

Original Research

A comparative study of intravenous dexmedetomidine v/s intravenous fentanyl for attenuation of hemodynamic responses to laryngoscopy and endotracheal intubation and following formation of pneumoperitoneum in laparoscopic elective abdominal surgeries under general anesthesia

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ABSTRACT

Background: The stress response to laryngoscopy and endotracheal intubation is a significant concern for anesthesiologists. Various medications have been used to attenuate this response, but none have achieved full effectiveness. **Objective:** To compare the effects of intravenous dexmedetomidine and fentanyl on hemodynamic responses to laryngoscopy and endotracheal intubation and following formation of pneumoperitoneum in laparoscopic elective abdominal surgeries under general anesthesia. **Methodology:** This prospective, double-blind, randomized comparative study was conducted on 100 patients undergoing laparoscopic abdominal surgeries under general anesthesia. Patients were randomly allocated into two groups: Group 1 (dexmedetomidine) and Group 2 (fentanyl). Hemodynamic parameters, including heart rate, mean arterial pressure (MAP), and oxygen saturation (SpO₂), were recorded at various time intervals. **Results:** The study found significant differences in heart rate and MAP responses between the two groups at various time intervals during surgery. Dexmedetomidine was more effective in attenuating the pressor response compared to fentanyl. The mean heart rate and MAP values were higher in Group 1 (dexmedetomidine) at pre-operative and intra-operative baseline, but decreased significantly after pneumoperitoneum. In contrast, Group 2 (fentanyl) showed an increase in mean heart rate and MAP values after pneumoperitoneum. **Conclusion:** The study concludes that dexmedetomidine is a more effective medication than fentanyl in attenuating the hemodynamic responses to laryngoscopy and endotracheal intubation and following formation of pneumoperitoneum in laparoscopic elective abdominal surgeries under general anesthesia. Dexmedetomidine maintains a stable heart rate and MAP, unlike fentanyl, which makes it a preferred choice for patients undergoing laparoscopic surgeries.

Keywords: Dexmedetomidine, Fentanyl, Hemodynamic Response, Laryngoscopy, Endotracheal Intubation, Pneumoperitoneum, Laparoscopic Surgery, General Anesthesia.

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Introduction

The Anaesthesiologist is greatly concerned about the stress reaction that occurs during direct laryngoscopy and endotracheal intubation. The haemodynamic response to laryngoscopy and intubation caused by unpleasant stimuli was initially documented by Reid and Brace in 1940.¹ Nevertheless, it has been noted that the cardiovascular reactions to tracheal intubation can be reduced by β -adrenergic inhibition.² Various methods and medications have been suggested to reduce the intensity of airway and cardiovascular reactions, but, none have achieved full effectiveness.³ Several medications, including lidocaine, opioids, esmolol, calcium channel blockers, magnesium sulfate, and propofol, have been demonstrated to reduce these responses. However, they all have some limitations and side effects.⁴ Several studies have investigated the use of α_2 adrenergic agonist chemicals, such as clonidine, as premedication in laparoscopic procedures.⁵⁻⁷ Dexmedetomidine, a more recent medication, exhibits a significant level of specificity with a ratio of α_2/α_1 of 1620:1, indicating that it functions as a complete α_2 agonist.⁸

Dexmedetomidine, a drug that activates α_2 -adrenoreceptors and has a distribution half-life of around 6 minutes, has been effectively employed to reduce the stress reaction to laryngoscopy.⁹ It exhibits a highly remarkable ability to significantly decrease the minimal alveolar concentration of volatile anesthetics. It provides other benefits such as pain relief, suppression of sympathetic activity, decrease in the occurrence of shivering, and reduction in the occurrence of respiratory depression.⁴ Dexmedetomidine is currently prescribed for sedating patients in the intensive care unit who are on mechanical ventilation, as well as for sedating patients who are not on a ventilator before or during surgical and other procedures.⁹

The current focus of anaesthetic research is to discover a "stress-free anesthetic method" that can reduce the neuroendocrine, inflammatory, and humoral reactions. Pain has been recognized as the fifth essential indicator. Poorly controlled acute pain can negatively impact the healing process. Anesthesia that relies on opioids provides stability to the cardiovascular system and reduces instances of stress during surgery.¹⁰ Fentanyl is a powerful, man-made painkiller that acts quickly and has a short period of effectiveness. It is highly lipophilic, has a small molecular weight, and is a synthetic opioid agonist commonly employed as an intravenous analgesic adjunct, a constituent of inhalation anesthesia, a component of balanced

anesthesia, and a neurolept analgesia agent. It is also utilized as the only anesthetic. As an analgesic, it is 75 to 125 times more powerful than morphine. The effect begins within 1-2 minutes after receiving the medication through an intravenous route and lasts for 1 hour. Therefore, it has been shown to be perfect for managing the brief physiological effects that occur after laryngoscopy and intubation.¹¹

The objective of this study is to evaluate and compare the impact of dexmedetomidine and fentanyl infusion on the stress response in patients who are undergoing elective laparoscopic operations while under general anesthesia.

