IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 4 Ser.4 (April. 2021), PP 13-18
www.iosrjournals.org

"Comparison of Fentanyl with Dexmedetomidine on attenuating the haemodynamic response to intubation: A randomized double blind clinical study".

Dr Amit Kumar Sahu[1], Dr Koshy Varghese[2], Dr Asif Ahmed[3],
Dr Shyam Sundar Sahu[4]

1 DNB Anaesthetist 2,3Specialist 4 Assistant professor
1,2,3 Deptt of Anaesthesia and Critical Care, Tata Main Hospital, Jamshedpur, India
4 Deptt of Paediatric Surgery, RIMS , Ranchi, India

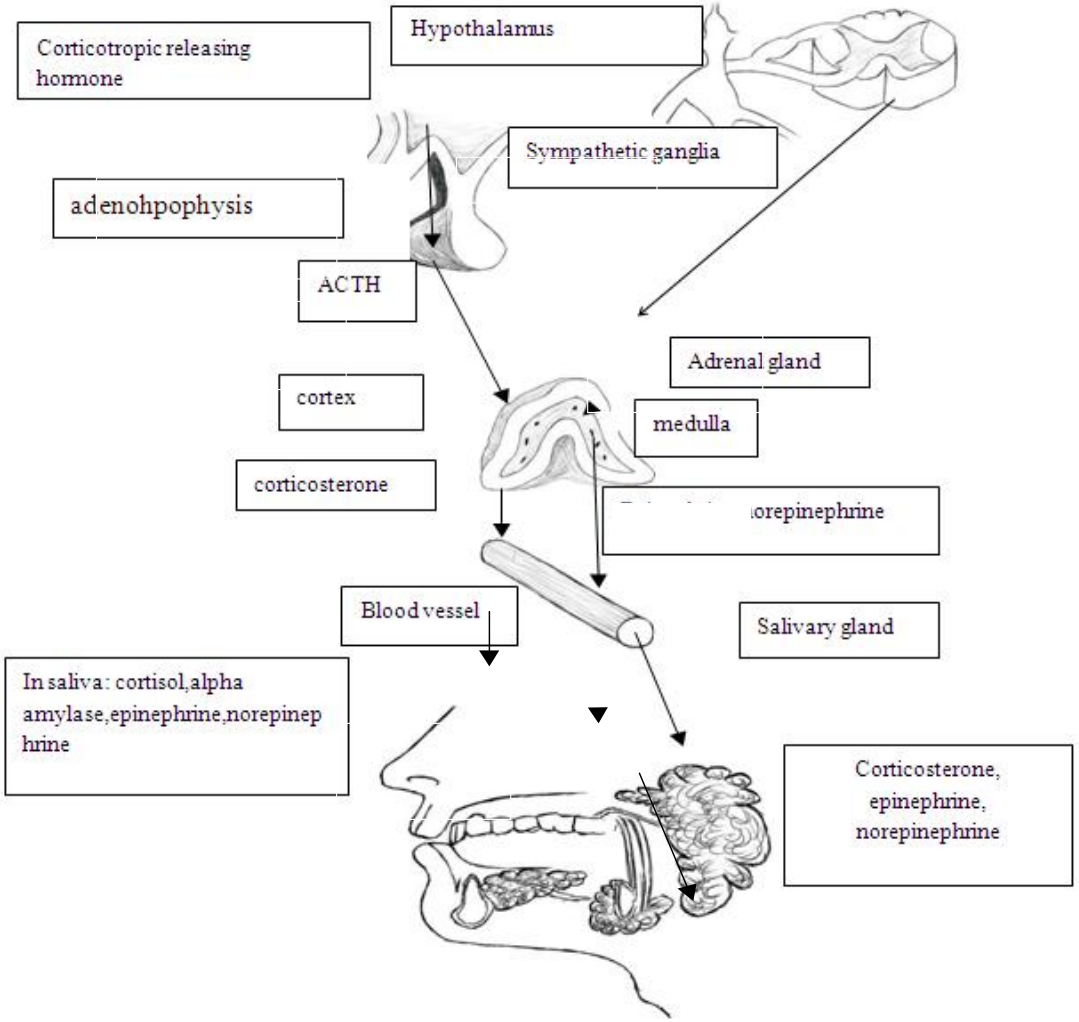
Abstract:-
Aim*: To compare the effect of intravenous Fentanyl with intravenous Dexmedetomidine on haemodynamic response to laryngoscopy & tracheal intubation in patients posted for elective surgical procedures and to study the safety and side effects of these drugs.*
Settings and Design: *Prospective, randomized & double blind study.*
Methods and Material: *100 elective surgical patients of aged 18 to 65 years were included in study. All patients underwent elective surgical procedures under general anaesthesia. Patients were randomized into two groups. Group F: Received Fentanyl 2µg/kg, Group D : Received Dexmedetomidine 1µg/kg.*
The following parameter (HR, SAP, MAP, DAP, and SpO2) levels were measured and recorded: - Average of three readings taken in operation theatre were considered as baseline and all other measurements were compared with the baseline.
Statistical analysis used*: All data were calculated as mean, standard deviation, percentage, Comparison of two mean tests and Chi-square test used*
Results*: When basal levels were compared with the measurements of the groups, it was found that during laryngoscopy and subsequent time intervals post intubation heart rate, systolic, diastolic, mean arterial pressures in Group D were lower than Group F.*
Conclusions: *Dexmedetomidine was superior then Fentanyl in the prevention of tachycardia. Dexmedetomidine also prevented systolic, diastolic, mean arterial pressure increases following intubation better than fentanyl.*
Key word- *Dexmedetomidine, Fentanyl, randomization, laryngoscopy, intubation*

