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RESEARCH ARTICLE

A Comparison of the Effect of Dexmedetomidine and Esmolol in Attenuating Stress Responses during Laparoscopic Surgeries

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ABSTRACT

Introduction: The creation of pneumoperitoneum leads to increased mean arterial pressure and systemic vascular resistance as a result of stimulation of the sympathetic system leading to increased release of catecholamines and vasopressin. In order to prevent these hemodynamic changes, various pharmacological agents like clonidine, esmolol, or dexmedetomidine are used. Hence, there is need for this study.

Materials and methods: A total of 60 patients were randomized into two equal groups: group D—dexmedetomidine was administered as loading dose 1 µg/kg administered slowly over 15 minutes before induction followed by maintenance infusion of 0.5 µg/kg/hour throughout the period of pneumoperitoneum. Group E—esmolol was administered as loading dose at 1 mg/kg administered slowly over 5 minutes before induction followed by maintenance infusion of 0.5 mg/kg/hour throughout the period of pneumoperitoneum. Intra-abdominal pressure was maintained at 12 to 14 mm Hg throughout the procedure. The infusions were discontinued immediately after the release of pneumoperitoneum. Heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were recorded at frequent intervals as per the pro forma. Data were analyzed using appropriate statistical tests.

Results and conclusions: As compared with esmolol, dexmedetomidine is more effective for attenuation of the pressor responses to pneumoperitoneum and thus achieving hemodynamic stability during laparoscopic surgeries ($p < 0.05$).

Keywords: Dexmedetomidine, Esmolol, Laparoscopic, Pneumoperitoneum.

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INTRODUCTION

Laparoscopic procedure has benefits over open surgical procedure in terms of minimal invasion, decreased tissue damage, decreased operative time, and morbidity. But the creation of pneumoperitoneum leads to increased heart rate and mean arterial pressure as a result of the involvement of sympathetic system leading to increased release of catecholamines and vasopressin.[1] These hemodynamic disturbances may be detrimental in patients with poor cardiac reserve. Hence, in order to prevent these hemodynamic changes, various pharmacological agents like clonidine, esmolol, or dexmedetomidine have been used.[2-4]

Dexmedetomidine is alpha-2 adrenergic receptor agonist that modulates the hemodynamic changes by inhibiting the release of catecholamines and vasopressin.[5] Esmolol, an ultrashort-acting cardioselective beta-1 antagonist, has also been used to control tachycardia and hypertension.[6] Hence, we performed this study so as to compare the efficacy of these two agents and also to compare the safety of these drugs.[7]

MATERIALS AND METHODS

This prospective randomized single-blind control study was conducted at Mahatma Gandhi Medical College and Hospital, Jaipur, India. A total of 60 patients were included in the study.

Inclusion Criteria

Age 20 to 60 years, American Society of Anesthesiologist (ASA) physical status I/II, either gender, posted for laparoscopic surgery to be performed under general anesthesia. The exclusion criteria included: ASA grade III/IV, hypertension, diabetes, ischemic heart diseases, cerebrovascular insufficiency, morbid obesity, age <20 or >60 years, allergy to study medications, renal/hepatic insufficiency, patients on antipsychotic, or antihypertensive medication. Pregnant or lactating females were also excluded. Patients were randomized with the help of chit in box method into two groups of 30 each.

Group D—Injection dexmedetomidine was administered as loading dose infusion at 1 µg/kg slowly over 15 minutes before induction followed by maintenance

infusion of 0.5 µg/kg/hour administered throughout the period of pneumoperitoneum.

Group E—Injection esmolol was administered as loading dose infusion at 1 mg/kg slowly over 5 minutes administered before induction followed by maintenance infusion of 0.5 mg/kg/hour continued throughout the period of pneumoperitoneum.

On arrival in operating room, standard monitoring was attached. All patients were preoxygenated with 100% O_2 for 5 minutes and induced with standardized doses of midazolam, fentanyl, and propofol intravenously. Orotracheal intubation was facilitated with injection Vecuronium bromide and achieved with cuffed endotracheal tube of size as appropriate. Anesthesia was maintained with oxygen:nitrous oxide (40:60), isoflurane, and injection Vecuronium. Throughout the procedure, intraabdominal pressure was maintained at <14 mm Hg. The infusions of the study drugs were discontinued immediately after the release of pneumoperitoneum. Reversal of neuromuscular blockade was achieved with injection Neostigmine and injection Glycopyrrolate.

