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A Comparative Study of the Haemodynamic Changes with Dexmedetomidine Vs Fentanyl during Laparoscopic Cholecystectomies under General Anaesthesia

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Abstract:
Introduction: *For the conduct of general anaesthesia, an ideal induction agent and effective premedication required that is the one without any serious systemic perturbations. Dexmedetomidine & Fentanyl has been used for blunting the haemodynamic pressor responses during laryngoscopy and endotracheal intubation but its use for attenuating the haemodynamic responses during laparoscopy is limited.*
Aims & Objectives: *To assess the haemodynamic responses during laryngoscopy and tracheal intubation after premedication with Dexmedetomidine & fentanyl.To assess the haemodynamic responses associated with pneumoperitoneum after premedication and pneumoperitoneum with Dexmedetomidine & fentanyl.*
Results: *Haemodynamic parameters, Sp02 and EtCO2 were recorded immediately after ET tube insertion.Mean heart rate, systolic, diastolic and mean arterial blood pressures were increased in both groups but values in group-d were lower than group-f which was statistically significant($p<0.05$).*
Conclusion: *It can be asserted from this study that Dexmedetomidine is a good pre-anaesthetic medication and much better agent than Fentanyl in respect of haemodynamic stability. There are no serious side effects in this premedicating dose of both the drugs.*
Keywords: *dexmedetomedine, fentanyl,laproscopic surgeries, premedication, pneumoperitoneum.*

I. Introduction

Laparoscopic procedure allows endoscopic access to the peritoneal cavity after insufflations of a gas (CO_2) to create space between the anterior abdominal wall and the viscera. The choice of anesthetic technique for the upper abdominal laparoscopic surgery is mostly limited to general anaesthesia .

For the conduct of general anaesthesia, an ideal induction agent and effective premedication required that is the one without any serious systemic perturbations.

Different medications like opioids, lidocaine, β blockers, nitroglycerine, nitroprusside, α-2 agonists, calcium channel blockers and benzodiazepines are being used now to attenuate these haemodynamic responses.

Dexmedetomidine a novel α-2 agonist, attenuates sympathoadrenal responses to tracheal intubation and reduces the dose of thiopentone Sodium[8]. Various studies have shown that it attenuates the haemodynamic responses of laryngoscopy, intubation, and extubation and it has a beneficial sedative property.

Fentanyl a μ-opioid receptor pure agonist possesses a potent analgesic property with a rapid and a short duration of action[9]. Fentanyl has been used for blunting the haemodynamic pressor responses during laryngoscopy and endotracheal intubation but its use for attenuating the haemodynamic responses during laparoscopy is limited[9] .

With these considerations the present study was designed to observe the different actions (mainly in attenuating haemodynamic responses) of both the above mentioned agents as premedicants in cases of laparoscopic cholecystectomies.

II. Aims And Objectives

1. To assess the haemodynamic responses during laryngoscopy and tracheal intubation after premedication with dexmedetomidine.
2. To assess the haemodynamic responses during laryngoscopy and tracheal intubation after premedication with fentanyl.
3. To assess the haemodynamic responses associated with pneumoperitoneum after premedication with dexmedetomidine.
4. To assess the haemodynamic responses associated with pneumoperitoneum after premedication with fentanyl.
5. To compare between Fentanyl and dexmedetomidine for attenuation of haemodynamic responses to laryngoscopy , tracheal intubation , and pneumoperitoneum during laparoscopic cholecytectomy under general anaesthesia.

III. Materials and Methods

1. Study Area & Period:

Done at Guntur Medical college / Government general hospital, Guntur. within period between 2015-2016.

2.Study Technique

After getting the institutional ethical committee approval and obtaining the written informed consents in the consent forms, adults aged between 18 and 60 years of either sex, in ASA grade I and II, scheduled to undergo laparoscopic cholecystectomy under general anaesthesia with endotracheal intubation will be included in the study.

Patients with ASA grade 3 and 4 ,history of allergy to any of the study drugs ,history of hypertension, chronic obstructive pulmonary disease, uncontrolled diabetes mellitus, ischaemic heart disease, valvular heart disease, left ventricular failure and atrioventricular conduction defects,and patients receiving other alpha 2 agonists like clonidine and other opioids will be excluded from the study.Patients will be premedicated either 10ml of dexmedetomidine in saline(1mcg/kg) 15 min before induction or 10ml of fentanyl in saline(2mcg/kg) 10 min before induction .This was prepared in a drip chamber of infusion set (paediatric) and was administered over a period of 10 mins.

