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Original Research

An evaluation of haemodynamic responses to tracheal intubation following intravenous dexmedetomidine and fentanyl in patients undergoing laparoscopic cholecystectomy

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Abstract

Background: Laryngoscopy and tracheal intubation are related to sympathetic stimulation and lead to hypertension and tachycardia. These changes in hemodynamics may increase the risk of myocardial ischemia. As a result, effective blunting of these unpleasant responses is required. This study aimed to compare the effects of dexmedetomidine and fentanyl bolus administration on attenuation of hemodynamic response to tracheal intubation in patients undergoing laparoscopic cholecystectomy surgeries.

Methodology: A total of 136 patients of both genders undergoing elective laparoscopic cholecystectomy surgeries satisfying inclusion criteria were randomly allocated into 2 groups (group D and group F). Group D received 1mcg/Kg of dexmedetomidine (Dexa) intravenous (IV) in 100ml of normal saline over 10 minutes and 5ml of normal saline over 3 minutes before induction. Group F received Inj. Fentanyl 2mcg/Kg diluted in 100 ml of normal saline over 10 minutes and 5ml of normal saline 3 minutes before induction. The patients were ventilated for 3 minutes by bag and mask. After 3 minutes of ventilation, endotracheal intubation was done. Vitals (systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate) were recorded from the time of intubation to 10 minutes after that at 1 minute interval.

Results: In both groups, heart rate increased significantly immediately following intubation ($p = 0.002$). In dexmedetomidine group heart rate, mean arterial pressure, systolic and diastolic blood pressures were significantly controlled at various time points in comparison to fentanyl group after laryngoscopy and intubation.

Conclusions: Dexmedetomidine in a dose of 1mcg/kg causes greater and sustained attenuation of haemodynamic response to endotracheal intubation among the patients of cholelithiasis undergoing laparoscopic cholecystectomy surgeries as compared to fentanyl. Therefore, it can be used as an effective alternative to opioids for induction of general anaesthesia in patients undergoing laparoscopic cholecystectomy surgery.

Keywords: Fentanyl; Dexmedetomidine; Tracheal Intubation; Cholecystectomy; Haemodynamic Response.

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Introduction:

Laparoscopic procedures leave less scars, cause less discomfort during the recovery period, needs less hospital stays, and have lower rates of morbidity and mortality, they are a fundamental part of modern surgical methods and are now considered the highest-quality option for many gallbladder surgeries.[1] Tracheal intubation and laryngoscopy are related to sympathetic stimulation and lead to hypertension and tachycardia.[2] These changes in hemodynamics may increase the risk of myocardial ischemia. As a result, effective blunting of these unpleasant responses is required.[3] Various prophylactic interventions have been tried to blunt this stress response; administration of local anesthetics, opioids, beta blockers, alpha 2 [α2] adrenergic agonists, vasodilators, magnesium, or increased concentrations of volatile anesthetic.[4] Fentanyl is a potent μ receptor agonist with rapid onset and relatively short duration of action, minimal respiratory depression, and has the ability to provide cardiovascular stability.[5] Despite these beneficial effects, fentanyl is known to cause bradycardia, nausea, vomiting, pruritus, and muscle rigidity. Moreover, availability of fentanyl in small hospitals is restricted due to tough narcotic laws.[6] Dexmedetomidine is a newer α2 receptor agonist having eight times higher affinity and α2 selectivity as compared with clonidine. Dexmedetomidine attenuates these potentially harmful cardiovascular reactions during induction of anesthesia and has been used in infusion for this purpose.[7-9] Opioid-based anesthesia offers hemodynamic stability and decreases intraoperative stress episodes. This study aims to compare the effects of dexmedetomidine and fentanyl bolus administration on stress attenuation during endotracheal intubation in patients undergoing laparoscopic cholecystectomy.

Material and Methods:

The current study was performed as a comparative cross- sectional observational study after obtaining approval from the Institutional Ethical Committee and informed consent from all the participants. The study populations included 136 patients of both genders undergoing elective laparoscopic cholecystectomy surgeries under general anesthesia of aged 18- 60 years, and with American Society of Anesthesiologists (ASA) physical status grade I and II.[10,11] Exclusion criteria were anticipated difficult intubation, history of myocardial, pulmonary, or endocrine diseases, diabetes mellitus, hepatic or renal impairment, and drug abuse or opioid addiction, surgical complication, and failure of laparoscopy. This study was conducted during the period of May 2023 to June 2024.