Hemodynamic variables were recorded at various time intervals: preoperative (baseline), just after the administration of study drug, immediately after induction, just after intubation, after creation of pneumoperitoneum and thereafter at regular intervals of 15 minutes, just after release of pneumoperitoneum, and then after 15 minutes. The quantitative data were expressed as mean ± standard deviation (SD) and qualitative data as percentage. The qualitative data were analyzed using Chi-square test and quantitative data were analyzed using Student's t-test; p-value < 0.05 was considered statistically significant.

RESULTS

The study groups were statistically identical (p > 0.05) (Table 1). The baseline heart rate was statistically identical in both groups. After administration of study drugs also, there was no statistically significant difference in the heart rate in both the groups. After induction and intubation there was increase in heart rate in group E but not in group D (Table 2 and Graph 1). After the creation of pneumoperitoneum and during pneumoperitoneum, there was significant increase in heart rate in group E as compared with group D (p = 0.001) (Table 2 and Graph 1). Similarly, there was

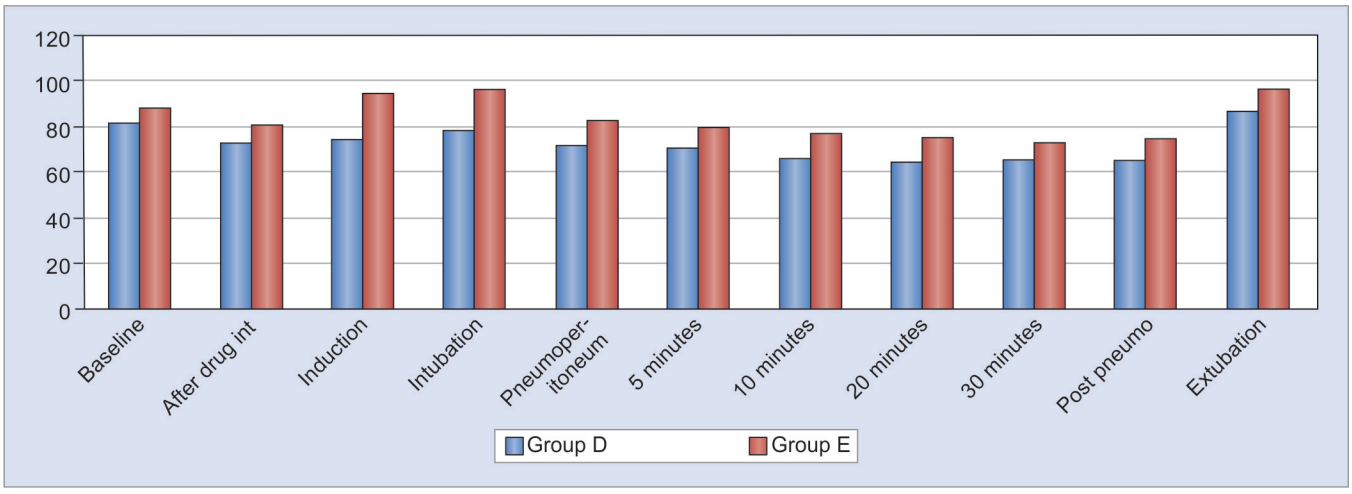
Table 1: Demographic variables

Groups		*Weight (kg)*	*Height (cm)*	*Age (yrs)*
D	No. of patients	30	30	30
	Mean	54.83	163.00	39.47
	SD	10.333	11.588	13.71
E	No. of patients	30	30	30
	Mean	58.60	158.40	40.60
	SD	10.820	9.511	13.04
p-value		0.173	0.098	0.744

