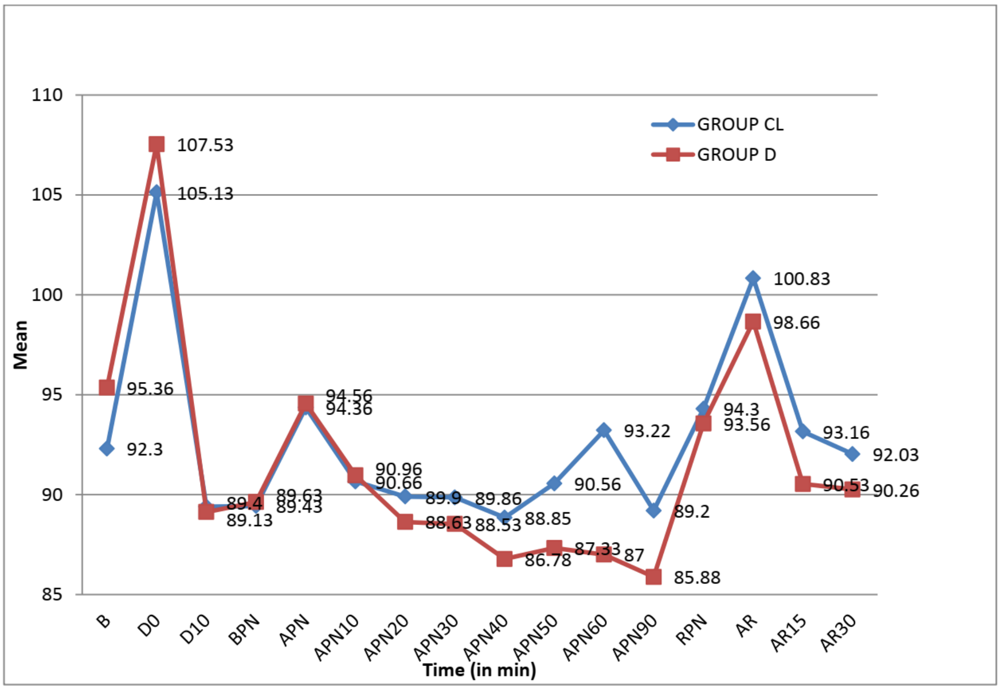
The observations were recorded and subjected to statistical analysis using students "t" test by statistics calculator SPSS 17. The observations recorded in all the groups were tabulated and statistical analysis carried out by using appropriate statistical software, SPSS 17. Student 't'-test for inter group comparison was used. p-value >0.05 was taken to be statistically insignificant & p-value <0.05 was taken statistically significant and p-value <0.01 taken to be statistically highly significant.

RESULTS

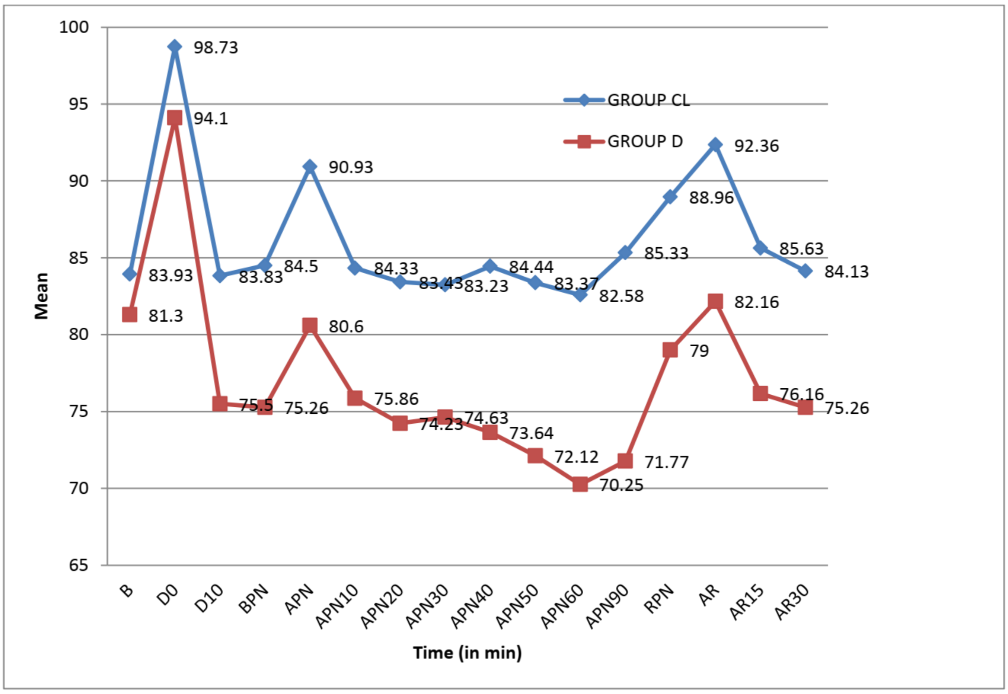
Data obtained from the patients involved in the study were analyzed. The mean age, weight, sex, type of surgery, duration of pneumoperitoneum, duration of anaesthesia, type of surgery and Ramsay sedation score after extubation were comparable in two study groups as shown in table. Preoperative heart rate, systolic, diastolic and mean blood pressure and blood sugar level were comparable in all the two groups.

