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Attenuation of the Hemodynamic Responses to Endotracheal Intubation with Gabapentin Versus Fentanyl: A Randomized Double Blind Controlled Study

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***Abstract**: Background and Aims: Laryngoscopy and tracheal intubation after induction of anaesthesia generate sympathoadrenal responses. We conducted a prospective, double blind, controlled clinical trial to examine whether a single preoperative dose of 800 mg gabapentin would be as effective as 2 micro/kg of intravenous (IV) fentanyl in blunting the hemodynamic response to endotracheal intubation Method: After approval from institutional ethical committee this double blind controlled study was carried out in the department of the anaesthesiology. Sixty patient age 20-60 year were allocated into two groups. One group received 2 micro/kg IV fentanyl ,and other group received 800 mg oral gabapentin. Gabapentin was administered 2 hours and fentanyl 5 min before induction of anaesthesia , Serial values of mean arterial pressure (MAP) and heart rate (HR) were compared among the two group and with the respective pre induction measurement. Result: Patient receiving oral gabapentin 800 mg alone show didn't remarkable decreases in heart rate and mean arterial pressure in response to endotracheal intubation . These hemodynamic changes were lesser in patient receiving IV fentanyl. Conclusion; It can be concluded from our study that Oral gabapentin does not produce significant reduction in laryngoscopy and endotracheal intubation induced sympathetic responses as compared to IV fentanyl.*

***Keywords**: Gabapentin, Fentanyl, Hemodynamic, Endotracheal Intubation.*

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I. Introduction

Laryngoscopy and endotracheal intubation evokes a transient sympathetic response manifesting as increase in heart rate, blood pressure and arrhythmias. Laryngoscopy and intubation often provoke hypertension and tachycardia[3,4]. Gabapentin was developed as an anticonvulsant.[5]. Gabapentin, a structural analogue of gamma-amino butyric acid, has been shown to have multi‑modal effects. It is used for premedication in adults, postoperative analgesia and preoperative anxiolysis and also prevents postsurgical pain. Fentanyl acts at opioid receptors and predominantly acts on μ receptors[6]. Fentanyl brings hemodynamic stability during perioperative period by its action on cardiovascular and autonomic regulatory areas.

II. Method

This prospective randomized double blind controlled study was carried out in the department of anesthesiology of our institution. After approval from institutional ethical committee we included sixty patients of either sex, aged 20 – 60 years of ASA status 1 and 2. A written informed consent was signed by all the patients involved in the study. The present study was done in two groups.

Study Design: Prospective randomized double blind controlled study

Study Location: This was a tertiary care teaching hospital based study done in Department of Anaesthesiology SMS Medical College & associated hospitals, Jaipur, Rajasthan, India

Study Duration: December 2017 to November 2018.

Sample Size: A sample size of 30 case in each group would be adequate to verify the expected minimum difference of 23.2(±11.9) percentage increase in heart rate after 1 min of intubation in gabapentin and fentanyl. This sample size is adequate to cover other study variable too. Hence 30 case will be taken in two group. Each group was consisting of 30 patients:

TAB GABAPENTIN (GROUP A): Patient was given tab gabapentin 800mg (2 hr prior to surgery) + inj. Normal saline 5ml (5min prior to surgery)

INJ FENTANYL (GROUP B): Patient was given inj. fentanyl 2µg/kg (5min prior to surgery) diluted in normal saline to make 5ml + placebo tab (2 hr prior to surgery).

Inclusion criteria:
1. Either sex
2. Aged 20-60 years.
3. ASA status 1 and 2
4. Scheduled for elective surgery.

Exclusion criteria:
1. Not willing to participate in study
2. Pregnant women
3. Patients with a history of drug or alcohol abuse.
4. Uncooperative patient
5. Morbid obese, difficult intubation.
6. Patient on antihypertensive & antidepressant.

The randomization was done by sealed envelope method. A total of 60 envelops (30 per group) were made, each envelope mentioning a particular study group. Study drug were loaded by and administered by another anesthesiologist to the patient. Base line heart rate and BP was recorded before induction and after intubation upto 15 min. The observed comparative hemodynamic changes are shown in table-1 for heart rate table-2 for systolic blood pressure table-3 for diastolic blood pressure and table-4 for mean arterial pressure.

