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KEY WORDS: GA, ASA, Drxmedetomidine, Fentanyl, Esmolol, Endotracheal Intubati

A COMPARATIVE STUDY OF INTRAVENOUS DEXMEDETOMIDINE, ESMOLOL AND FENTANYL FOR ATTENUATION OF HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANAESTHESIA

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ABSTRACT

The aim is to evaluate and compare the relative efficacy of intravenous dexmedetomidine, Esmolol and Fentanyl for attenuation of stress responses following laryngoscopy and endotracheal intubation in adult patients undergoing laparoscopic cholecystectomy under general anaesthesia.

INTRODUCTION

- The stress response following direct laryngoscopy and endotracheal intubation is an important concern for the anesthesiologist.
- The pressure response is known to be a sympathoadrenal response provoked by stimulation of the epipharynx and larynx. The nociceptive signals are conducted to the brain via glossopharyngeal and vagus nerve.
- During laryngoscopy, stimulation of proprioceptors at the base of the tongue increase in plasma catecholamine concentrations which result in tachycardia and hypertension. Subsequent orotracheal intubation recruits additional receptors that elicit augmented hemodynamic and epinephrine responses as well as some vagal inhibition of the heart.
- These changes are the maximum at 1 minute after intubation and last for 5-10 min.
- Dexmedetomidine is a highly specific and selective α2 adrenoreceptor agonist. It is currently used for sedation, anxiolysis, and analgesia without respiratory depression. It causes a dose-dependent reduction in a decrease in serum norepinephrine concentration, resulting in decreased heart rate and arterial blood pressure.
- Esmolol is an ultra-short acting, selective β-1 adrenergic receptor antagonist. It also reduces the force of contraction and heart rate. It has a rapid onset and a short duration of action. Hence, it permits rapid titration to a desired level of β-blockade on the administration during the perioperative period. However, it does not have an intrinsic sympathetic activity or membrane-stabilizing activity at therapeutic doses.
- Fentanyl is a phenylpiperidine derivative synthetic opioid agonist that is structurally related to meperidine and binds mu (μ) opioid G protein-coupled receptor. It has quick onset time, more considerable safety margin, dose-dependent respiratory depression and termination of effect, and relative cardiovascular stability. It attenuates the cardiovascular response by its direct action on opioid receptors, cardiovascular system, and indirectly by preventing the increase in plasma catecholamines concentration and decreasing the central sympathetic outflow.

AIMS AND OBJECTIVES

The study aims to evaluate and compare the relative efficacy of intravenous dexmedetomidine, Esmolol and Fentanyl for attenuation of stress responses following laryngoscopy and endotracheal intubation in adult patients undergoing laparoscopic cholecystectomy under general anaesthesia.

MATERIALS AND METHODS

Study Design: Hospital-based prospective, randomized, double-blind, comparative and interventional study.

Study Period: Two year, from September 2020 to September 2022.

Sample Size: The sample size was calculated based on the findings of previous studies [15,19,60, 63] and using statistical software G*Power (version 3.1.9.4).

Considering α= 0.05, power of the study (1-β)= 0.90, the effect size of 0.4 and number of groups= 3 with ratio 1 for all groups, the minimum sample size calculated is 84, i.e. 28 in each group. Considering dropout rate 5-10% we took a sample size of 90, i.e. 30 in each group.

OBSERVATIONS

1. Demographic Variables:

A. AGE:

Table 1.1 Mean Age

Age (years)	Mean	Std. Deviation	P Value
Group D	34.70	10.85	0.943
Group F	35.63	9.99	
Group E	35.00	11.53	

Table 1.1 shows the mean age of the patients in the three groups. It was observed that there was no significant difference (p-value > 0.05) in the mean age of the patients among the groups.

