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Original Research Article

Evaluation of attenuation of intubation response in simulated difficult airway: An entropy™-guided comparison between fentanyl and dexmedetomidine: A randomized, prospective, double-blinded study

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Abstract

Background and Aims: Laryngoscopy and endotracheal intubation often trigger a catecholamine surge due to reflex sympathetic stimulation, with more severe pressor responses in difficult airways. This study aimed to evaluate the effectiveness of dexmedetomidine and fentanyl in attenuating hemodynamic responses during simulated difficult intubation scenarios. Secondary outcomes including entropy values, adverse events, and intubation difficulty scale (IDS) scores were also assessed.

Materials and Methods: In this randomized, prospective, double-blinded study, 130 patients were divided into two groups: Group F (fentanyl, 2 µg/kg) and Group D (dexmedetomidine, 1 µg/kg). After drug administration and induction, a soft cervical collar was applied once state entropy reached <50, creating a standardized difficult airway scenario. Hemodynamic parameters, including heart rate (HR), mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO_2), and anaesthesia depth (state entropy [SE] and response entropy [RE]), were recorded at baseline, during drug administration, after induction, immediately post-intubation, and at specified intervals up to 10 minutes post-intubation. Adverse events and intubation difficulty scale (IDS) score were also documented.

Results: Dexmedetomidine showed superior control of heart rate immediately post-intubation ($P<0.05$) and up to 10 minutes post-intubation compared to fentanyl ($P<0.01$). No significant differences were observed in blood pressure measurements between groups ($P>0.05$). Dexmedetomidine was associated with lower entropy values ($P<0.01$), indicating better depth of anaesthesia. The fentanyl group experienced significant hypotension immediately post-induction.

Conclusion: Both dexmedetomidine (1 µg/kg) and fentanyl (2 µg/kg) effectively attenuate the intubation response during simulated difficult laryngoscopy and intubation. Dexmedetomidine offers superior heart rate control and depth of anaesthesia compared to fentanyl.

Keywords: Airway management; Cervical collar, Simulated difficult intubation; Dexmedetomidine, Fentanyl; Entropy.

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1. Introduction

Airway management is crucial in anaesthesia and emergency care. Laryngoscopy and intubation cause a surge in catecholamine levels, leading to hypertension, tachyarrhythmias, myocardial ischemia and intracranial hypertension.[1]

The magnitude of pressor response intensifies with increased duration and multiple attempts of intubation in difficult airway. With worsening of the laryngeal view during laryngoscopy there is need of increased anterior lifting force with the laryngoscope blade, reinstituting most favourable sniff position, making repeated attempts, manipulation of larynx externally, or opting for alternative devices to achieve intubation and all these factors increase the stress response to laryngoscopy.[2]

Fentanyl is a short acting synthetic opioid used during anaesthesia to dampen cardiovascular responses to noxious stimulation from laryngoscopy, intubation, surgical incision.[3-5] Dexmedetomidine, a selective α_2 agonist causes sympatholysis acting centrally and has sedative and analgesic effects. Fentanyl and dexmedetomidine are among the

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various pharmacological agents used to dampen the cardiovascular responses to laryngoscopy and intubation.

Entropy is used to track level of consciousness in patients receiving general anaesthesia or sedation.[6] The use of entropy ensures maintenance of uniform depth of anaesthesia and thus aids in preventing stress response that might inadvertently arise during airway handling in light plane of anaesthesia.

The predictors of difficult airway have inter-rater variabilities with low sensitivity, most of the patients with anticipated difficult airway might not have true difficult airway hence we created reversible 'difficult-to-intubate' situations with soft cervical collars to evaluate effectiveness of fentanyl and dexmedetomidine in suppressing intubation response in simulated difficult airway as primary outcome. Secondary outcomes were assessment of IDS score after simulation of difficult airway and adverse events during the study.

2. Materials and Methods

This prospective, randomized, double blinded clinical study was conducted after institutional ethical committee clearance (IRB number SDMIEC: 0355:2017) and prospective registration in CTRI- clinical trials registry – India (registration number: CTRI/2018/03/012355). 130 patients aged 18-55 years, belonging to ASA-PS I and II in whom airway difficulty was not anticipated and requiring endotracheal intubation for general anaesthesia to conduct elective surgeries at a tertiary care hospital, during December 2017 to May 2019 were enrolled for the study with written informed consent. Patients with predicted difficulty in airway management, heart rate less than 60 beats/min, ASA physical status III and IV, BMI <18 kg/m^2 and >40 kg/m^2, ischaemic heart disease, raised intracranial pressure, epilepsy, cerebrovascular disease, intraocular hypertension, hepatic, renal and other cardiac diseases, allergic to drugs in study, pregnant women, lactating mothers and those who refused to participate in the study were excluded (**Figure 1**).

