Original Research Paper

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PROSPECTIVE RANDOMIZED DOUBLE BLIND COMPARATIVE STUDY OF EVALUATING EFFICACY AND SAFETY OF TWO DIFFERENT DOSES OF FENTANYL FOR PREVENTION OF SYMPATHOMIMETIC RESPONSE TO LARYNGOSCOPY AND INTUBATION IN CONTROLLED HYPERTENSIVE PATIENTS

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ABSTRACT Laryngoscopy prior to intubation and intubation in itself produce significant hemodynamic stress response. Hypertension and tachycardia are common responses in normotensive patients and thought to be due to increased sympathetic activity due to increased plasma concentration of catecholamine following mechanical stimulation. Hypertensive patients have increased activity of the sympathetic nervous system and may exhibit an exaggerated hemodynamic response to the induction of anesthesia compared with normotensive patients. Marked increases in catecholamine concentration and in the sensitivity of peripheral vessels to catecholamine in these patients have been reported. 60 patients were divided in to 2 groups, Group A received 2mcg/kg and Group B received 3mcg/kg fentanyl intravenously 5minutes before induction. Sympathomimetic response was assessed during laryngoscopy, intubation, up to 20minutes after intubation. we conclude that intravenous fentanyl dose of 3mcg/kg provided satisfactory results for prevention of hemodynamic stress response to laryngoscopy and intubation in hypertensive surgical populations

KEYWORDS : Laryngoscopy, Intubation, Sympathomimetic response, Fentanyl

INTRODUCTION

Laryngoscopy and intubation are gold standard procedure for securing the airway in most of the patients undergoing operation under general anesthesia. Laryngoscopy prior to intubation and intubation in itself produce significant hemodynamic stress response. Increase in arterial pressure begins after about 15 seconds and peaks within 30-45 seconds after laryngoscopy; associated with significant rise in heart rate. Though this elevated hemodynamic response is usually transient, returns to base line within 10-15 minutes and well tolerated by healthy individuals without cardio-respiratory compromise, can prove disastrous in the patient with cardiac and neurological diseases.[1]

Complications of pressure response following laryngoscopy and intubation includes myocardial ischemia[4], cardiac failure and intracranial haemorrahge[5], and increases in intracranial pressure.[6] These complications may prove serious enough even on normotensive patients. In hypertensive patients undergoing surgery even an exaggerated response to laryngoscopy and intubation has been reported.[4] Hence, prevention of this stress response to laryngoscopy and intubation is highly desirable in surgical patients and specially so in hypertensive sub group.

Many methods have been tried to attenuate the hemodynamic response like use of inhalational agents, opioids, vasodilators, adrenergic and calcium channel blockers and local anesthetics.

Among opioids, fentanyl citrate has been identified as a most effective agent for this purpose. Fentanyl is effective in blunting stress response to intubation and has been used for this purpose in different doses titrationranging from 1.5µg/kg to 6µg/kg in different studies.[1,7-10]Most of the observers used 2 µg/kg of fentanyl for this purpose and the results show attenuation of response with this dose but 100% prevention of response is not achieved.[1-8] Studies using 4µg/kg of fentanyl or higher dose showed unacceptable degrees of adverse events.[9-10]

There is no study till date which used 3µg/Kg of Fentanyl and compared its effects in controlled Hypertensive population with 2 µg/kg of fentanyl. This prompted us to plan the present study to evaluate the efficacy and safety of two different doses of fentanyl (2µg and 3µg) to prevent hemodynamic stress response to laryngoscopy and intubation in controlled hypertensive patients.

AIMS AND OBJECTIVES

To assess the efficacy and safety of 2µg/kg and 3µg/kg of fentanyl as premedication in attenuating hemodynamic stress response to laryngoscopy and endotracheal intubation in controlled hypertensive patients in respect to following clinical parameters heart rate, blood pressure (systolic, diastolic) , mean arterial pressure.

