

TO STUDY EFFECT OF GABAPENTIN ON ATTENUATION OF PRESSOR RESPONSE TO DIRECT LARYNGOSCOPY AND TRACHEAL INTUBATION AND ON PERIOPERATIVE PAIN

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ABSTRACT

BACKGROUND

Endotracheal intubation was first described by Rowbotham and Magill in 1921.¹ In 1940 Reid and Brace first described hemodynamic response to Laryngoscopy and Intubation due to Noxious stimuli.² The circulatory responses to laryngeal and tracheal stimulation are due to sympathoadrenal stimulation.³ Laryngoscopy and Tracheal Intubation induces changes in circulating Catecholamine levels significantly. Norepinephrine, Epinephrine and Dopamine levels rise, but the raise in Norepinephrine levels is consistently associated with elevation of Blood pressure and Heart rate.⁴ Even though the elevation in Blood pressure and Heart rate due to Laryngoscopy and Intubation are brief, they may have detrimental effects in high risk patients including Myocardial Infarction, Cardiac failure, Intracranial haemorrhage and increases in Intracranial pressure.⁵ Many strategies have been advocated to minimize these hemodynamic adverse responses and aimed at different levels of the reflex arc.⁶ Block of the peripheral sensory receptors and afferent input is by topical application and infiltration of Local Anaesthetic to Superior laryngeal nerve. Block of central mechanism of integration and sensory input by drugs like Fentanyl, Morphine etc. Block of efferent pathway and effector sites IV Lignocaine, Beta blockers, Calcium channel blockers, Hydralazine etc. No single drug or technique is satisfactory.

The aim of this study is to evaluate the efficacy of Gabapentin in attenuating hemodynamic response to laryngoscopy and intubation in a placebo controlled double blind study.

MATERIALS AND METHODS

A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 150 patients posted for elective surgery divided into two groups and were randomly allocated Group 1 – placebo capsules with sugar and Group 2 – Gabapentin 300 mg capsules. Heart rate, systolic, diastolic blood pressure, mean arterial pressure were recorded at 1, 3, 5 and 10 minutes intervals from onset of laryngoscopy.

RESULTS

In Gabapentin group there was significant suppression of heart rate and blood pressure when compared to the control group which returned to baseline at the end of 10 minutes of laryngoscopy.

CONCLUSION

In patients with no drugs to attenuate the sympathetic response to laryngoscopy and intubation the maximum raise in heart rate and blood pressures were statistically and clinically very highly significant and can be detrimental in high-risk patients. Gabapentin significantly attenuates the sympathetic response to laryngoscopy and tracheal intubation.

KEYWORDS

Gabapentin, Laryngoscopy, Tracheal Intubation, Sympathetic Response.

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hemodynamic response to Laryngoscopy and Intubation due to Noxious stimuli.² The circulatory responses to laryngeal and tracheal stimulation are due to sympathoadrenal stimulation.³ Laryngoscopy and Tracheal Intubation induces changes in circulating Catecholamine levels significantly. Norepinephrine, Epinephrine and Dopamine levels rise, but the raise in Norepinephrine levels is consistently associated with elevation of Blood pressure and Heart rate.⁴ Even though the elevation in Blood pressure and Heart rate due to Laryngoscopy and Intubation are brief, they may have detrimental effects in high risk patients including Myocardial Infarction, Cardiac failure, Intracranial haemorrhage and increases in Intracranial pressure.⁵

Many strategies have been advocated to minimize these hemodynamic adverse responses and aimed at different levels of the reflex arc.⁶ Block of the peripheral sensory receptors and afferent input is by topical application and infiltration of Local Anaesthetic to Superior laryngeal nerve. Block of central mechanism of integration and sensory input by drugs like Fentanyl, Morphine etc. Block of efferent pathway and effector sites IV Lignocaine, Beta blockers, Calcium channel blockers, Hydralazine etc. No single drug or technique is satisfactory.

The present study is to evaluate the efficacy of Gabapentin in attenuation of pressor response to Laryngoscopy and Intubation with minimal side effects and better pharmacological profile.