The sample size was determined using data from a pilot study that examined differences in heart rate between the two anaesthetic techniques. To detect a clinically meaningful difference of 20% in heart rate between the groups, a power analysis was performed. Using a significance level (α) of 0.05 for 95% confidence and statistical power (1-β) of 80%, the calculated minimum sample size was 63 patients per group. To account for potential dropouts and ensure adequate power, sample size was increased to 65 patients per group. The sample size was calculated using the following formula for comparing means between two independent groups:

$$n = \frac{2(Z\alpha+Z\beta)^2 \times p \times q}{d^2}$$

$$n = \frac{2(1.96+0.842)^2 \times 0.8 \times 0.2}{(0.2)^2}$$

$n = 62.8$

where $p = \frac{p1+p2}{2}$

$q = 1-p$

$Z\alpha = 1.96$ at 5% α- error

$Z\beta = 0.842$ at 80% power

d = difference between two proportions or effect size

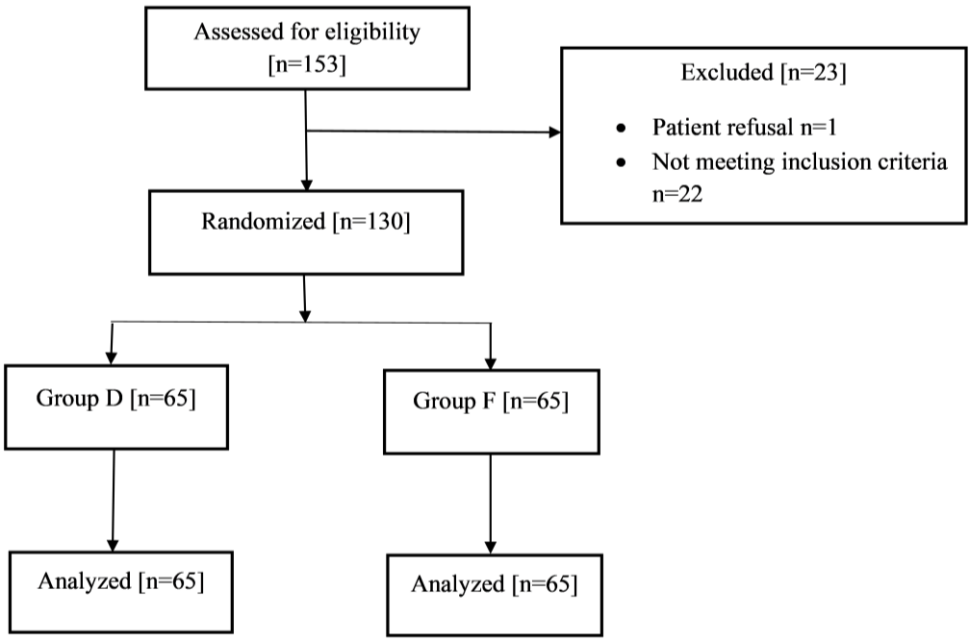

Figure 1: CONSORT flow diagram for the study. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl

All patients underwent thorough pre-operative evaluation. Written informed consent for the procedure was obtained. Patients were informed that they would be unaware of their assignment to either study group. Patients who consented to participate were kept fasting according to standard ASA guidelines and were premedicated with 150 mg of ranitidine and 0.5 mg of alprazolam orally.

Patients were randomly assigned to group F and group D using a sealed envelope method, with the envelopes being opened just before the patients were moved into the operating room. Following the transfer of patients to the operating room, entropy sensors were affixed to their foreheads. An intravenous line was secured with cannula of appropriate size. Heart rate (HR), mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO_2), state entropy (SE) and response entropy (RE) were measured and noted down (T_0).

Patients in group F received 20 ml of normal saline over 10 minutes using a syringe pump followed by injection fentanyl 2 μg/kg body weight 1 minute prior to induction. Patients in group D received intravenous dexmedetomidine 1 μg/kg body weight over 10 minutes using a syringe pump followed by 2-3 ml of normal saline 1 minute prior to induction. All the above mentioned haemodynamic and entropy parameters were recorded after study drug administration (T_1). All the study drugs (dexmedetomidine and fentanyl) were prepared by a person not administering anaesthesia and not involved in assessment of the patient, hence double blinding maintained.

Following preoxygenation, patients were induced with injection propofol 2 mg/kg IV, supplemented, if necessary, by 0.2 mg/kg propofol till SE value became less than 50. Anaesthesia was maintained with propofol infusion at 150 μg/kg/min. After induction (T_2) a reading of HR, MAP, SBP, DBP, SpO_2, SE and RE were noted. Check ventilation was done and when found adequate, neuromuscular blockade was achieved using injection vecuronium 0.1 mg/kg IV. The patient received mask ventilation with 100% oxygen for a duration of 3 minutes. Once state entropy reached <50, a soft cervical collar was applied to the patient to restrict neck movements creating a standardized difficult airway scenario.

