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"A COMPARATIVE STUDY OF ESMOLOL AND DEXMEDETOMIDINE ON HAEMODYNAMIC RESPONSES TO CARBON DIOXIDE PNEUMOPERITONEUM DURING LAPAROSCOPIC SURGERY."

Anaesthesiology

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ABSTRACT

Background: The advent of laparoscopic surgery has benefited the patient and surgeon, however creation of pneumoperitoneum for same has bearings during the perioperative period. These effects of pneumoperitoneum are associated with significant haemodynamic changes, increasing the morbidity of the patient.
Aim: The present study compared the efficacy of dexmedetomidine and esmolol on hemodynamic responses to CO2 pneumoperitoneum during laparoscopic surgery.
Material And Method: A total of 60 patients aged 20-50 y, American Society of Anaesthesiologists (ASA) physical status I or II, of either sex, planned for laparoscopic surgery were included. The patients were randomly divided into two groups of 30 each. Group D received dexmedetomidine bolus dose 1 mcg/kg IV in 100 ml NS and Group E received esmolol bolus dose 1 mg/kg IV in 10 ml of NS before creating pneumoperitoneum.
Measurement: Heart rate (HR), systolic blood pressure, diastolic blood pressure and mean arterial pressure (MAP) were recorded preoperative, vitals were recorded at intubation time, after intubation before creating pneumoperitoneum, after creating pneumoperitoneum, at 3,5,10 min and then every 10 min intervals till 30 min after pneumoperitoneum. Propofol induction dose, intraoperative fentanyl requirement and rescue drug were also recorded.
Result: In group D, there was no statistically significant increase in HR and blood pressure after pneumoperitoneum at any time intervals, whereas in Group E, there was a statistically significant increase in MAP and HR after pneumoperitoneum at 10, 20, and 30 min. There was a significant decrease in induction dose of propofol and intraoperative fentanyl requirement in Group D and E.
Conclusion: Dexmedetomidine is more effective than esmolol for attenuating the hemodynamic response to pneumoperitoneum in elective laparoscopic surgery. Dexmedetomidine and esmolol also reduced requirements of anaesthetic agents.

KEYWORDS

Pneumoperitoneum, Laproscopy surgery, General Anaesthesia

INTRODUCTION:

Laparoscopic procedures offer several advantages such as a reduction in stress response, postoperative pain, postoperative wound infection rate, intraoperative bleeding, short recovery time, and cosmetic appearance. Now a day's laparoscopy is a choice for many surgeries like cholecystectomy, appendicectomy, hysterectomy even as a diagnostic procedure also it is very frequently used. The hallmark of laparoscopy is the creation of pneumoperitoneum with carbon dioxide (CO_2). Immediately after pneumoperitoneum, plasma level of norepinephrine, epinephrine and plasma renin activity increases. The renin-angiotensin-aldosterone system is also activated by the increased catecholamine level. All these changes come together to contribute to elevated arterial pressure, increased systemic and pulmonary vascular resistance and reduced cardiac output.

Laparoscopy leads to ventilatory changes as the Pneumoperitoneum created decreases thoraco-pulmonary compliance by 30% to 50% in healthy and obese patients. Reduction in functional residual capacity and development of atelectasis due to elevation of the diaphragm and changes in the distribution of pulmonary ventilation and perfusion from increased airway pressure can be expected. Hypercapnia and pneumoperitoneum cause stimulation of the sympathetic nervous system causing catecholamine and vasopressin release. Different pharmacological agents like α_2 adrenergic agonists, beta-blockers and opioids, magnesium sulfate, nitroglycerine, are often used to attenuate circulatory response due to pneumoperitoneum and to provide hemodynamic stability during laparoscopy surgery.

Dexmedetomidine is a highly selective α-2 adrenergic agonist that has sedative, anxiolytic, sympatholytic and analgesic properties without producing significant respiratory depression. Its sympatholytic effect decreases mean arterial pressure (MAP) and heart rate (HR) by reducing norepinephrine release.

Esmolol, an ultrashort acting cardio selective β1 adrenoceptor antagonist, has been used to control tachycardia and hypertension. Esmolol blunts adrenergic responses to perioperative noxious stimuli effectively.

MATERIAL AND METHOD:

This prospective, randomized, study was conducted at B.J. Medical College and Civil Hospital, Ahmedabad and written informed consent were taken from the patients. A total of 60 patients, aged 20-60 y, ASA physical status I or II, of either sex, scheduled for elective laparoscopic surgery under general anaesthesia were taken as subjects for the study.