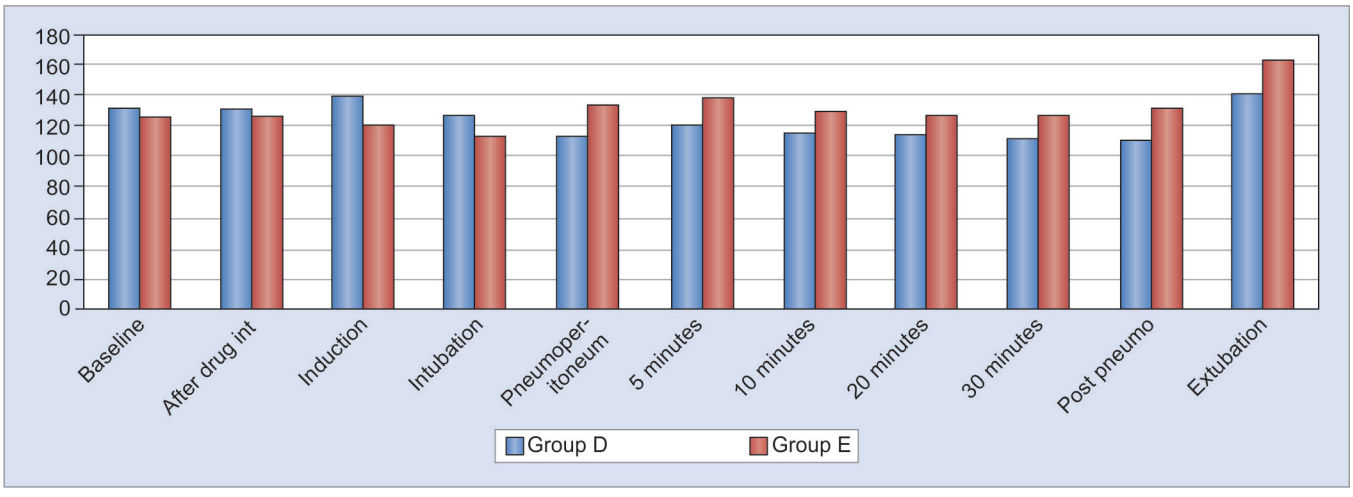
Table 2: Heart rate at various points of time

Groups		*Baseline*	*After drug int*	*Induction*	*Intubation*	*Pneumoperitoneum*	*5 min*	*10 min*	*20 min*	*30 min*	*Postpneumo*	*Extubation*
Group D	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	81.20	72.87	74.90	77.97	71.77	70.23	66.07	64.37	65.60	65.57	86.90
	SD	13.90	9.26	13.32	13.78	10.56	10.03	6.58	4.94	6.667	10.36	9.35
Group E	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	88.53	80.57	94.83	96.23	82.97	79.20	77.13	75.23	72.97	74.47	95.97
	SD	20.08	22.39	18.71	19.51	14.06	14.31	14.37	13.07	12.455	12.56	20.65
p-value		0.105	0.087	<0.001, S	<0.001, S	0.001	0.007	<0.001, S	<0.001, S	0.006S	0.004	0.032

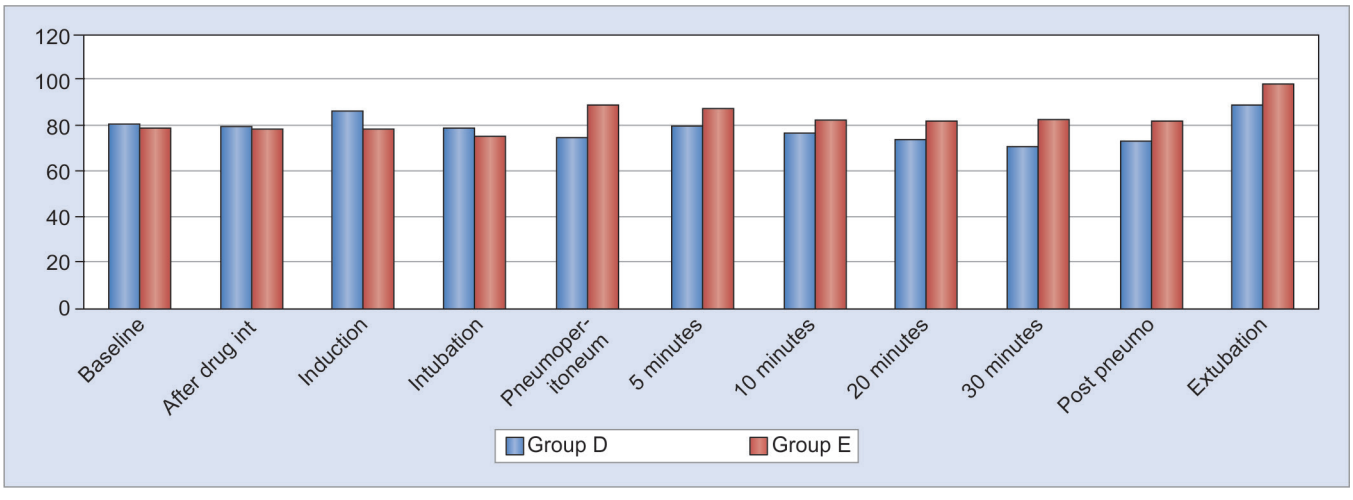
S: Significant



Graph 1: Heart rate at various points of time



Graph 2: Systolic blood pressure at various points of time



Graph 3: Diastolic blood pressure at various points of time

no significant difference in systolic blood pressure and diastolic blood pressure between groups at baseline, after administration of study drugs, induction, and intubation. Systolic blood pressure and diastolic blood pressure were higher in group E as compared with group D after creation of pneumoperitoneum and during pneumoperitoneum (Graphs 2 and 3; Tables 3 and 4, respectively). In addition, there was no significant difference in baseline mean arterial pressure between the groups. However, mean arterial pressure was significantly higher in group E as compared with group D at the time of creation of pneumoperitoneum and during pneumoperitoneum (Table 5 and Graph 4).