Date of Submission: 22-03-2021 Date of Acceptance: 06-04-2021

I. Introduction

Laryngoscopy and endotracheal intubation form the basic integral part of balanced anaesthesia wherein the airway is secured and controlled ventilation can be administered to the patient. However, undesired haemodynamic fluctuations are encountered with laryngoscopy and endotracheal intubation. These changes are especially in the form of an increase or decrease in heart rate, arterial blood pressure and myocardial oxygen demand along with cardiac rhythm disturbances[1], which were demonstrated as early as 1940s & 1950s [2].

Fig. Stress response in hypothalamus-pituitary-suprarenal and sympathoadrenal system.[1]



The occurrence of pressor response to tracheal intubation is caused by the following factors:-

(1) Reflex sympathoadrenal stimulation following laryngoscopy and tracheal intubation. There is consistent increase in plasma concentration of norepinephrine following tracheal intubation.

(2) Stimulation of cardio-accelerator nerves.

(3) Vagovagal reflex in which the vagus nerve mediates both the afferent and efferent pathways.

(4) Contributory factors: like anxiety, atropine premedication, reflex baroreceptor effect following fall of blood pressure after induction of anaesthesia, vagolytic action of certain muscle relaxants.

Dexmedetomidine is an imidazole derivative and highly selective alpha (α)-2-adrenergic receptor agonist[3,12] which decreases noradrenaline release resulting in attenuation of sympathoadrenal responses. Fentanyl is an opioid μ receptor agonist in high doses blunts the sympathetic response during intubation[4]. Studies in the west have also compared the two drugs for their efficacy, but a similar study with respective dosing in the Indian subpopulation is lacking.

II. Material and Methods

This prospective, randomized & double blind study was conducted in the Department of Anaesthesia and Critical Care, Tata Main Hospital, Jamshedpur which is a 940 bedded multidisciplinary teaching hospital. Total study population taken was 100. Time frame to address the study was from January 2015 to October 2016. ASA I and II patients of aged between 18 to 65 years undergoing elective surgical procedure under general anaesthesia with tracheal intubation were included. Patients with difficult intubation, emergency cases pregnant patients and on medications like beta blockers, opioids and α agonists were excluded from the study.