Aim of the Study

- Attenuation of pressor response to Laryngoscopy and Intubation was studied with various techniques like deep inhalational, deep general Anaesthesia and with various drugs like Midazolam, Morphine, Buprenorphine, Fentanyl, Sufentanil, Remifentanil, Droperidol, Clonidine, Metoprolol, Esmolol, Atenolol, Lignocaine, and were proven to be effective.
- The introduction of Gabapentin which is a relatively new drug, which was introduced as antiepileptic but proved to be effective in controlling neuropathic pain. The drug is well tolerated, as compared with older antiepileptics such as Carbamazepine.
- The aim of present study is to evaluate the efficacy of Gabapentin in attenuating hemodynamic response to Laryngoscopy and Intubation in a placebo controlled double blind study.

MATERIALS AND METHODS

A clinical comparative study of attenuation of sympathetic response to Laryngoscopy and Intubation was done in 150 patients posted for elective surgery.

Inclusion Criteria

- Age between 20 to 50 years of both the sexes.
- Patients with ASA grade I or II.
- Mallampati airway assessment of grade I and II.

Exclusion Criteria

- Age less than 20 and more than 50 years
- Patients with Hypertension, Diabetes, Immunocompromise and Pregnancy
- Predictably difficult airways.
- Obesity (BMI>30) and patients with known allergy to NSAIDS.
- Consumption of anti-hypertensives, sedatives, hypnotics, antidepressants drugs with effect on CNS. 150 cases are divided in to two groups.
- Group-1 was Control group. In this group placebo capsules were prepared after meticulously emptying of the Gabapentin capsules and filled with thin sugar.

- Group-2 was Gabapentin group. In this group patients received Gabapentin 300 mg at noon, 18 hours and 24 hours the day before surgery and at 6 a.m. on the morning of surgery.

Patients were pre-medicated with Omeprazole 40 mg orally night on day before surgery,

10 mg IV Metoclopramide 10 minutes before induction of anaesthesia, induced with Propofol 2.5 mg/kg, Vecuronium bromide 0.08-0.1 mg/kg. Patient was intubated and heart rate, systolic and diastolic blood pressure were recorded before and after administration of IV anaesthetic at 1, 3, 5 and 10 minute intervals from the onset of laryngoscopy.

Adequacy of ventilation was monitored clinically and SPO₂ was maintained at 99-100%.

OBSERVATION AND RESULTS

Analysis of Heart Rate

The difference in the heart rate between control and Gabapentin groups remain significant at immediately after Laryngoscopy and Intubation and at 1 min, 3 min and 5 min with p value being (<0.0001) and not much significant at 10 min post intubation. At 1, 3 and 5 minutes' post laryngoscopy the difference is very highly significant (p<0.001).

Time	Heart Rate		T Test P Value
	Control Mean ± SD	Gabapentin Mean ± SD	
Baseline	83.10 ± 7.393	86.60 ± 12.056	0.064
Pre-induction	87.21 ± 6.290	89.32 ± 7.763	0.099
Post induction	105.14 ± 11.485	89.66 ± 7.922	0.0001
1 Min	109.54 ± 7.867	93.96 ± 7.265	0.0001
3 Min	101.77 ± 8.883	91.40 ± 9.534	0.0001
5 Min	95.85 ± 7.769	89.04 ± 7.529	0.0001
10 Min	89.58 ± 7.482	86.08 ± 6.948	0.006

Table 1. Comparison of Heart Rate (in BPM) in Between Two Groups

Analysis of Systolic Blood Pressure

The difference in Systolic blood pressure between control and Gabapentin group remains statistically significant at post induction with p value being 0.0001, immediately after Laryngoscopy and Intubation and at 1 min, 3 min, 5 min and 10 min with P value being (<0.0001).