After this, direct laryngoscopy was performed using a Macintosh blade of suitable size; airway secured with cuffed endotracheal tube of appropriate size, passing orally and fixed at appropriate length after auscultation for equal air entry in both lungs. The number of attempts in laryngoscopy, total duration of laryngoscopy and intubation were noted. Each insertion of laryngoscope blade into the oral cavity was taken as an attempt at laryngoscopy. The time duration from insertion of laryngoscope into oral cavity to appearance of end tidal carbon dioxide waveform on the monitor was taken as total duration of laryngoscopy and intubation. A maximum of three attempts at laryngoscopy and 180 seconds of total duration of laryngoscopy and intubation was allowed, failure of which was managed by intubating after removing cervical collar.

Any episode of bradycardia (HR <45 beats/min) was treated with IV atropine 0.6 mg and drop in mean arterial blood pressure more than 20% from the baseline was treated with IV ephedrine 6 mg. Any rise in heart rate and mean arterial blood pressure more than 30% from the baseline was treated with IV esmolol 0.5-1 mg/kg.

Readings of HR, MAP, SBP, DBP, SpO_2, SE and RE were taken immediately post intubation (T_3), every minute for 5 minutes post intubation (T_{4-8}), 7 minutes (T_9) and 10 minutes (T_{10}) following intubation. The cervical collar was removed, and anaesthesia was maintained with propofol infusion at 150 μg/kg/min and controlled ventilation with IPPV, O_2, N_2O for 10 minutes post intubation. Further management of anaesthesia and analgesia intraoperatively and postoperatively was determined by the attending anaesthesiologist.

Both the study participants and anaesthesiologist administrating drug were unaware of group allotment of the patient and thus double blinding maintained.

The intubation difficulty scale (IDS) validated by Adnet and colleagues along with CL grade was used to assess airway difficulty after application of cervical collar.[2] Additional dose of propofol required for induction and adverse effects were also compared.

Data were collected, organized, and expressed as mean ± standard deviation. Analysis was performed using IBM SPSS Statistics (version 22.0 Evaluation). The unpaired sample t-test was employed for quantitative data, while the Chi-square test was used for qualitative data. A *P* value of <0.05 was deemed to be statistically significant and <0.01 was considered highly significant. *P* value of >0.05 was considered statistically insignificant.

3. Results

Both the groups had comparable demographic characteristics (**Table 1**). While comparing CL grading after applying cervical collar, most patients had CL 2a (n=51) and 2b (n=52) views. There were 12 patients with CL grade 1 and 15 patients with CL grade 3. The distribution of patients across these grades was comparable between the two groups (*P*>0.05). All parameters in the IDS score assessment remained statistically comparable in both the groups with no statistical difference in Mean IDS score (*P*>0.05) (**Table 2**).

Baseline mean heart rate was comparable in both the groups (*P*>0.05) (**Figure 2**) Mean heart rate throughout the study period was lower in group D when compared to group F (*P*<0.05) (**Table 3**). But this difference was clinically insignificant, as change in mean heart rate in both the groups remained <20% of baseline value.

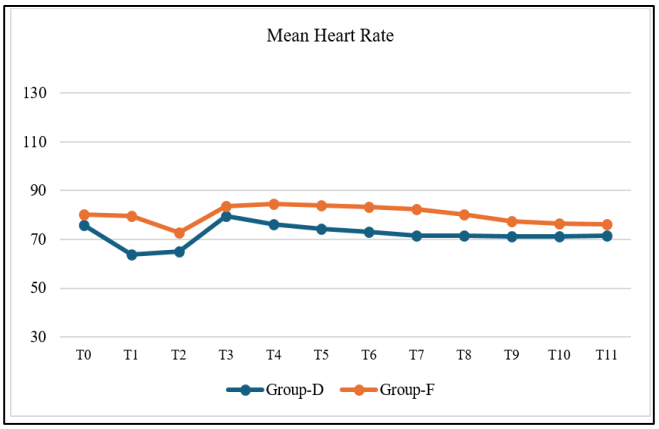

Figure 2: Comparison of mean heart rate among group D and group F. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl. T0-before test drug administration, T1-after test drug administration, T2-after induction, T3-immediate post intubation, T4- one minute post intubation, T5- two minutes post intubation, T6-three minutes post intubation, T7-four minutes post intubation, T8-five minutes post intubation, T9-seven minutes post intubation, T10-nine minutes post intubation, T11-ten minutes post intubation

Mean arterial pressure (MAP) was analogous in both the groups before test drug administration. MAP was noticed to be significantly lower in group D compared to group F after test drug administration (T_1) (P<0.05), while it was lower in group F after induction of anaesthesia (T_2) which was both statistically (P<0.01) and clinically significant (decrease in MAP >20% of baseline) (**Table 3**). MAP was comparable between two groups from the immediate post intubation period till end of study period (T_3-T_{11}) (P>0.05). (**Figure 3**)

