IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 5 Ver. 3 (May. 2018), PP 09-14
www.iosrjournals.org

To Evaluate the Effect of Pre-Operative Oral Gabapentin on Cardiovascular Response to Laryngoscopy and Tracheal Intubation

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Abstract
Background: *Many pharmacologic approaches have been tried to obtund the haemodynamic response to laryngoscopy but none has been proved entirely satisfactory, because either the reflex is blocked incompletely or because the method itself carries some additional risk.*
Aims and Objective: *Our study aims to assess the efficacy of oral Gabapentin 400mg in attenuating haemodynamic response to direct laryngoscopy and endotracheal intubation in ASA I/II normotensive patients undergoing elective upper abdominal surgeries under general anaesthesia.*
Materials and methods: *A prospective, randomized, placebo controlled, double blind clinical study was conducted on 60 normotensive patients (30 in each group), of either sex, undergoing elective upper abdominal surgeries under general anaesthesia.Patients were randomized to C or G group accordingly and received the respective capsules, that is, the Placebo Capsule B-Complex or Capsule Gabapentin 400 mg, 2 hours prior to surgery.*
Results*: As compared to Gabapentin group, control group patients showed significantly higher and sustained increase in heart rate, systolic and diastolic blood pressure, at 00 minutes immediately after intubation, 01, 03, 05, 10 minutes following intubation. The control group patients showed significantly higher and sustained increase in mean arterial pressure at induction and thereafter for 10 minutes (P < 0.001).*
Discussion: *In our study, Oral route was selected as it is safe, less costly and more acceptable than the parenteral route. In our study, heart rate was less affected (12.38%) as compared to blood pressure (2.68%) and changes in diastolic blood pressure were minimal 2.65%.*
Conclusion: *Gabapentin (400 mg), when given orally two hours prior to surgery effectively attenuates heart rate and blood pressure changes to direct laryngoscopy and tracheal intubation. Its effect on the heart rate is less as compared to blood pressure. Changes in diastolic blood pressure are minimal after intubation.*
Keywords*: Gabapentin, Haemodynamics, Intubation, Oral, Response*.

Date of Submission: 20-04-2018 Date of acceptance: 07-05-2018

I Introduction

Laryngoscopy and endotracheal intubation are integral parts of modern anaesthesia. A marked cardiovascular response with a rise in blood pressure and increase in pulse rate is often encountered during endotracheal intubation (King BD et al, 1951)[1].During their studies on efficacy of Gabapentin, several researchers (Fassoulaki et al 2006[15], Memis et al 2006[16], Koc et al 2007[17]] found that patients who received the drug were haemodynamically stable and had less significant pressor response during surgery. Gabapentin may inhibit central sensitization through an action on voltage-dependent Ca^{2+} channels, resulting in a direct post-synaptic or a pre-synaptic inhibition of Ca^{2+} influx that decreases excitatory amino acid neuro-transmission (Fink et al, 2000)[18].

With this background, we designed this clinical study to assess the efficacy of oral Gabapentin 400mg in attenuating haemodynamic response to direct laryngoscopy and endotracheal intubation in ASA I/II normotensive patients undergoing elective upper abdominal surgeries under general anaesthesia.

II Materials And Methods

A prospective, randomized, placebo controlled, double blind clinical study was conducted on 60 normotensive patients (30 in each group), of either sex, undergoing elective upper abdominal surgeries under general anaesthesia.

2.1 Inclusion criteria: Patients undergoing elective upper abdominal surgeries under general anaesthesia, ASA Grade I/II, Age between 20-40 years, Weight between 40-60 kg.

2.2 Exclusion criteria: Patient refusal, difficult intubation. (Malampatti Class III/IV, Restricted neck movements, Receding jaw, Oral masses, Cormack-Lehanne Grade>I) Drug or alcohol abuse, patients receiving sedatives, hypnotics and antidepressants, Cardiovascular and renal diseases, known allergy to gabapentin, patients suffering from any cardiovascular disorder, either controlled with drugs or uncontrolled (hypertension or ischemic heart disease or valvular heart disorders), history of acidity or gastro osophageal reflux.