Randomization and Grouping:

Patients fulfilling the inclusion criteria were randomly divided into two groups. The randomization list was generated into one of the two groups by a random number function using a computer generated table of random numbers, resulting in a list of 100 patients. The study drug was premixed to a volume of 10 ml and presented as coded syringes to the Anesthesiologist who was not an investigator in the study. All recordings were done by an Anesthesiologist blinded to the group allocation. The patients were randomly divided into two groups each (n=50) and study drug was administered over a period of 10 minutes:-

Group F (Fentanyl Group):- received Fentanyl 2µg/kg diluted to 10ml in 0.9% normal saline.

Group D (Dexmedetomidine Group):- received Dexmedetomidine 1µg/kg diluted to 10ml in 0.9% normal saline. The drug administrator and the person making the observation were blinded to the study. Intubation was done by an experienced anaesthesiologist not involved in the study.

III. Methodology

All patients were examined one day before and their lab results and consent were reviewed**.** At operation theatre fasting status confirmed, vascular access taken and patients were connected to pulse oximeter, electrocardiograph monitor and automated non-invasive blood pressure. Baseline (average of three readings) parameters of patients including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), rate pressure product (RPP) and peripheral oxygen saturation (SpO2) were recorded in the operation theatre.

Patients were pre-oxygenated and study drug given in infusion over 10min as per protocol. Induction done using Inj. Propofol 2mg/kg and Inj. Succinylcholine 2 mg / kg intravenously followed by laryngoscopy and intubation at single attempt within 15 sec were included in the study. Anaesthesia was maintained with oxygen/nitrous oxide (1:3), 0.8% to 1.5% isoflurane and Inj. vecuronium (initial intravenous bolus dose of 0.08 mg/kg followed by intermittent dose of 0.02 mg/kg) intravenously.

An average of three readings (T_0) taken in operation theatre were considered as baseline and all other measurements were compared with the baseline. Further readings are as: after study drug infusion(T_1), after induction agents given(T_2), immediately after intubation(T_3) and 1min(T_4), 3min(T_5), 5min(T_6), 7min(T_7) and 10 min(T_8) following intubation in all patients. The haemodynamic alterations like a decrease in MAP greater than 20% below the baseline value or SBP less than 90 mm of Hg were treated primarily by increasing the IV fluid infusion rate and then reducing isoflurane concentration. If hypotension (SBP< 90 mm of Hg) did not respond to fluid administration, then injection mephentermine 6mg IV was administered. Any incidence of bradycardia (HR <50/min) was treated with injection atropine 0.6 mg IV. Surgical incision was done following the completion of the initial 10 mins of monitoring. The patients were ventilated & end tidal CO_2 level was maintained between 30 and 35 mm Hg. Intraoperative HR, SBP, DBP, MAP, RPP and SpO_2 levels were recorded at 5 min intervals. Additional doses of injection fentanyl 1µg/kg were administered according to hemodynamic variables to all the groups as rescue analgesia.

At the end of the surgery all patients were reversed using neostigmine 0.05 mg/kg and atropine 0.02mg/kg IV. Patients were extubated after adequate recovery and then shifted to anaesthesia recovery room and monitored for 60 min for any side effects like respiratory depression, hypotension, bradycardia, drowsiness, shivering, nausea or vomiting.

IV. Observations

Both groups were compared for demographic data (age, sex, weight, height, BMI), duration of surgery, MP scores, ASA grading and laryngoscopy time were measured. Haemodynamic parameters (HR, SBP, DBP, MAP, RPP and SpO2) levels were measured and recorded along with any side effects.

V. Results

Table no- 1: Comparison of Demographic parameters, Mallampatti scores, Laryngoscopy time and Duration of surgery among Group F (Fentanyl) and Group D (Dexmedetomidine).

