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TO COMPARE THE EFFECTS OF DEXMEDETOMIDINE (WITHOUT BOLUS DOSE) AND PROPOFOL (SEDATIVE DOSE) ON ATTENUATION OF HEMODYNAMIC CHANGES DURING LAPAROSCOPIC SURGERIES

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Keywords:

Dexmedetomidine, Propofol, Laparoscopy surgeries, Hemodynamic changes

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ABSTRACT: Introduction: Laparoscopic surgery is one of the most important diagnostic and therapeutic tools in the present surgical era. Laparoscopic surgeries require insufflation of the abdomen with some gas; usually, Carbon Dioxide is called pneumoperitonium, which induces pathophysiologic changes that complicate anesthetic management. To prevent and counteract these effects, appropriate monitoring and pharmacological interventions are required. **Material and Method:** In an observational study, sixty (60) patients of ASA physical status I or II aged between 18-60 years of age, of either sex scheduled for elective laparoscopic surgeries under general anesthesia, were observed. Inj. Dexmedetomidine infusion and Inj. Propofol infusion started at a different dose. **Results:** Both the drugs maintain hemodynamic stability during laparoscopy but at the time of extubation propofol group showed rise in parameters while dexmedetomidine patients were calm. Dexmedetomidine without bolus, as infusion only does result in attenuation of hemodynamic responses. Omitting the bolus dose avoided the undesirable hemodynamic effects like bradycardia and hypotension. **Conclusion**: The infusions of a sedative dose of dexmedetomidine and propofol during laparoscopic surgery attenuate hemodynamic response to pneumoperitoneum and maintain hemodynamic stability. Dexmedetomidine can be used safely and effectively for attenuation of hemodynamic changes in laparoscopic surgeries and is very effective in the control of heart rate and systolic blood pressure changes.

INTRODUCTION: Laparoscopic surgery is one of the most important diagnostic and therapeutic tools in the present surgical era. Since 1987, when the first laparoscopic cholecystectomy was successfully performed by Phillipe Mouret, this has become the gold standard.

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The benefits of minimal access techniques include less pain, early mobilization, minimal scar and shorter hospital stay, which have further increased its applications [1].

This minimally invasive procedure requires pneumoperitonium for adequate visualization and operative manipulation. Laparoscopic surgeries require insufflation of the abdomen with some gas, usually, Carbon dioxide, called pneumoperitonium, which induces pathophysiologic changes that complicate anesthetic management. Pneumoperitonium affects several homeostatic systems leading to an alteration in acid-base balance, cardiovascular system, pulmonary physiology, and stress response. The extent of cardiovascular changes associated with pneumoperitonium includes an increase in mean arterial pressure, a decrease in cardiac output, an increase in systemic vascular resistance, which in turn, compromise tissue perfusion.

To prevent and counteract these effects, appropriate monitoring and pharmacological interventions are required. Such interventions include preloading with intravenous fluids, administration of general anesthesia with vasodilating anesthetics, direct vasodilators like Nitroglycerine [2], high doses of Opioids [3], infusion of Propofol, and centrally acting α2 agonists like Clonidine and Dexmedetomidine [4], Xylocard [5], oral Gabapentin [6].

The intervention may be associated with some undesirable side effects like sedation and respiratory depression with high dose opioids, raised cost with infusions of propofol or dexmedetomidine, tachycardia with nitroglycerine, *etc*.

The study is planned "To compare the effects of Dexmedetomidine (without bolus dose) and Propofol (sedative dose) on the attenuation of hemodynamic changes during laparoscopic surgeries."

Propofol is an alkyl phenol (2,6, diisoprop-pylphenol) and the most frequently used intravenous anesthetic agent. The most prominent effect of propofol is a decrease in systemic blood pressure associated with a decrease in cardiac output, stroke volume index, and systemic vascular resistance. It attenuates heart rate response to atropine and suppresses supraventricular tachycardia.

At sub-hypnotic doses, it has significant antiemetic property [7]. Thus, it is one of the most commonly used agents in laparoscopy for the purpose of control of hemodynamic changes.

Dexmedetomidine is a highly selective and potent α2 adrenergic agonist. Studies have shown that dexmedetomidine is 8 times more specific for α2 adrenoceptors than clonidine (ratios of α2:α1 activity, 1620:1 for dexmedetomidine, 220:1 for clonidine). Dexmedetomidine provides better perioperative hemodynamic stability than many agents now in use and may offer protection from ischemia due to the attenuated neuroendocrine response. Dexmedetomidine treated patients were more sedated at the time of arrival in the PACU, emerged more rapidly from anesthesia, required less volatile anesthetic to achieve hemodynamic endpoints, and had greater overall stability in the perioperative period with fewer episodes of tachycardia requiring intervention [8].

Dexmedetomidine being a novel agent, is not being used that often in laparoscopic surgeries, although it has a suitable pharmacological profile for the purpose of attenuation of hemodynamic changes.

So we have designed this study to compare Dexmedetomidine's effect on attenuation of hemodynamic response to laparoscopic surgeries with that of propofol.

MATERIALS AND METHODS: In this study, sixty (60) patients of ASA physical status I or II aged between 18-60 years of age, of either sex scheduled for elective laparoscopic surgeries under general anesthesia were observed and the observations were divided into two groups (each group containing 30 patients).

Group D: Inj. Dexmedetomidine 0.4 mcg/kg/hr was started immediately after intubation and was maintained between 0.2-0.7 mcg/kg/hr; infusion was stopped before 15-20 min to end of operation.

Group P: Inj. Propofol 50 mcg/kg/min IV was started immediately after intubation and was maintained between 25-75mcg/kg/min; infusion was stopped before 15-20 min to end of operation.

Exclusion Criteria: Patients with a history of significant respiratory, cardiovascular, renal diseases, history of allergy, psychiatric illness, and pregnancy were excluded from the study. Any surgery converted to open from laparoscopy was also excluded from the study.

Surgical Procedures Included: Surgeries like laparoscopic cholecystectomy, laparoscopic appen-dicectomy, laparoscopic hernioplasty, laparoscopic sleeve gastrectomy, and laparoscopic gastric bypass. Gynecological surgeries like laparoscopic ovarian cystectomy, laparoscopic-assisted vaginal hysterectomy, and total laparoscopic hysterectomy. Diagnostic laparoscopies were also included.

Study Site and Design: The study was conducted at Sterling hospital, Ahmedabad. This was a prospective observational study.

Study Period and Population: The study began from the ethical committee clearance date and continued till the end. Patients posted for elective laparoscopic surgery under general anesthesia at Sterling hospital, Ahmedabad, were included.