Study was carried out after getting approval from the Institutional Ethics Committee and informed consent was obtained for participation in the study from all patients. Tablet Alprazolam 0.5mg oral was given on the night prior to surgery; Patients were randomized to C or G group accordingly and received the respective capsules 2 hours prior to surgery with a sip of water. The capsule was given by an anaesthetist who was blinded for the study.

2.3 Study Medication:

G Group: Capsule Gabapentin 400 mg two hours prior to surgery.

Trade Name: GABANTIN400 (SUN PHARMACEUTICALS) Generic name: 1-(amino methyl) cyclohexane acetic acid

C Group: Placebo Capsule B-Complex

In the pre-operative area, patient was monitored for vital parameters and level of sedation, before shifting to operation theatre. Sedation score was assessed using the RAMSAY SEDATION SCALE (RSS).

Printout of ECG was taken when there was a change of >30% in the heart rate or any arrhythmia was noted. All the patients received Inj. Midazolam 0.02 mg/kg and Inj. Pentazocine 0.3 mg/kg I.V. as pre-medication; they were induced with Inj. Propofol 2-2.5mg/. Intubation was facilitated with Inj. Suxamethonium Hydrochloride 2 mg/kg.Laryngoscopy was done after 90 seconds with the McIntosh 3 laryngoscope blade by the same anaesthetist who was trained in the technique for 2 years. Patients were maintained on O_2 + N_2O (50% each) + Isoflurane (0.8%).Muscle relaxation was maintained using injection Vecuronium Bromide (0.1 mg/kg) after initiation of spontaneous respiration. $ETCO_2$ was also monitored during the study.

2.4 Parameters Measured:

Heart rate, Systolic, Diastolic and Mean arterial blood pressure were recorded before induction, 90 seconds after induction, 00 minute immediately after intubation, 01, 03, 05, 10 minutes after intubation by the anaesthetist who was blinded to the drug given. If the parameters did not return to baseline after 10 minutes and the increase was < 30% of baseline, then surgery was started. After that, further values were not taken into consideration. Cases where intubation was difficult, took more than 20 sec. and required more than one attempt were excluded from the study. For statistical analysis, heart rate or blood pressure change of ±30% were considered clinically significant. Patient were observed for 8 hours in the post-operative period for side-effects like somnolence, nausea, vomiting, ataxia and dizziness and treated accordingly if needed.

Incidences of all these parameters were recorded in both the groups. If there was hypotension as per definition in between 10 to 15 min, then fluid challenge was given. If not corrected by this, then Ephedrine 5 mg was given. If tachycardia was associated with hypertension, then Isoflurane% was increased. If there was bradycardia as per definition in above period, it was treated with injection Atropine 0.02 mg/kg.

III Statistical Analysis

Demographic parameters were analyzed by Student's t-test. Binary data like sex, ASA grade were analyzed by chi-square test. For finding statistical significance between the groups, unpaired t-test was applied to ascertain the pattern and magnitude of differences. A p value < 0.05 was considered as significant and p value < 0.01 was considered highly significant.

IV Results

Both the groups were comparable in terms of age, sex, weight and ASA grade. Mallampatti grading, laryngoscopy and time required for intubation were comparable in both the groups. The duration of surgery was comparable in both the groups (P=0.7921). The data thus obtained was divided in the following two groups:

Gabapentin group ('G' group) -Patients receiving Capsule Gabapentin 400 mg orally with sips of water prior to surgery.

Control group ('C' group) -Patients receiving Capsule B-Complex as placebo with sips of water prior to surgery.

The sedation score, which was assessed according to the Ramsay Sedation Scale, was comparable in both the groups. At the baseline, the time required for intubation, the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure in both groups were comparable.