	Group – F (n=50)	**Group – D (n=50)**
AGE	43.08 ± 12.91	45.72 ± 13
GENDER(M/F)	16/34	17/33
ASA(I/II)	23/27	19/31
WEIGHT(KG)	63.56 ± 12.65	67.24 ± 12.47
HEIGHT	162.34 ± 10.33	162.22 ± 9.02
B.M.I	24.08 ± 4.16	25.55 ± 4.41
MP(I/II/III)	19/21/10	12/26/12
LARYNGOSCOPY TIME	10.82 ± 1.06	11.02 ± 0.96
Duration of surgery	54.84 ± 28.61	56.62 ± 25.97

There was no difference between two groups according to demographic parameters like age, sex, ASA grading, height, weight, body mass index, Mallampatti scores, laryngoscopic time and duration of surgery as observed in table no- 1.

Table No-2: Comparison of mean heart rate among Group F (Fentanyl) and Group D (Dexmedetomidine) at different time intervals**:**

Time Interval	Group - F	Group – D	$\|t\|_{cal.}$	d.f	P – value
T_0 min	85.97 ± 14.59	83.19 ± 7.26	1.206	98	0.2306
T_1 min	82.6 ± 14.23	77.4 ± 7.27	2.301	98	0.0235
T_2 min	78.9 ± 14.44	72.64 ± 6.70	2.781	98	*0.0065*
T_3 min	94.12 ± 16.37	82.18 ± 5.69	4.872	98	*P<.0001*
T_4 min	96.02 ± 15.53	84.34 ± 4.37	5.119	98	*P<.0001*
T_5 min	93.74 ± 12.86	80.34 ± 4.14	7.014	98	*P<.0001*
T_6 min	89.08 ± 12.82	77.74 ± 3.97	5.975	98	*P<.0001*
T_7 min	85.3 ± 11.74	74.2 ± 3.81	6.359	98	*P<.0001*
T_8 min	80.38 ± 9.88	74.16 ± 3.15	4.241	98	*0.0001*

Mean heart rate was significantly lower in Group- D at most intervals particularly from T_3 to T_8 with $p < 0.0001$ as compared to Group- F when observed in table no-2.

Table No-3: Comparison of mean SBP among Group F (Fentanyl) and Group D (Dexmedetomidine) at different time intervals:-

Time interval	Group - F	Group – D	$\|t\|_{cal.}$	d.f	P – value
T_0 min	132.15 ± 11.81	132.61 ± 11.61	0.201	98	0.8414
T_1 min	126.04 ± 9.98	122.42 ± 4.61	2.328	98	*0.0219*
T_2 min	116.98 ± 8.39	112.34 ± 4.48	3.450	98	*0.0008*
T_3 min	144.36 ± 10.45	140.64 ± 5.32	2.243	98	*0.0271*
T_4 min	142.82 ± 10.55	135.68 ± 4.83	4.351	98	*P<.0001*
T_5 min	131.98 ± 9.49	126.6 ± 3.83	3.717	98	*0.0003*
T_6 min	121.96 ± 7.65	119.62 ± 3.19	1.996	98	*0.0487*
T_7 min	117.3 ± 5.63	115.22 ± 2.82	2.336	98	*0.0215*
T_8 min	113.96 ± 4.67	110.38 ± 6.33	3.218	98	*0.0017*

It showed that Group F (Fentanyl) and Group D (Dexmedetomidine) were comparable at T_0. The maximum rise in mean SBP found at T_3 with 144.36 mmHg for Group F (Fentanyl) and140.64mmHg. for Group D (Dexmedetomidine).