Time	Heart Rate		T Test P Value
	Control Mean ± SD	Gabapentin Mean ± SD	
Baseline	120.50 ± 7.507	119.70 ± 8.384	0.357
Pre-induction	125.59 ± 4.872	122.80 ± 8.444	0.034
Post induction	159.72 ± 21.951	123.80 ± 9.560	0.0001
1 Min	168.76 ± 14.52	134.20 ± 9.212	0.0001
3 Min	101.77 ± 8.883	91.40 ± 9.534	0.0001
5 Min	147.14 ± 10.649	127.12 ± 5.021	0.0001
10 Min	128.66 ± 11.404	122.00 ± 9.553	0.0001

Table 2. Comparison of Systolic Blood Pressure (in mm of Hg) in Two Groups

Analysis of Diastolic Blood Pressure

The difference in Diastolic blood pressure between control and Gabapentin groups remain significant at post induction with P-value being 0.0001, immediately after Laryngoscopy and Intubation and at 1 min, 3 min and 5 min with p-value being (<0.0001). At 10 min no significant difference in

Diastolic blood pressure as observed with P-value being 0.102. These differences in Diastolic blood pressures between control group and Gabapentin group remain statistically very significant at all times except at 10 min where is statistically insignificant.

Column 1	Column 2	Column 3	Column 4	Column 5
	Dias Tolic Blood Pressure			T Test
		Control	Gabapentin	
		Mean ± SD	Mean ± SD	P Value
Baseline		78.06 ± 8.053	79.28 ± 9.190	0.427
RE Induction		80.56 ± 7.744	79.44 ± 7.965	0.409
DST Induction		101.05 ± 11.7;	77.36 ± 7.148	0.0001
1 Min		105.04 ± 9.13!	85.52 ± 8.716	0.0001
3 Min		95.18 ± 8.046	81.80 ± 7.103	0.0001
5 Min		89.62 ± 8.69	77.44 ± 6.322	0.0001
10 Min		78.16 ± 5.860	75.76 ± 9.358	0.102

Table 3. Comparison of Diastolic Blood Pressure (in mm of Hg)

Analysis of Mean Arterial Pressure

In comparison to control group attenuation of mean arterial pressure is significant in Gabapentin group. The difference in Mean arterial pressure between control and Gabapentin groups remains significant immediately after Laryngoscopy and Intubation and at 1 min,3 min,5 min with p-value being (<0.0001).

3 Min	16326.88 ± 1539.203	11746.68 ± 1355.529	0.0001
5 Min	13988.98 ± 1890.336	11377.60 ± 1018.733	0.0001
10 Min	11547.98 ± 1593.905	10403.40 ± 977.93	0.0001

Table 5. Comparison of Rate Pressure Product (in mm of hg*BPM) in Two Groups

Time	Mean Arterial Pressure		T Test
	Control	Gabapentin	P Value
	Mean ± SD	Mean ± SD	
Baseline	91.69 ± 7.513	93.08 ± 8.595	0.333
Pre-Induction	95.60 ± 6.181	93.98 ± 7.288	0.181
Post Induction	120.52 ± 14.459	92.70 ± 6.541	0.0001
1 Min	126.57 ± 8.564	104.18 ± 12.008	0.0001
3 Min	116.53 ± 6.946	97.54 ± 5.786	0.0001
5 Min	108.70 ± 8.379	94.06 ± 5.257	0.0001
10 Min	94.70 ± 6.536	90.36 ± 8.962	0.003

Table 4. Comparison of Mean Arterial Pressure (in mm of Hg) in Two Groups

Analysis of Rate Pressure Product

The difference in rate pressure product between control and Gabapentin groups remain significant immediately and at 1 min, 3 min, 5 min and 10 min with p value being (<0.0001).