TABLE 1: Comparison of Heart Rate

TIME	HEART RATE (beats per minute)		'P' VALUE
	'G'GROUP (MEAN ± S.D.)	'C'GROUP (MEAN ± S.D.)	
Before Induction	86.13 ± 16.41	85.93 ± 11.99	0.9572
90 seconds after Induction	88.40 ± 15.24 P=0.2975	88.43 ± 11.88 P=0.2360	0.9925
00 minutes immediately after Intubation	96.80 ± 16.60 P=0.0000	107.00 ± 09.86 P=0.0000	0.0042
01 minute after Intubation	95.23 ± 15.60 P=0.0002	109.97 ± 11.90 P=0.0000	0.0001
03 minutes after Intubation	91.10 ± 16.88 P=0.0279	106.77 ± 12.96 P=0.0000	0.0002
05 minutes after Intubation	86.87 ± 15.72 P=0.6863	102.37 ± 12.67 P=0.0000	0.0001
10 minutes after Intubation	87.03 ± 16.19 P=0.6862	99.67 ± 14.45 P=0.0000	0.0023

'Thus, in G Group, mean heart rate was significantly higher at 00, 01 and 03 minutes and had come back to baseline 05 minutes after intubation where as in 'C' Group, there was an insignificant rise in heart rate and after intubation, the heart rate rose significantly from baseline which lasted for more than 10 minutes. The maximum change in the heart rate was seen immediately after intubation in the Gabapentin group. All the values in the Gabapentin group were significantly lower than the control group.10% of the patients in the Gabapentin group and 53.33% of the patients in the control group had tachycardia. None of the patients in both the groups had bradycardia. 2 patients in the control group had ventricular ectopics following intubation which were transient and did not require any treatment. One patient in the Gabapentin group had ventricular bigeminy and also the duration of intubation exceeded more than 20 seconds and one patient in the control group who had an unanticipated difficult intubation had bradycardia, required two attempts for intubation. Both the patients were excluded from the study

TABLE 2 – Comparison of Systolic Blood Pressure

TIME	SYSTOLIC BLOOD PRESSURE (mm Hg)		'P' VALUE
	'G'GROUP MEAN ± S.D.	'C'GROUP MEAN ± S.D.	
Before Induction	118.80 ± 10.96	117.67 ± 11.91	0.7027
90 seconds after Induction	105.60 ± 09.24 p=0.0000	102.63 ± 12.10 p=0.0000	0.2906
00 minutes immediately after Intubation	122.03 ± 09.26 p=0.1045	138.13 ± 18.10 p=0.0000	0.0001
01 minute after Intubation	120.57 ± 08.61 p=0.2978	137.67 ± 16.80 p=0.0000	0.0000
03 minutes after Intubation	112.53 ± 10.27 p=0.0007	132.17 ± 17.64 p=0.0001	0.0000
05 minutes after Intubation	107.30 ± 12.16 p=0.0000	124.97 ± 11.65 p=0.0113	0.0000
10 minutes after Intubation	107.63 ± 12.47 p=0.0000	118.20 ± 12.73 p=0.8543	0.0019

TABLE 3 - Comparison of Diastolic Blood Pressure

TIME	DIASTOLIC BLOOD PRESSURE (mm Hg)		'P' VALUE
	'G'GROUP MEAN ± S.D.	'C'GROUP MEAN ± S.D.	
Before Induction	76.73 ± 08.99	75.23 ± 08.57	0.5110
90 seconds after Induction	66.97 ± 08.54 p=0.0000	64.80 ± 10.77 p=0.0000	0.3917
00 minutes immediately after Intubation	78.77 ± 12.49 p=0.3096	91.20 ± 14.19 p=0.0000	0.0007
01 minute after Intubation	76.47 ± 08.52 p=0.8539	92.43 ± 14.63 p=0.0000	0.0000
03 minutes after Intubation	72.03 ± 09.08 p=0.0068	84.10 ± 12.28 p=0.0008	0.0001
05 minutes after Intubation	68.37 ± 11.07 p=0.0000	80.83 ± 12.53 p=0.0479	0.0001
10 minutes after Intubation	69.67 ± 10.97 p=0.0016	79.37 ± 09.68 p=0.0753	0.0006