Table No-4 Comparison of mean DBP among Group F (Fentanyl) and Group D (Dexmedetomidine) at different time intervals:-

Time interval	Group – F	Group – D	$\|t\|_{cal.}$	d.f	P – value
T_0 min	80.71 ± 7.50	81.82 ± 6.05	0.815	98	0.4173
T_1 min	77.06 ± 5.44	75.96 ± 3.66	1.186	98	0.2384
T_2 min	72.56 ± 5.37	73.22 ± 2.57	0.784	98	0.4350
T_3 min	89.72 ± 4.33	88.38 ± 2.78	1.841	98	0.0686
T_4 min	89.88 ± 3.92	88.92 ± 2.69	1.428	98	0.1565
T_5 min	83.88 ± 3.15	79.34 ± 3.43	6.893	98	*P<.0001*
T_6 min	76.9 ± 3.22	73.26 ± 2.93	5.912	98	*P<.0001*
T_7 min	71.8 ± 3.40	69.76 ± 2.98	3.191	98	*0.0019*
T_8 min	70.26 ±2.45	68.14 ± 3.33	3.626	98	*0.0005*

It showed that both Group F (Fentanyl) and Group D (Dexmedetomidine) were comparable in maintenance of DBP after intubation upto 1min after intubation. However, there was statistically significant prolonged attenuation of DBP observed in Group D (Dexmedetomidine) at T_5, T_6, T_7 and T_8 after intubation as compared to Group F (Fentanyl).

Table No-05 Comparison of mean MAP among Group F (Fentanyl) and Group D (Dexmedetomidine) at different time intervals:-

Time Interval	Group – F	Group – D	$\|t\|_{cal.}$	d.f	P – value
T_0 min	97.86 ± 7.73	98.75 ± 6.65	0.617	98	0.5385
T_1 min	93.22 ± 6.01	91.54 ± 3.31	1.731	98	0.0865

T_2 min	87.38 ± 5.42	86.22 ± 2.32	1.391	98	0.1673
T_3 min	107.16 ± 5.08	105.76 ± 2.40	1.762	98	0.0812
T_4 min	107.48 ± 4.17	104.46 ± 2.87	4.218	98	*0.0001*
T_5 min	99.84 ± 3.89	95.08 ± 2.45	7.321	98	*P<0.0001*
T_6 min	91.84 ± 3.47	88.64 ± 2.18	5.522	98	*P<0.0001*
T_7 min	86.98 ± 3.21	84.86 ± 2.07	3.925	98	*0.0002*
T_8 min	84.88 ± 2.32	82.18 ± 2.80	5.250	98	*P<0.0001*

It showed that both groups were comparable upto immediately after intubation phase. However, Group D (Dexmedetomidine) found to have strongly significant at T_4, T_5, T_6, T_7 and T_8 intervals than Group F (Fentanyl) in controlling mean MAP.

Table No 6- Comparison of mean RPP among Group F (Fentanyl) and Group D (Dexmedetomidine) at different time intervals:-

Time interval	Group – F	Group - D	$\|t\|_{cal.}$	d.f	P – value
T_0 min	11400 ± 2477.40	11036 ± 1431.08	0.900	98	0.3705
T_1 min	10444.96 ± 2244.78	9474.8 ± 974.98	2.803	98	*0.0061*
T_2 min	9258 ± 2039.72	8166.46 ± 896.03	3.464	98	*0.0008*
T_3 min	13645.08 ± 2964.13	11555.4 ± 871.07	4.783	98	*P<0.0001*
T_4 min	13749.8 ± 2706.10	114446 ± 740.87	5.810	98	*P<0.0001*
T_5 min	12375.82 ± 1950.27	10233.9 ± 598.54	7.424	98	*P<0.0001*
T_6 min	10874.18 ± 1783.82	9298.46 ± 520.36	5.996	98	*P<0.0001*
T_7 min	10006.88 ± 1462.49	8546.58 ± 433.87	6.769	98	*P<0.0001*
T_8 min	9159.68 ± 1181.27	8189.06 ± 612.84	5.157	98	*P<0.0001*

It showed Group C (Dexmedetomidine) was highly significant when compared to Group B (Fentanyl) at all-time intervals.

Side effects were not observed in any of the study groups.
Henceforth, Group D (Dexmedetomidine) causes minimal increase in myocardial oxygen demand following laryngoscopy and intubation and was found to be superior than both Group F (Fentanyl).