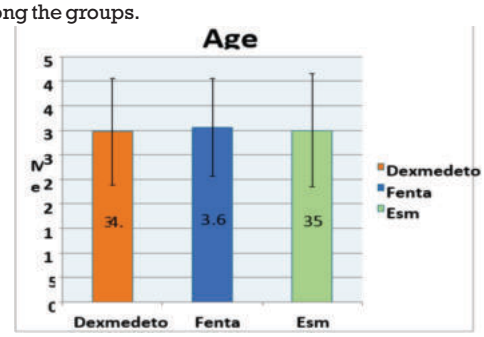

Figure 1.1 Comparison of the mean age of the patients among three intervention groups

B. Weight:

Table 1.2 Mean body weight

Weight (kg)	Mean	Std. Deviation	P Value
Group D	62.53	13.67	0.100
Group F	58.83	11.34	
Group E	66.13	13.81	

Table 1.2 shows the mean body weight of the patients in the three groups. It was observed that there was no significant difference (p-value > 0.05) in the mean body weight of the patients among the groups.

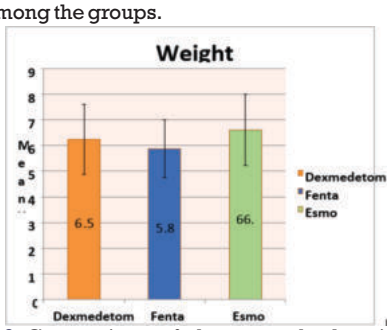

Figure 1.2 Comparison of the mean bodyweight of the patients among three intervention groups

C. Height:

Table 1.3 Mean Height

Height (cm)	Mean	Std. Deviation	P Value
Group D	168.73	7.07	0.068
Group F	169.97	7.57	
Group E	173.43	9.25	

Table 1.3 shows the mean height of the patients in the three groups. It was observed that there was no significant difference (p-value > 0.05) in the mean Height of the patients among the groups.

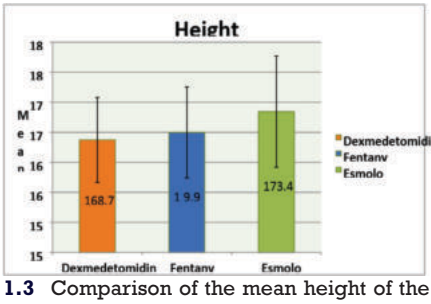

Figure 1.3 Comparison of the mean height of the patients among three intervention groups

D. Body Mass Index (BMI):

Table 1.4 Mean BMI

BMI (kg/m2)	Mean	Std. Deviation	P Value
Group D	21.97	4.65	0.288
Group F	20.43	4.06	
Group E	22.17	5.10	

Table 1.4 shows the mean BMI of the patients in the three groups. It was observed that there was no significant difference (p-value > 0.05) in the mean BMI of the patients among the groups.

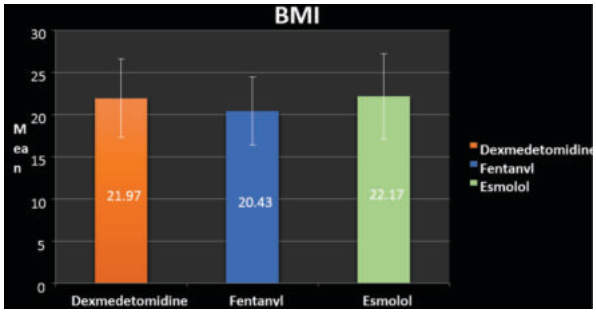

Figure 1.4 Comparison of the mean BMI of the patients among three intervention groups

E. Gender:

Table 1.5 Gender Distribution

Sex	Groups			Chisquare	P Value
	Group D	Group F	Group E		
	No. %	No. %	No. %	1.92	0.383
Male	07 23. 3	03 90	05 16. 7		
Female	23 76. 7	27 10	25 83. 3		
Tot al	30 100	30 100	30 100		

Table 1.5 shows the gender distribution of the patients in the three groups. It was observed that there was no significant difference (p-value > 0.05) in the sex distribution of the patients among the groups.