Material and Methods

The present prospective, double blind, randomized comparative study was carried in the Department of Anaesthesiology, Rama Medical college, Hapur, Uttar Pradesh among 100 patients undergoing laparoscopic abdominal surgeries under general anaesthesia and who satisfied inclusion and exclusion criteria. Ethical clearance was obtained from institutional ethical committee and informed written consent was obtained from patients before commencement of the present study.

The study included patients who were scheduled for elective laparoscopic surgery under general anesthesia (GA). Participants were of either sex and fell within the age range of 18 to 50 years. Additionally, patients were required to have an American Society of Anesthesiologists (ASA) physical status grade of either I or II, indicating that they were either healthy or had mild systemic disease.

The exclusion criteria comprised of patients with anticipated difficult airways, obesity (BMI >30 kg/m²), or a history of convulsions or allergies to study drugs were also excluded. Furthermore, patients with a history of significant medical conditions, including respiratory, cardiac, hepatic, renal, neurological, or endocrinological diseases (ASA Class III or above), were excluded. Pregnant women and lactating mothers were also not eligible to participate in the study. Patients who were unwilling to participate in the study were also excluded.

The 100 patients were randomly allocated into one of the two predefined groups (group 1 and 2) by using computer-generated random numbers. The study drugs were prepared, labelled with participants serial number and were given to the first investigator who was blinded to the group allocation. All intubations were performed by the second investigator who was blinded to the group allocation. The person observing and recording the hemodynamic parameters was also blinded from the group allocations.

Both the patients and the investigators were blinded to the group allocation. Group I, (50 patients)- Patients

received intravenous dexmedetomidine 0.75mcg/kg over 10 minutes as loading dose before induction of anaesthesia, then 0.2mcg/kg/h maintenance dose till 10 minutes following formation of pneumoperitoneum. In Group II, (50 patients)– Patients received intravenous fentanyl 2mcg/kg loading dose followed by infusion at the rate of 0.2 mcg/kg/hr as maintenance dose till 10 minutes following formation of pneumoperitoneum. Before the study, informed consent was obtained from patients, and they were kept nil per oral for 8 hours before surgery. Preanesthetic evaluation was done, and standard monitors were attached, including electrocardiogram, non-invasive blood pressure, and pulse oximetry. IV access was secured, and IV fluid was started according to standard perioperative fluid replacement therapy. Patients received midazolam and ondansetron as premedication. Induction of anesthesia was done with propofol and vecuronium, followed by direct laryngoscopy and intubation. Maintenance of anesthesia was done with oxygen, nitrous oxide, isoflurane, and intermittent bolus doses of vecuronium. Pneumoperitoneum was created, and intra-abdominal pressure was maintained at 12-14

mmHg. Hemodynamic parameters, including heart rate, blood pressure, and oxygen saturation, were recorded at various time intervals. Any complications or adverse events were also noted.

The data obtained was subjected to statistical analysis and relevant statistical tests were applied. Data entered in MS Excel was analyzed in SPSS software. P value <0.05 was considered significant during data analysis.

Results

Table 1 shows age group wise distribution of study subjects among two groups, Results revealed that from total 100 study participants 50 subjects were in group 1 and 50 subjects in group 2 , 28% subjects of group 1 and 36% subjects of group 2 belonged to age group of 21-30 years, 32% of group 1 and 20% of group 2 subjects belonged to 31-40 years age group and 40% subjects of group 1 and 44% of group 2 subjects belongs to 41-50 years It was statistically non significant (P=0.17).

Table 2 shows type of surgery wise distribution of study subjects and difference was statistically non significant (p=0.508).