MATERIALS & METHODS

60 patients of either gender between 20-50 years of age with ASA grading II(well controlled primary idiopathic hypertension, blood pressure ≤ 140/90)were divided into two groups of 30 each. Preoperative evaluation done on the day before surgery, Patients were fasted for 6 hours before surgery, due dose of anti-hypertensive drugs were given. Patients were randomly allocated into following 2 groups : Group A – Patients received 2mcg/kg fentanyl intravenously, 5 minutes before induction Group B - Patients received 3mcg/kg fentanyl intravenously, 5 minutes before induction

At operation theatre, iv access was established with 18/20G cannula. Monitoring for HR, NIBP (SB, DBP and MAP) and SpO_2 were established and baseline vital parameters were recorded.

Premedication- Inj.Glycopyrrolate 0.004mg/kg IV Inj.Ondansetron 0.15 mg/kg IV & Inj Midazolam 0.08mg/kg given 15minutes before induction.

All patients received a standard prescribed anesthetic protocol. After pre oxygenation with 100% oxygen for 3 minutes with facemask, anesthesia was induced with 2.5% thiopentone sodium intravenously slowly till loss of eyelash reflex. Following check ventilation, muscle paralysis was achieved by succinylcholine 2 mg/kg intravenously. When there was no response to train of four on peripheral nerve stimulation (ulnar nerve at wrist), trachea was intubated with sterile polyvinyl chloride, cuffed, disposable endotracheal tube (sized 8.0 or 8.5 mm in male and 7.0 or 7.5 in female).

Tube was attached to Bain's breathing system and after confirming successful intubation with end tidal CO_2 monitor and clinical examination, anesthesia was maintained with O_2 - N_2O (50-50), vecuronium bromide and sevoflurane (inhalational agent). IPPV was started. Tidal volume and ventilatory frequency were adjusted so as to maintain normocapnia (end tidal CO_2 40 ± 4 mmHg).

All the parameters selected (HR, SBP, DBP, MAP and SpO_2) were recorded at 5min after fentanyl injection, during laryngoscopy and intubation, at 1,3,5,10,15,20 minutes after intubation.

At the end of surgery, neuromuscular blockade was reversed with neostigmine 50µg/kg and glycopyrrolate 10µg/kg intravenously. After

satisfying the extubation criteria, trachea was extubated and patients were transferred to post anesthesia care unit.

STATISTICALANALYSIS

The data obtained in the study for various parameters are presented in the tabulated and graphical form. Using statistical software (graph pad Instat V3.0 software) mean and standard deviation was calculated for all the quantitative variables. Intra group comparison was made using the Repeated measures ANOVA and inter group comparison among the different groups were done using unpaired t test. Inter group comparison of qualitative data were done by chi square test. P value <0.05 considered statistically significant.

SAMPLE SIZE

Sample size calculation assuming α error being 0.05 and β error being 0.20 with a power of study 80% showed that 29 patients will be required per study group to detect the differences in hemodynamic stress response during laryngoscopy and intubation.

RESULTS

As shown in table 1,

Demographic profile in terms of age, gender and weight was comparable in both groups, **P>0.05.** As shown in table 2,

Intragroup comparison-

In group A, HR decreased from baseline within five minute of fentanyl premedication (4.59% decrease from baseline) (p<0.001). At the time of laryngoscopy and intubation, HR increased above pre-induction level, it was higher from baseline (03.50% higher from baseline) After intubation, HR started decreasing further with 7.76% maximum decrease noted at 20 min (p< 0.001).

In group B, HR decreased from baseline within five minute of fentanyl premedication (04.71% decrease from baseline) (p<0.001). At the time of laryngoscopy and intubation, HR increased (0.31 % increase above baseline) (p<0.05). Increase in HR during intubation continued up to five minutes. After five minutes of intubation, HR started decreasing from baseline with 8.61% maximum decrease noted at 20 min (p< 0.001).