The study started after taking clearance from the scientific committee and the ethical committee of the institution. The pre-anesthetic assessment was done on the day before surgery, informed written consent was taken, basic routine investigations advised and noted:

Premedication: Vital data like Pulse, BP, ECG and SPO2 were recorded after shifting patient to the operating room and before giving premedication.

All the patients were given premedication in the form of:

1. Inj. Glycopyrollate - 0.004 mg/kg i.v.
2. Inj. Ondansetron - 0.08 mg/kg i.v.
3. Inj. Fentanyl - 2.0 mcg/kg i.v.

Technique: General Anesthesia

Group D: In this group, Inj. Dexmedetomidine 0.4mcg/kg/hr was initiated immediately after intubation, and maintained between 0.2-0.7 mcg/kg/hr. The rate of infusion was titrated accordingly to maintain HR >60/min and systolic blood pressure >90mmHg.

Group P: Inj. Propofol 50 mcg/kg/min IV infusion was started immediately after intubation and maintained between 25-75 mcg/kg/min titrated accordingly to maintain HR >60/min and systolic blood pressure >90mmHg.

Induction: All the patients of group D and group P were induced with

- Inj. Sodium thiopental 5– 7 mg/kg i.v.
- Inj. Succinylcholine 1.5-2 mg/kg i.v.

Securing Airway: All the patients were intubated with a cuffed endotracheal tube of appropriate size.

Maintenance: Patients of both the groups were maintained with O_2+N_2O+ Sevoflurane (1.5-2%) + Inj. Atracurium 0.4 to 0.5 mg/kg and maintenance dose of 0.08-0.10 mg/kg intermittently.

In the case of bradycardia HR <60, infusion of the drug was stopped, and bolus dose of inj. atropine 0.6 mg i.v. given.

In case of hypotension, mean BP <60 mm of Hg, drug infusion was stopped, the concentration of sevoflurane reduced, and bolus dose of inj mephentramine 5 mg was given. The rate of infusion of i.v. fluid was increased.

If hypotension persisted, infusion of colloid like Hydroxyethyl starch was to be started and 100-200 ml bolus to be given. If the need occurred, infusion of inj noradrenaline was planned to be started at 0.05mcg/kg/min, rate to be increased if required.

Monitoring: Heart Rate, blood pressure (systolic, diastolic, and mean), SPO2, and $ETCO_2$ recorded before premedication, after premedication, after intubation, and at regular intervals throughout the surgery.

The $ETCO_2$ was maintained between 35-40 mmHg.

In cases where $ETCO_2$ raised after insufflation of gas, the ventilatory settings were adjusted to hyperventilate and washout CO_2. The respiratory rate increased to 16-20/min. The tidal volume decreased according to change in respiratory rate, upto 6 ml/kg; so as not to alter the minute volume significantly.

Reversal:

- Inj. Glycopyrrolate 8 mcg/kg i.v.
- Inj. Neostigmine 0.05mg/kg i.v.

The patients were extubated after adequate reversal of muscle relaxant adjudged by adequate spontaneous breathing and limb movement, return of consciousness and obeying of verbal command.

The patients were then shifted to a postoperative recovery room for observation and further management.

Statistical Analysis: Observations were compared, and results were expressed as mean ± SD, for the purpose of statistical analysis values before premedication were considered as baseline.

Statistical analysis was carried out using ANOVA and repeated ANOVA tests. P-value <0.05 was considered as significant, and value <0.001 was considered as highly significant. Statistical analysis was performed with SOFTWARE EPI INFO 7.0 and SPSS 15.0 (Statistical Package for the Social Sciences).

OBSERVATION AND RESULTS: Sixty patients were observed and compared using an infusion of inj. Dexmedetomidine (Group D n=30) and inj. Propofol (Group P n=30) in laparoscopic surgeries for their efficacy in attenuating the hemodynamic changes related to these surgeries.

TABLE 1: DEMOGRAPHIC DATA

		Group P (N=30)	Group D (N=30)
Age (yrs.)	Range	18-60	18-60
	Mean ± SD	40.60±12.11	42.67±10.34
Sex	Male	15	14
	Female	15	16
Type of surgery	Diagnostic lap	2	3
	Lap Appendicectomy	7	3
	Lap Cholecystectomy	11	17
	Lap Gastric bypass	3	0
	Lap Ovarian cystectomy	1	1
	Lap Sleeve gastrectomy	5	4
	Lap Hernioplasty	0	2
	Lap Total hysterectomy	1	0

As shown in **Table 1,** both the groups were comparable regarding age and sex; the table also depicts the various surgeries included and the number of cases included of each type. During intraoperative period End-tidal CO_2 and SPO_2 were maintained in both groups.

TABLE 2: COMPARISON OF HEART RATE (HR)

Time Interval (min)	Mean Heart Rate(beats/min)++ Group P	Group D
Before premed	90±15	92 ±14
After premed	96±16	99±16
After intubation	107±15	105±16
3	105±16	101±15
5	100±14	97±14
10	96±12	95±13
15	94±12	94±13
30	90±11	91±12
45	86±10	87±10
60	83±10	84±11
75	81±8	82±9
90	79±9	80±10
105	81±8	79±7
120	77±7	76±6
135	75±8	71±6

++ All results rounded off to a nearest integer

Results for both the groups were obtained by ANOVA (Analysis of Variance) statistical test. The probability of this result assuming the null hypothesis is less than 0.0001 (highly significant).

The table shows the mean and standard deviation values of heart rate for each time interval of both the groups. As can be observed from the table, the heart rate rises abruptly after intubation in both groups; due to the hemodynamic response to laryngoscopy. The heart rates then follow a decreasing trend in both the groups soon after the respective drug infusions are started. The trend continues till the end of surgery. The validity of which is confirmed by ANOVA test with the probability of less than 0.0001 (highly significant). No bradycardia was observed.