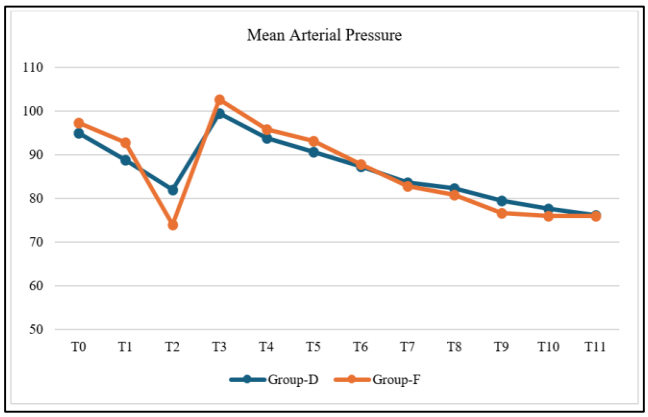

Figure 3: Comparison of mean arterial blood pressure among group D and group F. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl.

Mean SBP was also comparable between two groups before drug administration. Mean SBP was significantly lower after dexmedetomidine administration (T_1) in group D (P<0.05). Lower mean SBP was observed in group F compared to group D after induction (T_2) which was both statistically (P<0.01) (**Table 3**) and clinically significant (decrease in SBP >20% of baseline). Mean SBP was comparable between two groups statistically at all-time post intubation till 10 min (P>0.05), except at 7th minute post intubation (T_9) where it was lower in group F (P<0.05). (**Figure 4**)

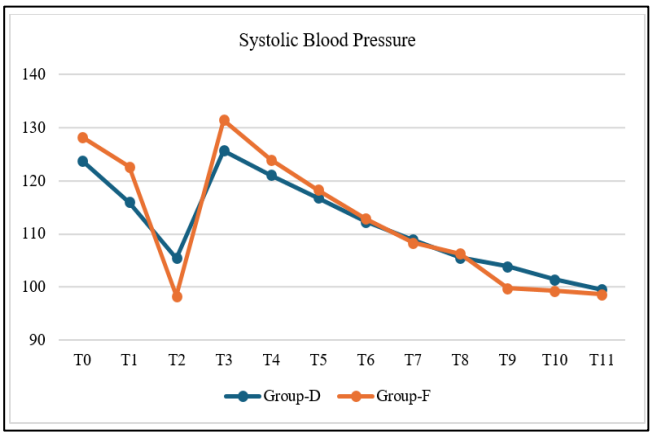

Figure 4: Comparison of mean systolic blood pressure among group D and group F. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl

Mean diastolic blood pressure was always statistically similar among both the groups during study period (P>0.05), except post induction (T_2) where it remained highly statistically lower in group F (P<0.01) and clinically significant. (**Table 3**) (**Figure 5**)

SpO_2 was always comparable between two groups during the study period except that it was statistically lower in group D after dexmedetomidine administration (T_1) when compared to group F. However, this was clinically insignificant (98.5±1.5%). No episode of clinically evident desaturation was noted in either of the group.

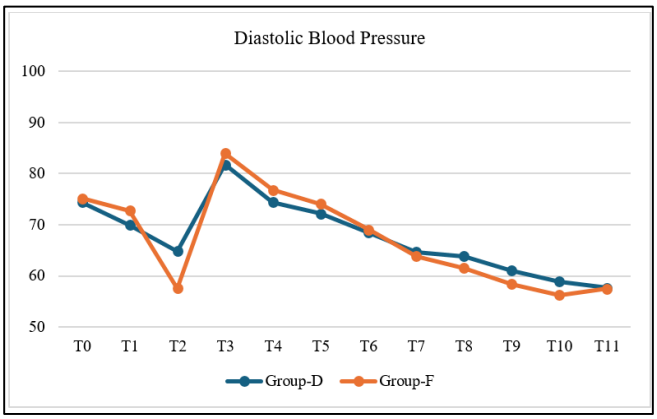

Figure 5: Comparison of mean diastolic blood pressure among group D and group F. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl

State entropy (SE) and response entropy (RE) values were comparable between two groups before test drug administration (**Table 4**). SE and RE values remained lower in group D when compared to group F during the entire study period which was statistically highly significant (P<0.01) (**Figure 6**, **Figure 7**)

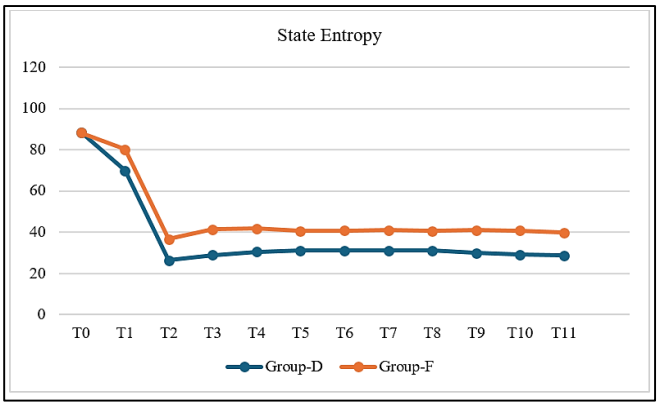

Figure 6: Comparison of mean state entropy values among group D and group F. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl.

