Original Research Article

Study of efficacy of dexmedetomidine and fentanyl for suppression of pressor response to pneumoperitoneum during laparoscopic surgeries

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Abstract

Background: Peritoneal insufflation in laparoscopic surgeries induces alterations of hemodynamics, characterized by decrease in stroke volume and cardiac output, elevation of mean arterial pressure, and increase of systemic and pulmonary vascular resistance. Present study was aimed to compare the effect of dexmedetomidine Versus fentanyl on hemodynamic response to tracheal intubation, following pneumoperitoneum and intraoperative period in patients undergoing laparoscopic surgery. **Material and Methods:** The present prospective, randomized comparative study in patients 18-60 years age, posted for planned laparoscopic surgery, ASA grade I/II, willing to participate in study were considered for present study. Patients were allocated randomly to the two groups using slips in box method. Immediately before induction, patients in the fentanyl group (Group F) received fentanyl 1µg/kg in normal saline and in the dexmedetomidine group (Group D) received dexmedetomidine 1 µg/kg in normal saline. **Results:** Age, gender, weight and ASA grading were comparable in the two groups. Distribution of systolic blood pressure (SBP) at various intervals between the two groups and p value is statistically significant at time of intubation, 15 min after pneumoperitoneum and at the time of extubation. Diastolic blood pressure (DBP) at various intervals between the two groups and p value is statistically significant at time of intubation, 15 min after pneumoperitoneum and at the time of extubation. Heart rate at various intervals between the two groups and p value is statistically significant at time of intubation, 15 min,30 min after pneumoperitoneum and at the time of extubation **Conclusion:** Intravenous premedication with infusion of dexmedetomidine 1mcg/kg over 10min as loading dose followed by 0.2mcg/kg/hr as maintenance is recommended for better haemodynamic stability during perioperative period despite high cost.

Keywords: dexmedetomidine, fentanyl, pressor response, laparoscopic surgeries.

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INTRODUCTION

Laparoscopic surgeries involve insufflation of a CO2 gas into the peritoneal cavity producing a pneumoperitoneum. Peritoneal insufflation induces alterations of hemodynamics, characterized by decrease in stroke volume and cardiac output, elevation of mean arterial pressure, and increase of systemic and pulmonary vascular resistance.[1] Hemodynamic changes are accentuated in high-risk cardiac patients Dexmedetomidine has analgesic, anxiolytic, sedative and sympatholytic properties. Dexmedetomidine also attenuates the

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haemodynamic response to tracheal intubation, decreases plasma catecholamine concentration during anaesthesia and decreases perioperative requirement of inhaled anesthetics.[2] The hypnotic response is probably mediated by activation of the α2 adrenoreceptors. Dexmedetomidine is proved to have antinociceptive effects and reduce the neurohumoral properties.[3] Fentanyl citrate is a narcotic analgesic interacting predominantly with the opioid μ receptor and exerting its principal pharmacological effect on CNS. Its primary action of therapeutic value is analgesia and sedation. It is extensively used for anesthetic and analgesic most often in operating room and ICU.[4] The study was aimed to compare the effect of dexmedetomidine Versus fentanyl on hemodynamic response to tracheal intubation, following pneumoperitoneum and intraoperative period in patients undergoing laparoscopic surgery.

MATERIAL AND METHODS

The present prospective, randomized comparative study was conducted in the Department of Anaesthesiology, Kamineni Institute of Medical Sciences, Narketpally for a period of 1 year. Institutional ethical committee approval was taken.

Inclusion criteria

- Patients 18-60 years age, posted for planned laparoscopic surgery, ASA grade I/II, willing to participate in study were considered for present study.

Exclusion criteria

- ASA grade III or greater
- Base line heart rate less than 60bpm, base line blood pressure less than 100/60mmHg
- Patients with history of hypertension, ischemic heart disease, heart block, left ventricular failure, heart block, severe renal or hepatic disease.
- Pregnant, lactating and menstruating females.
- Anticipated difficult intubation