The graphical representation of mean values for heart rate is as follows:

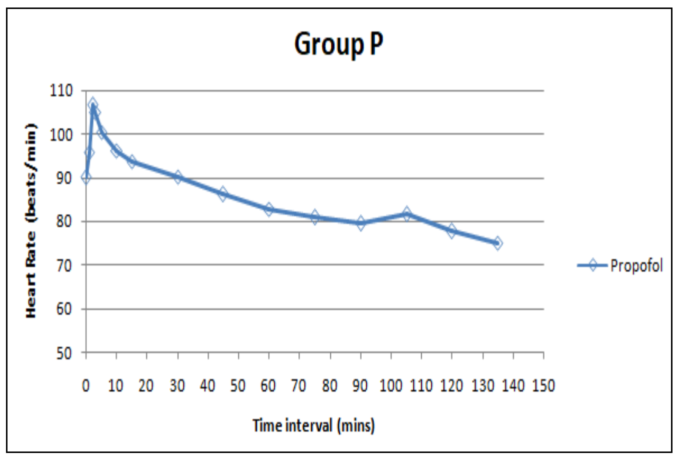

FIG. 1: GRAPH SHOWING MEAN HEART RATE (BEATS/MIN) AT DIFFERENT TIME INTERVALS (MINUTES) FOR GROUP P (PROPOFOL)

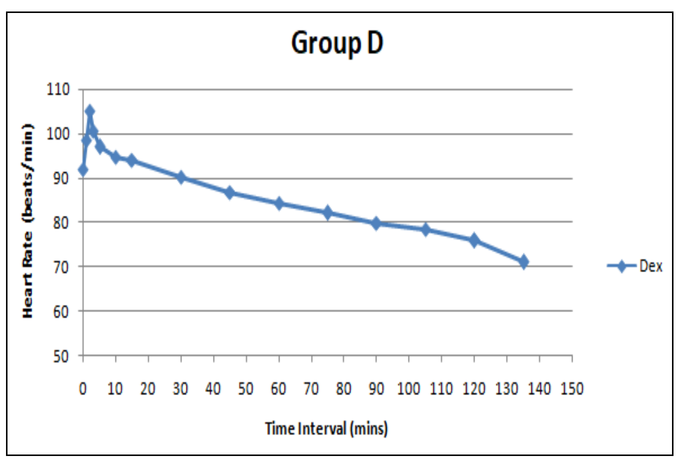

FIG. 2: GRAPH SHOWING MEAN HEART RATE (BEATS/MIN) AT DIFFERENT TIME INTERVAL (MINUTES) FOR GROUP D (DEXMEDETOMIDINE)

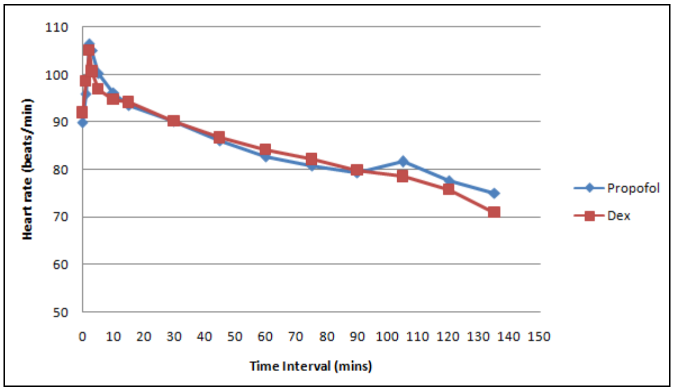

FIG. 3: GRAPH SHOWING MEAN OF HEART RATE (BEATS/MIN) AT DIFFERENT TIME INTERVALS (MIN) FOR BOTH THE GROUPS

From the above graph, one can conclude that initially, both the groups follow a similar trend, but after 75 minutes, group P has a continuous change in heart rate. In contrast, in group D, it is approximately stable.

So, finding statistically significant difference after 75 min using Repeated ANOVA statistical test we have

TABLE 3: COMPARISON OF DRUG EFFECT IN HEART RATE

Drug	Time interval (min)	p-value	Result	Interpretation
Group P	3-15	<0.001	S	Variability arises*
	15-45	<0.001	S	Variability arises
	45-75	<0.001	S	Variability arises
	75-135	0.194	NS	No Variability arises+
Group D	3-15	<0.001	S	Variability arises
	15-45	<0.001	S	Variability arises
	45-75	<0.001	S	Variability arises
	75-135	0.003	S	Variability arises

*: "variability arises" shows a change in heart rate is due to the effect of the drug

+: "no variability arises" shows a change in heart rate is not due to the drug

This table reinforces the interpretation from the graph of heart rate for both drugs that although both the drugs keep heart rate controlled, propofol is not as effective as dexmedetomidine in attenuating heart rate changes, especially after 75 minu.

This effect is observed as propofol is a short-acting drug; the effect is short-lived once the infusion is stopped; also, there is a change in heart rate due to reversal and extubation. This is in contrast to the effect of dexmedetomidine, which maintains heart rate on emergence from anesthesia even after stopping the infusion.

TABLE 4: COMPARISON OF SYSTOLIC BLOOD PRESSURE (SBP)

Time Interval (min)	Mean Systolic BP (mm Hg)++	
	Group P	Group D
Before premed	125±10	127±13
After premed	119±10	123±10
After intubation	136±11	148±13
3	131±10	133±9
5	125±8	124±9
10	122±8	122±7
15	120±6	120±11
30	117±6	117±8
45	114±6	114±8
60	113±5	111±7
75	111±6	110±9
90	110±5	111±11
105	112±5	108±6
120	114±5	107±4
135	113±5	104±2

++ All results rounded off to nearest integer

Results for both the groups were obtained by ANOVA (Analysis of Variance) statistical test. The probability of this result assuming the null hypothesis is less than 0.0001 (highly significant).

The table shows the mean and standard deviation values of systolic blood pressure for each time interval of both groups. As can be observed from the table, the systolic blood pressure rises sharply after intubation in both groups; due to the hemodynamic response to laryngoscopy. The systolic blood pressures then follow a decreasing trend in both the groups soon after the respective drug infusions are started. The trend continues till the end of surgery. The validity of which is confirmed by ANOVA test with the probability of less than 0.0001 (highly significant). No incidence of hypotension was observed.

The graphical representation of mean values for systolic blood pressures is as follows:

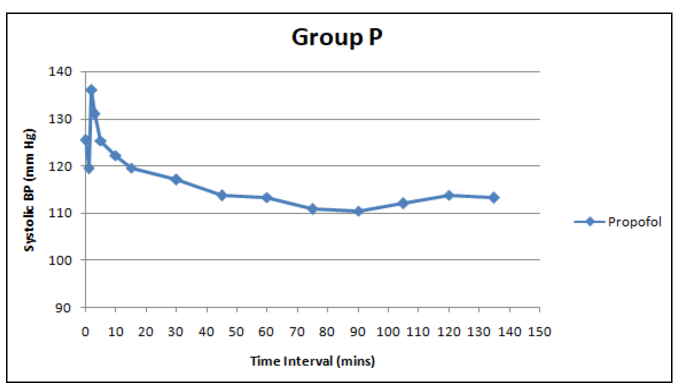

FIG. 4: GRAPH SHOWING MEAN SYSTOLIC BLOOD PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR THE GROUP P (PROPOFOL)