VI. Discussion

Haemodynamic responses to laryngoscopy and endotracheal intubation have been a topic of discussion since first observed by Reid et al[2] in 1940. These responses are transitory but in patients with ischemic heart disease, systemic hypertension and cerebrovascular diseases can result in deleterious effects like left ventricular failure, pulmonary oedema and myocardial ischemia. Therefore, there is a need to blunt this response[4,5].

In our study, Fentanyl was given at the dose of 2 µg/kg diluted in 10 ml normal saline over 10 min prior to induction given as infusion similar to study by Kharwar et al[5] and Ugur et al.[6]

Dexmedetomidine infusion of 1µg/kg done over 10 minutes in our study correlates with the studies conducted by Uysal et al,[7] Gogus et al[8] and this dose was found to be associated with lesser complications like severe bradycardia, hypotension and rhythm changes.

Comparison of Mean Heart rate: In our study Fentanyl leads to rise in mean HR by 11% whereas it was only 1% for Dexmedetomidine which correlates with study by Patel et al.[9] Dexmedetomidine is better than Fentanyl in controlling heart rate correlates with studies done by Gunalan et al.[10] Hence, Dexmedetomidine is better than Fentanyl in attenuating the tachycardic response to laryngoscopy and intubation. Dexmedetomidine is better than Fentanyl in controlling heart rate correlates with studies done by Jain V[11] and Gunalan et al.[10]

Comparison of Mean Systolic blood pressure: In the study conducted by Patel et al[9] it was observed that Dexmedetomidine significantly attenuates stress response at intubation with lower increase in SBP (6%) compared with Fentanyl (23%), which is similar to our study, in which SBP decreased in the Dexmedetomidine group.

Comparison of Mean Diastolic blood pressure: Dexmedetomidine had statistically significant value at T_5, T_6 ($p<0.0001$), T_7 ($p=0.0019$) & T_8 ($p= 0.0005$) when compared with Fentanyl which is in concordance with that of Gandhi et al[15] Jain V[11]. Dexmedetomidine exhibits a superior response compared to Fentanyl in controlling mean DBP.

Comparison of Mean MAP: Dexmedetomidine was found to have significantly superior effect than Fentanyl at T_5 with $P<0.0001$ and T_6, T_7 and T_8 with p-value < 0.05. Hence, Dexmedetomidine was found to have a superior effect than Fentanyl in attenuating MAP. This finding is in concordance with that of Aksu et al.[13]

Comparison of Mean rate pressure product: Rate pressure product is a measure of the stress put on the cardiac muscle based on the number of times it needs to beat per minute (HR) and the arterial blood pressure

that it is pumping against (SBP). Levels of RPP in excess of 20,000 are more commonly associated with angina pectoris and myocardial ischemia.
Calculated as:
Rate Pressure Product (RPP) = Heart Rate (HR) x Systolic Blood Pressure (SBP)
In our study, all three groups had comparable RPP at baseline (T_0) and there was no statistical difference. None of our observation shows an increased myocardial oxygen demand as all the values lies in low region (10000-14999) only. Dexmedetomidine had statistically significant control over mean RPP and lesser myocardial oxygen demand as compared to Fentanyl with $p< 0.0001$ at post-intubation periods of upto 10 min.

VII. Conclusion

Hence, we concluded that Dexmedetomidine is superior to Fentanyl. No side effects observed in our study. As we did not evaluate whether the hemodynamic responses measured for "several minutes" after intubation could affect perioperative outcomes [14,15] was limitation to our study. This study did not evaluate the patients on regular medications (like opioids, α_2 agonists, sedatives and β adreno-receptor blocking drugs) on the hemodynamic response to laryngoscopy and endotracheal intubation. Hence, larger studies are still required to validate the findings.