A pre anesthetic evaluation comprising of history of previous medical and surgical illness, previous anesthetic exposures, drug allergies and baseline investigations of blood, radiographs of chest and airway examination was done. All patients were explained about the procedure and its complications and informed consent obtained. Preoperative vital parameters in the form of baseline pulse, blood pressure and oxygen saturation was recorded. Patients were allocated randomly to the two groups using slips in box method. All patients were pre-medicated with intravenous Glycopyrrolate 4μg/kg, Ondansetron 15μg/kg. Immediately before induction, patients in the fentanyl group (Group F) received fentanyl 1μg/kg in normal saline and in the dexmedetomidine group (Group D) received dexmedetomidine 1 μg/kg in normal saline. Total volume of the study drug was adjusted to 50 ml and administered over a period of 10 min before induction. Followed by infusion dose of respective drugs at the rate of 0.2μg/kg/hr after the loading dose All patients were preoxygenated with 100% O2 for 3 minutes and were induced with Propofol 2mg/kg IV. Intubation was facilitated by using Vecuronium bromide 0.1mg/kg. The lungs were ventilated with 100% oxygen for 3 minutes. Intra-abdominal pressure was restricted to 10-14mmHg throughout the laparoscopic procedure. The patients were mechanically ventilated to keep ETCO2 between 35-40 mm hg. Anaesthesia was maintained with Vecuronium bromide and intermittent positive pressure ventilation with nitrous oxide and oxygen in the ratio of 50: 50 with 1% Isoflurane using circle absorber system connected to the Boyle's anesthetic workstation. Intra-abdominal pressure was restricted to 10-14 mmHg. EtCO2 was maintained below 35 mmHg at any course of the procedure. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SPO2, EtCO2 were recorded at various intervals as pre-operatively i.e. before premedication (baseline value), after induction, after intubation, 15 min, 30 min, 45min, 60 min,75 min,90min, extubation and post operatively. At the end of surgery, neuromuscular blockade was reversed with neostigmine 50 μg/ kg and glycopyrrolate10 μg/kg intravenously. After satisfying the extubation criteria, patient was extubated and transferred to post-operative ward. Patients were observed for any adverse events during postoperative period. The data was expressed as mean and standard deviation. Comparison between two groups at a time (inter-group comparison) was done using student's unpaired t- test. $P < 0.05$ was considered statistically significant, value < 0.01 was considered highly significant.

RESULTS

Total of 60 patients randomly allocated in two groups, to Group D (Dexmedetomidine) and Group F (Fentanyl) of 30 each undergoing elective laparoscopic surgeries, under GA were studied. Age, gender, weight and ASA grading were comparable in the two groups.

Table 1: General parameters

Parameters	Group D (n=30)	Group F (n=30)	P value
Age [years]	30.7 ± 7.611	29.23 ± 7.205	0.445
Weight [kg]	59.3 ± 3.33	59.9 ± 3.40	0.49
ASA Grade			
I	22 (73.33%)	23 (76.66%)	
II	8 (26.66%)	7 (23.33%)	

Distribution of systolic blood pressure (SBP) at various intervals between the two groups and p value is statistically significant at time of intubation, 15 min after pneumoperitoneum and at the time of extubation.

Table 2: Comparison of SBP between two groups at various intervals

Systolic blood pressure	Group D (n=30)	Group F (n=30)	P Value
Pre -op	124.3 ± 10.31	125 ± 10.2	0.792
Induction	112.46 ± 7.97	112 ± 7.30	0.816
Intubation	122.7 ± 10.4	130 ± 8.13	0.003
15min After PNP	123.7 ± 7.16	133 ± 6.81	0.0001
30 min After PNP	125.7 ± 6.13	127 5.54	0.392
45 min After PNP	123.7 ± 4.97	125 ± 5.18	0.325
60 min After PNP	124 ± 4.95	125 4 ±.82	0.431
Extubation	132.5 ± 3.73	134.6 ± 4.81	0.022
Post- op	126.8 ± 3.66	126 ± 4.47	0.451

Diastolic blood pressure (DBP) at various intervals between the two groups and p value is statistically significant at time of intubation, 15 min after pneumoperitoneum and at the time of extubation.

Table 3: Comparison of diastolic blood pressure between two groups at various intervals

Diastolic blood pressure	Group D (n=30)	Group F (n=30)	P Value
Pre -op	80.1 ± 8.87	77 ± 7.3	0.144
Induction	75.06 ± 8.84	72 ± 6.7	0.136
Intubation	78.9 ± 8.32	86.2 ± 4.56	0.0001
15min After PNP	80.2 ± 6.69	85 ± 4.8	0.0023
30 min After PNP	78.53 ± 5.77	79 ± 4.8	0.732
45 min After PNP	77.67 ± 4.61	75.9 ± 4.02	0.118
60 min After PNP	74.6 ± 3.9	75.7 ± 4.79	0.334
Extubation	80 ± 4.26	83.6 ± 4.91	0.003
Post- op	76.1 ± 3.79	77.5 ± 4.32	0.183

Heart rate at various intervals between the two groups and p value is statistically significant at time of intubation, 15 min,30 min after pneumoperitoneum and at the time of extubation