Patients will be induced with thiopentone sodium (5mg/kg). Endotracheal intubation will be facilitated with succinylcholine 1.5mg/kg. Anaesthesia will be maintained with 66% nitrous oxide in oxygen 0.5 to 1.5% sevoflurane and additional doses of vecuronium bromide. The tidal volume and the ventilator frequency will be adjusted and intermittent positive pressure ventilation (IPPV) will be continued by mechanical ventilator. Intra operative hydration will be maintained with Ringer's Lactate solution. Rescue drugs like atropine, epinephrine, Norepinephrine will be kept available.

Pneumoperitoneum will be created by insufflation with CO2 and the operation table will be tilted about 15 degree in Reverse Trendelenburg position. IAP will be kept below 15 mm Hg throughout the surgical procedure. All patients will receive 4 mg ondansetron intravenously before extubation.

Tracheal extubation will be performed with neostigmine (0.05mg/kg) and glycopyrrolate (0.01mg/kg).All patients will be monitored and heart rate, non invasive blood pressures (SBP, DBP, MAP) Sp02 and EtCO2 will be recorded perioperatively before induction, immediately after endotracheal intubation, before pneumoperitoneum, 15 and 30 minutes after pneumoperitoneum, after release of carbondioxide and after extubation. All data collected will be analysed statistically.

10.Plan For Statistical Analysis Of Data

Results would be summarised by usual descriptive measures such as mean and Standed Deviation for numerical variables and percentages for categorical variables. Haemodynamic parameters and other numerical variables would be compared between groups by student unpaired t-test and $p < 0.05$ would be considered statistically significant.

III. Observations And Results

The total number of patients of this study was sixty. These sixty patient were randomly divided into two groups, group D (n=30) and group F (n=30). The age of all the patients in this study was between 18 and 60 years

Table-1 : Age and weight distribution in both groups

	GROUP		P Value	Significance
	GROUP D	GROUP F		
	Mean ± Std. Deviation	Mean ± std. Deviation		
Age (years)	35.87 ± 10.44	37.07 ± 10.66	0.661	Not Significant
Body weight (Kgs)	53.2 ± 5.05	53.33 ± 5.24	0.920	Not Significant

P> 0.05 = NOT SIGNIFICANT

Gender

Distribution of patients according to gender in group- D and group- F.

Table-2 : Distribution of Gender

Gender	Group		Total	P Value	Significance
	Group D	Group F			
FEMALE	18(60)	15 (50)	33(55)	0.436	Not Significant
MALE	12(40)	15(50)	27(45)		
Total	30(100)	30(100)	60(100)		

Heart Rate

Mean± Standard Deviation of heart rate (beats per min) in Group-D and Group-F at different points of time.

Table-3 : Comparison of HR in both groups

	Group D	Group F		
	Mean ± Std. Deviation	Mean± Std. Deviation	P Value	Significance
Before Premedication	87.57 ± 5.41	87.07 ± 5.48	0.723	Not Significant
Before induction	81.07 ± 4.84	81.63 ± 4.82	0.651	Not significant
Immediately after ET Tube insertion	86.83 ± 4.26	92.83 ± 7.02	<0.001	Significant
Before Pneumoperitoneum	79.2 ± 3.15	81.87 ± 4.18	0.007	Significant
15 mins after Pneumoperitoneum	82.07 ± 2.79	86.37 ± 5.22	<0.001	Significant
30 mins after Pneumoperotoneum	83.57 ± 3	89.9 ± 5.24	<0.001	Significant
After Release of CO2	78.17 ± 2.39	82.53 ± 4.18	<0.001	Significant
After Extubation	86.63 ± 3.62	86.53 ± 4.89	0.929	Not Significant

p>0.05= NOT SIGNIFICANT

Table-3 showed (by using 'unpaired t test' and taking an alpha level of 5%) that there was no statistically significant difference of mean heart rate values between two groups (p>0.05) before premedication, before induction and after extubation. But, in other points of time there was significant difference between two groups (p>0.05) and heart rate was higher in Group-F.