Patients satisfying inclusion criteria were randomly allocated into 2 groups (group D and group F). Group D received 1mcg/Kg of dexmedetomidine (Dexa) intravenous (IV) in 100ml of normal saline over 10 minutes and 5ml of normal saline over 3 minutes before induction. Group F received Inj. Fentanyl 2mcg/Kg diluted in 100 ml of normal saline over 10 minutes and 5ml of normal saline 3 minutes before induction.

Preloading was done in all patients with multiple electrolyte injection type 1 (USP Pharmacopeia)[12]10 ml/kg over 15-20 minutes. Intravenous injection of 75 mcg of Palonosetron was given to all patients. After applying monitors, baseline hemodynamic parameters were noted. Following that the drug (dexmedetomidine or fentanyl) was given to the patient as per the group to which they belong over 10 minutes and after those vitals (systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate) will be noted.

Induction of anaesthesia was initiated thereafter. Premedication (Injection Glycopyrrolate and Inj. Midazolam) were given, followed by Injection Propofol and then Injection cisatracurium. The patients were ventilated for 3 minutes by bag and mask. After 3 minutes of ventilation, endotracheal intubation was done. Vitals (systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate) were recorded from the time of intubation to 10 minutes after that at 1 minute interval.

Statistical analysis: All the collected data was entered into Microsoft excel. Statistical Package for the Social Sciences (SPSS-28 version) software was used for all statistical analyses. Continuous variables are presented as mean with 95% confidence interval, and the t-test was applied to compare the difference of means between two groups after checking the normal condition. A p-value less than 0.05 were considered as statistical significance.

Results:

A total of 136 patients were recruited for the study and there was no dropout. There were 42.6% males and 57.4% females in dexmedetomidine group. But in fentanyl group there were 36.8% male and 63.2% females. The mean age of dexmedetomidine group was 41.94±11.44 years and 42.21±9.79 years of fentanyl group. In this study there were significant difference observed in BMI of both the groups ($p<0.05$). Mean BMI indicates that subjects of cholelithiasis were overweight in present study (Table 1).

Table 1: Demographic profile of patients.

Variables	Group D (N= 68)	Group F (N= 68)
Age	41.94±11.44	42.21±9.79
Weight	71.85±8.21	70.07±10.24
BMI	28.26±2.96	26.98±3.33
Sex		
Male	42.6%	36.8%
Female	57.4%	63.2%

Table 2: Distribution of mean ± SD of vitals after drug administration in subjects of both groups.

Vitals after drug administration	Group D (N= 68)	Group F (N= 68)	**P-Value**
HR	73.65±12.66	82.0±11.51	0.000
SBP	126.28±13.45	128.0±13.50	0.469
DBP	81.03±10.78	79.63±10.92	0.474
MAP	94.71±10.30	94.87±10.12	0.931