III. Figure And Table

Table-1 : Comparison of intra operative Heart rate (BPM) among study groups

Time	Group A	Group B	P value
Baseline (T1)	86.3 ± 10.4	87.7 ± 12	0.639
Before induction (T2)	85.9 ± 11.5	84.9 ± 11	0.724
After induction (T3)	78 ± 10.2	79.8 ± 8.9	0.469
Before intubation (T4)	77.3 ± 10.5	77 ± 10.6	0.913
Post intubation			
01 min (T5)	122.3 ± 13	108.3 ± 15	<0.001
3 min (T6)	116.5 ± 12.1	103.1 ± 13.8	<0.001
5 min (T7)	111.3 ± 8.5	98.3 ± 10.3	<0.001
10 min (T8)	105 ± 8	92.3 ± 7.8	<0.001
15 min (T9)	100.7 ± 17.9	85.3 ± 7.8	<0.001

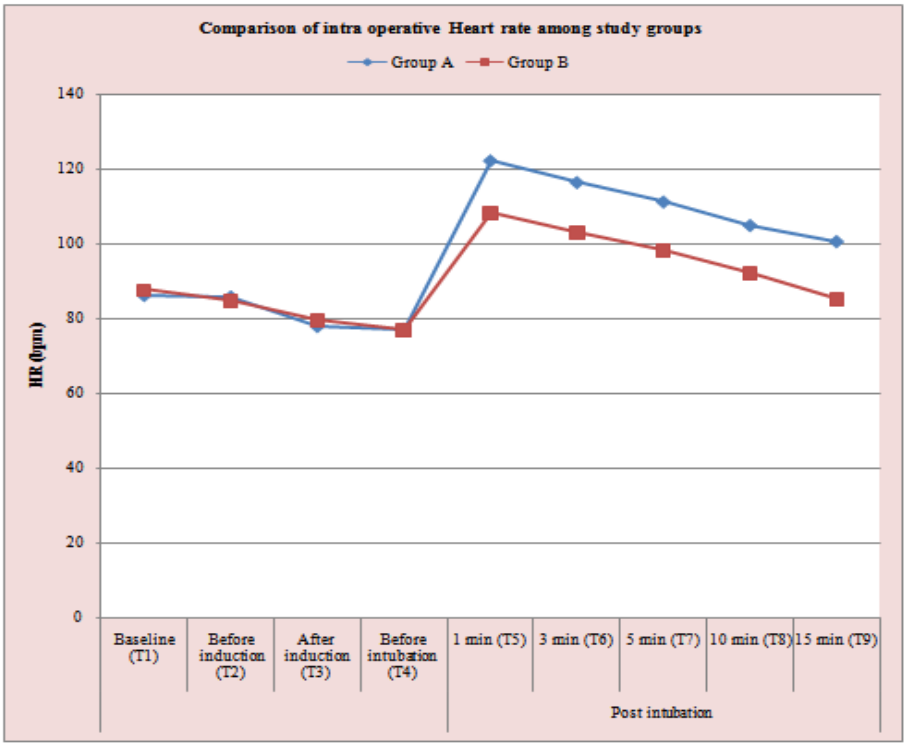


Table-2 : Comparison of intra operative SBP (mmHg) among study groups

Time	Group A	Group B	P value
Baseline (T1)	121.1 ± 10.3	126.3 ± 12.8	0.093
Before induction (T2)	128.1 ± 10.6	117.6 ± 13.1	0.001
After induction (T3)	113.5 ± 11.3	106.6 ± 13.1	0.033
Before intubation (T4)	117.4 ± 10.1	117.5 ± 13.1	0.974
Post intubation			
1 min (T5)	147.2 ± 13.8	124.6 ± 12.4	<0.001
3 min (T6)	141.4 ± 9	118.8 ± 12.4	<0.001
5 min (T7)	131.6 ± 8.9	122.5 ± 9.3	<0.001
10 min (T8)	125.5 ± 8.7	119.2 ± 8.3	0.006
15 min (T9)	118.6 ± 7.6	116.6 ± 10.1	0.398