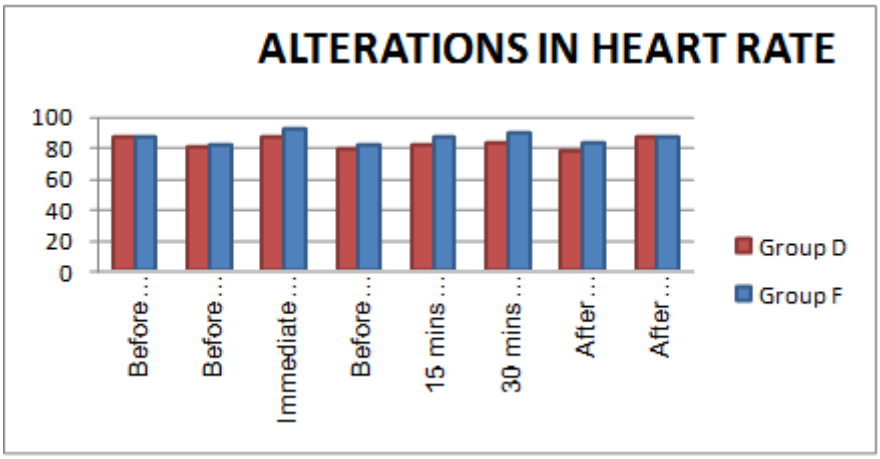

Fig : Bar Diagram showing alterations of Heart rate in both groups

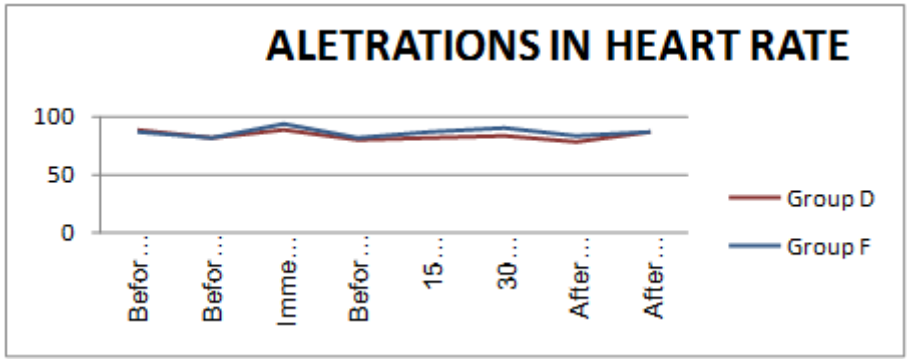

Fig : Line Diagram showing alterations of Heart rate in both groups

Systolic Blood Pressure

Mean ± Standard Deviation of Systolic Blood pressure (mmHg) in Group-D and Group –F at different points of time.

Table-4: Comparison of SBP in both groups

	GROUP D	**GROUP F**		
	Mean ± Std. Deviation	**Mean ± Std. Deviation**	**P value**	**Significance**
Before Premedication	123.2 ± 10.71	122.2 ± 10.16	0.712	Not Significant
Before Induction	112.5 ± 8.1	114.7 ± 9.03	0.325	Not Significant
Immediately after ET Tube insertion	133.37 ± 8.74	139.07 ±12.79	0.049	Significant
Before Pneumoperitoneum	113.23 ± 7.08	123.23 ± 9.06	<0.001	Significant
15 mins after Pneumoperitoneum	119.1 ± 5.77	128.83 ± 10.55	<0.001	Significant
30 mins after Pneumoperitoneum	122.9 ± 6.73	137.13 ± 11.5	<0.001	Significant
After Release of CO2	114.57 ± 5.75	123.6 ± 10.1	<0.001	Significant
After Extubation	129.87 ± 7.47	129.17 ± 6.79	0.706	Not Significant

p>0.05= NOT SIGNIFICANT

Table-4 showed that by using 'unpaired t test' and taking an alpha level of 5% there was no statistically significant difference of SBP values between two groups (p<0.05) before premedication, before induction and after extubation. But, in other points of time, there was significant difference between two groups (p<0.05) and SBP was higher in Group-F.