Table 1: Age group wise distribution of study subjects among two groups

Age Group (Years)	Group 1		Group 2	
	Frequency	Percent	Frequency	Percent
21-30	14	28.0	18	36.0
31-40	16	32.0	10	20.0
41-50	20	40.0	22	44.00
Total	50	100.0	50	100.0
Chi square value; p value	6.38;0.17			

Table 2: Type of surgery wise distribution of study subjects among two groups

Type of Surgery	Group 1		Group 2	
	Frequency	Percent	Frequency	Percent
IPOM	2	4.0	2	4.0
LAP APPENDICECTOMY	8	16.0	8	16.0
LAP CHOLE	30	60.0	28	56.0
LAP HERNIOPLASTY	8	16.0	10	20.0
LAP LIVER ABSCESS DRAINAGE	2	4.0	0	0.0
LAP FUNDOPLICATION	0	0.0	2	4.0
Chi square value; p value	4.291;0.508			

Table 3: Comparison of mean heart rate values between two groups at different time intervals

Time interval	Groups	Mean	SD	t value	p value
Pre operative	Group 1	95.32	11.70	2.357	0.02*
	Group 2	90.12	10.33		
Intra-operative baseline	Group 1	95.68	12.48	3.375	0.001*
	Group 2	88.72	7.55		
T1 (After drug infusion)	Group 1	93.16	13.20	3.823	<0.01*
	Group 2	84.84	7.92		
T2 (Just after Intubation)	Group 1	94.52	11.71	2.333	0.02*
	Group 2	90.12	6.38		
T3 (1 min after	Group 1	94.24	11.37		

intubation)	Group 2	93.24	5.69	0.556	0.58
T4 (3 mins after intubation)	Group 1	92.44	11.44	-2.091	0.04
	Group 2	96.28	6.16		
T5 (5 mins after intubation)	Group 1	90.68	10.72	-4.154	<0.01*
	Group 2	97.84	5.80		
T6 (1 min after pneumoperitoneum)	Group 1	89.64	10.67	-6.914	<0.01*
	Group 2	101.60	5.98		
T7 (3 mins after pneumoperitoneum)	Group 1	88.08	10.90	-9.059	<0.01*
	Group 2	104.64	6.95		
T8 (5 mins after pneumoperitoteum)	Group 1	86.44	10.04	-11.782	<0.01*
	Group 2	107.96	8.13		
T9 (10 mins after pneumoperitoneum)	Group 1	82.52	16.58	-10.502	<0.01*
	Group 2	110.36	8.75		

The study compared mean heart rate values (table 3) between two groups at different time intervals. The results showed that group 1 had a higher mean heart rate than group 2 at pre-operative, intra-operative baseline, and after drug infusion, with statistically significant differences (P=0.02, P=0.001, and P<0.01, respectively). However, after intubation, the mean heart

rate in group 2 increased, and the difference between the two groups became statistically significant at 3, 5, and 10 minutes after pneumoperitoneum (P<0.01). The results suggest that there are significant differences in heart rate response between the two groups at various time intervals during surgery.

Table 4: Comparison of mean MAP values between two groups at different time intervals

Time interval	Groups	Mean	SD	t value	p value
Pre operative	Group 1	104.72	6.04	5.524	<0.01*
	Group 2	97.60	6.82		
Intra-operative baseline	Group 1	105.32	6.11	6.311	<0.01*
	Group 2	97.76	5.87		
T1 (After drug infusion)	Group 1	102.96	6.20	8.103	<0.01*
	Group 2	93.64	5.27		
T2 (Just after Intubation)	Group 1	101.80	5.76	2.337	.021*
	Group 2	99.16	5.53		
T3 (1 min after intubation)	Group 1	100.04	4.99	-0.267	0.79
	Group 2	100.32	5.50		
T4 (3 mins after intubation)	Group 1	98.92	4.62	-3.329	.001*
	Group 2	102.08	4.87		
T5 (5 mins after intubation)	Group 1	97.28	4.68	-6.017	<0.01*
	Group 2	103.00	4.82		
T6 (1 min after pneumoperitoneum)	Group 1	95.12	5.21	-11.263	<0.01*
	Group 2	106.52	4.91		
T7(3 mins after pneumoperitoneum)	Group 1	93.40	4.85	-15.672	<0.01*
	Group 2	108.52	4.80		
T8 (5 mins after pneumoperitoteum)	Group 1	91.64	4.72	-18.568	<0.01*
	Group 2	108.84	4.54		
T9 (10 mins after pneumoperitoneum)	Group 1	88.88	4.35	-21.853	<0.01*
	Group 2	109.80	5.18		

The study compared mean arterial pressure (MAP) values (table 4) between two groups at different time intervals. The results showed that group 1 had a higher mean MAP than group 2 at pre-operative and intra-operative baseline, with statistically significant differences (P<0.01). After drug infusion, the difference remained statistically significant (P=0.021). However,

after intubation and pneumoperitoneum, the mean MAP in group 2 increased, and the difference between the two groups became statistically significant at 3, 5, and 10 minutes after pneumoperitoneum (P<0.01). The results suggest that there are significant differences in MAP response between the two groups at various time intervals during surgery.