As shown in Table 2 and 3, there was a significant decrease in systolic and diastolic blood pressure after induction in both groups. However immediately after intubation, both groups showed an increase in systolic and diastolic blood pressure. As compared to Gabapentin group, control group patients showed significantly higher and sustained increase in systolic and diastolic blood pressure at 00 minutes immediately after intubation, 01, 03, 05, 10 minutes following intubation (P=0.0001, P=0.0000, P=0.0000, P=0.0000 and P=0.0019 respectively for systolic blood pressure and P=0.0007, P=0.0000, P=0.0001, P=0.0001 and P=0.0006 for diastolic blood pressure respectively).When the mean arterial pressure between two groups were compared, control group patients showed significantly higher and sustained increased in mean arterial pressure at induction and thereafter for 10 minutes (P < 0.001).In the Gabapentin group, mean arterial pressure changed by 2.68% and by 19.54% in the control group immediately after intubation.16.67% of the patients in the control group had hypertension (a 30% increase from the baseline) which lasted for not more than 3 minutes. Hypotension was not observed in our study.

TABLE 4 - Percentage Change in Gabapentin group in Heart rate, Systolic, Diastolic and Mean Arterial Pressure immediately after intubation with respect to Baseline.

PARAMETERS	PERCENTAGE CHANGE (%)
HEART RATE	12.38
SYSTOLIC BLOOD PRESSURE	2.72
DIASTOLIC BLOOD PRESSURE	2.65
MEAN ARTERIAL PRESSURE	2.68

In the Gabapentin group, heart rate was less affected as compared to blood pressure and minimal changes were observed in diastolic blood pressure.

V Discussion

The cardiovascular responses to intubation may have serious consequences, including myocardial ischemia, dysrhythmias, and at times, even cardiac arrest (Bruder et al, 1992)[2].Deep anaesthesia (King BD et al, 1951)[1], topical anaesthesia (Sklar BZ et al 1992[5], Takita et al 2001[6], Venus B et al 1984[4], Robert K Stoelting et al[13,21,3]), opioids like Fentanyl, Alfentanil, Remifentanil (Maguire AM et al, 2001)[7], calcium channel blockers like Verapamil, Diltiazem, Nicardipine (Jyotsna Wig et al, 1994)[12], beta blockers like Esmolol, Labetalol, Landiolol (Kindler CH et al 1996[9], Miller DR et al 1991[8], Ramanathan J et al 1988[10], Yamazaki A et al 2005[11]), Nitroglycerin (Hill AB et al, 1981)[14] have been tried with varying success. Gabapentin has been used by Kong et al (2007)[22] for the management of more acute conditions. Hence we planned to conduct a prospective, randomized, double blind, clinical study to assess effect of preoperative oral Gabapentin on pressor response to direct laryngoscopy and endotracheal intubation. Normotensive patients were included in the study as the pressor response is exaggerated in patients with hypertension (Prys-Roberts et al, 1971)[23]. We used the inclusion and exclusion criteria similar to the ones used by Fassoulaki et al (2006)[15] and Koc et al (2007)[17].In our study, oral Gabapentin 400 mg single dose was administered 2 hours prior to surgery. Oral route was

selected as it is safe, less costly and more acceptable than the parenteral route. The bioavailability of Gabapentin varies inversely with dose. So we have used the optimum dose of 400 mg. Gabapentin was given orally two hours prior to surgery because of the following reasons (Rose et al, 2002)[19]:

1. Peak plasma concentration after oral administration is attained in 2 -3 hours at the time of intubation.
2. Gabapentin is absorbed rapidly in part by the L-amino acid transport system.
3. Pharmacological actions following Gabapentin administration are due to the activity of the parent compound; Gabapentin is not appreciably metabolized in humans.