In group F, 14 patients required an additional dose of propofol (>2 mg/kg) during induction to achieve a state entropy (SE) value of <50, compared to 3 patients in group D, a difference that was statistically significant. In group F, 10 patients (13% of the total study population) experienced hypotension, defined as a decrease in mean arterial pressure (MAP) >20% from baseline, immediately after induction. This was effectively managed with a 6 mg bolus of intravenous (IV) ephedrine. Additionally, 2 patients (3% of the total in group F) developed hypertension, defined as an increase in MAP >30% from baseline, following intubation; this was treated with 0.5 mg/kg of IV esmolol.

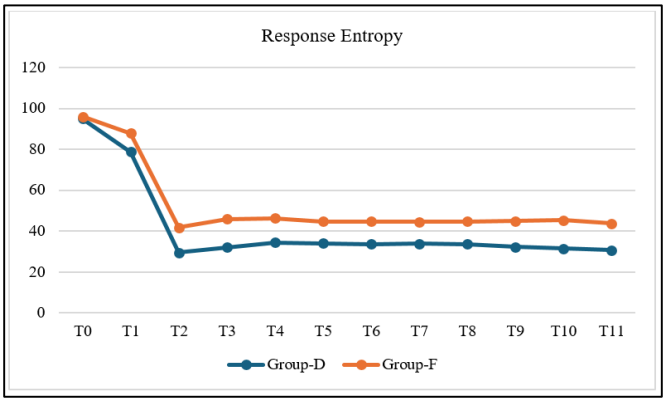

Figure 7: Comparison of mean response entropy values among group D and group F. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl

Total of 12 patients had tears from the eye post intubation of which 7 were in group F and 5 were in group D. Limb movements were seen in 2 patients both belonging to group F while attempting mask ventilation post induction of anaesthesia before administration of skeletal muscle relaxant. In both the groups these signs of lighter plane of anaesthesia were seen while SE value was <50 and incidence of these signs were statistically comparable among both groups.

Table 1: Demographic makeup of the enrolled patients

Demographic makeup	**Group-D**	**Group-F**	***P* value**
Age (years), Mean ± SD	31.45±10.08	35.17±10.70	0.356
BMI, Mean ± SD	23.16 ± 3.07	22.53 ± 3.68	0.294
Gender			
Male	28	30	0.724
Female	37	35	
ASA-PS			
I	60	55	0.170
II	5	10	

Values are presented as mean ± SD, numbers. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl. BMI: body mass index, ASA-PS: American Society of Anaesthesiologists physical status.

Table 2: Distribution of CL grade, comparison of parameters of IDS scores and distribution of IDS score

CL grade	**Group-D n=65**	**Group-F n=65**	***P* value**
1	4	8	0.325
2a	26	25	
2b	26	26	
3	9	6	
Duration of laryngoscopy and intubation in seconds	46.60 ± 24.38	50.48 ± 30.80	0.427
Number of attempts in laryngoscopy and intubation			
1	61	55	0.303
2	2	4	
3	1	5	
4	1	1	

Table 2 Continued…			
Number of additional operators			
Nil	65	63	0.154
One	0	2	
Alternative intubation technique used			
Nil	50	59	0.056
Bougie	15	6	
Need of excessive lifting force			
No	11	16	0.279
Yes	54	49	
IDS Score after application of soft cervical collar			
0	4	8	0.057
1	8	13	
2	37	28	
3	7	6	
4	7	1	
5	1	5	
6	0	2	
7	0	1	
8	1	0	
9	0	1	

Values are presented as mean ± SD, numbers. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl. CL grade: Cormack-Lehane grade, IDS: intubation difficulty scale.