Table 5: Comparison of mean SPO2 values between two groups at different time intervals

Time interval	Groups	Mean	SD	t value	p value
Pre operative	Group 1	98.08	0.98	-0.425	0.671
	Group 2	98.16	0.88		
Intra-operative baseline	Group 1	98.08	0.99	5.706	<0.01*
	Group 2	59.27	48.08		
T1 (After drug infusion)	Group 1	98.32	0.68	0.949	0.345
	Group 2	98.16	0.98		
T2 (Just after Intubation)	Group 1	100.00	0.00	3.5	.001*
	Group 2	99.80	0.40		
T3 (1 min after intubation)	Group 1	100.00	0.00	2.585	.013*
	Group 2	99.88	0.33		
T4 (3 mins after intubation)	Group 1	99.84	0.37	-1.228	0.223
	Group 2	99.92	0.27		
T5 (5 mins after intubation)	Group 1	99.92	0.27	2.214	.030*
	Group 2	99.76	0.43		
T6 (1 min after pneumoperitoneum)	Group 1	99.88	0.33	-1.476	0.144
	Group 2	99.96	0.20		
T7 (3 mins after pneumoperitoneum)	Group 1	100.00	0.00	1.429	0.159
	Group 2	99.96	0.20		
T8 (5 mins after pneumoperitoteum)	Group 1	99.84	0.37	-1.228	0.223
	Group 2	99.92	0.27		
T9 (10 mins after pneumoperitoneum)	Group 1	99.92	0.27	1.738	0.086
	Group 2	99.80	0.40		

The study compared mean SpO₂ values between two groups at different time intervals (table 5). The results showed that there were no significant differences in SpO₂ values between the two groups at pre-operative, intra-operative baseline, and after drug infusion. However, significant differences were found just after intubation, 1 minute after intubation, and 5 minutes after intubation, with group 1 having higher SpO₂ values. After pneumoperitoneum, the differences in SpO₂ values between the two groups were not statistically significant at 1, 3, 5, and 10 minutes. The results suggest that while there were some significant differences in SpO₂ values between the two groups during intubation, these differences were not sustained after pneumoperitoneum.

Discussion

Endotracheal intubations are commonly performed to secure definitive airway in the operation theater (OT) but it has an associated high level of risk.¹² Unfortunately, it results in an undesirable sequence of pathophysiological reactions. This could lead to negative consequences in the specific group of patients who have other comorbid health conditions.¹³ Approximately 40%-45% of patients who undergo endotracheal intubations in the operation theater (OT) experience complications, which can include severe hypotension, severe hypoxemia, and cardiac arrest. Severe cardiovascular collapse is a frequently occurring

consequence following endotracheal intubation in the operation theater (OT). It is crucial to identify risk factors for circulatory collapse during endotracheal intubation in order to prevent or minimize this severe consequence.¹²

In the present study, both the fentanyl group and the dexmedetomidine group experienced a rise in HR during pneumoperitoneum; however, the HR in the fentanyl group remained above the baseline after 10 minutes following formation of pneumoperitoneum, whereas the HR in the dexmedetomidine group reverted to baseline after 10 minutes following formation of pneumoperitoneum. Similar to our study, **Meena R et al¹⁴** and **Kataria AP et al¹⁵** observed that dexmedetomidine significantly attenuated the heart rate (HR) response to pneumoperitoneum compared to fentanyl. Dexmedetomidine maintained HR at or slightly below baseline levels during the pneumoperitoneum period. In contrast, the fentanyl group consistently had higher HR levels than baseline during the intraoperative period, with statistically significant differences between the two groups (**p<0.05**).¹⁴ **Kataria AP et al¹⁵** also reported a similar trend, with dexmedetomidine causing a greater reduction in HR after induction, and fentanyl resulting in elevated HR levels after pneumoperitoneum.