References

[1]. Jakusenko N, Kopeika U, Mihelsons M, Nagobade D, Vija Putniņa A, Pavārs A. Comparison of stress response performing endotracheal intubation by direct laryngoscopy, fibreoptic intubation and intubation by the glidescope laryngoscope. In Proceedings of the Latvian Academy of Sciences. Section B. Natural, Exact, and Applied Sciences. 2008 Jan 1 (Vol. 62, No. 4-5, pp. 176-181).
[2]. Reid L C, Brace D E. Irritation of respiratory tract and its reflex effect upon heart. Surg., Gynaec. and Obst. Feb 1940 ; 70 : 157-162.
[3]. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs. 2000 Feb;59(2):263-8.
[4]. Gupta S, Tank P. A comparative study of efficacy of esmolol and fentanyl for pressure attenuation during laryngoscopy and endotracheal intubation. Saudi journal of anaesthesia. 2011 Jan 1;5(1):2.
[5]. Kharwar RK, Kumar R, Tiwary PK, Suwalka U, Prakash S. A comparison of intravenous dexmedetomidine v/s inj. fentanyl for attenuation of hemodynamic responses during laryngoscopy and intubation after propofol induction. NJIRM 2014 ; 5:71–5.
[6]. Ugur B, Ogurlu M, Gezer E, Aydin ON, Gürsoy F. Effects of Esmolol, Lidocaine and Fentanyl on haemodynamic responses to endotracheal intubation. Clinical drug investigation. 2007 Apr 1;27(4):269-77.
[7]. Uysal HY, Tezer E, Turkoglu M, Aslanargun PN, Basar H. The effects of dexmedetomidine on hemodynamic response to tracheal intubation in hypertensive patients: A comparison with esmolol and sufentanyl. Journal of Research in Medical Sciences. 2012 Jan 4;17(1).
[8]. Gogus N, Akan B, Serger N, Baydar M. The comparison of the effects of dexmedetomidine, fentanyl and esmolol on prevention of hemodynamic response to intubation. Brazilian Journal of Anesthesiology (English Edition). 2014 Oct 31;64(5):314-9.
[9]. Patel CR, Engineer SR, Shah BJ, Madhu S. Effect of intravenous infusion of dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: A study with entropy analysis. Indian journal of anaesthesia. 2012 Nov 1;56(6):542.
[10]. Gunalan S, Venkatraman R, Sivarajan G, Sunder P. Comparative evaluation of bolus administration of dexmedetomidine and fentanyl for stress attenuation during laryngoscopy and endotracheal intubation. Journal of clinical and diagnostic research: JCDR. 2015 Sep;9(9):UC06
[11]. Jain V, Chandak A, Ghosh A, Golhar M. Comparison of dexmedetomidine and fentanyl for attenuation of the hemodynamic response to laryngoscopy and tracheal intubation. Ain-Shams Journal of Anaesthesiology. 2015 Apr 1;8(2):236-43
[12]. Aho M, Lehtinen AM, Erkola O, Kallio A, Korttila K. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. Anesthesiology. 1991 Jun;74(6):997-1002.
[13]. Aksu R, Akin A, Biçer C, Esmaoğlu A, Tosun Z, Boyaci A. Comparison of the effects of dexmedetomidine versus fentanyl on airway reflexes and hemodynamic responses to tracheal extubation during rhinoplasty: A double-blind, randomized, controlled study. Current therapeutic research. 2009 Jun 30;70(3):209-20.
[14]. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian journal of anaesthesia. 2011 Jul 1;55(4):352.
[15]. Gandhi S, Goyal V, Radhakrishnan K, Balakrishnan M. Comparison of Dexmedetomidine with Fentanyl in Attenuation of Pressor Response during Laryngoscopy and Intubation. IOSR Journal of Pharmacy. 2014;2(4):28-38.

Dr Amit Kumar Sahu, et. al. "Comparison of Fentanyl with Dexmedetomidine on attenuating the haemodynamic response to intubation: A randomized double blind clinical study."*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(04), 2021, pp. 13-18.