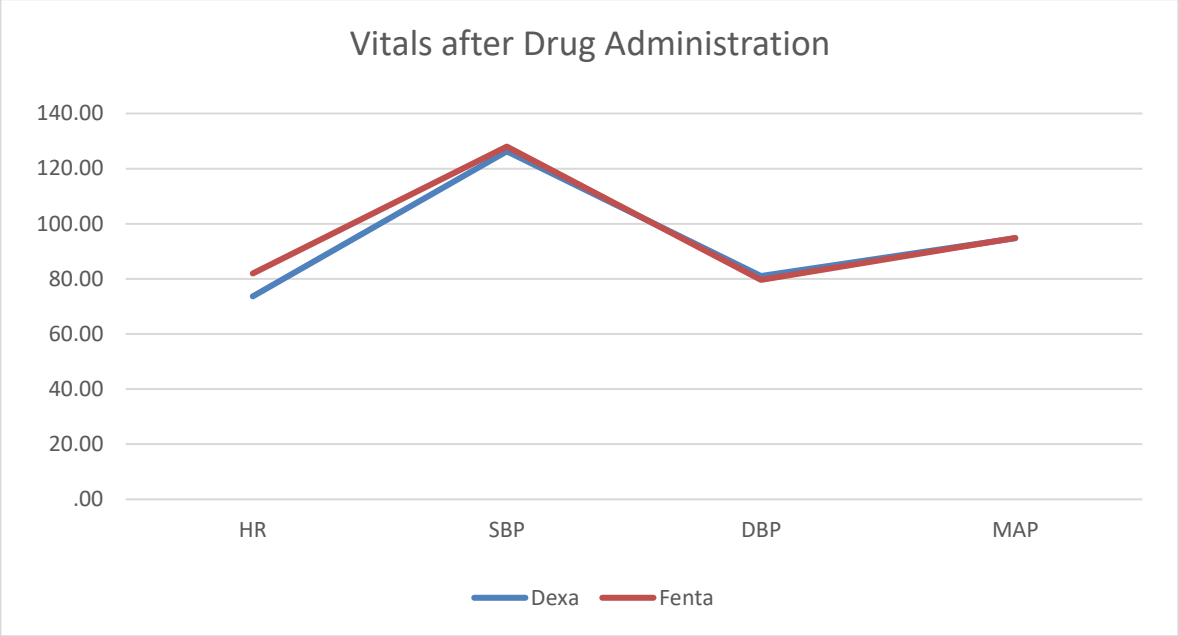

Figure 1: Distribution of mean ± SD of vitals after drug administration in subjects of both groups.

Table 2 and Figure 1 depict the distribution of mean ± SD of vitals after drug administration in subjects of both groups. Statistically significant difference was observed in HR after drug administration among both groups.

Table 3: Inter- group comparison of heart rate at various time points after drug intervention and following intubation.

Time	**Heart Rate**		
	Group D (N= 68)	Group F (N= 68)	**P-Value**
At 0 Min	82.76±10.74	88.69±10.79	0.002
At 1 Min	81.93±10.363	86.94±10.36	0.005
At 2 Min	81.04±10.72	88.03±10.39	0.000
At 3 Min	80.57±9.89	88.71±9.83	0.000
At 4 Min	80.18±10.78	88.32±11.03	0.000
At 5 Min	79.9±11.1	87.69±11.01	0.000
At 6 Min	80.15±11.29	87.46±10.63	0.000
At 7 Min	80.12±11.65	88.41±10.43	0.000
At 8 Min	79.71±11.59	87.96±10.06	0.000
At 9 Min	79.50±11.67	87.59±11.22	0.000
At 10 Min	78.72±11.34	87.85±11.74	0.000

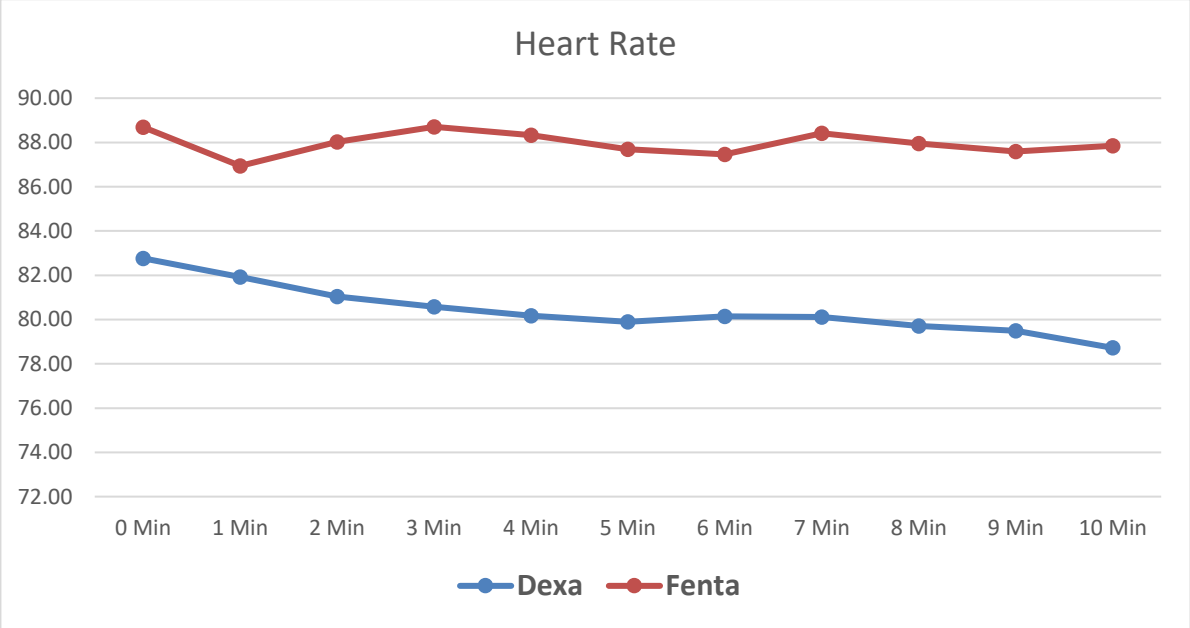

Figure 2: Inter- group comparison of heart rate at various time points after drug intervention and following intubation.