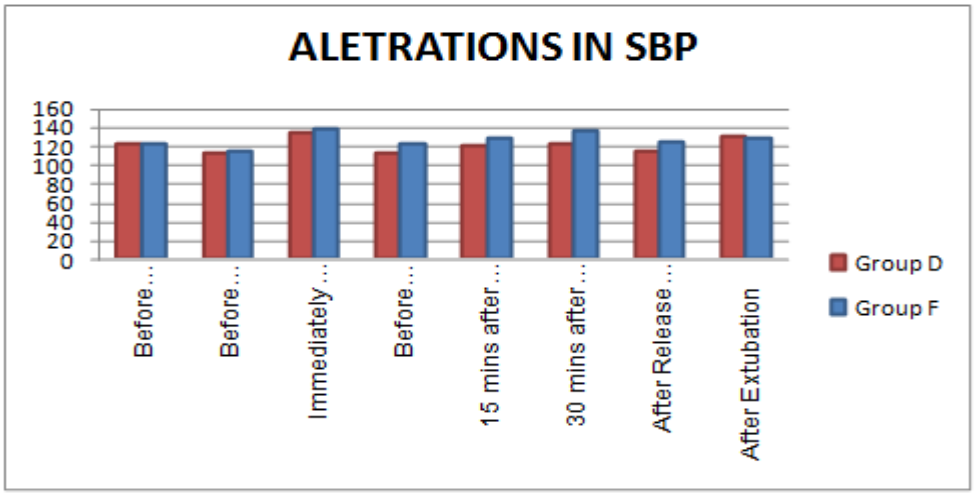

Fig: Bar Diagram showing alterations of SBP in both groups

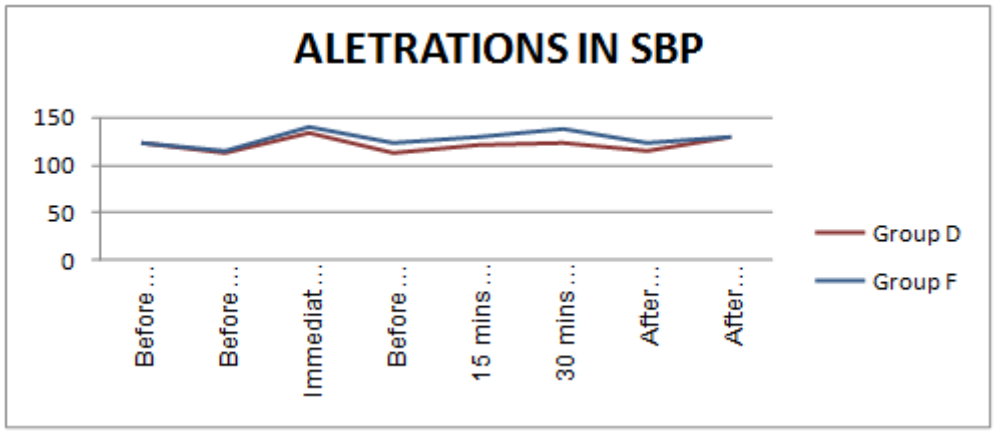

Fig: Line Diagram showing alterations of SBP in both groups

Diastolic Blood Pressure

Mean± Standard Deviation of Diastolic Blood Pressure (mmHg) in Group –D and Group – F at different points of time.

Table-5: Comparison of DBP in both groups

	Group D	GROUP F		
	Mean ± Std. Deviation	Mean ± Std. Deviation	P Value	Significance
Before Premedication	85.63 ± 4.41	84.9 ± 4.7	0.536	Not significant
Before induction	76.63 ± 4.45	77.43 ± 4.49	0.491	Not Significant
Immediately after ET Tube insertion	82.17 ± 4.65	92.3 ± 7.46	<0.001	Significant
Before Pneumoperitoneum	76.7 ± 3.64	78.87 ± 4.41	0.042	Significant
15 mins after Pneumoperitoneum	79.2 ± 3.63	83.57 ± 5.66	0.001	Significant
30 mins after Pneumoperotoneum	81.5 ± 3.25	87.67 ± 6.56	<0.001	Significant
After Release of CO2	77.03 ± 3.31	81.9 ± 4.77	<0.001	Significant
After Extubation	85.13 ± 4.27	84.53 ± 7.98	0.718	Not Significant

p>0.05= NOT SIGNIFICANT

Table-5 showed that by using 'unpaired t test' and taking an alpha level of 5% , there was no statistically significant difference of DBP values between two groups (p>0.05) before premedication and before induction. But, in other points of time, there was significant difference between two groups (p<0.05) and DBP was higher in Group –F.