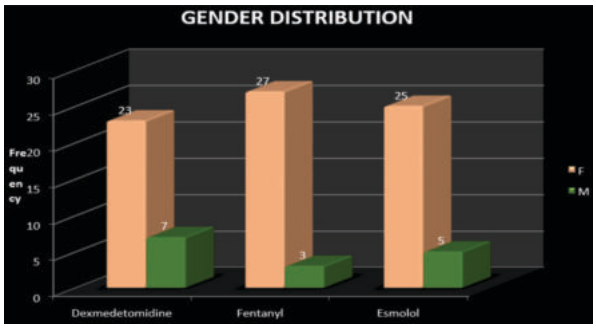

Figure 1.5 Comparison of the gender of the patients among three intervention groups

F. ASA Physical Status:

Table 1.6 ASA physical status distribution

ASA Physical Status	Groups						Chisquare	P Value
	Group D		Group F		Group E			
	No.	%	No.	%	No.	%	1.50	0.473
Grade I	17	56.7	21	70	17	56. 4		
Grade II	13	43.3	09	30	13	43. 3		
Total	30	100	30	100	30	100		

Table 1.6 shows the distribution of the patients according to ASA Physical Status grading in the three groups. It was observed that there was no significant difference (p-value > 0.05) among the groups.

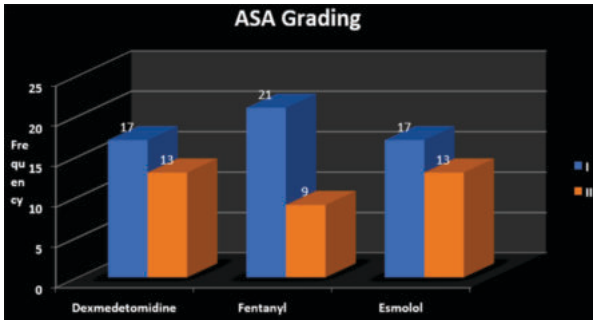

Figure 1.6 Comparison of the patients among three intervention groups according to ASA Grade:

2. Comparison of preoperative vitals measurements:

Preoperative Vitals	Group D (MEAN ± SD)	Group F (MEAN ± SD)	Group E (MEAN ± SD)	P value
HR	87.30 ± 12.31	87.10 ± 8.73	88.77 ± 8.83	0.78
SBP	126.00 ± 10.92	125.87 ± 9.47	124.60 ± 9.86	0.84
DBP	81.40 ± 9.43	79.87 ± 8.24	80.13 ± 7.29	0.75
MAP	94.16 ± 6.22	93.00 ± 5.14	94.82 ± 7.62	0.54
RR	17.80 ± 1.19	17.63 ± 1.59	18.33 ± 1.06	0.10
SPO2	99.40 ± 0.62	99.30 ± 0.75	99..43 ± 0.63	0.72

Table 2 shows the comparison of preoperative HR, SBP, DBP, MAP, RR, and SPO2 in the three groups. It was observed that there was no significant difference (p-value > 0.05) among the groups.

3. Intraoperative hemodynamic Parameters: A. Heart Rate (HR):

Table 3.1 Comparison of heart rates among the groups

Time Interval (min)	Group D (Mean±SD)	Group F (Mean±SD)	Group E (Mean±SD)	P-Value

T0 = Baseline (before the start of infusion of study drugs)	86.23±8.01	87.67±6.76	86.03±8.01	0.66
T1 = after completion of the study drug infusion	82.97±10.50	88.47±5.79	85.80±10.18	0.07
T2 = just after laryngoscopy &intubation	80.83±7.32	87.90±7.31	89.03±8.78	<0.01
T3 = 1 min after intubation	78.93±11.67	83.43±9.86	86.63±7.45	0.012
T4 = 3 min after intubation	79.37±10.13	84.67±9.14	87.07±8.81	0.007
T5 = 5 min after intubation	81.50±8.55	86.17±7.47	88.93±7.47	0.002
T6 = 10 min after intubation.	80.93±8.87	84.70±9.24	88.07±9.16	0.012