Table 3 and Figure 2 depicts the inter-group comparison of heart rate at various time points after drug intervention and following intubation. Simple main effect analysis showed that heart rate changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points.

Table 4: Inter- group comparison of MAP at various time points after drug intervention and following intubation.

Time	**MAP**		
	Group D (N= 68)	Group F (N= 68)	**P-Value**
At 0 Min	99.63±8.1	95.38±9.82	0.007
At 1 Min	94.04±9.16	92.19±10.26	0.271
At 2 Min	87.60±8.26	88.56±9.46	0.524
At 3 Min	84.79±8.39	85.5±10.40	0.717
At 4 Min	80.91±9.76	84.56±9.21	0.029
At 5 Min	80.34±8.98	84.32±10.80	0.011
At 6 Min	79.84±7.43	84.07±12.29	0.010
At 7 Min	79.32±7.14	84.94±11.93	0.000
At 8 Min	80.09±9.02	85.76±12.72	0.002
At 9 Min	81.57±9.54	85.82±12.37	0.026
At 10 Min	79.9±8.21	87.01±11.14	0.000

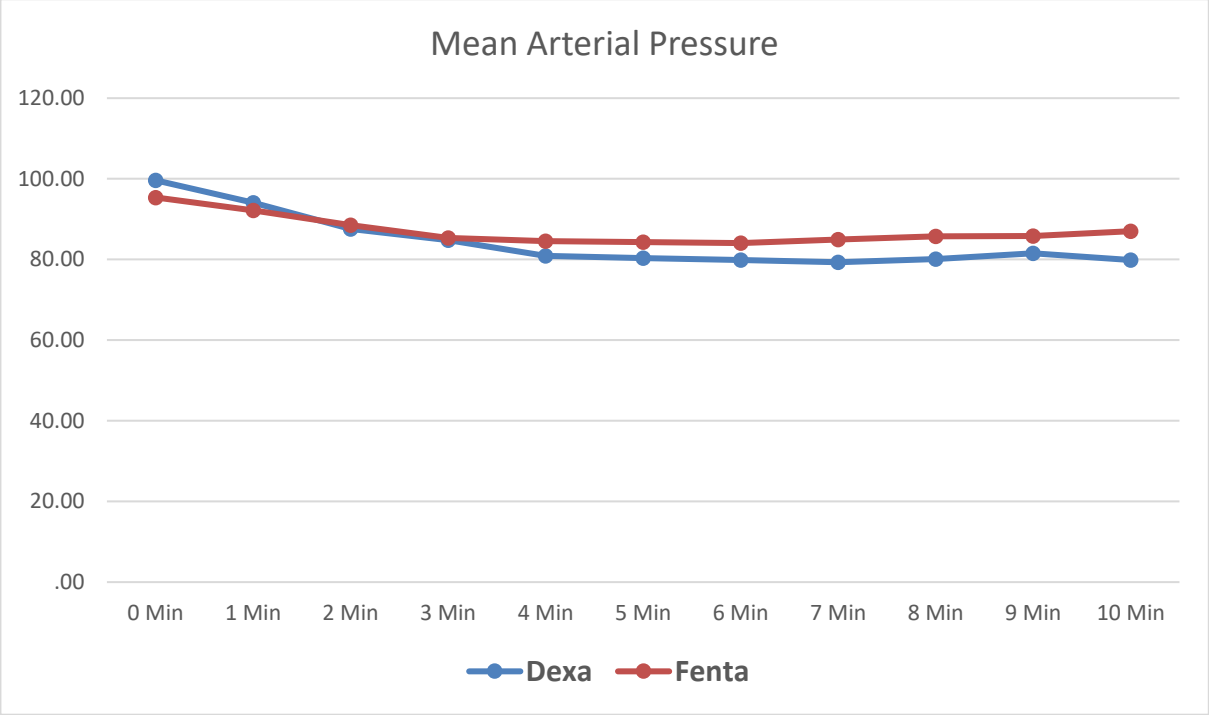

Figure 3: Inter- group comparison of MAP at various time points after drug intervention and following intubation.