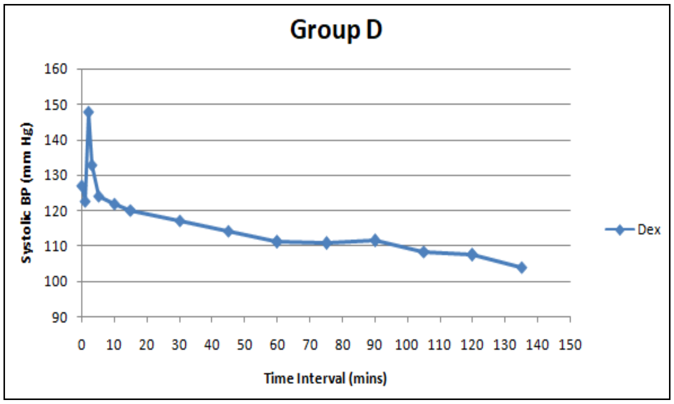

FIG. 5: GRAPH SHOWING MEAN SYSTOLIC BLOOD PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR THE GROUP D (DEXMEDETOMIDINE)

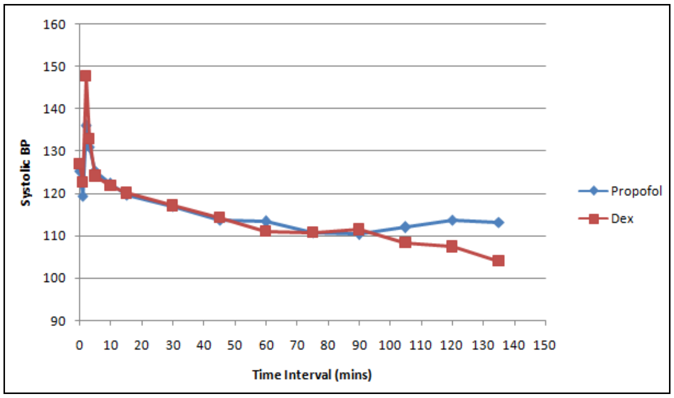

FIG. 6: GRAPH SHOWING MEAN SYSTOLIC BLOOD PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR BOTH THE GROUPS

From the above graph, one can conclude that initially, both the groups follow a similar trend, but after 75 min, group P has a continuous change in systolic blood pressure, whereas in group D it is approximately stable.

So once again, finding statistically significant difference after 75 min using Repeated ANOVA statistical test we have

TABLE 5: COMPARISON OF DRUG EFFECT IN SYSTOLIC BLOOD PRESSURE

Drug	Time interval (min)	p-value	Result	Interpretation
Group P	3-15	<0.001	S	Variability arises*
	15-45	<0.001	S	Variability arises
	45-75	<0.001	S	Variability arises
	75-135	0.535	NS	No Variability arises+
Group D	3-15	<0.001	S	Variability arises
	15-45	<0.001	S	Variability arises
	45-75	<0.001	S	Variability arises
	75-135	0.023	S	Variability arises

*: "variability arises" shows a change in systolic blood pressure is due to the effect of the drug
+: "no variability arises" shows a change in systolic blood pressure is not due to the drug

This table reinforces the interpretation from the graph of systolic blood pressure for both drugs that although both the drugs keep heart rate controlled, propofol is not as effective as dexmedetomidine in attenuating systolic blood pressure changes, especially after 75 min.

This effect is observed as propofol is a short-acting drug; the effect is short lived once the infusion is stopped; also, there is a change in systolic blood pressures due to reversal and extubation.

This is in contrast to the effect of dexmedetomidine, which maintains systolic pressure on emergence from anesthesia even after stopping the infusion.

TABLE 6: COMPARISON OF DIASTOLIC BLOOD PRESSURE (DBP)

Time Interval (min)	Mean Diastolic BP (mm Hg)++	
	Group P	Group D
Before premed	82±8	82±7
After premed	79±8	80±6
After intubation	91±9	99±6
3	87±9	90±6
5	84±8	82±5
10	82±6	80±5
15	81±6	80±9
30	77±5	77±6
45	76±6	76±6
60	75±4	74±6
75	73±6	73±6
90	73±5	73±7
105	75±7	72±4
120	77±6	71±4
135	76±9	69±3

++ All results rounded off to nearest integer

Results for both the groups were obtained by ANOVA (Analysis of Variance) statistical test. The probability of this result assuming the null hypothesis is less than 0.0001 (highly significant).

The table shows the mean and standard deviation values of diastolic blood pressure for each time interval of both groups. As can be observed from the table, the diastolic blood pressure rises suddenly after intubation in both groups; due to the hemodynamic response to laryngoscopy. The diastolic blood pressures then follow a decreasing trend in both the groups soon after the respective drug infusions are started. The trend continues till the end of surgery. The validity of which is confirmed by ANOVA test with the probability of less than 0.0001 (highly significant). No incidence of hypotension was observed.

The graphical representation of mean values for diastolic blood pressures is as follows:

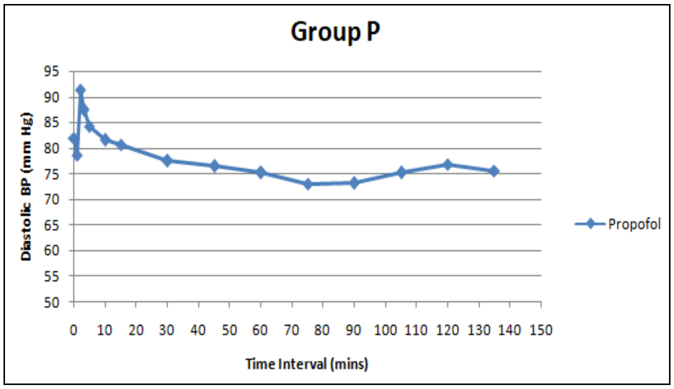

FIG. 7: GRAPH SHOWING MEAN DIASTOLIC BLOOD PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR THE GROUP P (PROPOFOL)

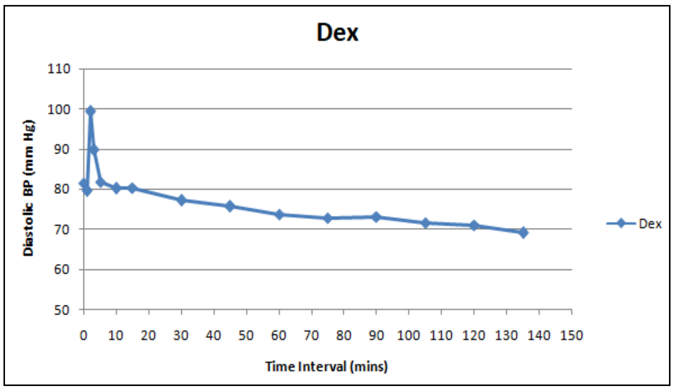

FIG. 8: GRAPH SHOWING MEAN DIASTOLIC BLOOD PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR THE GROUP D (DEXMEDETOMIDINE)