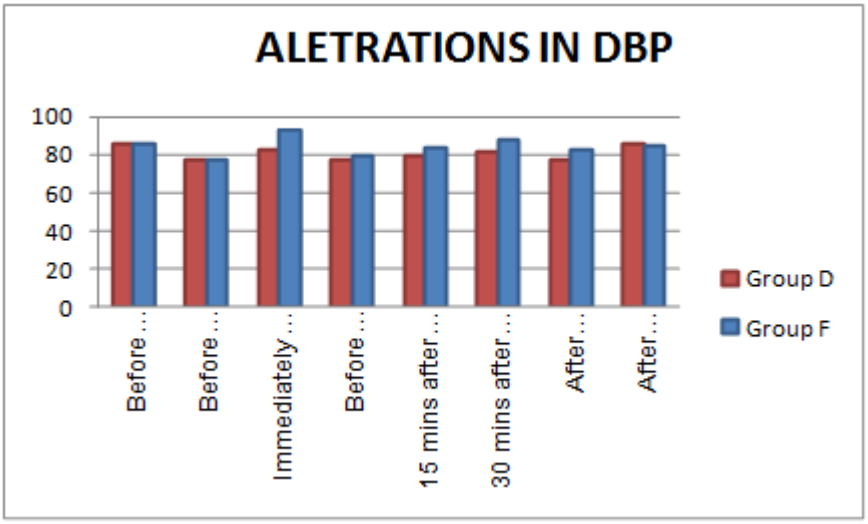

Fig: Bar Diagram showing alterations of DBP in both groups

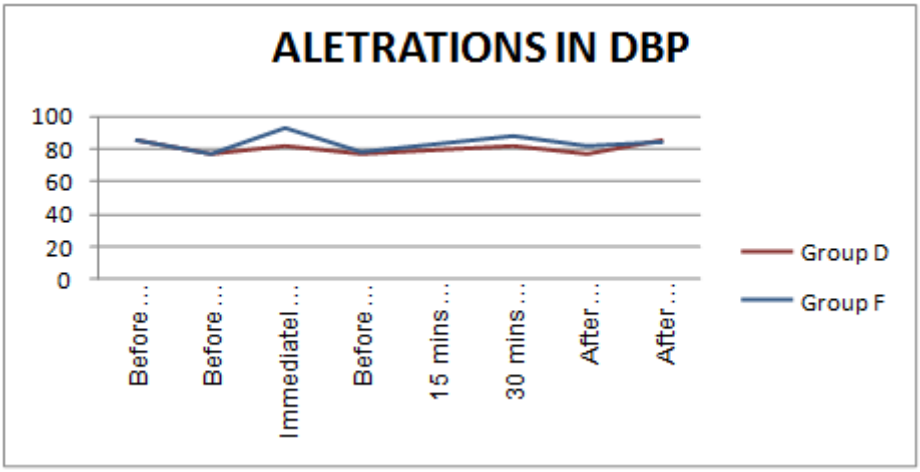

Fig: Line Diagram showing alterations of DBP in both groups

Mean Arterial Pressure

Mean ± Standard Deviation of Mean Arterial Pressure (mmHg) in Group –D and Group –F at different points of time.

Table-6: Comparison of MAP in both groups

	GROUP D	**GROUP F**		
	Mean ± Std. Deviation	**Mean ± Std. Deviation**	**P Value**	**Significance**
Before Premedication	95.87 ± 5.89	94.9 ± 6.29	0.542	Not Significant
Before induction	88.53 ± 5.44	89.8 ± 5.82	0.387	Not Significant
Immediately after ET Tube insertion	99.17 ± 5.81	107.83 ± 9.09	<0.001	Significant
Before Pneumoperitoneum	88.87 ± 4.49	93.67 ± 5.59	0.001	Significant
15 mins after Pneumoperitoneum	92.5 ± 4.23	98.6 ± 7.05	<0.001	Significant
30 mins after Pneumoperitoneum	95.33 ± 4.26	104.13 ± 7.99	<0.001	Significant
After Release of CO2	89.5 ± 3.93	95.83 ± 6.06	<0.001	Significant
After Extubation	100 ± 5.11	99.37 ± 6.57	0.679	Not Significant

p>0.05 = NOT SIGNIFICANT

Table -6 showed (by using 'unpaired t test' and taking an alpha level of 5%) that there was no statistically significant difference of MAP values between two groups (p>0.05) before premedication, before induction and after extubation. But, in other points of time there was significant difference between two groups (p<0.005) and MAP was higher in Group- F.