A thorough preoperative check-up with general physical examination was done along with all routine investigations like haemoglobin, renal function tests, serum electrolytes, random blood sugar, coagulation profile, chest X-ray PA view and ECG. All the patients were kept nil by mouth after the previous midnight of surgery. After written informed consent, patient will be taken on O.T table & baseline monitoring and all standard monitors including non-invasive blood pressure (NIBP), pulse oximetry (SpO2), electrocardiogram (ECG) and capnography (EtCO2) were attached. After establishing intravenous access using an 18G cannula, ringer lactate was started and pre-operative vital parameters were recorded.

All patients were premedicated with Inj. glycopyrrolate (0.004mg/kg), Inj. fentanyl (1 mcg/kg) and Inj. Ondansetron 0.15mg/kg intravenously. After preoxygenation with 100% O2 for three minutes, patients were induced with Inj. propofol (2 mg/kg) intravenously in both groups, intubation was done with Inj. succinylcholine (2mg/kg). Anaesthesia was maintained with O_2 , 0.6% isoflurane, and intermittent bolus dose of vecuronium.

- Group E patients received bolus dose of 1mg/kg IV in 10 ml of NS esmolol before pneumoperitoneum.
- Group D patients received bolus dose of 1 µg/kg IV in 100 ml NS dexmedetomidine before pneumoperitoneum.

CO_2 was insufflated into the peritoneal cavity to create pneumoperitoneum. Intra-abdominal pressure (IAP) was maintained up to 12 mmHg throughout the laparoscopic procedure. All the patients were positioned in a head-up tilt of 15°. The patients were mechanically ventilated to keep end-tidal CO_2 between 30 and 40 mmHg. Injection paracetamol 1000 mg was infused IV in every patient. Isoflurane discontinued 15 minutes before the end of surgery to facilitate rapid emergence from anaesthesia. Neuromuscular blockade was reversed with Inj. neostigmine 0.05 mg/kg and Inj. glycopyrrolate

0.008 mg/kg were given immediately after completion of surgery. Extubation was done after adequate recovery from the effects of neuromuscular blockade.

After clinical recovery Patients were shifted to recovery room and observed for 2 hours for immediate postoperative complication e.g. nausea, vomiting, shivering, sedation, hypotension, bradycardia etc. were recorded and managed accordingly.

Intra operatively any hypotension (MAP <20% preoperative) was managed with a fluid bolus of normal saline 250-300 ml. If hypotension did not respond to fluid administration, then inj. mephentermine 5 mg i.v. was administered. If hypotension did not respond to 2 repeat doses of mephentermine then dopamine infusion was started to maintain the blood pressure. Any incidence of bradycardia (HR < 50/min) was treated with inj. atropine 0.6 mg i.v. Hypertension (MAP >20% preoperative) was managed with nitroglycerine infusion.

The sample size is calculated by power analysis, using a two-sample t test, with a two-sided type I error of 5% (α=0.05) and power at 80.37 (α=0.19). Therefore 25 patients in each group are needed. We enrolled 30 patients in each group to account for potential dropouts or protocol violations.

RESULT:

The demographic data and changes in hemodynamic parameters are presented in a tabular form.

Table 1 Age Distribution

	Group D(n=30)	Group E(n=30)	P Value
Age (Years) Mean SD	33.5±9.036	31.57±7.925	0.3827

No statistically significant difference was found between two groups (p>0.05).

Table 2 Weight Distribution

	Group D (n=30)	Group E (n=30)	P Value
Weight(kg) Mean ±SD	55.86 ±11.74	59.83±11.11	0.1838

Both groups were comparable in weight distribution. There was no statistically significant difference between both groups(p>0.05)

Table 3 Sex Distribution

Gender	Group D No. of patient	Group D Percentage	Group E No. of patients	Group E Percentage
Male	6	20%	6	20%
Female	24	80%	24	80%
Total	30	100%	30	100%

Both the groups were comparable in sex distribution.

Table 4 Comparison Of Changes In Mean Heart Rate ± S.D. Between Two Groups

Time Interval	Group D(n=30)		Group E(n=30)		P
	MEAN	S.D.	MEAN	S.D.	value
Baseline	88.93	11.63	85.4	13.43	0.29
Intubation	94.5	11.15	88.43	14.96	0.174
Before Pneumoperitoneum	97.06	9.87	90.2	13.44	0.02
After Pneumoperitoneum	97.56	10.25	86.1	13.23	0.004
3 MIN	94.5	11.10	83.23	13.56	<0.001
5MIN	90.5	10.83	80.1	14.80	0.003
10 MIN	87.8	11.26	78.86	14.64	0.01
20 MIN	86.3	10.92	87.3	14.02	0.759
30 MIN	85.06	10.82	93.2	12.78	0.01

This table shows the comparison of changes in mean heart rate at various pre-determined time interval and p value to determine the significance of changes in heart rate between both the groups. There was significant fall in heart rate observed at before pneumoperitoneum and after pneumoperitoneum and at 3 min, 5 min, 10 min after pneumoperitoneum in group E patients. There is significant fall in heart rate at 30 min after pneumoperitoneum in group D patients.

