Research Article

Effect of Gabapentin on Pressor Response to Laryngoscopy and Tracheal Intubation: A Double Blind Randomized Placebo Controlled Study

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Abstract:

The effects of gabapentin on arterial pressure and heart rate were compared at induction of anaesthesia and at tracheal intubation in a prospective randomized double blind study. Fourty patients of American society of Anaesthesiologists (ASA) physical status I undergoing elective surgery were divided in two groups of twenty each. Twenty patients received oral placebo (Group P), and 20 patients received 900 mg of gabapentin (Group G), 2 hours prior to induction of anaesthesia. Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Heart rate (HR) were recorded one minute before and after induction of anaesthesia, immediately after intubation and 1,3,5 and 10minutes after intubation. Changes in SBP were statistically insignificant in both the groups. In the gabapentin group, at 0 and 5 minutes, the DBP was significantly less than the placebo group ($p<0.05$). There was a significant decrease in heart rate in Group G as compared to Group P ($p<0.05$).Pre medication with 900 mg gabapentin, 2 hours before induction of anaesthesia attenuates the tachycardia associated with laryngoscopy and intubation but not the pressor response completely.

Key Words: Gabapentin, Laryngoscopy, Intubation, Haemodynamic responses

Introduction:

Tracheal intubation provokes a marked sympathetic response manifested as tachycardia and hypertension, which is potentially deleterious in some patients. Apart from hypertension and tachycardia, dysrhythmias and myocardial ischemia can occur (Brandt, 1996). The mechanism for these reflex cardiovascular changes is unknown, but the drop may be a result of reflex sympathetic action perhaps involving the baroreceptor system provoked by stimulation of the epipharynx and laryngopharynx.

Several techniques have been proposed to prevent or attenuate the haemodynamic responses following laryngoscopy and intubation, such as deepening of anaesthesia, omitting cholinergic premedication, pre-treatment with vasodilators such as nitroglycerine (Mikawa et al, 1992), beta blockers (Coleman et al, 1980), calcium channel blockers (Puri & Batra, 1988; Nishikawa & Namiki, 1989) and opioids (Maguire et al, 2001; Dahlgren & Messeter, 1981).

Recently gabapentin has been used in randomised controlled trials to treat acute postoperative pain and to reduce postoperative opioid requirements (Fassoulaki et al, 2006 ; Thomson et al, 1989). In these studies with gabapentin, it was noticed that patients remained haemodynamically stable. Thus, we found it worthy of evaluation as to whether gabapentin has an effect on changes in blood pressure and heart rate during laryngoscopy and tracheal intubation or not.

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Material and Methods:

This prospective, randomized, double blind and placebo controlled study was performed on forty patients undergoing elective surgery under general anaesthesia. Patients with ASA grade I in the age group of sixteen to sixty years were included in the study. Patients were divided into groups of 20 each. Group P received oral placebo in the form of 3 sugar filled in emptied gapapentien capsule two hours before the surgery and Group G received three gabapentin capsules (300 mg each) were 2 hours before Surgery. Patients were familiarized with verbal rating scale (VRS) for sedation. Ranitidine 150mg was given the night before surgery at 10 pm to all patients.

Exclusion criteria were: anticipated difficult intubation, ASA physical status II or above, history suggestive of hiatus hernia and gastroesophageal reflux, patients with body weight >20% of ideal body weight, consumption of anti hypertensive, sedatives, hypnotics and antidepressant drugs; patients with nervous system disorders and history of drug hypersensitivity.

Informed consent was taken from all patients after approval from ethical committee.

Anaesthetic Technique:

In the operation theatre, intravenous ringer lactate solution was started. All patients received intravenous ondansetron 0.1mg/kg and tramadol 2.0 mg/kg 10 minutes before induction of anaesthesia. Standard monitors were attached like heart rate, blood pressure, ECG and pulse oximeter.