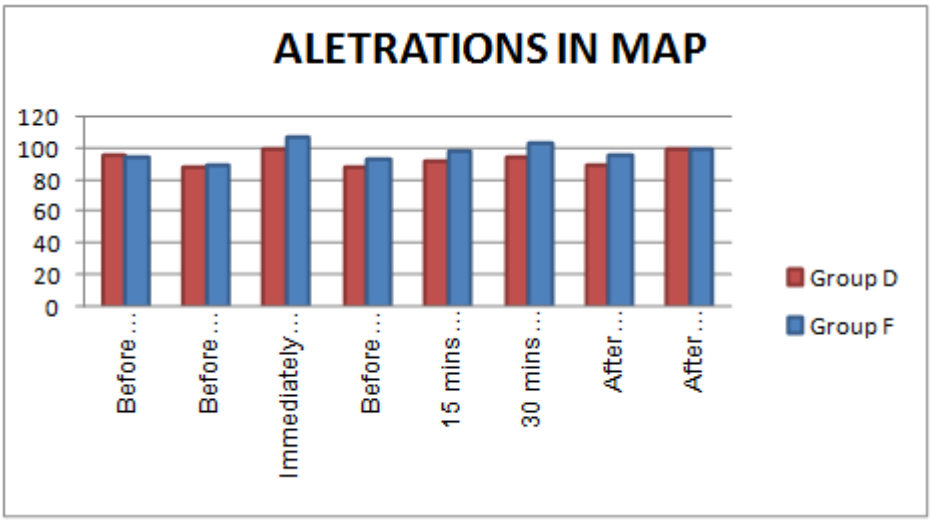

Fig: Bar Diagram showing alterations of MAP in both groups

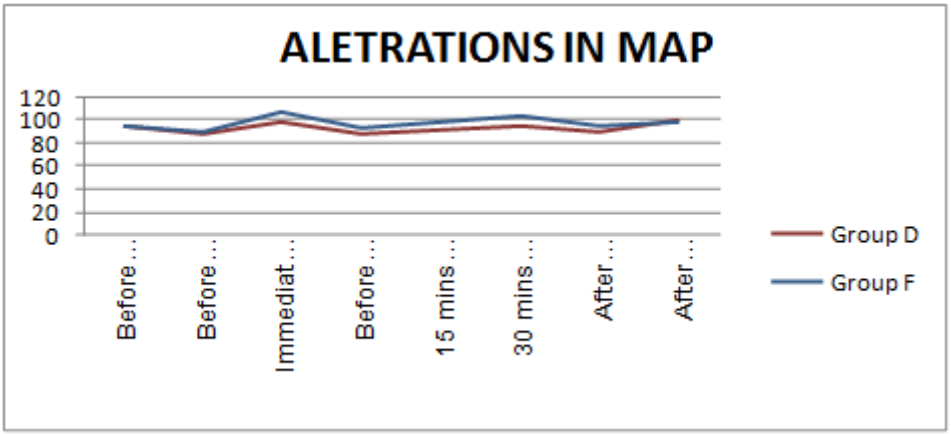

Fig: Line Diagram showing alterations of MAP in both groups

SPO_2

Mean + Standard Deviation of SpO2 in Group-D and Group-F at different points of time.

Table-7: Comparison of SPO_2 in both groups

	GROUP D	**GROUP F**		
	Mean ± Std. Deviation	**Mean ± Std. Deviation**	**P Value**	**Significance**
Before Premedication	98.07 ± 1.2	97.7 ± 1.34	0.270	Not Significant
Before induction	98.73 ± 0.74	98.47 ± 1.14	0.286	Not Significant
Immediately after ET Tube insertion	97.87 ± 0.82	98 ± 0.91	0.553	Not Significant
Before pneumoperitoneum	98 ± 0.74	97.83 ± 1.18	0.514	Not Significant
15 mins after Pneumoperitoneum	97.5 ± 0.82	97.97 ± 1.19	0.082	Not Significant
30 mins after pneumoperitoneum	98.77 ± 0.73	99.03 ± 1.19	0.299	Not Significant
After Release of CO_2	98 ± 0.74	98.13 ±1.22	0.612	Not Significant
After Extubation	97.87 ± 0.86	97.63 ± 1.25	0.402	Not Significant

p>0.05= NOT SIGNIFICANT

$Etco_2$

Mean ± standard Deviation of $EtCO_2$ in Group-D and Group- F at different points of time.

Table-8: Comparision of $EtCO_2$ in both groups

	GROUP D	**GROUP F**		
	Mean ± Std. Deviation	**Mean ± Std. Deviation**	**P Value**	**Signification**
Before Induction	31.3 ± 1.09	31.4 ± 1.55	0.773	Not Significant
Immediately After ET Tube Insertion	31.4 + 1.09	31.87 + 1.7	0.208	Not Significant
Before Pneumoperitoneum	31.37 + 0.96	32.07 + 1.82	0.068	Not Significant
15 Min After Pneumoperitoneum	33.13 + 0.9	32.63 + 1.61	0.143	Not Significant
30 Mins After Pneumoperitoneum	32.73 + 1.36	32.93 + 1.76	0.625	Not Significant
After Release Of CO2	32.5 + 1.08	32.63 + 1.77	0.726	Not Significant
After Extubation	32.77 + 1.04	33.23 + 2.1	0.279	Not Significant

p>0.05= NOT SIGNIFICANT

Table-8 showed (by using 'unpaired t test' and taking an alpha level of 5%) that there was no statistically significant difference of ETCO2 values (p>0.05) between two groups in different points of time.