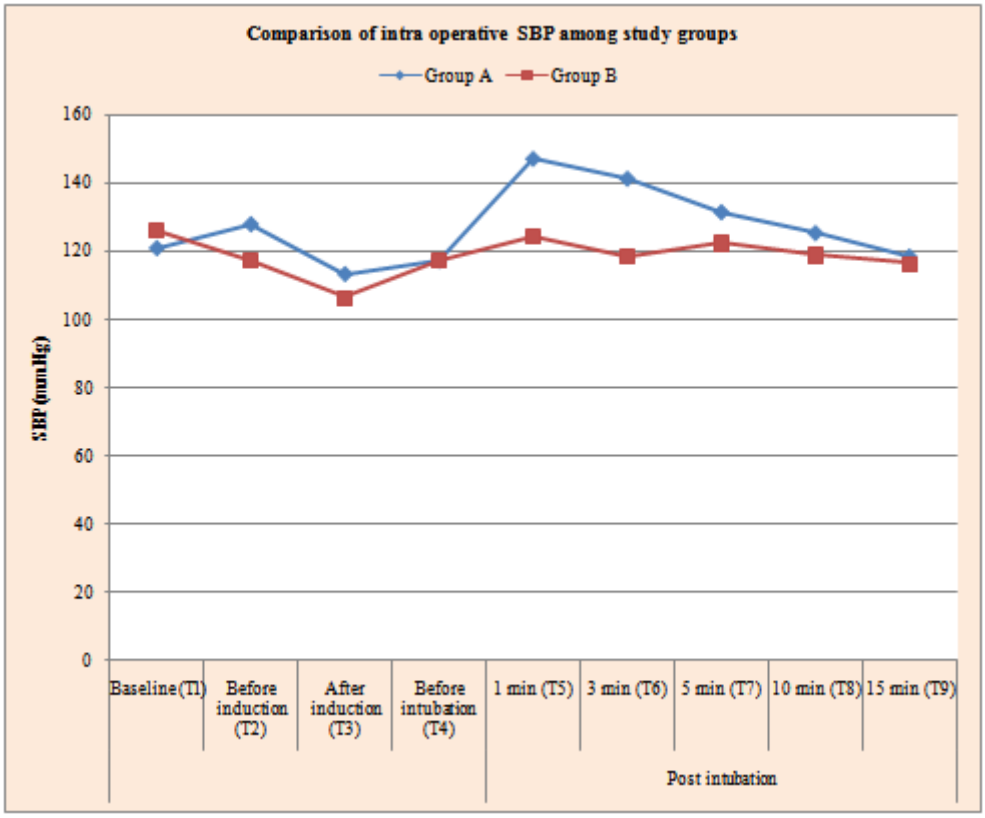


Table-3 : Comparison of intra operative DBP (mmHg) among study groups

Time	Group A	Group B	P value
Baseline (T1)	78.6 ± 7.8	84.9 ± 8.6	0.005
Before induction (T2)	82.1 ± 7.7	82.4 ± 9.8	0.884
After induction (T3)	72 ± 7.7	73.4 ± 9.8	0.539
Before intubation (T4)	74.7 ± 9.2	76.4 ± 9.8	0.474
Post intubation			
1 min (T5)	107.2 ± 9.1	90.1 ± 9	<0.001
3 min (T6)	100.1 ± 5.6	86.4 ± 9.8	<0.001
5 min (T7)	90.7 ± 6.3	80.9 ± 7.5	<0.001
10 min (T8)	84.4 ± 5.1	76.4 ± 7	<0.001
15 min (T9)	76.9 ± 6.1	75.3 ± 7.2	0.365