After tracheal intubation, end tidal carbon dioxide monitoring was initiated, paracetamol infusion was given over 15 minutes with 15 mg/kg body weight and injection diclofenac sodium aquous was given intravenously with a dose of 1 mg/kg body weight. All patients were preoxygenated for 3minutes. Anaesthesia was induced with oxygen, nitrous oxide, and propofol 2mg/kg of body weight. Vecuronium 0.1mg/kg was used to facilitate tracheal intubation. All intubations were performed by experienced anaesthesiologist. The duration of laryangoscopy and intubation was limited to the minimum possible time of 30 seconds and was done in a single attempt. Anaesthesia was maintained with nitrous oxide 66%, oxygen 33%, halothane 0.5% and vecuronium.

Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were recorded one minute before and after administration of the intravenous anaesthetic agent. The next reading was taken immediately after intubation and cuff inflation and was labelled as the 0 reading. Subsequent readings were taken at 1,3,5 and 10 minutes. Continuous intra operative monitoring of heart rate and blood pressure was done at every 5 minutes. Neuromuscular block was reversed with neostigmine 0.05mg/kg and atropine 0.02mg/kg intravenously. After tracheal extubation and on awakening from anaesthesia, patients were assessed for postoperative sedation using an 11 point VRS (with 0= no sleepiness to 10= almost asleep) at 0, 1, 6, 11 and 24 hours.

Statistical Analysis:

Data was analyzed on computer software. Characteristics of the patients of the two groups and changes in SBP, DBP and HR between the two groups were compared with independent *t*- tests. The sedation score was compared using the mann witney (non parametric) test. Somnolence and dizziness amongst the patients in the two groups were analyzed using the *chi-square* test.

Results:

It was found that the two study groups were comparable with respect to age, sex, height, weight and duration of surgery (Table I). The mean age was 42.55 yrs in the gabapentin group (group G) while it was 42.7 yrs in the placebo group (group P). Similarly, the mean height was 149cms in the group G and 150.2cms in group P. The mean weight also did not differ much; 54.75kg v/s 52.35kg. The duration of anaesthesia was 123.5mins in group G and 128 mins in Group P.

The baseline values of SBP were comparable (127.70mmHgvs 126.80mmHg) in both the groups (Table II). After adiministering propofol, there was a fall in SBP followed by a rise after laryngoscopy and intubation in both the groups . The trend of fall towards the base line values was similar in both the groups at 0,1,3,5 and 10 mins after intubation.

The sedation scores in the present study were significantly higher in the group G at 0 and 1 hour in the postoperative period (Table V).

Table I: Patient characteristics in each group.

	N	Group	Mean± S.D.	*p*-value
Age (yrs)	20	G	42.55±7.38	0.993
		P	42.7±8.48	
Height (cms)	20	G	149.0±3.35	0.35
		P	150.2±4.36	
Weight (kg)	20	G	54.75±8.94	0.37
		p	52.35±7.74	
Duration (mins)	20	G	123.5±16.14	0.32
		P	128±10.43	

Discussion:

Tracheal intubation is a noxious stimulus, tending to provoke a marked sympathetic response manifested as tachycardia and hypertension which is potentially deleterious in some patients. Various agents effectively attenuate this response, including anaesthetics, analgesics, adrenergic blocking agents and vasodilators. This has been a fertile area for clinical investigation, spawning numerous studies of the various techniques which might be expected to modify the haemodynamic response to intubation. Some patients unquestionably require careful haemodynamic control during induction of anaesthesia and intubation. Even a transient hyperdynamic response may cause serious complication in patients with symptomatic aortic aneurysm, recent myocardial infarction, cerebral

Table II: SBP before and after intravenus (i.v.) induction agent and at 0,1,3,5, and 10 mins after tracheal intubation and Cuff inflation in the gabapentin and placebo group.

Group		Before i.v.	After i.v.	0 min	1 min	3 min	5 min	10 min
G	Mean	127.70	117.8	128.7	119.2	112.7	107.6	104.0
n=20	± SD	10.67	10.86	11.116	10.462	11.526	10.515	11.079
P	Mean	126.80	114.65	138.65	124.25	114.85	109.25	105.90
n=20	± SD	11.423	11.735	20.630	18.157	12.704	11.026	10.422
t-value		0.25	0.88	1.89	1.065	0.548	0.471	0.561
p-value		0.798	0.384	0.67	0.293	0.578	0.641	0.580

Table III: DBP before and after intravenus (i.v.) induction agent and at 0 , 1, 3, 5 and 10 min after tracheal intubation.

