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Comparison of Dexmedetomidine and Clonidine for Attenuation of Hemodynamic Responses during Laparoscopic Hysterectomy.

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ABSTRACT

To compare hemodynamic variations following premedication with or clonidine during laparoscopic hysterectomy. This study is a prospective cross-sectional randomized double blinded controlled trial was conducted for a period of three months in sree balaji medical college, chennai. After taking institutional ethical clearance and consent from patients, 80 patients of ASA Grade I and II undergoing elective laparoscopic hysterectomy were included in the study. Patients were allocated into two groups. Group A received dexmedetomidine and Group B received clonidine .Baseline clinical parameters were recorded. Group A patients loading dose of dexmedetomidine infusion 1 µg/kg was started and continued for 15 minutes. In Group B clonidine in 2µg/kg infused over 15 min. before induction. Following induction with intravenous propofol, endotracheal intubation was facilitated by vecuronium. Anaesthesia was maintained by nitrous oxide and oxygen and sevoflurane. Muscle relaxation was achieved by intermittent bolus doses of vecuronium. The patients were mechanically ventilated to keep EtCO2 between 35 and 40 mm Hg. Residual neuromuscular block was reversed by an appropriate dose of neostigmine and glycopyrrolate. All patients were shifted to HDU post-op. Sedation Score was documented. In comparison to group B, attenuation of heart rate, Systolic blood pressure, diastolic blood pressures were significantly more in group A. but sedation was slightly more in group A patients. In an attempt to attenuate both the effects of laryngoscopy and insufflations with carbon dioxide in laparoscopic surgery infusions of dexmedetomidine and clonidine were run all through the procedures in the present study and it was found that use of both attenuated the hemodynamic responses. However dexmedetomidine being found to be more effective.

Keywords: Clonidine, dexmedetomidine, hemodynamic responses, laparoscopic hysterectomy.

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INTRODUCTION

Laparoscopic surgery presents several challenges for the anaesthesiologist. The patient position required and the establishment of pneumoperitoneum has significant effects on the hemodynamic. Maximal hemodynamic changes are observed with the pneumoperitoneum and the patients in the Trendelenburg position [1,2]. The lithotomy position also leads to auto-transfusion by redistributing blood from vessels of the lower extremities into the central body compartment, in turn increase preload. Various cardiac abnormalities (Bradyarrhythmias, dysrhythmias, and asystole) can occur during insertion of laparoscopic ports or during insufflation of abdomen. Sudden stretching of the peritoneum can precipitate areflexive, and sometimes profound increase in vagal tone. Clonidine, a central sympatholytic drug have beneficial pharmacological properties which is dose dependent sedation, analgesia, anxiolysis and without relevant respiratory depression. It posses beneficial effects on hemodynamic changes during laryngoscopy and endotracheal intubation and reduces bleeding. It also attenuates stress responses to painful stimuli, improves the intraoperative hemodynamic stability, reduces the incidence of perioperative myocardial ischemic episodes in patients and decreases anaesthesia requirements during surgery [3,4]. Pre-medication with clonidine reduces the requirement for propofol, which may be a pharmacokinetic effect. Dexmedetomidine also belongs to the class of α2 agonist; it has well known sedation, analgesia and opioid sparing effect. It was approved in the USA in late 1999,gained remarkable attention for sedation and analgesia in ICU.Compared with clonidine, dexmedetomidine is about 16 times more specific for α 2 receptors. The present study was conducted, to compare hemodynamic changes in different phases of surgery during laparoscopic hysterectomy following use of dexmedetomidine or clonidine [5-7].

SUBJECTS AND METHODS

This prospective cross-sectional randomised double blind controlled trial was conducted in a time period of 3 months in a tertiary care hospital in Chennai sree balaji medical college after obtaining institutional ethical clearance and informed consent of patients.

Inclusion criteria

Hundred subjects in the age group of 45-60 years and of ASA Grade I and II undergoing elective laparoscopic, Hysterectomies were included in the study [8]. Patients were allocated into two groups using an online randomizer, Group A and B. Group A (n =40) received dexmedetomidine and Group B (n = 40) received clonidine [9,10].

Exclusion criteria

ASA ≥III, pregnant mothers, BMI ≥35,reported adverse reactions to any of the drugs included in the study, and chronic or acute intake of sedatives, analgesics, or any other drug affecting the metabolism of anaesthetics used, any chronic pain syndrome, history of seizures, medication use that affects cytochrome P450-3A4 or P450-1A2 metabolism (including smokers and tobacco addicts) [11]. Following proper history, physical assessment and review of laboratory investigations, the procedure for/complications of general anaesthesia was explained to the patients. All patients eligible for the study had the following information documented: Medication list, age, sex, height, weight, body mass index, serum urea, fasting sugar, serum creatinine, calculated creatinine clearance, Liver Function Tests, serum electrolytes, coagulation profile, ECG, Chest X-Ray, primary diagnosis, and scheduled procedure. Airway Assessment was done. Patients who were predicted to have difficult intubation were excluded.