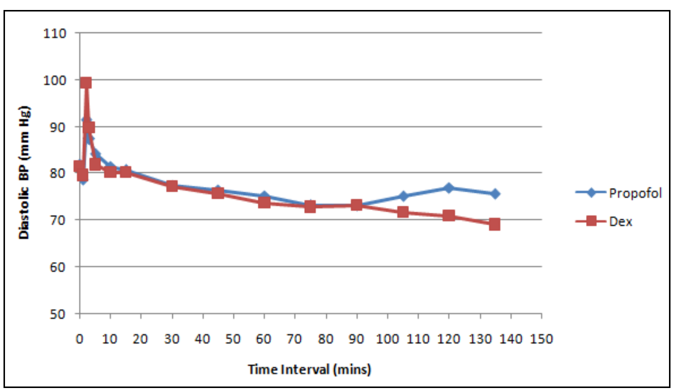

FIG. 9: GRAPH SHOWING MEAN DIASTOLIC BLOOD PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR BOTH THE GROUPS

From the above graph, one can conclude that initially, both the groups follow a similar trend of control and stability, but after 75 minutes, different trends in diastolic blood pressure are observed in the two groups.

Comparing the above findings using the Repeated ANOVA statistical test we have.

TABLE 7: COMPARISON OF DRUG EFFECT IN DIASTOLIC BLOOD PRESSURE

Drug	Time interval (min)	p-value	Result	Interpretation
Group P	3-15	<0.001	S	Variability arises*
	15-45	<0.001	S	Variability arises
	45-75	0.010	S	Variability arises
	75-135	0.438	NS	No Variability arises+
Group D	3-15	0.892	NS	No Variability arises
	15-45	<0.001	S	Variability arises
	45-75	<0.001	S	Variability arises
	75-135	0.001	S	Variability arises

*: "variability arises" shows a change in diastolic blood pressure is due to the effect of the drug

+: "no variability arises" shows a change in diastolic blood pressure is not due to the drug

This table reinforces the interpretation from the graph of diastolic blood pressure for both drugs, that both the drugs keep diastolic blood pressure controlled but towards the end, *i.e.*, after 75 min difference in effect is noted. However, the statistical analysis shows that the diastolic pressure values observed after 75 min are not due to the effect of the drug in both groups. This effect is due to hemodynamic changes associated with reversal and extubation. Also, it is worthwhile to note that even though the graph and mean values observed show the continued stabilizing effect of dexmedetomidine till the end, this could not be proved statistically for diastolic blood pressure values.

TABLE 8: COMPARISON OF MEAN ARTERIAL PRESSURE (MAP)

Time Interval (min)	Mean Arterial Pressure (mm Hg)++	
	Group P	Group D
Before premed	96±8	97±9
After premed	92±8	94±7
After intubation	106±9	115±7
3	102±9	104±6
5	98±7	96±5
10	95±6	94±5
15	94±5	94±9
30	91±5	90±6
45	89±6	89±6
60	88±4	86±6
75	86±6	85±7
90	86±5	86±8
105	87±6	84±4
120	89±6	83±4
135	88±7	80±3

++ All results rounded off to a nearest integer

Results for both the groups were obtained by ANOVA (Analysis of Variance) statistical test. The probability of this result assuming the null hypothesis is less than 0.0001 (highly significant).

The table shows the mean and standard deviation values of mean arterial pressure for each time interval of both groups. As can be observed from the table, the mean arterial pressure rises sharply after intubation in both groups; due to the hemodynamic response to laryngoscopy.

The mean arterial pressures then follow a decreasing trend in both the groups soon after the respective drug infusions are started. The trend continues till the end of surgery. The validity of which is confirmed by ANOVA test with the probability of less than 0.0001 (highly significant). No incidence of hypotension was observed.

The graphical representation of mean values for the mean arterial pressure is as follows:

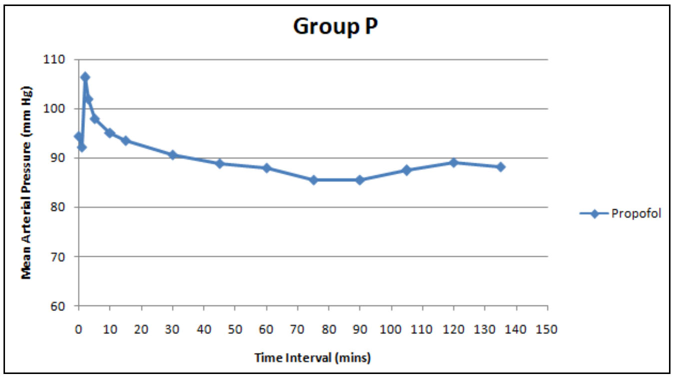

FIG. 10: GRAPH SHOWING MEAN ARTERIAL PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR THE GROUP P (PROPOFOL)

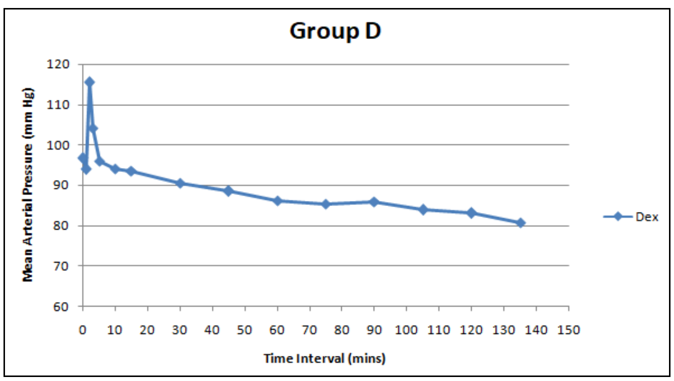

FIG. 11: GRAPH SHOWING MEAN ARTERIAL PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR THE GROUP D (DEXMEDETOMIDINE)

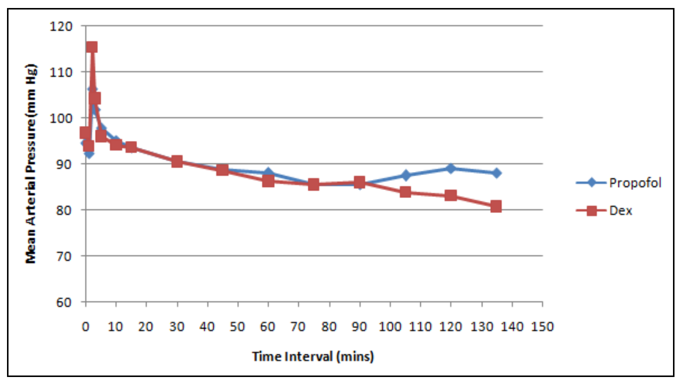

FIG. 12: GRAPH SHOWING MEAN ARTERIAL PRESSURE (mm OF Hg) AT DIFFERENT TIME INTERVALS (MIN) FOR BOTH THE GROUPS

TABLE 9: COMPARISON OF DRUG EFFECT IN MEAN ARTERIAL PRESSURE

Drug	Time interval (min)	p-value	Result	Interpretation
Group P	3-15	<0.001	S	Variability arises*
	15-45	<0.001	S	Variability arises
	45-75	0.001	S	Variability arises
	75-90	0.001	S	Variability arises
	90-135	0.434	NS	No Variability arises+
Group D	3-15	<0.001	S	Variability arises
	15-45	<0.001	S	Variability arises
	45-75	<0.001	S	Variability arises
	75-135	0.666	NS	No Variability arises
	135-180	0.193	NS	No Variability arises