Patients in our study were induced with Injection Propofol 2-2.5 mg/kg and Injection Vecuronium bromide 0.1mg/kg.Time required for intubation was comparable in both the groups. The cardiovascular response to the act of tracheal intubation is a reflex phenomenon with the afferent stimuli carried over both glossopharyngeal and vagal pathways. Such stimuli activate suprasegmental and hypothalamic sympathetic centres to cause a peripheral sympathoadrenal response with release of adrenaline and noradrenaline (Burstein et al, 1950)[20.] In our study, heart rate was less affected (12.38%) as compared to blood pressure (2.68%) and changes in diastolic blood pressure were minimal 2.65%. Another important property of Gabapentin is absence of serious adverse effects.

The incidence of sedation was 16.67% (sedation score=3) up to 3 hours postoperatively. The sedation observed with Gabapentin is less than that with opioids (Dirks et al, 2002)[24].Two patients receiving Gabapentin reported dizziness for 2 hours and required no intervention.

The cost of capsule Gabapentin is Rs.11/capsule. One vial of Esmolol costs Rs.300, one ampoule of Fentanyl costs Rs.35 and one ampoule of Clonidine costs Rs.25. This makes Gabapentin a cost-effective alternative to conventional expensive drugs. Thus, oral Gabapentin 400 mg given 2 hours prior to surgery

Attenuates the cardiovascular response to laryngoscopy and intubation.

2. Has less effect on the heart rate as compared to blood pressure. Changes in diastolic blood pressure were minimal after intubation in patients receiving Gabapentin.

VI Conclusion

From our clinical study, it can be concluded that:

1. Laryngoscopy and endotracheal intubation are associated with an increase in arterial blood pressure and heart rate.
2. Gabapentin (400 mg), when given orally two hours prior to surgery effectively attenuates heart rate and blood pressure changes to direct laryngoscopy and tracheal intubation. Its effect on the heart rate is less as compared to blood pressure. Changes in diastolic blood pressure are minimal after intubation.
3. There are only few side effects of oral Gabapentin (400 mg) in the form of sedation and dizziness which are tolerated well and require no further interventions.
4. Oral Gabapentin 400 mg is safe, acceptable and cost-effective compared to the drugs administered parenterally.

We recommend oral Gabapentin 400 mg two hours prior to surgery for attenuation of the pressor response particularly for the patients having less basal heart rate, patients on beta blockers, patients with heart block and patients in whom beta blockers are contraindicated.

References

[1]. King BD, Harris LC Jr, Griefenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during anaesthesia. Anaesthesiology 1951; 12: 556-66.
[2]. Bruder N, Ortega D, Granthil C. Consequences and prevention methods of haemodynamic changes during laryngoscopy and intratracheal intubation. Ann Fr Anaesth Reanim. 1992; 11(1): 57-71.
[3]. Stoelting RK. Circulatory response to laryngoscopy and tracheal intubation with or without prior oropharyngeal viscous Lidocaine. Anaesth Analg. 1977; 56(5): 618-21.
[4]. Venus B, Polassani V, Pham CG. Effects of aerosolized Lidocaine on circulatory responses to laryngoscopy and tracheal intubation. Crit Care Med. 1984; 12(4): 391-
[5]. Sklar BZ, Lurie S, Ezri T, Krichelli D, Savir I, Soroker D. Lidocaine inhalation attenuates the circulatory response to laryngoscopy and endotracheal intubation. J Clin Anaesth. 1992; 4(5): 382-5.
[6]. Takita K, Morimoto Y, Kemmotsu O. Tracheal Lidocaine attenuates the cardiovascular response to endotracheal intubation. Can J Anaesth. 2001; 48(8): 732-6.
[7]. Maguire AM, Kumar N, Parker JL, Rowbotham DJ, Thompson JP. Comparison of effects of Remifentanil and Alfentanil on cardiovascular response to tracheal intubation in hypertensive patients. Br J Anaesth. 2001; 86(1): 90-3.
[8]. Miller DR, Martineau RJ, Wynands JE, Hill J. Bolus administration of Esmolol for controlling haemodynamic response to tracheal intubation: The Canadian Multi-Center Trial. Can Jour Of Anaesth 1991; 38: 849-10
[9]. Kindler CH, Schumacher PG, Schneider MC, Urwyler A. Effects of intravenous Lidocaine and/or Esmolol on haemodynamic responses to laryngoscopy and intubation: A double-blind, controlled clinical trial. Clin Anaesth. 1996; 8(6): 491-6.
[10]. Ramanathan J, Sibai BM, Mabie WC, Chauhan D, Ruiz AG. The use of Labetalol for attenuation of the hypertensive response to endotracheal intubation in preeclampsia. Am J Obstet Gynecol. 1988; 159(3): 650-4.
[11]. Yamazaki A, Kinoshita H, Shimogai M, Fujii K, Nakahata K, Hironak Y, Iranami H, Hatano Y. Landiolol attenuates tachycardia in response to endotracheal intubation without affecting blood pressure. Can J Anaesth. 2005; 52: 254-4