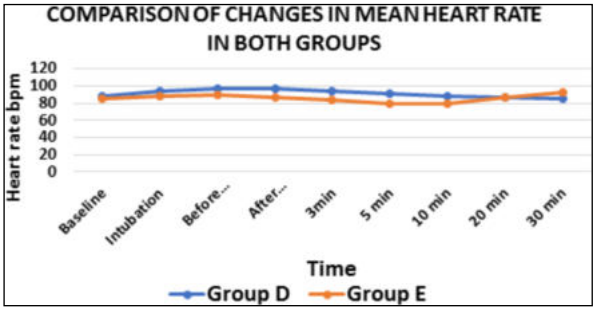

Chart 1

Table 5 Comparison Of Changes In Mean Systolic Blood Pressure ± S.D > Between Both Groups

Time Interval	Group D(n=30)		Group E(n=30)		P Value
	MEAN	S.D.	MEAN	S.D.	
Baseline	122.46	10.83	123.36	13.43	0.751
Intubation	126.4	9.67	130.06	14.96	0.145
Before Pneumoperitoneum	129.46	9.66	129.56	13.44	0.965
After Pneumoperitoneum	130.73	9.28	126.8	13.23	0.184
3 MIN	127.33	8.80	126.9	13.56	0.916
5 MIN	124.06	8.78	127.76	14.80	0.336
10 MIN	122.8	9.01	129.73	14.64	0.011
20 MIN	120.93	10.03	129.26	14.02	0.002
30 MIN	120.86	11.23	129.86	12.78	0.002

This table shows the comparison of changes in mean systolic blood pressure at various predetermined time interval and P value to determine the significance of the changes in between both groups. After pneumoperitoneum immediately in both groups mean systolic blood pressure were higher than baseline systolic blood pressure. There was significant difference of systolic blood pressure observed between both the groups after 10 min, 20 min, 30 min of pneumoperitoneum. There was low values of systolic blood pressure in group D as compare to group E.

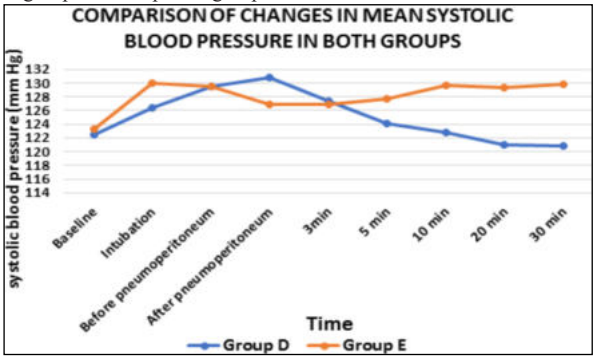

Chart 2

Table 6 Comparison Of Changes In Mean Diastolic Blood Pressure ± S.D. Between Both Groups

Time Interval	Group D (n=30)		Group E (n=30)		P Value
	MEAN	S.D.	MEAN	S.D.	
Baseline	76.26	6.53	76.13	8.92	0.949
Intubation	80	5.89	82.66	8.60	0.168
Before Pneumoperitoneum	81.4	5.94	82.46	7.45	0.545
After Pneumoperitoneum	82.26	5.72	81.4	9.33	0.669
3 MIN	80.4	5.85	82.06	11.44	0.483
5 MIN	76.8	5.59	84.73	10.85	<0.001
10 MIN	75	5.34	85.46	9.90	<0.001
20 MIN	74	5.11	87.26	9.47	<0.001
30 MIN	74.13	5.65	90.53	9.12	<0.001

This table shows the comparison of changes in mean diastolic pressure at various predetermined time interval and P value to determine the significance of the changes in diastolic blood pressure between both groups. There was significant difference of diastolic blood pressure observed between both the groups. Group D shows lower values of mean diastolic blood pressure at 5min,10min, 20min and 30min after

pneumoperitoneum as compared to group E.