Intergroup comparison-

During laryngoscopy and intubation, HR increased from baseline in group A (3.50% increase from baseline) compared to only 0.31% increase in group B So, in both the groups HR increased, but increase in HR was lower in group B than in group A. (p< 0.001). As shown in table 3,

Intragroup comparison-

In group A, MAP decreased from baseline within five minute of fentanyl premedication (05.60% decrease from baseline) (p<0.001). At the time of laryngoscopy and intubation, MAP was higher than pre-induction level (01.21% higher from baseline) (p<0.001).). After intubation, MAP started decreasing further with 03.70% maximum decrease noted at 20 min (p< 0.001).

In group B, MAP decreased from baseline within five minute of fentanyl premedication (07.11% decrease from baseline) (p<0.001). At the time of laryngoscopy and intubation, MAP decreased (02.61% decrease from baseline) (p<0.001). After intubation, MAP started decreasing further with 07.14% maximum decrease noted at 20 min (p< 0.001).

Intergroup comparison-

In group A, during laryngoscopy and intubation, MAP increased 01.21% from baseline (p< 0.001) and in group B MAP decreased 02.61% from baseline (p< 0.001). So, during laryngoscopy and intubation MAP increased in group A and decreased in group B from baseline (p< 0.001). It means hemodynamic stress response to laryngoscopy and intubation was prevented in group B, while it could not be prevented in group A.

DISCUSSION

Now a day in modern anesthesia and surgery, main concern is a safe outcome of the patients. The anesthetic drugs, complicated surgical procedures and the patient condition due to co-existing medical diseases increase the risk of outcome which leads to increase in mortality and morbidity. To prevent this, understanding the series of physiological changes (stress response) due to anesthesia and surgery is the most important. The body reacts to external stimuli, which trigger a reflex response leads to a complex interplay of substances between the hypothalamic-pituitary-axis, the classical neuro-endocrinal hormone system and autonomic nervous system and is called as "stress response" or "alarm reaction".[12-14]

Endotracheal intubation using a laryngoscope needs elevation of the epiglottis and exposure of the glottis; is a stressful noxious force stimulus. This stimulates laryngeal and tracheal sensory receptors, conducted to the brain via glossopharyngeal and vagus nerve, resulting in marked increase in the secretion of sympathetic amines like adrenaline and noradrenaline, they leads to increase in blood pressure, heart rate and tachyarrhythmia which is called "cardiovascular stress response".[11]

Among all the drugs used to reduce hemodynamic response, Opioids have advantage of having perioperative role in anaesthesia. Opioids has various advantages like no histamine release, no bronchospasm, cardio stability, rapid onset and short duration of action. Fentanyl suppresses the hemodynamic response by increasing the depth of anesthesia and decreasing sympathetic discharge. For these reasons we selected fentanyl among the opioid as premedication for preventing hemodynamic stress response to intubation.

Timing of fentanyl administration before laryngoscopy and intubation is important. Onset of fentanyl action starts within minutes after intravenous injection and reaches its peak at 5 minutes which is why fentanyl was injected 5 minutes before starting induction so as to acquire the maximum efficacy of fentanyl at the time of laryngoscopy and intubation.

In present study, 2mcg/kg fentanyl witnessed 3.50% increase in HR above baseline at the time of laryngoscopy and intubation compare to only 0.31% rise in HR when 3mcg/kg fentanyl was used. SBP, DBP, MAP all decreased compare to baseline in both the groups, but decrease was higher when 3mcg/kg fentanyl was used compare to 2mcg/kg of fentanyl. Still, none of the patients in 3mcg/kg fentanyl group developed hypotension as the average decrease in SBP 7.99%, in DBP 11.94%, and MAP 7.14% compare to baseline.

None of the patient in either group developed any sign of respiratory depression in post-operative period as per the defined criteria for respiratory depression. Hence 3mcg/kg of fentanyl does not produce higher sedation and is equally safe as 2mcg/kg of fentanyl.

CONCLUSIONS

From the present study it is concluded that fentanyl in the dose of 3mcg/kg 5 mins before induction is more appropriate dose in terms of efficacy and safety for preventing hemodynamic stress response to laryngoscopy and intubation in hypertensive surgical population compare to 2mcg/kg of fentanyl.

