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Dexmedetomidine versus Fentanyl as Pre-medication for Prevention of Adverse Haemodynamic Changes during Laryngoscopy and Endotracheal Intubation.

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ABSTRACT

BACKGROUND: Laryngoscopy and endotracheal intubation commonly lead to stimulation of sympathoadrenal system giving rise to adverse haemodynamic changes. These may lead to deleterious effects in susceptible patients. One of the approaches to reduce these harmful effects amongst many is the use of premedication like -2 agonist or opioids. Dexmedetomidine and Fentanyl have been tried successfully towards this end.

AIM: This study was carried out to compare the efficacy of Dexmedetomidine versus Fentanyl as premedication in prevention of haemodynamic changes of laryngoscopy and intubation.

MATERIAL AND METHODS: 110 patients of both genders and of ASA grade 1 and II, making two groups Group D and F of 55 each. Group D patients received Dexmedetomidine 0.6 µg per kg and
Group F received Fentanyl 2µg per kg as premedication given intravenously ten minutes before laryngoscopy. Changes in Heart Rate (HR) and Mean Arterial Pressure (MAP) during laryngoscopy
and endotracheal intubation were studied and analysed.

CONCLUSION: Dexmedetomidine 0.6µg per kg as premedication proves to be better as compared to
Fentanyl 2µg per kg in preventing adverse haemodynamic changes during laryngoscopy and intubation.

KEYWORDS : Dexmedetomidine, Fentanyl, Haemodynamic Changes, Laryngoscopy and Intubation.

INTRODUCTION

Endotracheal intubation has always been an integral part of administering anaesthesia and in Management of critically ill patient and in practice even today since its description by Rawbotham and Magill in 1921. Laryngoscopy and endotracheal intubation are although not free from adverse effects. Reid and Bruce[1] in 1940 and Kayhan Z et al[2] described response to laryngeal and tracheal stimulation as reflex sympathoadrenal stimulation. Transient hypertension and tachycardia is probably of no consequence in healthy individuals, but is hazardous to the patients with hypertension, myocardial insufficiency or cerebrovascular diseases[3]. Such patients are susceptible to pulmonary oedema, myocardial infarction and cerebrovascular accident[4,5] and acute Left ventricular failure, dysrhythmias and intracranial bleed[6]. Various pharma cological and non- pharmacological methods have been used to attenuate the hemodynamic response to laryngoscopy and tracheal intubation. None of these have proved to be ideal, hence it lays the rationale to continue the quest for an anaesthetic technique and/or a drug that effectively suppresses all the hazardous response to obnoxious stimuli with a maximum margin of safety.

α-2 agonists have a potential benefit for use, as they possess various advantages such as hypnotic, sedative, anxiolytic, sympatholytic, and analgesic properties.

The advantages of IV Dexmedetomidine and clonidine as premedication are, sedation, analgesia, anxiolysis and improved haemodynamic stability.

Opioids have also been successfully used to blunt the hemodynamic response to intubation. Opioids act as an agonist at stereospecific opioid receptors at presynaptic and postsynaptic sites in the central nervous system, principally the brainstem and spinal cord and in peripheral tissues outside the Central Nervous System[7]. Fentanyl citrate is a p - opiate receptor agonist. As anm, analgesic, fentanyl is 75 to 125 times more potent than morphine[7].

We conducted this project to study the efficacy of Dexmedetomidine versus fentanyl in preventing the hemodynamic response particular ly Heart Rate (HR) and Mean Arterial Pressure (MAP) to laryngosco py and endotracheal intubation.

MATERIAL AND METHODS

We conducted this study on 110 healthy adult patients of ASA grade I or II in the age group of 18-60 Years undergoing elective surgeries under General anaesthesia who consented to participate in study.

Patients with other comorbid conditions were excluded.

STUDY CONDUCT: -

It was a prospective and observational study carried out in a tertiary care teaching hospital, over 2 years, after obtaining the necessary approval from the Institutional Ethical Committee. Patients were evaluated by detailed history and examination. A valid, written Informed consent was taken from all the patients for participating in the study after explaining the procedure in the local language.

PATIENT GROUPS:

Two groups of 55 each, depending upon the drug administered:-
Group D –Inj. Dexmedetomidine (0.6 µg/kg diluted in 5ml saline IV).
Group F – Inj. Fentanyl (2 µg/kg diluted in 5ml saline IV).

SAMPLE SIZE:

The sample size was calculated by comparing MAP at one minute after intubation(Highest increase in MAP signifying pressor response to laryngoscopy in both the Groups) for the Power of Study to be 80% and Confidence Interval to be 95%. The minimum sample size calculated was found to be 98 (49 in each group) and we used a sample size of 110 (55 in each group).

On arrival in the operation theatre, multi-parameter monitors were attached and baseline vital parameters were recorded. Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure

(DBP), Mean Arterial Pressure (MAP) were recorded before pre-medication and 10 minutes after pre-medication.

With patient in supine position, the respective study solutions were administered intravenously through a syringe pump at a rate of 0.5ml/min, 10 minutes before laryngoscopy and intubation.