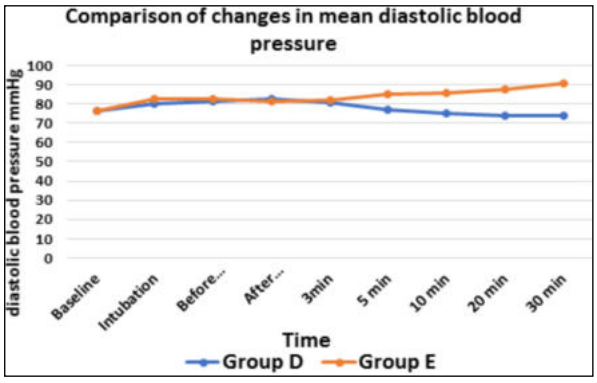

Chart 3

Table 7 Comparison Of Intra Operative And Post-operative Complications In Both The Groups

Intra Operative Complication	Group D(n=30)	Group E(n=30)
Bradycardia	0	0
Hypotension	0	0

Post Operative Complication	Group D(n=30)	Group E(n=30)
Nausea	0	0
Vomiting	0	0
Bradycardia	0	0
Hypotension	0	0
Shivering	0	0
Sedation	0	0

None of the patient in both the groups developed complications like bradycardia and hypotension intra operatively. None of the patient in both the groups developed complications like nausea, vomiting, bradycardia, hypotension, shivering and sedation post operatively.

DISCUSSION:

Our study confirms that dexmedetomidine and esmolol were successfully used to control hemodynamic changes during pneumoperitoneum in laparoscopic cholecystectomy however dexmedetomidine is more effective than esmolol to attenuate these changes.

Laparoscopic surgery is considered a minimally invasive procedure. Pneumoperitoneum using CO2 for laparoscopic surgery causes a rapid and immediate increase in plasma catecholamines and vasopressin, possibly due to an increase in intraperitoneal pressure and stimulation of the peritoneum by CO2. The increase in these stress hormones induces a cardiovascular response characterized by abrupt elevations of arterial pressure, SVR and HR. The increase in these hemodynamic values significantly increases the incidence of myocardial ischemia, infarction and other complications. Our study used comparison of dexmedetomidine and esmolol because both of these drugs are short acting, reduce catecholamines release and no postoperative complication.

Previous studies report that dexmedetomidine infusion rates ranging from 0.2 to 10 mcg/kg/hr have been used. The studies with higher dose had more incidences of hypotension and bradycardia. Most study used dexmedetomidine loading dose 1 mcg/kg over 10-15 minutes followed by continuous infusion 0.2 to 0.5 mcg/kg/hr for maintenance and concluded that dexmedetomidine attenuates the increase in heart rate and blood pressure by altering the stress-induced sympathoadrenal response. In this study, we used dexmedetomidine bolus dose 1 mcg/kg IV in 100 ml NS before pneumoperitoneum.

β-Adrenergic receptor antagonists have also been used by various authors during surgery with the intention to attenuate the stress response and decrease unwanted perioperative hemodynamic changes. We used Inj. Esmolol 1mg/kg IV diluted in 10 ml NS slowly. Koivusalo et al., suggested that an effect of esmolol on hemodynamic response to CO2 pneumoperitoneum is mediated by blockade of peripheral β-adrenergic receptors. In addition to this it decreased the intraoperative fentanyl requirement and also protected against renal vasoconstriction. Ozturk et al., also confirmed that esmolol had an opioid sparing effect during the intraoperative and immediate postoperative period in laparoscopic surgery.

Priya et al., noted that single dose of dexmedetomidine and esmolol were effective in controlling rise of pulse and blood pressure during extubation phase and dexmedetomidine is more effective than esmolol because of its additional analgesic and sedative actions. We also found same results with these two drugs during whole pneumoperitoneum period.

In our study,

- The demographic profile of the patients in terms of age, body weight and sex were comparable in both the groups and there was no significant difference.
- There was increase in the heart rate, systolic blood pressure and diastolic blood pressure at the time of CO_2 insufflation for laparoscopy in both groups.
- Esmolol shown significant reduction in heart rate after CO_2 insufflation and till 10 minutes after pneumoperitoneum, but after that there was increase in heart rate throughout. Dexmedetomidine shown better control of heart rate after 10 minutes of pneumoperitoneum and it continued throughout pneumoperitoneum.
- There was significant difference in attenuation of systolic and diastolic blood pressure in both the group. At time of insufflation Group D showed an increase in systolic and diastolic blood pressure which was within 20% of the baseline and after that blood pressure throughout time were in control in group D. In Group E there was significant increase in systolic and diastolic blood pressure starting from CO2 insufflation to pneumoperitoneum period.
- No serious side effects or complications were found in any of the study groups. There was no delay in recovery in any group patients.

There are some limitations to our study: (1) the no of patients is too small for broad generalizations (2) plasma catecholamines and antidiuretic hormone levels were not assessed by us to know the degree of suppression of neurohumoral pathway (3) we did not measure the postoperative fentanyl requirement and extubation criteria.

CONCLUSION:

We emphasize the use of dexmedetomidine and esmolol for attenuation of hemodynamic response to pneumoperitoneum in laparoscopic surgeries. Dexmedetomidine is more effective than esmolol in preventing such hemodynamic responses in laparoscopic surgery. In addition, dexmedetomidine and esmolol also reduce the intraoperative fentanyl requirement.

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