Table 3: Comparison of hemodynamics

Time Point	Description	HR Group-D (Mean ± SD)	HR Group-F (Mean ± SD)	HR *P* value	MAP Group-D (Mean ± SD)	MAP Group-F (Mean ± SD)	MAP *P* value	SBP Group-D (Mean ± SD)	SBP Group-F (Mean ± SD)	SBP *P* value	DBP Group-D (Mean ± SD)	DBP Group-F (Mean ± SD)	DBP *P* value
T_0	Before drug	75.9 ± 12.3	80.1 ± 12.7	0.06	94.9 ± 10.9	97.3 ± 10.8	0.202	123.8 ± 12.5	128.3 ± 14.9	0.06	74.4 ± 9.0	75.2 ±12.7	0.679
T_1	After drug	63.9 ± 9.8	79.6 ± 13.3	0.0	88.8 ± 10.1	92.8 ± 12.1	0.04	116.0 ± 14.1	122.7 ± 16.8	0.01	70.0 ± 9.7	72.8 ±10.8	0.115
T_2	After induction	65.0 ± 8.0	72.8 ± 11.0	0.0	81.9 ± 11.3	73.9 ± 9.7	0.0	105.5 ± 15.4	98.3 ± 13.6	0.006	64.9 ±10.7	57.6 ± 9.9	0.0
T_3	Immediate post intubation	79.7 ± 10.5	83.6 ± 11.4	0.04	99.5 ± 12.7	102.6±15.6	0.203	125.7 ± 16.1	131.5 ± 20.0	0.07	81.8 ±13.2	84.0 ±14.5	0.378
T_4	1 min post intubation	76.2 ± 9.8	84.7 ± 10.5	0.0	93.7 ± 9.8	95.8 ± 14.7	0.352	121.1 ± 13.4	124.0 ± 21.5	0.348	74.4 ±10.6	76.8 ±12.1	0.231
T_5	2 min post intubation	74.4 ± 9.7	84.0 ± 11.4	0.0	90.6 ± 9.9	93.1 ± 14.1	0.247	116.8 ± 12.6	118.3 ± 18.3	0.578	72.2 ± 9.6	74.1 ±12.2	0.333
T_6	3 min post intubation	73.2 ± 9.2	83.4 ± 11.7	0.0	87.3 ± 9.8	87.7 ± 14.2	0.857	112.3 ± 12.0	112.9 ± 18.0	0.841	68.5 ± 9.3	69.1 ±13.4	0.756
T_7	4 min post intubation	71.7 ± 9.6	82.3 ± 13.1	0.0	83.6 ± 10.3	82.8 ± 12.0	0.673	108.9 ± 12.2	108.4 ± 15.0	0.833	64.7 ± 9.8	63.9 ±12.0	0.678
T_8	5 min post intubation	71.7 ± 9.8	80.1 ± 12.3	0.0	82.3 ± 9.2	80.7 ± 11.8	0.394	105.6 ± 16.9	106.3 ± 15.0	0.797	63.9 ± 9.4	61.6 ±11.0	0.209
T_9	7 min post intubation	71.1 ± 9.5	77.3 ± 11.5	0.001	79.5 ± 8.6	76.6 ± 9.1	0.06	103.9 ± 11.2	99.8 ± 11.4	0.04	61.1 ± 8.9	58.4 ± 9.6	0.09
T_{10}	9 min post intubation	71.2 ± 9.2	76.5 ± 10.1	0.002	77.6 ± 8.7	76.0 ± 9.1	0.298	101.4 ± 11.4	99.3 ± 10.8	0.269	58.9 ± 9.1	56.3 ±10.1	0.129
T_{11}	10 min post intubation	71.6 ± 9.7	76.2 ± 10.9	0.01	76.1 ± 8.9	76.0 ± 9.1	0.954	99.6 ± 12.0	98.6 ± 11.7	0.637	57.7 ± 9.2	57.5 ±11.0	0.319

Values are presented as mean ± SD. Group-D: dexmedetomidine, Group-F: fentanyl.

Table 4: Comparison of mean state entropy and response entropy values

Parameters		State entropy			Response entropy		
		Group-D (n=65)	Group-F (n=65)	*P* value	Group-D (n=65)	Group-F (n=65)	*P* value
		Mean ± Std. Deviation	Mean ± Std. Deviation		Mean ± Std. Deviation	Mean ± Std. Deviation	
Before drug	T_0	88.5 ± 3.4	88.3 ± 3.8	0.788	95.0 ± 3.4	96.0 ± 2.0	0.06
After drug	T_1	70.0 ± 15.7	80.3 ± 16.1	0.000	78.8 ± 16.3	88.0 ± 16.2	0.002
After induction	T_2	26.4 ± 9.6	36.6 ± 8.9	0.000	29.6 ± 11.6	41.9 ± 10.7	0.000
Immediate post intubation	T_3	28.9 ± 9.9	41.4 ± 11.1	0.000	32.1 ± 11.0	46.0 ± 12.5	0.000
1 min post intubation	T_4	30.5 ± 9.4	41.8 ± 9.1	0.000	34.4 ± 10.5	46.4 ± 9.4	0.000
2 min post intubation	T_5	31.1 ± 8.7	40.5 ± 9.5	0.000	34.1 ± 10.0	44.7 ± 8.9	0.000
3 min post intubation	T_6	31.0 ± 9.6	40.8 ± 9.4	0.000	33.6 ± 10.4	44.7 ± 9.6	0.000
4 min post intubation	T_7	31.2 ± 10.3	41.0 ± 9.9	0.000	33.8 ± 10.7	44.6 ± 9.7	0.000
5 min post intubation	T_8	31.2 ± 10.4	40.7 ± 8.8	0.000	33.6 ± 11.0	44.8 ± 9.1	0.000
7 min post intubation	T_9	30.0 ± 10.7	41.1 ± 9.2	0.000	32.4 ± 12.2	45.0 ± 10.1	0.000
9 min post intubation	T_{10}	29.1 ± 10.8	40.8 ± 8.6	0.000	31.6 ± 10.7	45.4 ± 9.1	0.000
10 min post intubation	T_{11}	28.7 ± 10.0	39.8 ± 8.3	0.000	30.8 ± 10.8	43.7 ± 8.9	0.000

Values are presented as mean ± SD. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl.