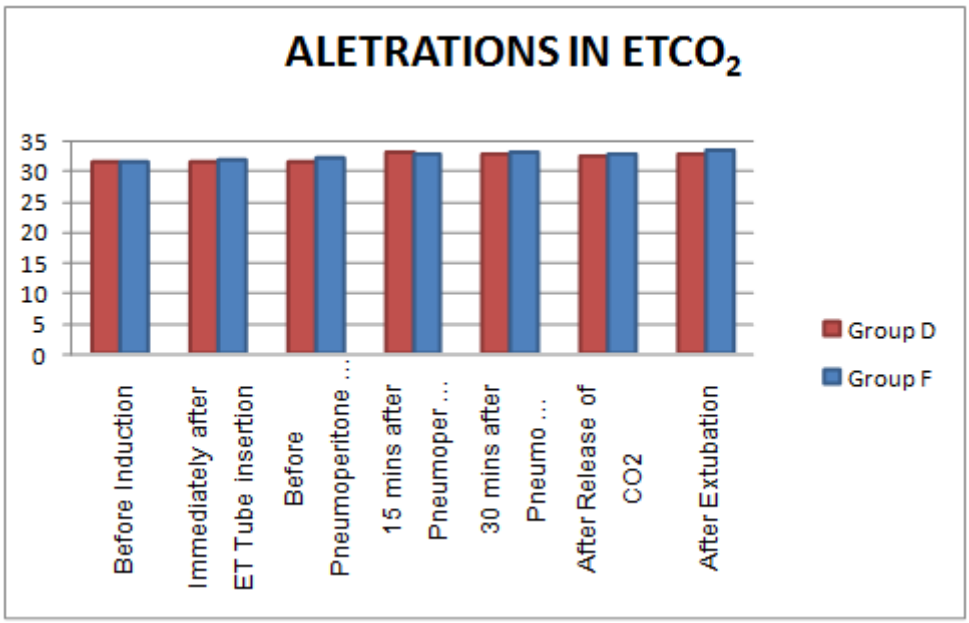

Fig: Bar Diagram showing alterations of $ETCO_2$ in both groups

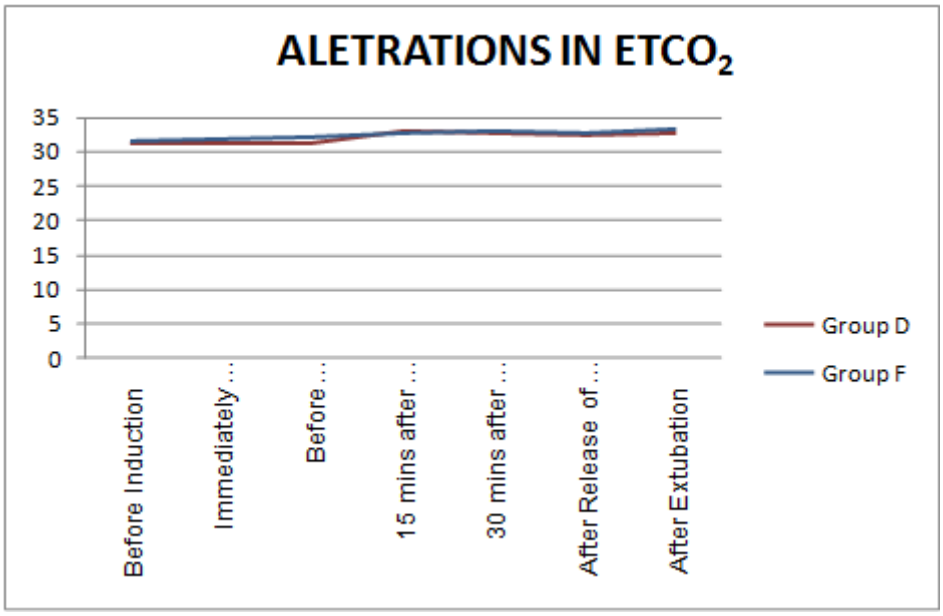

Fig1: Line Diagram showing alterations of $ETCO_2$ in both groups

IV. Discussion

Sixty ASA grade 1 and II patients of either sex, undergoing general anaesthesia were selected for this study after thorough pre-operative evaluation and taking informed consent. Age range of the patients was between 18 and 60 years.

Group D:- Patients received 10 ml of dexmedetomidine in saline (1 mcg/kg) 15 min before induction.

Group F:- Patients received 10 ml of fentanyl in saline(2mcg/kg) 10 min before induction

Mean age of the patients was 35.87 ± 10.44 years in group-D and 37.07 ± 10.66 years in group-F. Mean body weight of the patients in group-F was 53.33 ± 5.24 kgs and in group-D was 53.2 ± 5.05 kgs(Table-1). Group-F had 15 females (50%) and 15 males (50%) whereas group-D had 18 females (60.0%) and 12 males(40.0%). No statistically significant difference was observed in age, sex and body weight between two groups ($p>0.05$).

Mean heart rates in group-D and group-F were 87.57 ± 5.41 beats/minute and 87.07 ± 5.48 beats/minute respectively. Mean systolic blood pressure in group-D was 123.2 ± 10.71 mmHg and in group-F was 122.2 ± 10.16 mmHg. Mean diastolic blood pressure in group-D was 85.63 ± 4.41 mmHg and in group-F was 84.9 ± 4.7 mmHg. Mean arterial blood pressure in group-D was 95.87 ± 5.89 mmHg and in group-F was 94.9 ± 629 mmHg.

There was no statistically significant difference between the two groups regarding above mentioned haemodynamic parameters before premedication ($p>0.05$ in all cases).

Mean SpO_2 of group-D patients was 98.07 ± 1.2 and in group-F patients was 97.7 ± 1.34 , the difference between which was not statistically significant ($p>0.05$).