Methods

On the day of surgery all basic clinical parameters were documented. Intravenous line was gained and for Group A patients, loading dose of dexmedetomidine infusion 1µg/kg was started and continued for 15 minutes. In group B clonidine 2µg/kg infused over 15 minutes before induction. Drugs were diluted to a by an investigator who do not know about the study. The anaesthetist in charge of the patient start the infusion and he is blinded to which group the patient belong. After proper pre-oxygenation patients were given 1 µg/kg of fentanyl citrate intravenously. Anaesthesia was induced with propofol, administered at a rate of 20 mg per 5

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seconds until patient goes for complete anesthesia,endotracheal intubation was facilitated by muscle relaxant vecuronium.Anaesthesia was maintained by nitrous oxide, oxygen (50% +50%) and sevoflurane. Signs of inadequate analgesia, defined as an increase of heart rate and MAP of more than 20% of baseline, were to be managed by a bolus dose of fentanyl 0.5µg/kg). Muscle relaxation was achieved by intermittent bolus doses of vecuronium. The patients were mechanically ventilated to keep EtCO2 between 35 and 40 mm Hg. Following parameters were recorded throughout the procedure: Continuous ECG (lead‑II) and Heart rate, SpO2, Non invasive arterial blood pressure (SBP, DBP), measurement of EtCO2. The target BIS range was 40‑60 for surgical anaesthesia. All surgical procedures were one to one to one and half hour long. Readings were taken during laryngoscopy and tracheal Intubation and 1 min, 5 mins, 10 mins, 30 mins, 60 mins, and 90 mins, following laryngoscopy and tracheal intubation. At the end of the surgical procedure, residual neuromuscular block was reversed by an appropriate dose of neostigmine and glycopyrrolate. All patients were shifted to high dependency unit. Post-op O2 for 2 hours was administered to all patients. Sedation Score was assessed. Postoperative sedation, Heart rate, SpO2**,** Systolic blood pressure (SBP)**,** Diastolic blood pressure (DBP) was monitored for 24 hours following surgery. Results were expressed as number of occurrences, percentage and mean (SD). Data were summarized as Mean ± SD. Groups were compared by independent Student's t test. Groups were also compared by two factor repeated measure analysis of variance (ANOVA). Discrete (categorical) variables were compared by chi-square ($\chi 2$) test. A two-sided ($\alpha=2$) p value less than 0.05 ($p<0.05$) was considered statistically significant [12].

Table 1: Comparison of the heart rate responses

Heart rate (beats/min)	Mean (SD)		*P* value
	Group A	Group B	
Baseline	87.4(8.1)	87.5 (8.2)	0.11
At induction	91.2 (7.7)	104.8 (8.8)	<0.001**
1 Min after induction	88.5 (7.3)	108.7 (7.9)	<0.001**
5 Min after induction	86(7.1)	109.9 (8.1))	<0.001**
10 Min after induction	96.4(8.1)	113.4 (7.1)	<0.001**
30 Min after induction	84.1(3.1)	82.3 (2.4)	0.56
60 Min after induction	84.5(2.9)	84.2 (2.5)	0.51
90 Min after induction	83.1(1.8)	83.2 (1.8)	0.59
P value, **Highly significant			