Table: Showing Demographic Variables of Two Groups

Demographic data	Group CL	Group D
Age	35.16±8.49	36.53±7.85
Weight (kg)	53±6.45	50.90±5.28
Sex (female)	86.67%	97.67%
Duration of pneumoperitoneum (min)	58.4±17.78	62.73±17.80
Duration of anaesthesia (min)	85±9.73	91.16±18.36
Type of surgery Laparoscopic cholecystectomy	93.33	100%
Laparascopic hernia	6.67	-
Ramsay sedation score after extubation (mean+SD)	1.73±0.69	2.20±0.96



Graph-1-Statistical Analysis of Mean (± SD) Mean Arterial Pressure (mmHg)



Graph-2: Statistical Analysis of Mean Pulse Rate (bpm)

DISCUSSION

Laparoscopic procedure uses insuflation of carbon dioxide(pneumoperitoneum) that causes significant haemodynamic variation [8, 9] like adverse cardiovascular and pulmonaryeffects like decreased cardiac output, increased arterial pressures, increased systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) [8, 9] and it also decreases FRC [10] and thoracopulmonary compliance [11].

For maintaining the hemodynamic stability during period of pneumoperitoneum, various medicinal methods have been adopted since time like, beta blockers [12], Ca channel blocker, vasodilators [13], lidocaine [14], adrenoreceptor blockers [15], opioids [16], pregabalin [17], magnesium sulfate [18], remifentanil [19].

Clonidine and dexmedetomidine are selective and potent specific α- 2 agonists [25]. Nowadays, α-2 agonist due to their beneficial effects like sedation, analgesia, attenuation of stress response and reduction of inhalational agents requirement has been studied to attenuate laparoscopy related adverse responses. Clonidine and dexmedetomidine are the two currently used drugs with dexmedetomidine having higher selectivity for alpha 2 receptors and a shorter half life [26]. Both these drugs significantly reduce the release of catecholamines, predominantly having an effect on systemic vascular resistance and improve intra and postoperative haemodynamic stability by stabilizing the changes in heart rate, arterial pressure and cardiac output.

The present study was conducted to evaluate and compare the effects and efficacies of clonidine and dexmedetomidine on HR, SBP, DBP and MAP during pneumoperitoneum. This study was also aimed to observe any untoward effects of study drugs and effect on sedation after extubation.

Selected groups were comparable for the demographic variables like age and weight parameters, type of surgery, sex, duration of pneumopeitoneum and duration of anaesthesia with P> 0.05. Effect of intubation and laryngoscopy induced stress response, creation of pneumoperitoneum, reversal of pneumoperitoneum and extubation was seen over heart rate, SBP, DBP and MAP in both the groups but was significantly less in the dexmedetomidine (D) group compared to the clonidine (CL) group showing better stability of the hemodynamic vitals in the patients given dexmedetomidine intraoperatively.

Hazra R *et al.*, [27] conducted a study in which they administered iv clonidine 1µg/kg, iv dexmedetomidine 1µg/kg and normal saline in three different groups, 15 minutes prior to induction. They observed significant reduction ($p<0.05$) in heart rate after intubation, 10, 20 and 30 minutes after pneumoperitoneum, after release PNP and after extubation in dexmedetomidine group compared to clonidine and control group. These findings are very similar to our study which stated that dexmedetomidine provides better heart rate control as compared to clonidine and control group in laparoscopic surgeries.

Kumar S *et al.*, [28] conducted a study with 2µg/kg iv clonidine and 1 µg/kg iv dexmedetomidine, over 10 minutes before induction. They observed that SBP stablising effect of dexmedetomidine lasted till extubation, while clonidine was less effective in preventing haemodynamic response to extubation. Similarly DBP and MAP increased towards the end of procedure in clonidine group .In our study no such finding were observed. Significant changes in SBP observed at 40 and 50 minutes after pneumoperitoneum and MAP at 60 minutes after pneumoperitoneum, it may occur incidentally.

Lawrence CJ *et al.*, [29], Bhattacharjee DP *et al.*, [30] and Gupta K *et al*., [31] supported the fact that use of dexmedetomidine in lower dose (1µg/kg) provides better arterial pressure control during pneumoperitoneum in laparoscopic surgeries.

Godki PK *et al.,* [32] found dexmedetomidine infusion can be continued safely through extubation and no episodes of respiratory depression noted in postoperative period.

CONCLUSION

Following conclusions are drawn from the present study-

- Creation of pneumoperitoneum in laparoscopic abdominal surgeries produces significant increase of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP).
- Both intravenous clonidine and intravenous dexmedetomidine caused decrease in all haemodynamic parameters (HR, SBP, DBP and MAP) during pneumoperitoneum in laparoscopic abdominal surgeries.
- Dexmedetomidine and clonidine are equally effective in controlling blood pressure during pneumoperitoneum in laparoscopic surgeries but heart rate is better controlled by dexmedetomidine.
- Dexmedetomidine produces higher sedation as compared to clonidine but no respiratory complications.
- No untoward effects and or complications were observed with both study drugs.

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