Group		Before i.v.	After i.v.	0 min	1 min	3 min	5 min	10 min
G	Mean	81.00	74.90	85.45	78.32	73.05	68.21	67.21
n=20	±SD	7.248	7.174	11.190	11.480	9.554	8.237	7.729
P	Mean	85.25	77.70	94.50	83.75	77.40	75.05	72.90
n=20	±SD	7.853	8.355	14.562	13.490	12.927	11.954	10.427
t-value		1.791	1.146	2.216	1.376	1.228	2.104	1.97
p-value		0.083	0.263	0.034*	0.185	0.242	0.045*	0.062

Table IV: HR before and after intravenus (i.v.) induction agent and at 0,1,3,5,10 mins after tracheal intubation and Cuff inflation in the gabapentin and the placebo group.

Group		Before i.v.	After i.v.	0 min	1 min	3 min	5 min	10 min
G	Mean	89.70	83.00	97.05	92.50	87.90	82.35	77.50
n=20	±SD	13.800	12.465	17.191	14.490	13.676	12.067	8.382
P	Mean	94.55	89.40	110.85	104.90	99.10	92.85	84.45
n=20	±SD	16.491	12.882	14.317	13.058	12.649	13.136	11.732
t-value		1.012	1.606	2.608	2.858	2.702	2.64	2.151
p-value		0.32	0.119	0.009*	0.007*	0.011*	0.012*	0.038*

Table V: Sedation scores in the post operative period at 0,1,6,11,24 hours after surgery.

Group		0 Hr	1 Hrs	6 Hrs	11 Hrs	24 Hrs
G	Mean	3.20	2.80	1.40	1.00	1.00
n=20	± SD	1.005	1.005	.821	0.000	.000
P	Mean	1.85	1.35	1.05	1.05	1.00
n=20	± SD	.336	.489	.224	.224	.000
t-value		5.99	6.22	2.169		
p-value		<0.0001**	<0.0001**	0.074	0.317	1.000

*Significant (p<0.05), ** Highly Significant (p<0.0001)

Table VI: Occurrence of dizziness at 0,1,6,11 and 24 hours after surgery.

Group		0 Hrs	1 Hrs	6 Hrs	11 Hrs	24 Hrs
G	Present	19	19	0	0	0
n = 20	Absent	1	1	20	20	20
P	Present	9	5	0	0	0
n = 20	Absent	11	15	20	20	20
χ^2-value		11.90	20.417			
p-value		0.001*	<0.0001**	----	----	----

*Significant ($p<0.05$), ** Highly Significant ($p<0.0001$)

aneurysm, or intracranial hypertension.

Known or suspected ischaemic heart disease is by far the most common indication for modifying the haemodynamic response to intubation. The value of haemodynamic control in these patients is somewhat controversial. Myocardial ischaemia is a frequent consequence of induction and intubation especially if tachycardia occurs.

Perioperative myocardial ischaemia has been associated with postoperative myocardial infarction, and a causal relationship has been postulated (Mikawa et al, 1992; Fassoulaki & Kaniaris, 1983). Therefore, elimination of ischaemia at the time of intubation might prevent infarction. Modification of the haemodynamic response to intubaton is a laudable objective and is clearly indicated in a small subgroup of patients in whom a single hyperdyanamic episode may cause a catastrophe.

A variety of drugs have been used to control this haemodynamic response (Memis et al, 2006). Recently, gabapentin was found to be effective in attenuating the pressor response to tracheal intubation in various studies. Memis et al (2006), noticed that 800 mg of gabapentin, administered orally 1 hour before the surgery, was found to be effective in reducing the noxious stimuli to larangoscopy and intubation, thereby attenuating the hemodynamic response. Misra et al (2011), demonstrated that 900 mg of gabapentin administered orally 2 hours before induction of anaesthesia, abolished the hemodynamic response after skull pin insertion. With this background, in this study, 900 mg of gabapentin was given two hours before intubation and results were analyzed.