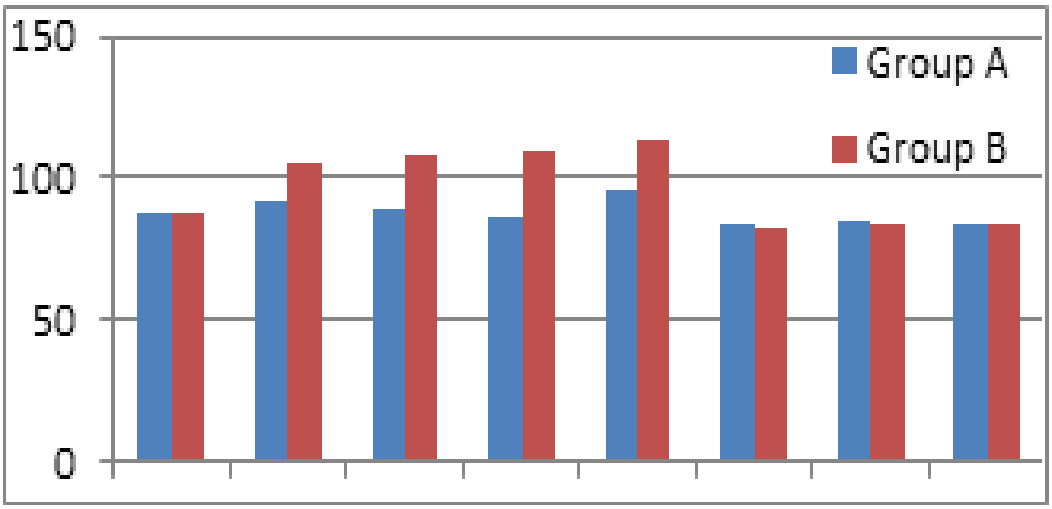

Figure 1

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RESULTS

There was no significant difference in age, sex, weight, height, ASA grading, resting heart rate, blood pressure, between the 2 groups.

Group A

There was a small percentage(3%) of increase in heart rate during intubation initially the pulse rate is 87.4 and there was a small increase in heart rate and maintained till end of surgery almost maintaining in the range of 83 [Table 1 and Figure 1].if we compare the systolic blood pressure initially it was around 120 and at the start of surgery it raised a little of 15 followed by a dip at the end of surgery around 110 with a small variation of around 4.5 %[Table 2 and Figure 2] [13,14]. The mean preoperative Diastolic Blood Pressure in this group was found to be 74mm of Hg. At intubation the mean Diastolic blood pressure was 1.5% higher than baseline Diastolic blood pressure and it was maintained till the end with small dip of 2.3%varaition [Table3and Figure3].

Group B

At the start of surgery it was in arrange of 85 pulse rate which increase to around 20% during intubation and maintained in a 10% increase throughout surgery [Table 1 and Figure 1].if we consider the systolic blood pressure initially which was 120 get a 20.2% increase around 145mm of Hg and maintained almost around 10% increase in pressure throughout surgery and at the end it maintained at 130.3 mm of Hg [Table 2 and Figure 2]. The same figure like systolic blood pressure increase the diastolic also showed a 10% increase [Table 3 and Figure 3]. In comparison to group B, attenuation of heart rate, Systolic blood pressure, diastolic blood pressure were significantly more in group A ($P < 0.001$). There was a small increase in sedation score in group B [15].

Table 2: Comparison of systolic blood pressure

Systolic blood pressure (mm of Hg)	Mean (SD)		*P* value
	Group A	Group B	
Baseline	121.1 (6.8)	120.2(6.9)	0.79
At induction	119.9 (6.1)	145.7(22.1)	<0.001**
1 Min after induction	121.3 (6.3)	141.8 (7.9)	<0.001**
3 Min after induction	117.9 (6.4)	142.9(8.3)	<0.001**
10 Min after induction	110.2 (7.5)	138.9 (8.5)	<0.001**
30 Min after induction	119.4 (1.6)	122.4(1.7)	0.17
60 Min after induction	122.5 (2.7)	124.6 (2.5)	0.29
90 Min after induction	125.3 (3.7)	126.8 (2.7)	0.15