Table 4 and Figure 3 depict inter-group comparison of MAP at various time points after drug intervention and following intubation. Simple main effect analysis showed that MAP changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points. Significant control was observed on mean arterial pressure in dexmedetomedine group than fentanyl groups.

Table 5: Inter-group comparison of SBP at various time points after drug intervention and following intubation

Time	**Systolic Blood Pressure**		
	Group D (N= 68)	Group F (N= 68)	**P-Value**
At 0 Min	128.34±11.65	121.99±22.45	0.053
At 1 Min	121.78±9.89	120.51±11.36	0.505
At 2 Min	115.01±8.47	114.34±9.92	0.673
At 3 Min	110.75±9.76	111.34±10.17	0.711
At 4 Min	106.74±8.80	109.69±10.11	0.066
At 5 Min	105.25±9.75	108.18±10.43	0.063
At 6 Min	103.94±9.31	109.40±12.98	0.003

At 7 Min	104.31±9.06	108.76±12.73	0.011
At 8 Min	104.53±10.46	111.53±14.49	0.000
At 9 Min	105.65±10.73	111.40±14.61	0.007
At 10 Min	105.53±8.99	110.88±13.64	0.006

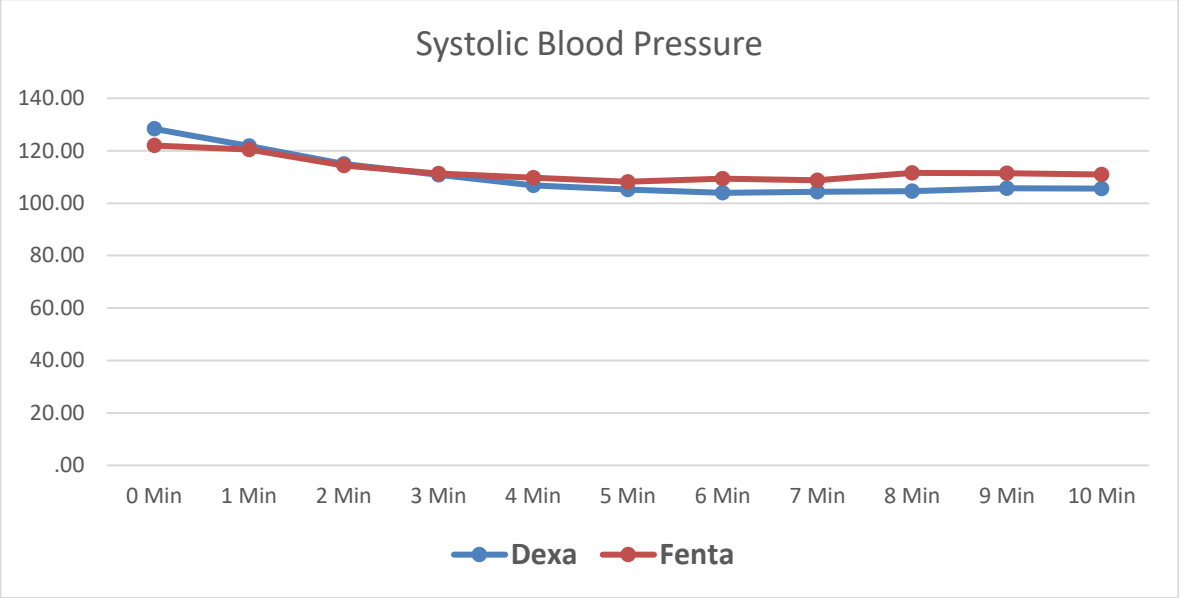

Figure 4: Inter-group comparison of SBP at various time points after drug intervention and following intubation.

Table 5 and Figure 4 depict inter-group comparison of SBP at various time points after drug intervention and following intubation. Simple main effect analysis showed that SBP changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points (at 6 min, 7 min, 8 min, 9 min and 10 min). Significant control was observed on systolic blood pressure in dexmedetomedine group than fentanyl groups.