APPENDICES:

TABLE 1- DEMOGRAPHIC PROFILE OF PATIENTS

Demographic Profile	Group A (n=30)	Group B (n=30)	Intergroup P value
	Mean ± SD	Mean ± SD	
Age (years)	36.33 ± 7.45	39.3 ± 7.6	0.131
Sex (male/ female)	(17/13)	(16/14)	0.795
Weight (Kg)	68.5 ± 7.0	66.33 ± 5.88	0.198

TABLE 2- CHANGES IN HEART RATE

HR (beats/minute)	Group A (n=30)			Group A (n=30)			Intra group
	Mean ± SD	% change From baseline	Intra group p value	Mean ± SD	% change From baseline	Intra group p value	
Baseline	95.80 ± 2.91			94.80 ± 2.75			0.178
15 minutes after premedication	93.46 ± 3.22	2.44	<0.001	93.51 ± 3.50	1.36	<0.001	0.136
5 Min after fentanyl (pre induction value)	91.40 ± 3.29	4.59↓	<0.001	90.53 ± 3.19	4.71↓	<0.001	<0.001

During laryngoscopy and intubation	99.16 ± 1.96	3.50↑	<0.001	95.10 ± 2.0	0.31↑	<0.001		<0.001
After intubation (min)	1	104.03 ± 1.49		<0.001	100.13 ± 1.52		<0.001	<0.001
	3	106.10 ± 1.42		<0.001	102.20 ± 1.39		<0.001	<0.001
	5	105.23 ± 1.95		<0.001	101.36 ± 1.90		<0.001	<0.001
	10	100.30 ± 1.89		<0.001	96.23 ± 1.90		<0.001	<0.001
	15	92.43 ± 1.97		<0.001	88.50 ± 1.92		<0.001	<0.001
	20	88.36 ± 1.82	7.76↓	<0.001	86.63 ± 1.83	8.61↓	<0.001	<0.001

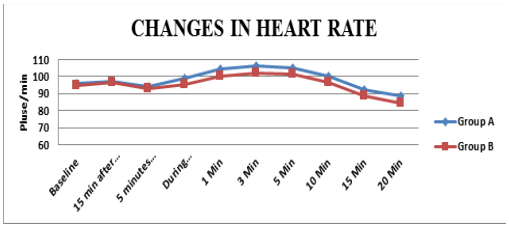
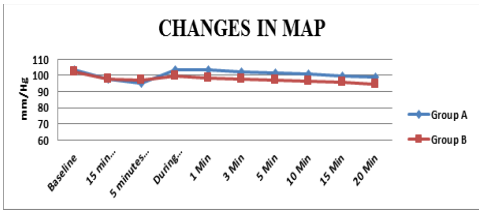


TABLE 3- CHANGES IN MAP (MEAN ARTERIAL PRESSURE)

HR (beats/minute)	Group A (n=30)			Group A (n=30)			Inter group P value
	Mean ± SD	% change From baseline	Intra group p value	Mean ± SD	% change From baseline	Intra group p value	
Baseline	102.56 ± 2.19			102.10 ± 2.26			0.121
15 minutes after premedication	97.86 ± 2.27	4.58↓	<0.001	97.66 ± 2.35	4.34↓	<0.001	0.739
5 Min after fentanyl (pre induction value)	96.93±2.30	5.60↓	<0.001	95.23 ± 2.30	7.11↓	<0.001	<0.001
During laryngoscopy and intubation	103.80 ± 2.85	1.21↑	<0.001	99.43 ± 2.81	2.61↓	<0.001	<0.001
After intubation (min)	103.40 ± 2.56		<0.001	98.10 ± 2.45		<0.001	<0.001
	102.46 ± 2.52		<0.001	97.80 ± 2.48		<0.001	<0.001
	101.56 ± 2.60		<0.001	97.06 ± 2.59		<0.001	<0.001
	100.73 ± 2.75		<0.001	96.50 ± 2.68		<0.001	<0.001
	99.76 ± 2.73		<0.001	95.83 ± 2.70		<0.001	<0.001
	98.76 ± 2.63	3.70↓	<0.001	94.80 ± 2.65	7.14↓	<0.001	<0.001



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