*: "variability arises" shows change in mean arterial pressure is due to the effect of drug
+: "no variability arises" shows change in mean arterial pressure is not due to the drug

From the above graph, one can conclude that initially, both the groups follow a similar trend of control and stability, but after 75 min, different trends in mean arterial pressure are observed in the two groups.

Comparing the above findings using the Repeated ANOVA statistical test, we have.

This table reinforces the interpretation from the graph of mean arterial pressure for both drugs that both the drugs keep mean arterial pressure controlled but towards the end *i.e.*, after 75 min difference in effect is noted.

However, the statistical analysis shows that after 90 min, the mean arterial pressure values observed are not due to the effect of the drug in group P whereas in group D mean arterial pressure values are not due to drug effect earlier than group P, *i.e.*, after 75 min. This effect is due to hemodynamic changes associated with reversal and extubation. Also, it is worthwhile to note that even though the graph and mean values observed show the continued stabilizing effect of dexmedetomidine till the end, this could not be proved statistically for mean arterial pressure values.

No any bradycardia, hypotension, or any other significant side effect were observed during our study.

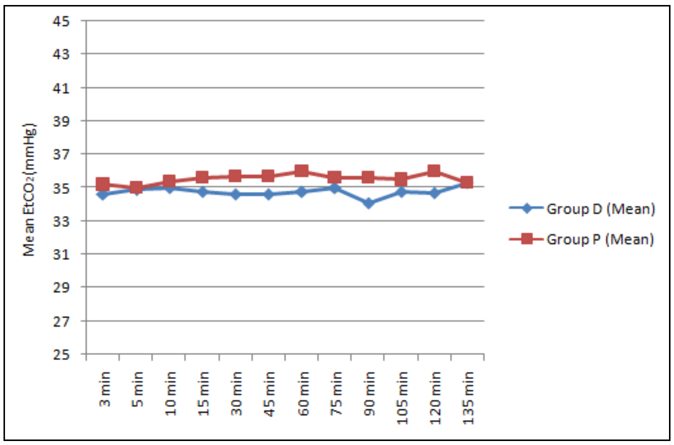

FIG. 13: GRAPH SHOWING MEAN END TIDAL CARBON DIOXIDE ($EtCO_2$) IN BOTH GROUPS DURING INTRA-OPERATIVE PERIOD

The graph shows that there was no significant change in mean end-tidal carbon dioxide ($EtCO_2$) in both groups during the intra-operative period.

DISCUSSION: In laparoscopic surgery, CO_2 is routinely used to create pneumoperitoneum and elevation of intra-abdominal pressure with raised diaphragm causes various adverse effects on the cardiovascular system. Plasma levels of catecholamines and vasopressin are increased immediately after pneumoperitoneum. Increased catecholamine level activates the renin-angiotensin-aldosterone system (RAAS), leading to characteristic hemodynamic alterations such as decreased cardiac output, elevated arterial pressure and increased systemic and pulmonary vascular resistance [29].

Patients with normal hearts can cope with these changes, but patients with compromised cardiac function may not be able to tolerate the hemodynamic changes. Various drugs have been used to attenuate the hemodynamic responses to pneumoperitoneum during laparoscopic surgery. Beta-adrenergic blocking agents like esmolol and $alpha_2$ agonists like clonidine and dexmedetomidine [4] have been used to attenuate the rise in MAP and HR. In our study, we compared dexmedetomidine and propofol for attenuation of cardiovascular responses in laparoscopic surgery.

Dexmedetomidine, a highly selective alpha 2 agonist, has significant sympatholytic and hemodynamic stability.

Dexmedetomidine provides better perioperative hemodynamic stability than many agents now in use and may offer protection from ischemia due to the attenuated neuroendocrine response. Dexmedetomidine treated patients were more sedated at the time of arrival in the PACU, emerged more rapidly from anesthesia, required less volatile anesthetic to achieve hemodynamic endpoints, and had greater overall stability in the perioperative period with fewer episodes of tachycardia requiring intervention [8].

Dexmedetomidine being a novel agent, is not being used that often in laparoscopic surgeries, although it has a suitable pharmacological profile to attenuate hemodynamic changes.

Propofol is an alkyl phenol (2,6, diisopropylphenol) and the most frequently used intravenous anesthetic agent.

The most prominent effect of propofol is decrease in systemic blood pressure associated with decrease in cardiac output, stroke volume index, and systemic vascular resistance.

It attenuates heart rate response to atropine and suppresses supraventricular tachycardia.

Thus it is one of the most commonly used agents in laparoscopy for the purpose of control of hemodynamic changes.

Thus we conducted this study to compare the effects of the two drugs regarding hemodynamic changes in laparoscopic surgeries. Our aim was to study the attenuating effect of dexmedetomidine and propofol for heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure during laparoscopic surgery. Infusion of dexmedetomidine and propofol was started after intubation and maintained throughout the surgery and stopped before 15-20 min to end of operation.

The study began after clearance from the scientific committee and ethical committee of the institution. A total of sixty patients undergoing laparoscopic surgeries in our hospital were observed after taking written and informed consent and the results obtained were compared for the purpose of this study. As mentioned earlier, patients were divided into two groups; both groups were comparable demographically. Hemodynamic parameters *viz*. heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial blood pressure were observed at regular intervals.

SPO_2 and $ETCO_2$ were also observed, and both remained in the normal, acceptable range throughout the observation period for all patients. No, any hypoxia or hypercarbia was noted. Also, during the intraoperative period, End-tidal CO_2 and SPO_2 were maintained in both groups. There was no significant change between the two groups

We observed that all the hemodynamic constants were raised significantly after intubation in both the groups; due to the hemodynamic response to laryngoscopy. The hemodynamic parameters then followed a decreasing trend in both the groups soon after the respective drug infusions are started. The trend continued till the end of surgery. No incidence of bradycardia, hypotension, or any other side effect was observed.