- After 10 mins of premedication with the study solutions, HR, SBP, DBP and MAP, SPO2 and EGG were recorded.
- After pre-oxygenation for 3 min, patients were induced with inj.thiopentone (4-7 mg/kg) i.v. and
- inj. Suxamethonium (2mg/kg) i.v. followed by laryngoscopy and intubation.
- All parameters under study were recorded at following time points:

T1: Before premedication
T2: 10 minutes after premedication
T3: 30 seconds after endotracheal intubation
T4: 1 minute after intubation and later every minute for ten minutes, labelled as T5 through to T13.

- All intubations were accomplished within 15 seconds by expert anaesthesiologists. After intubation, patients were maintained with Isoflurane (0.4 % v/v), O2 (50%), N2O (50%) and
- Vecuronium 0.1 mg /Kg and respiration was controlled.
- Neuromuscular blockade was reversed with Glycopyrrolate and Neostigmine at the end of surgery,
- under continuous monitoring.

Statistical analysis:
All data were entered into a pro forma in excel sheet (M.S. Office 2016), optimized for SPSS (Statistical Package for Social Science [SPSS] version 19.0 for Windows, SPSS, Inc.) and subjected to statistical analysis. A probability of $p<0.05$, was considered significant.

DISCUSSION:
Many researchers are studying the methods for attenuation of hemodynamic response. These hemodynamic responses need to be attenuated to decrease associated risk of myocardial ischemia, myocardial infarction, cerebral hemorrhage and raised intraocular tension in high-risk patients. These are by far the most important of the indications for attenuation of hemodynamic response to laryngoscopy and tracheal intubation[8].

Fentanyl is administered widely for attenuation of sympathetic response to laryngoscopy and intubation.[9] Blunting of sympathetic response is dose dependent. Fentanyl at 6 μg/kg completely abolishes, whereas at 2 μg/kg significantly attenuates, HR and MAP increase during laryngoscopy and intubation.[9]

Dexmedetomidine is a highly selective α 2 agonist. Hypotension is caused by activation of receptors in the brain and spinal cord level, inhibiting neuronal firing. Presynaptic activation of α2 adrenergic receptors inhibits release of norepinephrine, postsynaptic activation in the central nervous system inhibits sympathetic activity and, therefore, can decrease MAP and HR. Effects on hemodynamics are mediated by inhibition of central sympathetic outflow.[10]

Demographic profile
On the analysis of demographic data, the mean age and mean weight as well the mean duration of Laryngoscopy showed no significant difference in both the groups.

Effect on Heart rate: (Table I)
Comparison between the mean HR values of patients in the two groups demonstrated that there was no statistically significant difference until administration of premedication ($P > 0.05$).

TABLE. I: COMPARISON OF MEAN AND STANDARD DEVIATION OF HEART RATE IN BETWEEN TWO GROUPS AT ALL TIME POINTS

Time Points	Heart Rate per minute		Mean Difference	Student's Unpaired 'T' Test Value	P Value	Significance
	Group D	Group F				
	Mean + SD	Mean + SD				
T1	81.84 ± 9.21	83.53 ± 10.30	1.691	0.908	0.366	Not Significant
T2	69.67 ± 8.24	81.58 ± 10.32	11.909	6.69	<0.0001	Significant
T3	75.80 ± 8.41	94.47 ± 9.87	18.673	10.684	<0.0001	Significant
T4	77.89 ± 8.96	96.45 ± 10.96	18.564	9.725	<0.0001	Significant
T5	80.82 ± 8.42	101.44 ± 10.88	20.618	11.114	<0.0001	Significant
T6	81.98 ± 9.18	100.15 ± 10.79	18.164	9.509	<0.0001	Significant
T7	77.47 ± 9.32	97.75 ± 10.26	20.273	10.848	<0.0001	Significant
T8	75.91 ± 9.59	95.80 ± 10.62	19.891	10.306	<0.0001	Significant
T9	74.96 ± 9.56	94.75 ± 10.97	19.782	10.081	<0.0001	Significant
T10	73.05 ± 9.34	93.67 ± 10.40	20.618	10.942	<0.0001	Significant
T11	72.82 ± 9.60	92.78 ± 10.61	19.964	10.346	<0.0001	Significant
T12	71.67 ± 9.63	91.76 ± 10.40	20.091	10.515	<0.0001	Significant
T13	70.98 ± 9.52	90.80 ± 10.54	19.818	10.349	<0.0001	Significant

By applying Student's unpaired 'T' test, there is a significant difference between mean values of HR from time point T_2 to T_{13} when group D compared with group F ($p<0.05$). There is no significant difference between mean values of HR at time point T1 in both the groups. There was maximum decrease in HR at time point T2 in both groups which was found to be highly significant ($p < 0.0001$), but there was greater degree of decrease in Group D. This decrease reached the base line (time point T1) at time point T6 in Group D and thereafter the mean HR decreased below the baseline till time point T13. Whereas in Group F, after the decrease in mean HR at time point T2, it increased significantly above the base line till T5 which again approached the base line at time point T13. The variation in mean HR from baseline at all the time intervals was greater in Group F as compared to Group D. The decrease in HR after laryngoscopy and intubation was more profound in Group D as compared to Group F. These findings are comparable with those of **Scheinin B et al.**[11] as well as those of **Aho M et al.,**[12] **Sagar Gandhi et al.**[13] and **Kharwar et al**[14]**.** These observations are also in concordance with those in the study by **Vaibhav Jain et al.**[15], in which they used Inj. Dexmedetomidine in a higher dose of 1μg/kg.