Table 4: Comparison of heart rate between two groups at various intervals

Heart rate	Group D (n=30)	Group F (n=30)	P Value
Pre -op	77.3 ± 7.25	80 ± 5.3	0.105
Induction	78.36 ± 5.14	76 ± 8.4	0.194
Intubation	72.07 ± 5.39	86 ± 5.4	0.0001
15min After PNP	71 ± 4.72	86 ± 4.2	0.0001
30 min After PNP	75.3 ± 5.63	78.2 ± 5.09	0.040
45 min After PNP	74.33 ± 4.759	75.5 ± 4.22	0.317
60 min After PNP	74.7 ± 4.316	74.8 ± 4.29	0.928
Extubation	76.1 ± 3.78	85.9 ± 5.44	0.0001
Post- op	74.97 ± 4.37	76.6 ± 4.58	0.163

DISCUSSION

In laparoscopic surgery, CO2 is routinely used to create pneumoperitoneum. Elevated intra-abdominal pressure induced by pneumoperitoneum and CO2 itself produce some adverse effects on the cardiovascular system. Immediately after pneumoperitoneum, plasma level of norepinephrine, epinephrine and plasma renin activity is increased. Increased catecholamine level activates the renin-angiotensin-aldosterone-system (RAAS) leading to some characteristic haemodynamic alterations which include:

1. Decreased cardiac output (25-35%)
2. Elevated mean arterial pressure.
3. Increased systemic / pulmonary vascular resistance.[5]

To attenuate this hemodynamic response, a wide variety of agents such as beta blockers, α2 agonists, magnesium sulphate, opioids, vasodilators, and gasless are being used both during premedication and induction, to negate the hemodynamic variations.[6] In a study by Jaakola *et al.*,[7] found decreased BP and HR during intubations following the administration of 0.6 μg/kg bolus of dexmedetomidine preoperatively. After intubation, maximum heart rate was 18% and the maximum IOP was 27%, less in the dexmedetomidine group compared with the patients treated with placebo. Within 10 min after intubation, maximum systolic and diastolic arterial pressures were also significantly smaller in the dexmedetomidine group. Lawrence *et al.*,[8] noted that a single dose of dexmedetomidine (2μg/kg) before induction of anesthesia attenuated the hemodynamic response to intubation and extubation. The haemodynamic response to tracheal intubation and extubation was reduced in the dexmedetomidine group as was intra-operative heart rate variability; postoperative analgesic and anti-emetic requirements and peri- operative serum catecholamine concentrations were lower in the dexmedetomidine group. Similar findings were noted in present study. Sukminder *et al.*[9] studied attenuation of pressor response and dose sparing of opioids anesthetics with pre-operative dexmedetomidine with 1mcg/kg of dexmedetomidine and 2mcg/kg fentanyl pre operatively in respected groups. The pressor response to laryngoscopy, intubation, surgery and extubation were effectively decreased by dexmedetomidine, and were highly significant on comparison. The mean dose of fentanyl and isoflurane were also decreased significantly (>50%) by the administration of dexmedetomidine. The mean recovery time was also shorter in group D as compared with group F. Amar Prakash kataria *et al.*[10] evaluated the efficacy of dexmedetomidine and fentanyl in attenuation of pressor responses to laryngoscopy, intubation and pneumoperitoneum in laparoscopic cholecystectomy. They noted that requirements of additional opioids and inhalational agents are more with the group F than with that of the group D. Use of dexmedetomidine has reduced the use of the induction, inhalational agents and analgesics. Jayshree P Vaswani *et al.*[11] compared the effect of dexmedetomidine vs fentanyl on hemodynamic response in patients undergoing

laparoscopic surgery. Dexmedetomidine significantly attenuates stress response at intubation with lesser increase in HR (5% Vs 18%), SBP (9% Vs 19%) and DBP (3% Vs 15%), MAP (2% Vs 15%) as compared to fentanyl ($p<0.05$). In several study reports, dexmedetomidine infusion rates ranging from 0.1 to 1.0 µg/kg/hr have been used. The studies with higher infusion rates had more incidences of adverse effects like hypotension and bradycardia.[9,12] The patient group received dexmedetomidine significantly lowered the HR,SBP,DBP and MAP and also reduced the analgesic requirements and inhalational agents intra operatively than the group received the fentanyl. The incidence of the side effects like hypotension and bradycardia was minimal with the dexmedetomidine. The incidence of pruritus and bradycardia were also minimal with the fentanyl. Limitations of present study were small sample size, parameters such as cardiac output, systemic vascular resistance and serum catecholamine levels were not measured.

CONCLUSION

Intravenous premedication with infusion of dexmedetomidine 1mcg/kg over 10min as loading dose followed by 0.2mcg/kg/hr as maintenance dose still surgery is over in patients scheduled for elective laparoscopic procedures., may be recommended for better haemodynamic stability during perioperative period despite high cost.

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