However, differences, in the end, were observed, as follows

1. Heart Rate and Systolic Blood Pressure: Both the drugs keep heart rate and systolic blood pressure under control, but propofol is not as effective as dexmedetomidine in attenuating heart rate and systolic blood pressure changes, especially after 75 min.

This was observed as propofol is a short-acting drug, and so the effect was short-lived once the infusion was stopped also, there is a change in heart rate and systolic blood pressure due to hemodynamic response of reversal and extubation. This was in contrast to the effect of dexmedetomidine, which maintained heart rate and systolic blood pressure on emergence from anesthesia even after stopping the infusion.

2. Diastolic Blood Pressure: Both the drugs keep diastolic blood pressure control, but towards the end, i.e., after 75 min difference in effect was noted, but statistics showed that the diastolic pressure values observed after 75 min were not due to the effect of the drug, in both the groups. This might have been the effect of hemodynamic changes associated with reversal and extubation. Also, it is worthwhile to note that even though the graph and mean values observed show the continued stabilizing effect of dexmedetomidine till the end, this could not be proved statistically for diastolic blood pressure values.

3. Mean Arterial Pressure: Both the drugs keep mean arterial pressure controlled but towards the end *i.e.,* after 75 min difference in effect was noted due to the hemodynamic changes associated with reversal and extubation. Although the graph and mean values observed show the continued stabilizing effect of dexmedetomidine till the end, this could not be proved statistically for mean arterial pressure values as well.

Thus, we can say that both the drugs maintain hemodynamic stability during laparoscopy but at the time of extubation propofol group showed a rise in parameters while dexmedetomidine patients were calm. Heart rate and systolic blood pressure statistical analysis support this finding. This attenuating effect of dexmedetomidine at extubation could not be proved statistically for diastolic blood pressure and mean arterial pressure.

A lot of studies have been conducted on these two drugs and their hemodynamic effects. Our findings are corroborative with earlier studies.

Yao XH [11,] in his study on " The effects of propofol target-controlled infusion (TCI) and sevoflurane inhalational anesthesia on the hemodynamics and postoperative recovery in patients undergoing laparoscopic cholecystectomy," concluded that Propofol TCI and sevoflurane inhalational anesthesia, both are effective in inducing good anesthetic effect, maintaining hemodynamic stability and ensuring rapid recovery in operations such as laparoscopic cholecystectomy. Our study supports his finding that propofol infusion helps in maintaining hemodynamic stability, and we also found that its effect is comparable to dexmedetomidine in attenuating hemodynamic changes in laparoscopic surgeries.

Juckenhöfel S, Feisel C, Schmitt HJ and Biedler A[12] designed a study to investigate the differences between TIVA with propofol/remifentanil (P/R) and balanced anesthesia with sevoflurane/fentanyl (S/F) in gynecological laparoscopic surgery. During maintenance of anesthesia, heart rate in patients with S/F was significantly higher (P/R:HR max +16/-10; S/F:HR max +24/-0.). They concluded that compared with patients given balanced anesthesia with sevoflurane and fentanyl, TIVA with propofol and remifentanil proved to be particularly suited for gynecological laparoscopic surgery. Its major advantages are hemodynamic stability, significantly shorter times of emergence, and exceptional acceptance by the patients. In our study, also the heart rate is controlled by use of propofol, and hemodynamic stability also is observed.

Erk G. *et al.*, [13] compared anesthesia efficacy between target controlled propofol infusion (TCI) and sevoflurane inhalational anesthesia in laparoscopic cholecystectomy. Both groups were effective in inducing good anesthetic effect, maintaining hemodynamic stability, and ensuring rapid recovery. In our study, also propofol helps in maintaining hemodynamic stability.

Like Alka Shah and R N Adaroja [14] found that heart rate and blood pressure decreased more in propofol group compared to sevoflurane group, but patients were heamodyanamic stable in both groups; in their study of fifty patients. We also found that the use of propofol causes significant lowering of heart rate and blood pressure, but in our study, the effect of propofol was not greater than other groups, *i.e.*, dexmedetomidine. In our study, also, both groups were hemodynamically stable.

Tanskanen PE, Kyttä JV, Randell TT, and Aantaa RE [15] studied Dexmedetomidine as an anaesthetic adjuvant in patients undergoing intracranial tumor surgery: in a double-blind, randomized, and placebo-controlled study. Fifty-four patients scheduled for elective surgery of supratentorial brain tumor were randomized to receive in a double-blind manner a continuous DEX infusion (plasma target concentration 0.2 or 0.4 ng ml(-1)) or placebo, beginning 20 min before anesthesia and continuing until the start of skin closure. They found that the median percentage of time points when systolic blood pressure was within more or less than 20% of the intraoperative mean was 72, 77, and 85, respectively (P<0.01), DEX-0.4 group differed significantly from the other groups. DEX-0.4 group differed in the heart rate variability from placebo (93 *vs.* 82%, P<0.01). Their conclusion was that DEX increased perioperative hemodynamic stability in patients undergoing brain tumor surgery.

Likewise, we also found that using dexmedetomidine increased perioperative stability.

Turgut N *et al.*, [17] in their study “To show the effects of Dexmedetomidine on perioperative hemodynamics, propofol consumption, and postoperative recovery when used for general anesthesia in patients undergoing spinal laminectomy” concluded that propofol-dexmedetomidine is suitable for patients undergoing elective spinal laminectomy and provides stable perioperative hemodynamic responses. Our study supports their findings.

De La Mora-González JF [19] conducted the study “Hemodynamic effects of dexmedetomidine--fentanyl *vs.* nalbuphine--propofol in plastic surgery” on sixty patients. The patients were divided into two parallel groups. A group received dexmedetomidine-fentanyl, and the comparison group received nalbuphine--propofol, both with same dose of midazolam. They found that in both groups, hemodynamic constants decreased intra-operatively. Dexmedetomidine--fentanyl decreased more than in the nalbuphine--propofol (systolic blood pressure, p = 0.006; diastolic blood pressure, p = 0.01 and heart rate, p = 0.007). They concluded that Dexmedetomidine shows the same cardiovascular stability but with the absence of respiratory depression. In our study also hemodynamic constants decreased intraoperatively in both the groups, and dexmedetomidine was found to be more effective in attenuating hemodynamic changes.

El-Tahan MR *et al.*,[21)] studied "Efficacy of dexmedetomidine in suppressing cardiovascular and hormonal responses to general anesthesia for caesarean delivery: a dose-response study." 68 parturients scheduled for elective caesarean delivery under general anesthesia were randomly allocated to receive either placebo, or 0.2, 0.4 or 0.6 µg/kg/h intravenous dexmedetomidine (n=17 per group) 20 min before induction. They found that after induction, patients receiving dexmedetomidine had smaller increases in heart rate (P<0.001) than those in the placebo group. Patients who received 0.4 and 0.6 µg/kg/h infusions of dexmedetomidine showed slower heart rates (-21.5% and -36%, respectively; P<0.001), lower mean blood pressures (-17% and -25%, respectively; P<0.001) and higher sedation scores for the first 15 min after extubation and greater uterine tone (P<0.002).