In the study canducted by Memis et al (2006), patient receiving 400 mg of gabapentine 1 hour prior to surgery in the operation theatre showed significant increase in blood pressure associated with tracheal intubation compared to baseline level. In comparison, there was a significant decrease in heart rate and arterial pressure after intubation at 1,3,5 and 10 minutes in patients who received 800 mg gabapentin oral and 8mg dexamethasone intravenous one hour before surgery, than in patients who received 800 mg gabapentin alone preoperatively (Kovac, 1996). In a similar study by Koc et al (2007) it was seen that haemodynamics at 1,3,5 and 10min after tracheal intubation were found to be significantly lower in patient receiving a combination of 800mg gabapentin oral and 8mg dexamethasone intravenus one hour before surgery, than in patient who received either gabapentin 800 mg or dexamethasone 8mg alone.

In the present study, the comparison of DBP readings in both the groups revealed similar finding (Table III). The baseline values were similar in both the groups i.e 81mmHg in group G and 85.25mmHg in group P. There was a precipitous fall after administration of IV induction agent. Laryngoscopy led to an increase in DBP followed by a consistent decrease towards the baseline values over the next 10 mins. Inter group comparison was significant only at 0 and 5 mins. However, in the study of Fassoulaki et al (2006), patients in the group G showed lower DBP values at 0,1,3, 5 and 10 minutes.

The baseline heart rate was again comparable in both the groups in the present study (Table IV). The same was true for the readings after administration of intravenous induction agent. There was an apparent increase in heart rate in both the groups after laryngoscopy and intubation but the increase was significantly less in group G at all times. These findings are markedly different to those of Fassoulaki et al (2006), where there was an increase in heart rate in both the groups after laryngoscopy and intubation.

Memis et al (2006), observed a significant decrease in heart rate in patients who received 800 mg of gabapentin one hour preoperatively. Patients receiving placebo and 400 mg gabapentin showed a significant increase in heart rate associated with tracheal intubation compared to baseline levels than the patients who received 800 mg gabapentin. They concluded that gabapentin 800 mg given one hour before the operation blunted the arterial pressure and heart rate increase in first 10 minutes due to endotracheal intubation. Koc et al (2007)observed that the heart rate at 1, 3, 5, and 10 minutes after tracheal intubation was significantly lower in patients receiving a combination of gabapentin 800 mg orally and dexamethasone 8 mg intravenous, given one hour before the surgery than in patients who received either drug alone.

Dizziness was experienced by a large number of patients in group G but these effects were seen only till 2 hours after surgery as later the affect of gabapentin wore off. Gabapentin has been shown to be well tolerated and effective in the management of the pain associated with post herpetic neuralgia (Parsons et al, 2004). It is assumed that adverse events occurring with gabapentin are dose related. Parsons et al (2004) observed that the three most common adverse events were dizziness, somnolence and peripheral edema. In the present study peripheral edema was not observed in any patient.

Overall, it appears that pre-operative gabapentin blunts the heamodynamic response to intubation. Single and multiple doses have comparable haemodynamic effects. Arterial pressure and heart rate responses have been shown to be greater when the duration of laryngoscopy exceeds 30 second. The mechanism of gabapentin in controlling this haemodynamic response remains unknown. Since gabapentin inhibits membrane VGCCs (Voltage gated calcium channels) it is possible that it may have a similar action to calcium channel blockers (Sarantopoulos et al, 2002). Oral administration of gabapentin 900mg, two hours prior to induction of anaesthesia, is a simple and practical method for attenuating pressure response to laryngoscopy and tracheal intubation after standard elective induction.

Conclusion:

Pre-treatment with gabapentin 900 mg two hours before the induction of anaesthesia effectively attenuates the tachycardia associated with laryngoscopy and intubation but not the pressor response completely.

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