Table 3.1 shows the patient's heart rate before starting (T0) and after completion (T1) of the study drug infusion, just after laryngoscopy & intubation (T2), 1 minute (T3), 3 minutes (T4), 5 minutes (T5) and 10 minutes (T6) after intubation in 3 groups. It was observed that there was no significant difference in HR at T0 and T1 time points (p-value > 0.05) among the groups. The difference was statistically significant among the groups at T2, T3, T4, T5, and T6. (p<0.05)

Figure 3.1 Comparison of the heart rates among three intervention groups:

B. Systolic blood pressure (SBP):

Table 3.2 Comparison of SBP among the groups

Time Interval (min)	Group D (Mean±S.D)	Group F (Mean±S.D)	Group E (Mean±S.D)	P Value
T0 = Baseline (before the start of infusion of study drugs)	130.60±8.49	129.80±7.99	130.83±7.56	0.87
T1 = after completion of the study drug infusion	122.67±13.19	125.53±11.001	118.50±7.13	0.04
T2 = just after laryngoscopy & intubation	118.80±8.72	124.20±9.30	117.87±4.70	0.005
T3 = 1 min after intubation	121.40±7.49	124.00±9.63	117.70±8.37	0.019
T4 = 3 min after intubation	121.27±8.49	126.63±9.98	117.77±9.75	0.002
T5 = 5 min after intubation	128.03±10.37	125.23±9.65	120.10±8.86	0.007
T6 = 10 min after intubation.	126.47±8.18	125.67±11.56	122.33±9.61	0.234

Table 3.2 shows the patient's SBP before starting (T0) and after completion (T1) of the study drug infusion, just after laryngoscopy & intubation (T2), 1 minute (T3), 3 minutes (T4), 5 minutes (T5) and 10 minutes (T6) after intubation in 3 groups. It was observed that there was no significant difference in SBP at T0 and T6 time points (p-value > 0.05) among the groups. The difference was statistically significant among the groups at T1, T2, T3, T4, and T5. (p<0.05)

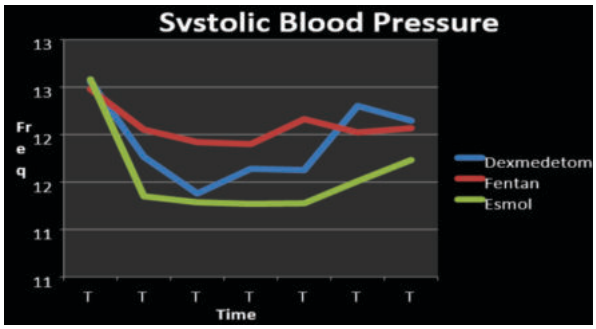

Figure 3.2 Comparison of the SBP among three intervention groups:

C. Diastolic blood pressure (DBP):

Table 3.3 Comparison of DBP among the groups

Time Interval (min)	Group D (Mean±S.D)	Group F (Mean±S.D)	Group E (Mean±S.D)	P Value
T0 = Baseline (before the start of infusion of study drugs)	81.87±9.22	81.90±9.66	79.63±7.91	0.535
T1 = after completion of the study drug infusion	72.67±10.82	83.20±7.00	79.37±7.84	<0.01
T2 = just after laryngoscopy &intubation	76.47±12.23	82.90±7.67	76.93±8.67	0.020
T3 = 1 min after intubation	72.53±6.56	79.83±9.91	78.47±8.71	0.003
T4 = 3 min after intubation	74.30±7.86	84.80±7.46	79.40±7.28	<0.01
T5 = 5 min after intubation	78.87±10.75	82.67±7.25	78.00±9.54	0.12
T6 = 10 min after intubation	78.53±7.55	79.20±10.51	77.20±11.27	0.73