Table 6: Inter-group comparison of DBP at various time points after drug intervention and following intubation

Time	**Diastolic Blood Pressure**		
	Group D (N= 68)	Group F (N= 68)	**P-Value**
At 0 Min	86.99±8.35	81.87±9.24	0.000
At 1 Min	81.54±9.45	80.59±11.27	0.579
At 2 Min	75.53±8.96	76.44±9.96	0.576
At 3 Min	72.99±8.76	74.01±11.41	0.534
At 4 Min	69.99±9.59	73.26±9.57	0.045

At 5 Min	68.71±9.53	74.22±11.45	0.001
At 6 Min	68.41±7.31	72.82±12.07	0.009
At 7 Min	67.72±7.27	74.22±12.46	0.000
At 8 Min	69.10±9.92	74.38±12.47	0.005
At 9 Min	70.07±9.64	74.29±12.53	0.031
At 10 Min	58.63±9.13	76.10±11.41	0.000

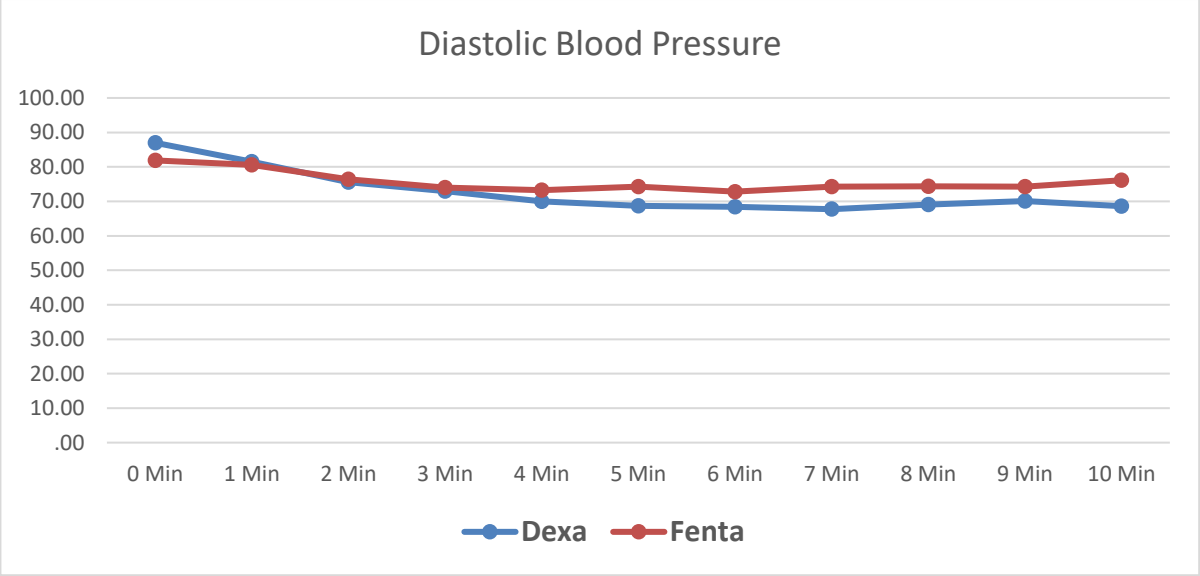

Figure 5: Inter-group comparison of DBP at various time points after drug intervention and following intubation.

Table 6 and Figure 5 depict inter-group comparison of DBP at various time points after drug intervention and following intubation. Simple main effect analysis showed that DBP changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points (from 4 to 10 minutes successively). Significant control was observed on diastolic blood pressure in dexmedetomidine group than fentanyl groups.

Discussion:

In this study compared to fentanyl, dexmedetomidine was more effective in preventing an increase in the hemodynamic response following intubation and laryngoscopy. As intraoperative analgesics with better and consistent hemodynamic control, alpha-2 agonists are becoming more and more popular due to their sympatholytic, anti-nociceptive, and sedation qualities.[13] To maintain stable hemodynamics during surgery, various combinations of pharmacological agents such as opioids, beta blockers, calcium channel blockers, combined alpha and beta blockers, lignocaine and alpha-2 receptor agonists have been tried.[14-16]

In this study there were 42.6% males and 57.4% females in dexmedetomidine group. But in fentanyl group there were 36.8% male and 63.2% females. In present study the prevalence of females was more in both groups in comparison to males undergoing laparoscopic cholecystectomy surgeries. Like the present study results Coelho et al. also found more prevalence of females (67.2%) undergoing laparoscopic cholecystectomy surgeries than males (32.8%).[17] Dhamnetiya et al. has also concluded that females have higher risk of gallstone formation than males.[18] This is because gender is one of the most salient risk factors for gallstone disease. At all ages, women are generally at higher risk of cholelithiasis than men because of women's naturally higher estrogen levels, multiparty or ingestion of estrogen-based oral contraceptives.[19]