Table 3: Systolic blood pressure at various points of time

Groups		*Baseline*	*After drug int*	*Induction*	*Intubation*	*Pneumoperitoneum*	*5 min*	*10 min*	*20 min*	*30 min*	*Postpneumo*	*Extubation*
Group D	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	132.63	131.73	139.90	127.53	114.57	121.27	117.60	115.57	113.57	111.90	141.43
	SD	15.83	18.26	30.99	24.40	13.90	13.67	13.33	13.71	14.292	10.89	21.90
Group E	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	126.90	127.93	121.50	114.57	133.60	139.17	131.20	127.70	127.77	133.33	163.37
	SD	21.72	17.98	18.15	20.46	25.55	21.27	16.48	16.24	16.761	19.01	23.62
p-value		0.247	0.420	0.007	0.030	0.001	<0.001, S	0.001	0.003	0.001, S	<0.001, S	<0.001, S

S: Significant

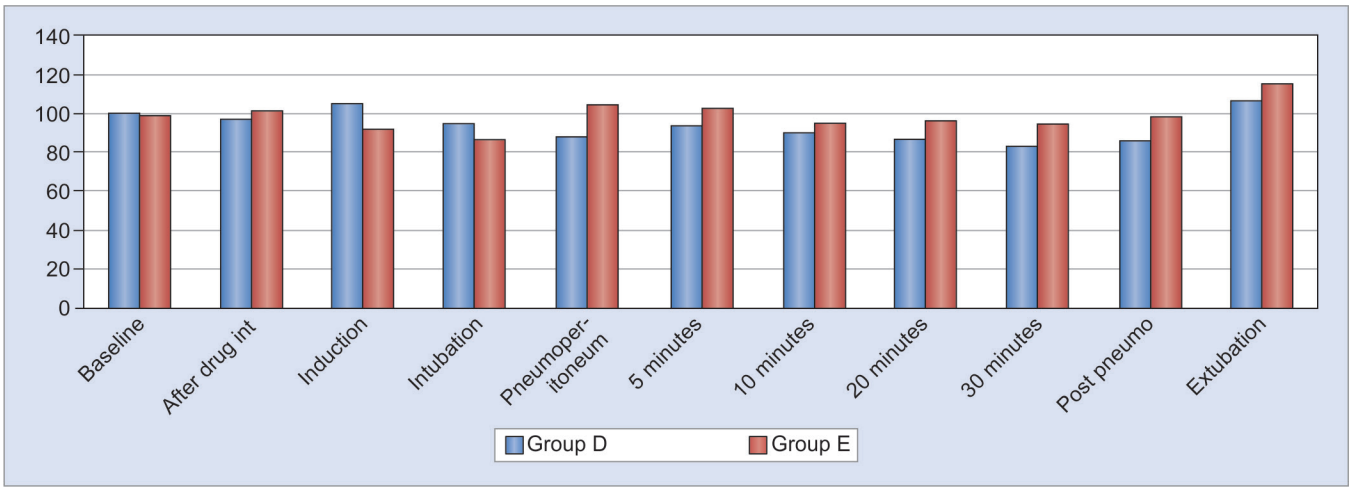
Table 4: Diastolic blood pressure at various points of time

Group		*Baseline*	*After drug int*	*Induction*	*Intubation*	*Pneumoperitoneum*	*5 min*	*10 min*	*20 min*	*30 min*	*Postpneumo*	*Extubation*
Group D	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	81.13	79.77	86.60	78.47	74.53	79.50	76.57	74.13	71.33	72.63	88.23
	SD	11.187	10.938	18.135	15.368	13.140	13.703	12.218	12.111	12.729	9.880	12.716
Group E	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	78.83	78.07	78.50	75.87	87.63	87.30	82.13	81.80	81.40	81.43	97.63
	SD	8.342	10.362	10.624	10.040	14.368	12.978	12.116	11.784	11.631	11.218	11.822
p-value		0.370	0.539	0.039	0.441	0.001	0.027	0.082	0.016	0.002, S	0.002	0.004