Their conclusion was that the preoperative administration of dexmedetomidine 0.4 and 0.6 µg/kg/h is effective in attenuating the maternal hemodynamic and hormonal responses to caesarean delivery under sevoflurane anesthesia without adverse neonatal effects. In this study bolus of dexmedetomidine was not used, and the direct infusion was started, we adopted the same approach in our study and observed a similar result that is administering the drug without bolus, as infusion only does result in attenuation of hemodynamic responses. Also, dexmedetomidine proved to be more effective in comparison to propofol.

Ickeringill M *et al.,*[23] investigated the hemodynamic effects and the efficacy of a continuous infusion of dexmedetomidine without a loading dose in 50 patients having had cardiac surgery (n = 33), complex major surgery (n = 9) and multiple trauma (n = 8). Dexmedetomidine was commenced at an initial rate of 0.2 to 0.4 microg/kg/h (depending on whether anesthetic or sedative agents had already been used), and rescue analgesia and sedation were administered with morphine and midazolam, respectively. Dexmedetomidine was an effective sedative and analgesic in this group of complex surgical and trauma patients with pronounced benefit in the cardiac surgery group. Omitting the loading dose avoided undesirable hemodynamic effects without compromising sedation and analgesia.

Our study strongly supports the finding of this study, as we also omitted the loading dose of dexmedetomidine, and no bradycardia or hypotension was observed.

Bakhamees HS and colleagues[25] evaluated the effect of dexmedetomidine on anesthetic requirements during surgery, hemodynamic, recovery profile, and morphine use in the postoperative period. Eighty adult patients scheduled for elective laparoscopic Roux-en-Y gastric bypass surgery were randomly assigned to one of two study groups; Group D (40 patients) received dexmedetomidine (0.8-microg/kg bolus, 0,4 microg kg^{-1}) h) and Group P (40 patients) received normal saline (placebo) in the same volume and rate. Patients who received dexmedetomidine showed significant decrease of intraoperative and postoperative mean blood pressure, heart rate. They concluded that the intraoperative infusion of dexmedetomidine decreased the total amount of propofol and fentanyl required to maintain anesthesia, offered better control of intraoperative and postoperative hemodynamics, decreased postoperative pain level, decreased the total amount of morphine used and showed a better recovery profile compared with placebo. Our study corroborates with their finding of a decrease in intraoperative mean blood pressure and heart rate with the use of dexmedetomidine.

Tufanogullari B *et al.*,[26] designed a prospective, randomized, double-blind, and placebo-controlled dose-ranging study to evaluate the effect of Dexmedetomidine on both early and late recovery after laparoscopic bariatric surgery. Eighty consenting ASA II-III morbidly obese patients were randomly assigned to 1 of 4 treatment groups: (1) control group received a saline infusion during surgery, (2) Dex 0.2 group received an infusion of 0.2 microg x kg(-1) x h(-1) IV, (3) Dex 0.4 group received an infusion of 0.4 microg x kg(-1) x h(-1) IV, and (4) Dex 0.8 group received an infusion of 0.8 microg x kg(-1) x h(-1) IV. Although the intraoperative hemodynamic values were similar in the four groups, arterial blood pressure values were significantly reduced in the Dex 0.2, 0.4, and 0.8 groups compared with the control group on admission to the postanesthesia care unit (PACU) (P < 0.05). They concluded that adjunctive use of an intraoperative Dex infusion (0.2-0.8 microg x kg($^{-1}$) x h($^{-1}$)) decreased fentanyl use, antiemetic therapy, and the length of stay in the PACU. When used during bariatric surgery, a dexmedetomidine infusion rate of 0.2 microg x kg($^{-1}$) x h($^{-1}$) is recommended to minimize the risk of adverse cardiovascular side effects. We also found that using dexmedetomidine infusion in low dose minimized the adverse cardiac events but attenuation of hemodynamic changes was adequate.

Poonam S Ghodki, Shailini K Thombre, Shalini P Sardesai, and Kalpana D Harnagle [28] studied dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery by entropy monitoring. They found 62.5% reduction in the induction dose of propofol was observed in dexmedetomidine group. They found Dexmedetomidine is a good anesthetic adjuant that decreases the requirement of anesthetics and opioids, attenuates sympatho-adrenal response, and maintains the stable hemodynamic and adequate depth of anesthesia. Our study supports their findings as we also observed that dexmedetomidine not only attenuated the cardiovascular changes associated with laparoscopy but also maintained the hemodynamic stability.

To conclude, different agents have been tried to minimize stress response of laparoscopic surgery with hemodynamic stability. Our study shows that infusions of a sedative dose of propofol a duringnd dexmedetomidine in low dose during laparoscopic surgery attenuate hemodynamic response to pneumoperitonium and maintain hemodynamic stability. We were able to demonstrate that administering the drug dexmedetomidine without bolus, as infusion only does result in attenuation of hemodynamic responses. Also, omitting the bolus dose avoided the undesirable hemodynamic effects like bradycardia and hypotension. The drug dexmedetomidine (Group D) in the dose 0.2-0.7mcg/kg/hr proved to be a better agent considering the hemodynamic stability it provided especially at extubation even after the infusion was stopped as compared to Propofol (Group P) in the dose of 25-75mcg/kg/min where also hemodynamic stability was observed but effect ended soon after the drug infusion was stopped. Dexmedetomidine in the above-mentioned dose can be used safely and effectively for attenuation of hemodynamic changes in laparoscopic surgeries and is very effective in the control of heart rate and systolic blood pressure changes.

CONCLUSION: The infusions of a sedative dose of dexmedetomidine and propofol during laparoscopic surgery attenuate hemodynamic response to pneumoperitonium and maintain hemodynamic stability. We were able to demonstrate that administering the drug dexmedetomidine without bolus, as infusion only does result in attenuation of hemodynamic responses. Also, omitting the bolus dose avoided the undesirable hemodynamic effects like bradycardia and hypotension. The drug dexmedetomidine (Group D) in the dose 0.2-0.7mcg/kg/hr proved to be a better agent considering the hemodynamic stability it provided especially at extubation even after the infusion was stopped as compared to Propofol (Group P) in the dose of 25-75 mcg/kg/min where also hemodynamic stability was observed but effect ended soon after the drug infusion was stopped. Dexmedetomidine in the above-mentioned dose can be used safely and effectively for attenuation of hemodynamic changes in laparoscopic surgeries and is very effective in the control of heart rate and systolic blood pressure changes.

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