Table 5: Comparison of additional dose of propofol required for induction of anaesthesia targeting state entropy value of <50.

Additional dose of propofol required for induction	Groups		Total	*P* value
	Group-D	Group-F		
Not required	62	51	113	0.04
Required	3	14	17	
Dosage	**Group-D**	**Group-F**	**Total**	
10 mg	0	5	5	
20 mg	2	4	6	
30 mg	1	4	5	
70 mg	0	1	1	
Total	3	14	17	

Values are presented as numbers. Group-D: recipients of dexmedetomidine, Group-F: recipients of fentanyl.

4. Discussion

This prospective randomised study aimed to compare the effectiveness of dexmedetomidine and fentanyl in attenuating the intubation response in a simulated difficult airway scenario among patients undergoing elective surgery under general anaesthesia. Of the 130 patients included, 52 (40%) presented with a restricted laryngoscopic view classified as Cormack-Lehane (CL) grade 2b, and 15 (11.5%) had a CL grade 3 view. These conditions were achieved by creating reversible "difficult-to-intubate" scenarios using a soft cervical collar, as described in previous studies.[7-13]

Stoelting RK suggests that the ideal duration for laryngoscopy is less than 15 seconds.[14] However, in our study, the average duration of laryngoscopy and intubation exceeded 15 seconds in both groups, meeting the criteria for prolonged laryngoscopy. Among the study population, 5 patients (3.84%) had an intubation difficulty scale (IDS) score greater than 5, indicating moderate to major difficulty in tracheal intubation. Conversely, the majority—113

patients (86.92%)—had an IDS score between 1 and 5, reflecting slight to moderate intubation difficulty.[15]

Reduction in mean heart rate from the baseline was 15.8% after dexmedetomidine administration and the same was 0.6% in fentanyl group. In group D, the rise in mean heart rate occurred immediately after intubation (79.7±10.5), representing a 5% rise from baseline. In contrast, in group F, the highest increase in mean heart rate was observed 1-minute post-intubation (84.7±10.5), corresponding to a 5.7% increase from baseline. Heart rate reverted to baseline value by 2 min post intubation in group D while the same was 5 minutes post intubation in group F. Patel C et al used sevoflurane-fentanyl 2 μg/kg in 30 patients taken as control group and sevoflurane-dexmedetomidine 1 μg/kg before induction, followed by infusion of 0.2 to 0.8 μg/kg/hour in 30 patients taken as test group.[16] They observed 10% escalation in pulse rate from initial baseline condition in the dexmedetomidine group in contrast to 17% rise in the fentanyl group at intubation (P<0.05). Keniya M et al found the escalation in heart rate after intubation was 21% in group C, receiving isoflurane-fentanyl (1 μg/kg) as compared to 7% in group D, receiving isoflurane-fentanyl (1 μg/kg)-dexmedetomidine (1 μg/kg before induction and infusion of 0.2 to 0.7 μg/kg/h in intraoperative period).[17] The heart rate values in the dexmedetomidine group were consistently lower than those in the fentanyl group, and this difference was statistically discernable across all time intervals, like the observations in other studies on intubation response by Patel C et al, Keniya M et al and Sulaiman S et al akin to our study, hence making dexmedetomidine the preferred drug to suppress sympathoadrenal response in patients with coronary artery disease and fixed cardiac output states, where control of heart rate is prima facie especially when difficult airway is anticipated.[16-18]

In the dexmedetomidine group, the immediate post-intubation increase in systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) was 1.5%, 9.9%, and 4.8% from baseline, respectively. In the fentanyl group, the corresponding increases were 3.2%, 12.2%, and 5.4%. These differences were statistically insignificant, suggesting that both fentanyl and dexmedetomidine, at the doses used in this study, effectively mitigated the intubation response during difficult laryngoscopy and intubation.

However, the dexmedetomidine group demonstrated a statistically significant reduction in SBP and MAP (6.42% and 6.3%, respectively) following administration prior to induction. In contrast, the fentanyl group exhibited a more pronounced decrease in SBP, DBP, and MAP (23.3%, 23.4%, and 24.04%, respectively) post-induction with propofol. This decline was both statistically significant (P<0.05) and clinically relevant (>20% reduction from baseline). The greater hemodynamic impact in the fentanyl group highlights the need to titrate the propofol dose to maintain state entropy (SE) values below 50 while ensuring hemodynamic stability.