The mean age of dexmedetomidine group was 41.94±11.44 years and 42.21±9.79 years of fentanyl group. Similarly, Festi et al also concluded that cholelithiasis is ten times more likely in people aged 40 and more due to a decline in the activity of cholesterol 7 α -hydroxylase, the limiting enzyme for bile acid synthesis; as this enzymatic activity decreases, and biliary cholesterol increases, the aging individual experiences cholesterol saturation and decreasing mobility of gallbladder emptying.[20]

In this study there were significant differences observed in BMI of both the groups ($p<0.05$). Mean BMI indicates that subjects of cholelithiasis were overweight in the present study. Sarrami et al, also suggested a strong association between obesity and cholelithiasis reaffirms the role of excess adiposity in gallstone formation.[21] Similar to our study results Baddam et al. also concluded that as the BMI increases, the likelihood of cholelithiasis also increases.[22] The pathophysiological mechanisms by which obesity increases the risk of developing cholelithiasis is due to the increase in plasma insulin levels, because higher levels of plasma insulin stimulate activity of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase causing a cholesterol hypersecretion.[23,24] In this study at the time of drug administration no significant difference was observed in other hemodynamic parameters except heart rate.

In present study simple main effect analysis showed that heart rate changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points (i.e. from 0 to 10 minutes) after drug intervention and following intubation. In the present study, heart rate was significantly decreased in the dexmedetomidine group when compared to fentanyl group immediately after study drug and there was statistically significant reduction in heart rate for up to 10 min after intubation in the dexmedetomidine group. Similarly, Ramsay et al. also found decrease in heart rate after the doses of dexmedetomedine.[25] Mahiswar et al. also reported that dexmedetomedine significantly lowered the increase in heart rate.[26]

In the present study simple main effect analysis showed that MAP changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points (i.e. from 4 to 10 minutes) after drug intervention and following intubation. Significant control was observed on mean arterial pressure in dexmedetomidine group than fentanyl group. Similarly, Jaakola et al., did a study with dexmedetomidine in a dose of 0.6mcg/kg and observed that dexmedetomidine reduces the increase in heart rate and mean arterial blood pressure during intubation.[27]

Simple main effect analysis also showed that SBP changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points (at 6 min, 7 min, 8 min, 9 min and 10 min) after drug intervention and following intubation. Significant control was observed on systolic blood pressure in dexmedetomidine group than fentanyl group. In the present study simple main effect analysis showed that DBP changed significantly in dexmedetomidine group in comparison to fentanyl group at various time points (from 4 to 10 minutes successively) after drug intervention and following intubation. Significant control was observed on diastolic blood pressure in dexmedetomidine group than fentanyl group. Present

study results are comparable to the study done by Bekker et al, who reported that dexmedetomidine, given at a similar dose, was effective in blunting the increase in systolic BP perioperatively, although it did not increase the incidence of hypotension or bradycardia.[28] Bruder et al. also reported that dexmedetomidine can effectively decrease the stress response, reducing a hemodynamic response after intubation and laryngoscopy.[29] Laha et al., studied the effects of preinduction loading dose of dexmedetomidine 1 mcg/kg on attenuation of sympathoadrenal responses and requirements of anaesthetic agents. They concluded that administration of dexmedetomidine not only attenuates the rise in mean heart rate, systolic blood pressure after intubation at 1, 2, 3 and 5 min but also significantly reduces the requirement of anaesthetic drugs.[30]

Dexmedetomidine was more efficient in preventing a rise in the hemodynamic response to intubation and laryngoscopy as compared to fentanyl. It was because dexmedetomidine inhibits the release of neurotransmitters at the end of nerves, causing a reduction in levels of norepinephrine in plasma that creates cardiovascular stabilization. Even though less effective, fentanyl can reduce a hemodynamic response by suppressing pain cues, lowering the central sympathetic tone and increasing vagal tone activation.[31]

Conclusion:

It was therefore concluded that the dexmedetomidine in a dose of 1mcg/kg causes greater and sustained attenuation of stress response to endotracheal intubation among the patients of cholelithiasis undergoing laparoscopic cholecystectomy surgeries. It may be considered as an alternative to opioids for this purpose.

Conflicts of Interest: The authors declare no conflicts of interest.

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