Thus, Dexmedetomidine is more effective in obtunding the increase in HR after laryngoscopy and intubation as compared to fentanyl.

Effect on Mean Arterial Pressure (MAP):TABLE II.
Comparison between the mean MAP values of patients in the two groups demonstrated that there was no statistically significant difference until administration of premedication ($P > 0.05$)

TABLE. II: COMPARISON OF MEAN AND STANDARD DEVIATION OF MEAN ARTERIAL PRESSURE IN BETWEEN TWO GROUPS AT ALL TIME POINTS

Time Points	Mean Arterial Pressure (mmHg)		Mean Difference	Student's Unpaired 'T' Test Value	P Value	Significance
	Group D	Group F				
	Mean + SD	Mean + SD				
T1	95.87 ± 4.69	94.18 ± 3.82	1.691	2.075	.040	Not Significant
T2	82.69 ± 4.71	88.91 ± 3.95	6.218	7.510	<0.0001	Significant
T3	88.24 ± 5.02	93.16 ± 4.00	4.927	5.690	<0.0001	Significant
T4	89.96 ± 4.73	96.05 ± 4.02	6.091	7.277	<0.0001	Significant
T5	93.96 ± 5.06	104.58 ±4.85	10.618	11.230	<0.0001	Significant
T6	90.58 ± 4.88	102.27 ±4.96	11.691	12.466	<0.0001	Significant
T7	87.67 ± 4.77	101.36 ±5.45	13.691	14.023	<0.0001	Significant
T8	85.71 ± 4.88	98.42 ± 4.07	12.709	14.832	<0.0001	Significant
T9	84.64 ± 4.94	96.35 ± 4.01	11.709	13.638	<0.0001	Significant
T10	82.56 ± 4.79	93.87 ± 4.05	11.309	13.362	<0.0001	Significant
T11	82.42 ± 5.08	93.00 ± 3.87	10.582	12.291	<0.0001	Significant
T12	80.05 ± 4.58	91.29 ± 4.03	11.236	13.665	<0.0001	Significant
T13	77.44 ± 4.76	90.49 ± 4.11	13.055	15.382	<0.0001	Significant

By applying Student's Unpaired 'T' test, there is a significant difference between mean values of MAP from time point T2 to T13, when Group D is compared with Group F ($p<0.05$). There is no significant difference between mean values of MAP at time point T1 in both the groups. There was maximum decrease in MAP at time point T2 in both the Groups that was found to be significant, but there was greater degree of decrease in Group D. This decrease approached the base line (time point T1) at time point T3 in group F where as in group D it took longer duration and approached baseline at the time point T5. The MAP did not rise above the baseline in Group D, whereas in Group F, the rise in MAP above the baseline was significant, peaking at time point T5, which again approached the baseline at T9 followed by a decrease below the baseline until time point T13.

On comparing the mean values of MAP at time points T1 toT13, in Group D, the variation was minimal whereas in Group F, there was a greater range of variation. After laryngoscopy and intubation, the MAP increased in both the groups. At time point T5 that is, 2 minutes after endotracheal intubation in Group F, the MAP increased progressively to reach a peak of 104.58±4.85 mm of Hg. The increase in MAP from baseline after laryngoscopy was 1.99% in Group D as compared to 11.04% in Group F. Thus, the increase in post laryngoscopic values of MAP was much higher in Group F than in Group D. Thereafter, the MAP decreased in both the groups but the degree of decrease was more in Group D. In Group D, the MAP remained below the baseline (time point T1) throughout after laryngoscopy. However, in Group F, the MAP remained above the baseline until time point T9 that is, till 6 minutes after laryngoscopy and intubation.

These findings coincide with those of **Sagar Gandhi et al**.[13], **Kharwar et al.**[14] **Vaibhav Jain et al.**[15] and **N. Turgut et al.**[16]However, N.Turgut et al had used Fentanyl in dose of 1μg/kg. Thus, Dexmedetomidine is more efficient in suppressing the increase in MAP value after laryngoscopy and intubation, as compared to fentanyl.

CONCLUSION

This study concludes that the dosage of 0.6 μg/kg IV of Dexmedetomidine, as premedication is more effective in suppressing the rise in Heart Rate and Mean Arterial Pressure during laryngoscopy as compared to fentanyl in a dose of 2 μg/kg IV, hence to prevent the adverse haemodynamic changes during laryngoscopy and intubation, Dexmedetomidine in a dose of 0.6 μg/kg IV is recommended.

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