Table 3.3 shows the patient's mean DBP before starting (T0) and after completion (T1) of the study drug infusion, just after laryngoscopy & intubation (T2), 1 minute (T3), 3 minutes (T4), 5 minutes (T5) and 10 minutes (T6) after intubation in 3 groups. It was observed that there was no significant difference in DBP at T0, T5, and T6 time points (p-value > 0.05) among the groups. The difference was statistically significant among the groups at T1, T2, T3, and T4. (p<0.05)

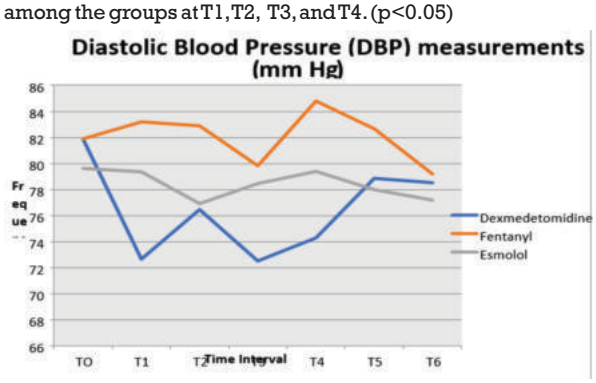

Figure 3.3 Comparison of the DBP among three intervention groups:

D. Mean arterial pressure (MAP):

Table 3.4 Comparison of MAP among the groups

Time Interval (min)	Group D (Mean±S.D)	Group F (Mean±S.D)	Group E (Mean±S.D)	P Value

T0 = Baseline (before the start of infusion of study drugs)	98.91±7.61	99.86±4.09	100.16±5.19	0.689
T1 = after completion of the study drug infusion	97.31±6.43	94.03±4.29	94.60±4.95	0.043
T2 = just after laryngoscopy &intubation	97.17±5.37	94.12±3.03	96.50±3.82	0.015
T3 = 1 min after intubation	95.35±5.07	91.78±5.42	95.38±4.29	0.007
T4 = 3 min after intubation	93.22±4.36	90.75±5.86	94.29±4.98	0.026
T5 = 5 min after intubation	94.60±6.35	93.43±3.72	94.20±4.52	0.656
T6 = 10 min after intubation	93.65±3.75	94.09±3.01	94.51±3.88	0.649

Table 3.4 shows the patient's mean MAP before starting (T0) and after completion (T1) of the study drug infusion, just after laryngoscopy & intubation (T2), 1 minute (T3), 3 minutes (T4), 5 minutes (T5) and 10 minutes (T6) after intubation in 3 groups. It was observed that there was no significant difference in MAP at T0, T5, and T6 time points (p-value > 0.05) among the groups. The difference was statistically significant among the groups at T1, T2, T3, and T4. (p<0.05)

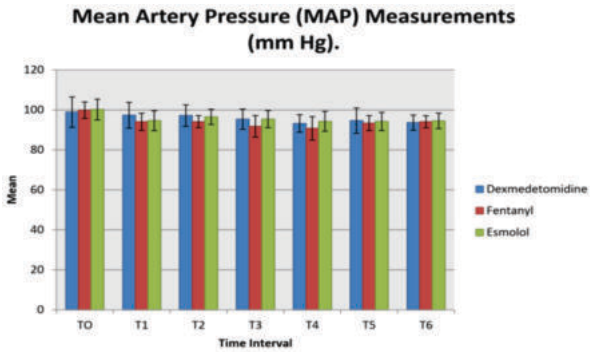

Figure 3.4 Comparison of the MAP among three intervention groups:

D. Oxygen Saturation (SPO2):

Table 3.5 Comparison of SPO2 among the groups

Time Interval (min)	Group D (Mean±S.D)	Group F (Mean±S.D)	Group E (Mean±S.D)	P value
T0 = Baseline (before the start of infusion of study drugs)	99.87±0.35	99.60±0.72	99.70±0.65	0.22
T1 = after completion of the study drug infusion	99.77±0.57	99.67±0.55	99.80±0.48	0.61
T2 = just after laryngoscopy &intubation	99.57±0.86	99.60±0.67	99.63±0.67	0.94
T3 = 1 min after intubation	99.57±0.63	99.50±0.63	99.57±0.73	0.90
T4 = 3 min after intubation	99.73±0.58	99.57±0.73	99.60±0.50	0.54
T5 = 5 min after intubation	99.47±0.63	99.47±0.78	99.70±0.47	0.27
T6 = 10 min after intubation	99.20±0.80	99.50±0.63	99.43±0.86	0.29

Table 3.5 shows the patient's mean SPO2 before starting (T0) and after completion (T1) of the study drug infusion, just after laryngoscopy & intubation (T2), 1 minute (T3), 3 minutes (T4), 5 minutes (T5) and 10 minutes (T6) after intubation in 3 groups. It was observed that there was no significant difference in SPO2 at any time point (p-value > 0.05) among the groups.

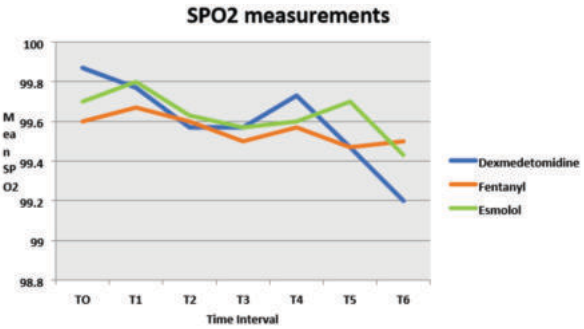

Figure 3.5 Comparison of the SPO2 among three intervention groups:

4. Complications/Adverse events:

Table 4 Comparison of Adverse events among the groups

Side Effects	Group D (n=30)	Group F (n=30)	Group E (n=30)	χ^2 Value	P value
	n (%)	n (%)	n (%)		
Nausea	6(20)	2 (6.7)	6 (20.0)	2.71	0.26
Vomiting	0 (0)	0 (0)	2 (6.7)	4.09	0.1 3
Bradyca rdia	3 (10)	4 (8.0)	3 (10)	0.27	0.8 7
Respiratory depression	0 (0)	2 (3.3)	0(0)	4.09	0.1 3
Dyspnea	2 (6.7)	0 (0)	2 (6.7)	2.09	0.3 5
Shivering	1(3.3)	1(3.3)	3 (10)	1.69	0.4 3
Hypotension	2 (6.7)	0 (0)	2 (6.7)	2.09	0.3 5

Table 4 shows the comparison of complications or adverse events. It was observed that there was no significant difference (p-value > 0.05) among the groups.

The following observations were obtained after statistical analysis:

1. The demographic profile (Age, Sex, weight, height, BMI, and ASA grade) were comparable among the three groups.
2. There was no significant difference in baseline HR, SBP, DBP, MAP, RR and SPO2 among the three groups.
3. Following the study drug infusion completion, HR fell from baseline in groups D and E but increased in group F. The difference in HR was statistically significant after laryngoscopy & intubation, 1 min, 3 min, 5 min, and 10 min after intubation. dexmedetomidine was found to attenuate the HR more effectively than fentanyl and esmolol.
4. Reduction of SBP, DBP, and MAP were recorded in all three groups from the baseline values. The differences were statistically significant among the groups starting after drug infusion to up to 3 minutes after intubation. Dexmedetomidine and esmolol were found to be more effectively reduced BP than fentanyl.
5. The comparison of the incidence of side effects among the group was statistically insignificant (p>0.05). Our patients had no cough, apnea, or laryngospasm episodes.

CONCLUSION

Intravenous dexmedetomidine, was found to be more effectively attenuate the stress responses following laryngoscopy and endotracheal intubation than esmolol and fentanyl in adult patients undergoing laparoscopic cholecystectomy under general anaesthesia. The side effects profile was comparable among the three agents.

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