Our findings align with those of Patel et al., who reported reductions in SBP and DBP of 6% and 9%, respectively, following dexmedetomidine infusion.[16] However, their observation of significantly lower post-intubation SBP (6% vs. 23%) and DBP (7% vs. 20%) in the dexmedetomidine group compared to the fentanyl group contrasts with our study. This discrepancy may be explained by the continuation of dexmedetomidine infusion (0.2–0.8 μg/kg/h) after the initial loading dose in their study, unlike our protocol, where no infusion was administered after the bolus dose of 1 μg/kg.

Similarly, Keniya et al. observed an increase in SBP by 40% in the control group versus 8% in the dexmedetomidine group and an increase in DBP by 25% versus 11%, respectively (P<0.05).[17] Both groups in their study received IV fentanyl (1 μg/kg), and the test group also received dexmedetomidine (1 μg/kg over 10 minutes) with a maintenance infusion (0.2–0.7 μg/kg/h) post-intubation. This use of a continuous infusion may explain the greater hemodynamic stability observed in their dexmedetomidine group compared to ours.

Conversely, Das et al. found no significant differences in SBP or DBP between their dexmedetomidine (1 μg/kg) and fentanyl (1 μg/kg) groups up to 15 minutes post-intubation, aligning more closely with our results.[19] These variations across studies highlight the importance of protocol differences, such as the use of continuous infusions, in determining hemodynamic outcomes.

In group F, 10 patients (13% of the total group) experienced hypotension, defined as a decrease in MAP >20% from baseline, immediately after induction of anaesthesia. This was effectively treated with a 6 mg bolus of intravenous (IV) ephedrine. These findings align with the study by Uzumcugil et al., who compared dexmedetomidine (1 μg/kg)–propofol and fentanyl (1 μg/kg)–propofol combinations for laryngeal mask airway (LMA) insertion and observed a greater reduction in both SBP and MAP in the fentanyl group 90 seconds post-induction, similar to our results.[20]

In the present study, 2 patients (3% of the total study population) in group F developed hypertension (MAP increase >30% from baseline) following intubation, which was managed with 0.5 mg/kg IV esmolol. The endpoint for achieving adequate anaesthesia during induction was defined as an SE value of 50, based on the findings of Iannuzi et al., who reported that loss of consciousness typically occurs at SE values between 42.2 and 60.4.[21]

Patients in group D demonstrated significantly lower state entropy (SE) and response entropy (RE) values after administration of the study drug compared to group F throughout the study period, with this difference being highly

statistically significant (P<0.001). Furthermore, the additional propofol dose required to achieve SE values <50, beyond the standard 2 mg/kg, was notably lower in the dexmedetomidine group than in the fentanyl group.

These findings collectively suggest that dexmedetomidine reduces the required propofol dose for induction and provides a greater depth of anaesthesia when co-administered with propofol compared to the fentanyl-propofol combination. This highlights the enhanced anaesthetic-sparing effect of dexmedetomidine, which may be advantageous in clinical practice.

Dexmedetomidine and fentanyl have been extensively studied for their ability to mitigate the sympathetic response to laryngoscopy and intubation in patients with normal airways. However, in cases of difficult airways, this response is exaggerated due to prolonged laryngoscopy, multiple attempts, and the increased anterior lifting force required during direct laryngoscopy. Our findings support the use of both dexmedetomidine and fentanyl as anaesthetic adjuvants in managing the exaggerated pressor response in anticipated and unanticipated difficult airway scenarios.

5. Limitations

Our study had few limitations. The sympathetic response to laryngoscopy and intubation was assessed clinically through heart rate (HR) and blood pressure (BP) measurements, rather than by directly measuring blood catecholamine levels, which could have provided a more precise evaluation of the stress response. Additionally, despite simulating difficult airway conditions, we were unable to achieve a 100% incidence of difficult laryngoscopy and intubation; only 3% of patients in our study had an Intubation Difficulty Scale (IDS) score >5, indicating moderate to severe difficulty. Finally, adverse events occurring beyond the study period were not recorded, limiting our ability to assess potential long-term complications or outcomes.

6. Conclusion

Both dexmedetomidine (1 μg/kg) and fentanyl (2 μg/kg) given intravenously attenuate intubation response in patients with difficult laryngoscopy and intubation requiring excessive lifting force, longer duration of laryngoscopy and multiple attempts during intubation. Dexmedetomidine (1 μg/kg) demonstrates superior control of heart rate compared to fentanyl (2 μg/kg) and provides a greater depth of anaesthesia, as evidenced by significantly lower state entropy and response entropy values. These findings highlight the potential advantage of dexmedetomidine as an anaesthetic adjuvant in managing difficult airway scenarios.

7. Source of Funding

None.

8. Conflict of Interest

None.

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