S: Significant

Table 5: Mean blood pressure at various points of time

Groups		*Baseline*	*After drug int*	*Induction*	*Intubation*	*Pneumoperitoneum*	*5 min*	*10 min*	*20 min*	*30 min*	*Postpneumo*	*Extubation*
Group D	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	100.23	96.97	105.50	95.43	88.03	93.43	90.37	86.83	84.17	85.90	106.47
	SD	11.973	13.576	23.365	19.197	11.657	13.177	12.238	11.528	12.078	9.607	14.802
Group E	N	30	30	30	30	30	30	30	30	30	30	30
	Mean	99.10	100.83	92.90	87.03	102.37	101.73	95.30	95.57	93.87	98.50	114.70
	SD	14.688	18.819	11.610	10.679	16.927	13.978	11.481	11.735	13.203	13.143	16.346
p-value		0.744	0.365	0.010	0.041	0.000	0.021	0.113	0.005	0.004S	0.000	0.045



Graph 4: Mean blood pressure at various points of time

Hypotension was observed in one patient in group D which responded well to intravenous bolus of 200 mL Ringer's lactate. There were no other complications in either group.

DISCUSSION

The creation of pneumoperitoneum during laparoscopic surgeries caused a rapid increase in plasma catecholamines and vasopressin leading to elevated arterial pressure, systemic vascular resistance, and heart rate. Increase in hemodynamic parameters leads to increase in the incidence of complications like myocardial ischemia and infarction.[7] To attenuate these hemodynamic changes, various pharmacological agents were used. In the present study, dexmedetomidine and esmolol were compared because both are short-acting and inhibit the release of catecholamines.

Dexmedetomidine is highly selective alpha-2 adrenergic receptor agonist that provides excellent sedation and analgesia with minimal respiratory depression.[8] Esmolol is an ultrashort-acting, cardioselective beta-1 receptor antagonist having little sedative effect, but no analgesic activity.[6,9] In a study it was observed that esmolol had an opioid sparing effect during and immediately after laparoscopic surgeries.[10] The pharmacologic profiles of both agents suggest that they could be a suitable anesthetic adjuvant for attenuation of hemodynamic responses as a result of pneumoperitoneum. Moreover, they do not interfere with the recovery process. In a study it was observed that intramuscular administration of dexmedetomidine during gynecologic laparoscopy leads to dose-dependent attenuation of mean arterial blood pressure and heart rate, which increased due to intubation and laparoscopy.[11]

Bhattacharjee et al[12] have used dexmedetomidine in a bolus dose of 1 µg/kg intravenously before pneumoperitoneum followed by maintenance infusion of 0.2 to 0.5 µg/kg/hour and observed that it is effective in attenuating the adverse hemodynamic response to pneumoperitoneum. In our study, similar doses of dexmedetomidine were administered and we observed that it is effective in attenuating adverse hemodynamic responses.

Apart from this, beta-adrenergic receptor antagonist has also been used by various authors during laparoscopic surgeries so as to attenuate the hemodynamic responses. Some researchers have used esmolol in an initial bolus of 1 mg/kg before pneumoperitoneum and followed by an infusion of 0.2 mg/kg/hour. They observed that esmolol was effective in attenuating the increase of heart rate and arterial pressure during laparoscopic surgeries.[13] In yet another study, administering the single dose, it was reported that dexmedetomidine was more effective in preventing the rise in heart rate and blood pressure during extubation because of its additional analgesic and sedative action.[14] Shams et al[15] used same loading and infusion dose of dexmedetomidine and esmolol in functional endoscopic sinus surgeries for providing hypotensive anesthesia and found that dexmedetomidine is more effective than esmolol with added advantages of its sedative effects. In a study comparing esmolol and dexmedetomidine with control group, it was observed that both the drugs were effective in attenuating pressor responses during laparoscopic surgeries.[16] In yet another study, it was observed that esmolol was better in terms of stability of heart rate as compared with the dexmedetomidine group which showed a better control in blood pressure.[17] However, in our study, we observed that dexmedetomidine group was better in terms of stability of both heart rate and blood pressure as compared with esmolol group. We did not compare the observations with control group.

CONCLUSION

Thus, we conclude that dexmedetomidine is better than esmolol in prevention of pressor responses to pneumoperitoneum created during laparoscopic surgeries.

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