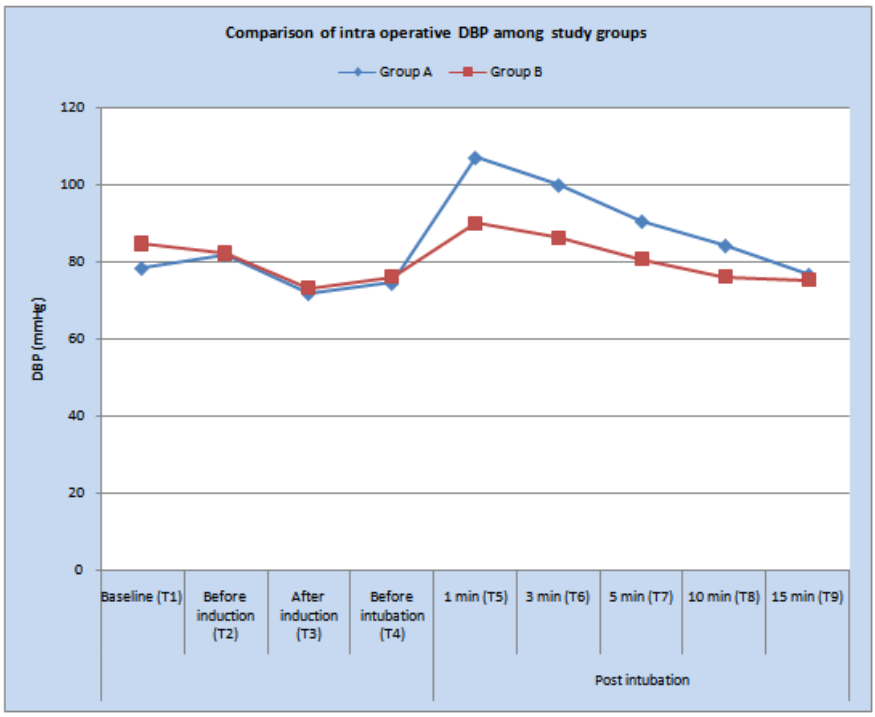
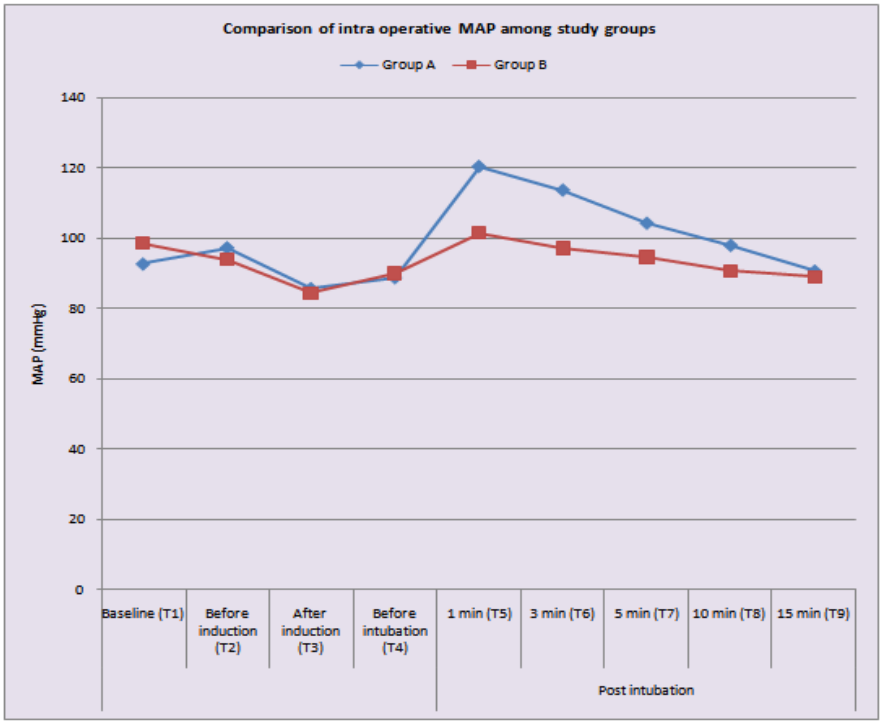


Table- 4: Comparison of intra operative MAP (mmHg) among study groups

Time	Group A	Group B	P value
Baseline (T1)	92.8 ± 7.3	98.7 ± 9.3	0.009
Before induction (T2)	97.4 ± 8.1	94.1 ± 10.3	0.171
After induction (T3)	85.8 ± 8.4	84.5 ± 10.2	0.575
Before intubation (T4)	88.9 ± 8.7	90.1 ± 10.2	0.623
Post intubation			
1 min (T5)	120.5 ± 10.1	101.6 ± 9.4	<0.001
3 min (T6)	113.8 ± 6	97.2 ± 10	<0.001
5 min (T7)	104.4 ± 6.8	94.8 ± 7.4	<0.001
10 min (T8)	98.1 ± 5.9	90.7 ± 6.9	<0.001
15 min (T9)	90.8 ± 6.1	89.1 ± 6.8	0.312