[12]. Wig J, Sharma M, Baichoo N, Agarwal A. Nicardipine and Verapamil attenuate the pressor response to laryngoscopy and intubation. Can J Anaesth. 1994; 41(12): 1185-8
[13]. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with Sodium Nitroprusside. Anaesth Analg. 1979; 58: 116-4.
[14]. Hill AB, Bowley CJ, Nahrwold ML, Knight PR, Kirsh MM, Denlinger JK. Intranasal administration of Nitroglycerine. Anaesthesiology 1981; 54: 346-8
[15]. Fassoulaki A, Melemeni A, Paraskeva A, Petropoulos G. Gabapentin attenuates the pressor response to direct laryngoscopy and tracheal intubation. Br J Anaesth 2006; 96: 769-73.
[16]. Memis D, Turan A, Karamanlioğlu B, Seker S, Türe M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol. 2006; 23(8): 686-90.
[17]. Koc S, Memis D, Sut D. The preo-perative use of Gabapentin, Dexamethasone and their combination in varicocele surgery: A Randomized Controlled Trial. Anaesth Analg 2007; 105(4): 1137-42.
[18]. Fink K, Meder W, Dooley DJ, Gothert M. Inhibition of neuronal Ca^{2+} influx by Gabapentin and subsequent reduction of neurotransmitter release from rat neocortical slices. Br. J. Pharmacol. 2000; 130: 900-7.
[19]. Rose MA, Kam A. Gabapentin: Pharmacology and its use in pain management. Anaesthesia, 2002; 57: 451-12.
[20]. Burstein CL, Woloshin G, Newman W. Electrocardiographic studies during endotracheal intubation: Effect during anaesthesia and intravenous Procaine. Anaesthesiology 1950; 11: 299-14
[21]. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: Influence of duration of laryngoscopy with or without prior Lidocaine. Anaesthesiology 1977; 47: 381-8
[22]. Kong VKF, Irvin. Gabapentin: A Multimodal perioperative drug? Br J Anaesth 2007; 99: 775-86
[23]. Prys-Roberts C, Greene LT, Melcohe R. Study of anaesthesia in realtion to hypertension. II Heamodynamic consequences of induction and endotarcheal intubation. Br J Anaesth. 1971; 40: 531
[24]. Dirks J, Fredensborg BB, Christensen D, Fomsgaard JS, Flyger H, Dahl JB**.** A randomized study of the effects of single-dose Gabapentin versus placebo on postoperative pain and Morphine consumption after mastectomy. Anaesthesiology 2002; 97: 560-4.

Dr Sumeet chugh ." To Evaluate the Effect of Pre-Operative Oral Gabapentin on Cardiovascular Response to Laryngoscopy and Tracheal Intubation."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 5, 2018, pp 09-14.