P value, **Highly significant

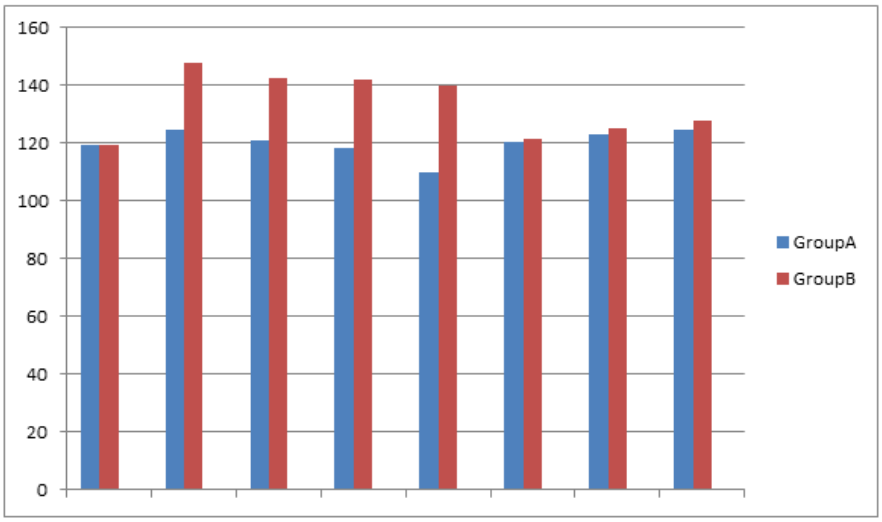

Figure 2

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Table 3: Comparison of diastolic blood pressure			
Diastolic blood pressure (mm of Hg)	**Mean (SD)**		***P* value**
	Group A	**Group B**	
Baseline	75.1 (3.22)	75.6 (3.21)	0.23
At induction	77.8 (4.10)	92.1 (3.97)	<0.001**
1 Min after induction	76.2 (4.53)	90.8 (3.73)	<0.001**
3 Min after induction	73.3 (4.83)	89.1 (3.33)	<0.001**
10 Mins after induction	71.1 (5.61)	87.7 (4.11)	<0.001**
30 Min after induction	81.1 (2.32)	80.7 (2.89)	0.17
60 Min after induction	81.4 (2.30)	82.3 (1.19)	0.35
90 Min after induction	81.2 (2.10)	82.1 (2.15)	0.51
P value, **Highly significant			

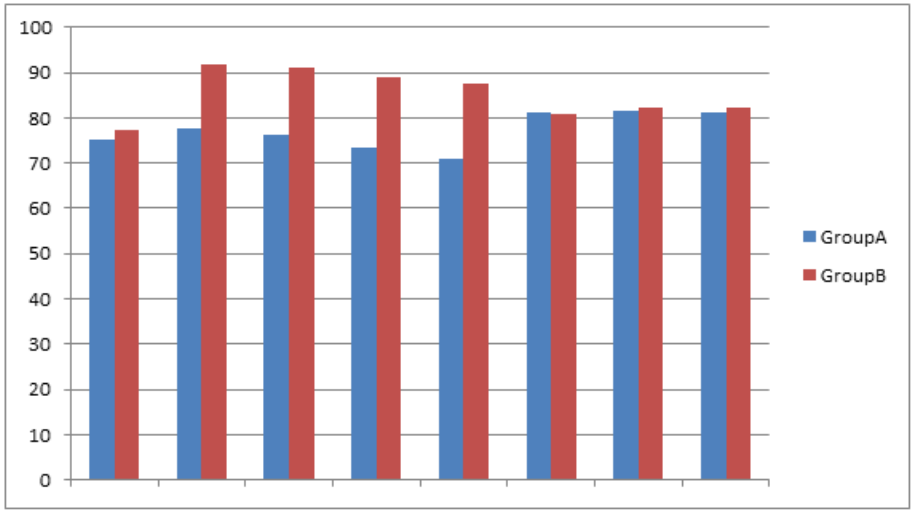

Figure 3

DISCUSSION

In high risk patients the sequence anaesthesia, laryngoscopy is associated with marked hemodynamic changes and autonomic reflex activity which makes concern**.** Marked fluctuations often seen in geriatric patients. Autonomic nervous system abnormality in geriatric patients manifest as a hyperkinetic circulation characterized by elevation in heart rate and blood pressure. Loss of cardiovascular reflexes causes tachycardia at rest and vagal tone decrease with increasing age. Sympathetic nervous system activity increases with age and decrease in response to adrenergic receptor stimulation and decreased baroreceptor sensivity is seen. Our study, we selected an optimal age range of 45 to 60 years. Readings were taken throughout surgery. The rationality was that up to 5 mins, the effect of sympathetic surge due to laryngoscopy and intubation will be present; at 10 mins, effect of pneumoperitoneum and change in position will start taking effect; by 30, and 60 mins, the persistent effect of pneumoperitoneum will be observed and by 90 mins, the effect of extubation will be prominent. In comparison to group B, attenuation of heart rate, Systolic blood pressure, diastolic blood pressure (at 1 min, 5 min and 10 min) were significantly more in group A ($P < 0.001$) [16]. Attenuation of hemodynamic responses at 30 mins, 60 mins and 90 mins were comparable in both groups with a small increase in group A. Administration of dexmedetomidine before induction and intraoperatively improves perioperative hemodynamic stability. Dexmedetomidine premedication is considered to be safe without episodes of hypotension, bradycardia, low oxygen saturation, nausea, vomiting [17-19]. In our study, both dexmedetomidine and clonidine lowered the hemodynamic response to intubation but clonidine was found to be more effective in attenuating the sympathetic response.

CONCLUSION

We conclude in our study, to attenuate both the effects of laryngoscopy and insufflations with carbon dioxide in laparoscopic hysterectomy, infusions of either of the drugs dexmedetomidine or clonidine found to be useful however dexmedetomidine being more effective but with small sedative effect more than clonidine.

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