Time	Rate Pressure Product		T Test P Value
	Control Mean ± SD	Gabapentin Mean ± SD	
Baseline	10061.40 ± 1355.041	10486.08 ± 1666.587	0.122
Pre-Induction	10988.33 ± 1087.690	10987.76 ± 1400.120	0.998
Post Induction	16940.44 ± 3600.052	11093.28 ± 1238.260	0.0001
1 Min	18733.72 ± 1988.485	12784.28 ± 1365.938	0.0001

DISCUSSION

Our results showed that Gabapentin attenuated the pressor response to tracheal intubation, as SAP and DAP, HR were significantly lower in the Gabapentin vs the control group. The cardiovascular responses to laryngoscopy and tracheal intubation are well known and linked with increases in Catecholamines in blood levels. Several techniques have been proposed to attenuate such responses.⁷ Tachycardia and rhythm disturbances as a result of intubation were attenuated by omitting Atropine as premedication.⁸ Nitroglycerin administrated intranasally, attenuated the hypertensive response to Laryngoscopy and Intubation but tachycardia was observed in both the nitroglycerin and the control group.⁹ Also, IV Lidocaine prevented the increase in Mean arterial blood pressure but had no effect on the HR.¹⁰

Fassoulaki et. al have done study on forty-six patients undergoing abdominal hysterectomy for benign disease were randomly allocated to receive Gabapentin 1600 mg or placebo capsules at 6 hourly intervals starting the noon before surgery. Systolic, Diastolic arterial blood pressure and Heart rate were recorded before and after the anaesthetic and at 0,1,3,5 and 10 min after tracheal intubation. They observed difference in heart rate and diastolic blood pressure with regard to time (p=0.0001).¹¹

Memis D, et al, studied the effects of Gabapentin on arterial pressure and heart rate at induction of anaesthesia and tracheal intubation in a randomized double-blind study. Ninety normotensive patients (ASA I) undergoing elective surgery were divided into three groups of 30 patients each. Prior to surgery, group I received oral placebo, group II

received 400 mg Gabapentin and group III received 800 mg Gabapentin. After induction, heart rate and mean arterial pressure were recorded at baseline, 1, 3, 5, 10, 15 min after intubation. Patients receiving placebo and 400 mg Gabapentin showed a significant increase in blood pressure and heart rate associated with tracheal intubation with p-value being <0.001, <0.001, <0.005, 0.005 respectively.¹²

Vida Ayatollahi et.al, conducted study in 30 patients aged 30-70 years, ASA physical status I or II, who underwent micro laryngeal surgery. The night before surgery, 15 patients (Group G) received 100 mg Gabapentin and 15 patients (Group P) received a placebo. Ninety minutes before operation, they received 800 mg Gabapentin (Group G), or a placebo (Group P). Heart rate, systolic, diastolic and mean arterial pressure were measured on the night before, on the morning of the procedure, at arrival to the operating room as baseline, before and after induction, 1, 3 min after tracheal intubation. They concluded that 800 mg Gabapentin given 90 min before a procedure attenuates the rise of diastolic pressure and mean arterial pressure in the first 15 min after micro laryngoscopy surgery, but has no effect on systolic blood pressure or heart rate with P-value being 0.01.¹³

The most recent studies regarding prevention of hemodynamic changes after Laryngoscopy and Tracheal intubation investigate the effect of Remifentanil, an opioid with very rapid onset and very short duration of action. Remifentanil 1 micro gm/kg followed by 0.5 micro gm/kg /min attenuated the pressor response to intubation but was associated with Bradycardia and /or Hypotension.¹⁴ Other workers found that remifentanil 0.5 micro gm/kg did not prevent Hypertension and Tachycardia during rapid sequence induction. However, Remifentanil 1 micro gm/kg was effective while 1.25 micro/kg in some patients caused Hypotension.¹⁵

CONCLUSION

The present study is a Double blinded comparative study conducted in 150 patients belonging to ASA grades I & II. One group received Placebo capsules and the other group received Gabapentin 300 mg orally half an hour before induction preoperatively.

We conclude that laryngoscopy and tracheal intubation are noxious stimuli which causes transient increase in heart rate and blood pressure. This effect is transient but dangerous in patients with comorbid conditions like diabetes, hypertension, cardiovascular diseases and intracranial hemorrhage conditions. Many techniques and drugs have been suggested to blunt this autonomic response but none of them are satisfactory, hence need further study.

Gabapentin significantly attenuate the pressor response to laryngoscopy and tracheal intubation.

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