Systolic, diastolic blood pressures, mean arterial blood pressure, heart rate, Sp02 and EtCO2 (with mask ventilation during preoxygenation) were recorded as pre induction values. We observed that the differences in values between the two groups were not statistically significant ($p>0.05$).

During induction, patients were preoxygenated with 100% oxygen for 3 minutes and injection glycopyrrolate 0.2 mcg/kg iv was given at the same time. Patients were induced with thiopentone sodium (5mg/kg). Endotracheal intubation was facilitated with succinylcholine (1.5 mg/kg). Thiopentone sodium was selected for induction since it still continues to be the most popular agent for induction.

In normovolemic patients thiopentone sodium 5mg/kg i.v can transiently decrease 10-20mm Hg of blood pressure and increase the heart rate by 15-20 beats/min.[128] There is increase in catecholamine levels, both noradernaline and adrenaline[128.] Haemodynamic parameters, Sp02 and EtCO2 were recorded immediately after ET tube insertion.Mean heart rate, systolic, diastolic and mean arterial blood pressures were increased in both groups but values in group-D were lower than group-F which was statistically significant($p<0.05$).

These results were very similar to Vaibhav jain et al, who found that an intravenous infusion of dexmedetomidine at 1 µg/kg administered 10 min before laryngoscopy and endotracheal intubation can be recommended over fentanyl at 2 µg/kg to attenuate the sympathetic response to laryngoscopy and endotracheal

intubation with minimal side effects. Sagar et all,found that DEXMEDETOMIDINE when used as I.V. premedicant in dose of 0.6 µg/kg provides beneficial effect in attenuation of pressor response to laryngoscopy and endotracheal intubation as compare to FENTANYL in dose of 2 µg/kg.

The difference in Sp02 and EtCO2 between the two groups were not statistically significant ($p>0.05$).

Anaesthesia was maintained with 66% nitrous oxide in oxygen, 0.5-1.5% sevoflurane and additional doses of vecuronium bromide. Pneumoperitoneum was created by insufflations with CO2 and the operation table was tilted about 15 degree in reverse trendelenburg position. Intra abdominal pressure was kept below 15 mmHg throughout the surgical procedure. After completion of the surgical procedure, neuromuscular blockade was reversed by Inj neostigmine 0.05 mg/kg iv along with lnj glycopyrrolate 0.2 mg iv for each 1 mg of neostigmine .Patients were extubated after airway reflexes returned.

Haemodynamic parameters (HR,SBP,DBP,MAP), Sp02 and ETCO2 were recorded before pneumoperitoneum, 15 minutes after pneumoperitoneum, 30 minutes after pneumoperitoneum, after release of CO2 and after extubation . The values of mean heart rate, systolic, diastolic and mean arterial pressures were lower in group-D than group-F which were statistically significant but the differences in Sp02 and EtCO2 between the two groups were not statistically significant.

Ghodki et al[130] used dexmedetomidine 1 µg/kg intravenously over 15 min before induction followed by maintenance infusion of 0.2 µg/kg/h and observed favorable vasopressor response during laryngoscopy, with minimal change in BP with pneumoperitoneum. In the present study, a single dexmedetomidine bolus of 1 µg/kg was used before induction and similar hemodynamic control was noted.

We could trace three studies in the literature (Vaibhav jain et al,Sagar Gandhi et al, Bikramjit Das et al) comparing Dexmedetomidine with fentanyl regarding attenuation of haemodynamic response to laryngoscopy and tracheal intubation;which proved Dexmedetomidine is to be more effective.

But we found no literature on comparing Dexmedetomidine with fentanyl regarding attenuation of haemodynamic responses during laparoscopic cholecystectomy.i.e during creation and maintenance of pneumoperitoneum and immediately after extubation.

Supplemental oxygen was given to all patients after extubation till stabilization. In the present study, no patient in either group showed any peri-operative ECG abnormality (ST segment abnormality or others).

V. Conclusion

1. Haemodynamic stability is well maintained and the surge in blood pressures and heart rate during laryngoscopy, intubation, pneumoperitoneum are controlled well with dexmedetomidine except at the time of extubation because the effect of dexmedetomidine has already abated.
2 Fentanyl maintains haemodynamic stability during laryngoscopy and intubation, but is not as good as Dexmedetomidine ,and has no action at the time of pneumoperitoneum and extubation.
3. Both Dexmedetomidine and Fentanyl do not produce any side effects like change in Sp02, EtCO2 or ECG changes.

In conclusion ,it can be asserted from this study that Dexmedetomidine is a good pre-anaesthetic medication and much better agent than Fentanyl in respect of haemodynamic stability. There are no serious side effects in this premedicating dose of both the drugs.

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