In our study, the heart rate decreased from baseline value after drug infusion in both groups and the difference among both groups was statistically

significant ($p < 0.05$). However, just after intubation, heart rate increased and reached to baseline values in both groups. Later, 3 minutes after intubation, mean values decreased in dexmedetomidine group and increased in fentanyl group and this trend continued upto 5 minutes after intubation, at 1 min after pneumoperitoneum and till 10 minutes after pneumoperitoneum. Our study's findings on the effects of laryngoscopy and intubation are consistent with Bajwa S et al.¹⁶ The dexmedetomidine group had a significantly lower average heart rate (HR) 20 minutes after administration compared to the fentanyl group ($P = 0.02$). After anesthesia administration, both groups showed a significant reduction in HR and mean arterial pressure (MAP) ($P < 0.001$). However, laryngoscopy and intubation led to a significant rise in HR and MAP in the fentanyl group compared to the dexmedetomidine group ($P < 0.001$). The dexmedetomidine group showed a faster rate of decline and stabilization of heart rate. Similarly, Saraf R et al¹⁷ and Jaakola ML et al¹⁸ observed a substantial decrease in heart rate after the administration of dexmedetomidine at a dosage of 0.6 $\mu\text{g}/\text{kg}$. Talke P et al¹⁹ demonstrated that dexmedetomidine infusion resulted in minimal increases in heart rate (HR) and noradrenaline levels. The sympatholytic characteristics of dexmedetomidine contributed to this hemodynamic effect by modulating plasma norepinephrine and urine normetanephrine elevations. In contrast to the placebo group, the dexmedetomidine group had lower norepinephrine levels after anesthesia.

Our study's findings differ from those of Shukla S et al¹³, who reported increased heart rate values from baseline over 10 minutes after intubation in both groups. In contrast, our study found that heart rate values decreased in the dexmedetomidine group.

Our study found that both groups experienced a fall in mean arterial pressure (MAP) after anesthesia induction, with a statistically significant fall in the dexmedetomidine group and a rise in the fentanyl group. The dexmedetomidine group showed less fluctuation in systolic blood pressure (SBP), diastolic blood pressure (DBP), and MAP after intubation and pneumoperitoneum. Similar findings were reported by Bajwa S et al¹⁶ and Neil L et al.²⁰ The studies by Bajwa S et al¹⁶ and Neil L et al²⁰ also found that dexmedetomidine maintained hemodynamic stability better than fentanyl during intubation and surgery. Dexmedetomidine was associated with a smaller increase in blood pressure during intubation and pneumoperitoneum, and a faster return to baseline values. These findings suggest that dexmedetomidine may be a better choice than fentanyl for maintaining hemodynamic stability during surgery. In another

corresponding study, Vora KS et al²¹ reported that dexmedetomidine when used as an adjuvant in general anesthesia for laparoscopic procedures, dexmedetomidine produced a stable hemodynamic profile during the perioperative phase and successfully reduced the pressor response to intubation and extubation, which reduced the need for strong inhalational agents and additional analgesics.

Further, Yildiz M et al²² found that a single dose of dexmedetomidine (1 $\mu\text{g}/\text{kg}$) effectively prevented cardiovascular hemodynamic response during laryngoscopy and endotracheal intubation. Dexmedetomidine also reduced the need for additional opioid medication. Ozkose Z et al²³ reported that a single dose of dexmedetomidine (1 $\mu\text{g}/\text{kg}$) reduced mean arterial pressure (MAP) by up to 20%. Dexmedetomidine's central sympatholytic activity and α_2 -adrenoceptor activation contribute to its hemodynamic stabilizing effects. Rabie A et al²⁴ found that a continuous intravenous infusion of dexmedetomidine (0.6 $\mu\text{g}/\text{kg}/\text{h}$) minimized stress response, coughing, postoperative nausea and vomiting, and pain medication needs after laparoscopic cholecystectomy. Jain V et al⁵⁵ found that dexmedetomidine effectively reduced the sympathetic response to laryngoscopy and intubation, with significant decreases in heart rate, systolic blood pressure, and diastolic blood pressure compared to fentanyl.

The current study was constrained by the absence of a group that received a placebo for comparison. Furthermore, there were no assessments made for cardiac output, systemic vascular resistance, or plasma catecholamine or stress hormone levels. Enhancing the precision of invasive blood pressure monitoring is possible. The objective of studying cerebral perfusion pressure is to guarantee patient safety, however the utilization of Bispectral Index (BIS) offers a more enlightening approach to quantify the level of anesthesia. This is crucial because changes in the depth of anesthesia can potentially affect the patient's hemodynamics.

Conclusion

To conclude, administration of dexmedetomidine was reported to have a more effective attenuation in the pressor response compared to fentanyl to laryngoscopy and endotracheal intubation and following formation of pneumoperitoneum in laparoscopic elective abdominal surgeries under general anaesthesia.

Unlike fentanyl, dexmedetomidine administration maintains a stable heart rate, mean arterial pressure (MAP), at specific time intervals after tracheal intubation and pneumoperitoneum. Dexmedetomidine

is a potent medication that effectively mitigates the body's reaction to tracheal intubation during rapid sequence induction, unlike fentanyl.

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