IV. Discussion

The hemodynamic response to laryngoscopy and intubation, comprising of elevation in heart rate and rise in systolic and diastolic pressure, are well known. The magnitude of hemodynamic changes observed may depend on various factors such as depth of anesthesia, whether any measure has been taken prior to airway manipulation, the anesthetic agent used, the duration of laryngoscopy and attempt of intubation. The principal mechanism in hypertension and tachycardia is sympathetic response, which may be the result of increase in catecholamine activity. Gabapentin may act in a manner similar to calcium channel blockers in controlling the hemodynamic response associated with laryngoscopy and intubation.[8]] Fentanyl is a potent, synthetic narcotic analgesic with a rapid onset and short duration of action. It is extremely lipid soluble, has a low molecular weight and is a synthetic opioid agonist which is popularly used as intravenous analgesic supplement, component of inhalation anaesthesia, balanced anaesthesia and neurolept analgesia and also as a sole anaesthetic. It is 75 to 125 times more potent than morphine as an analgesic [2]

Memis et al observed a significant decrease in heart rate in patients who received 800 mg of gabapentin one hour preoperatively[7]. Singhal SK et al in their study found that where thiopentone has been used as the induction agent, gabapentin has not been shown to be as effective as other agents such as clonidine[9]. Bafna U et al in their study has shown that the effects of gabapentin on hemodynamic variables during laryngoscopy and intubation may be dose-related up to a dose of 1000 mg.[11] Parida S et al in their study found that gabapentin against fentanyl to blunt the hemodynamic response to laryngoscopy and intubation seems to suggest that it is unlikely to add significant benefits to standard perioperative drug regimens that utilize thiopentone as the induction agent.[1] Fassoulaki et al in his study found that there was an increase in heart rate after laryngoscopy and intubation. Fentanyl brings hemodynamic stability during perioperative period by its action on cardiovascular and autonomic regulatory areas. It decreases sympathetic tone and increases parasympathetic tone. Fentanyl inhibits pituitary adrenal response directly or indirectly via hypothalamus. It attenuates the response at 2μg/kg IV given before laryngoscopy and intubation. Optimal time of administration is 5 minutes before laryngoscopy and intubation[12].

The potential for life threatening complication associated with these responses is also well documented. Intravenous anaesthetic induction agents do not adequately or predictably suppress the circulatory responses evolved by endotracheal intubation initiating laryngoscopy, so additional pharmacological measures like use of volatile anesthetics, topical and intravenous lidocaine, opioids, vasodilators, SNP, NTG, calcium channel blockers and β blockers have been tried by various authors. Therefore, it has become imperative to develop a novel technique or drug to prevent these potentially hazardous responses. In our study we compared randomly two drugs oral gabapentin 800 mg and inj. Fentanyl 2μg/kg to attenuate hemodynamic response during laryngoscopy and endotracheal intubation.

- There were no statistically significant differences in the demographic parameters such as Age, Weight, Sex and ASA physical status among the study groups .
- The mean baseline variables(HR,SBP,DBP,MAP,,SpO_2) were almost similar in both the groups as desired in study population was achieved for appropriate randomization, Preoperatively all patients were awake and above parameters observed after premedication and just before intubation, in both groups mean HR,SBP.DBP,MAP were decreased from baseline were statistically non significant.
- After 1 min of intubation, HR was increased in both the groups but more in gabapentin group than fentanyl group. There was rise in SBP, DBP, and MAP in gabapentin group from baseline value but in fentanyl group ,SBP,DBP and MAP were little decreased from baseline value.It was statistically significant ($p<0.05$).
- After 3 min of intubation HR was not return to baseline in both groups and difference was still statistical significant. All other parameters like SBP, DBP, MAP were decreased from baseline in both groups with non-significant difference. After that SBP, DBP and MAP were remained its trends till 15 min post intubation in both groups.
- After15 min of intubation HR was still above from baseline in group A but it was nearer to the baseline in group B.The mean oxygen saturation remained above 98% in both groups at all the point of study. There was no significant differences in oxygen saturation were noted at various of the study between the two group.
- The incidence of complications (hypotension bradycardia nausea and vomiting) were more with gabapentin group except respiratory depression which was found more in fentanyl group but the difference was not significant. Hence IV fentanyl (2μg/kg) is better option to attenuate the hemodynamic response as compare to oral gabapentin 800μg/kg.

V. Conclusion

It is concluded from our study that IV fentanyl (2µg/kg) controls the hemodynamic response to laryngoscopy and endotracheal intubation much better as compared to oral gabapentin(800mg) without any significant side effect.

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