Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2016/393

Original Article

Comparison of Oral Metoprolol and Oral Pregabalin for Suppression of Hemodynamic Responses to Laryngoscopy and Tracheal Intubation

Valli Sathyamoorthy[1], Nandhini Kumar[2], Bhavani Muthukrishnan[3], J Mohamed Ali[4]

[1]Professor, Department of Anaesthesiology, Government Kilpauk Medical College, Chennai, Tamil Nadu, India, [2]Senior Resident, Department of Anaesthesiology, Government Kilpauk Medical College, Chennai, Tamil Nadu, India, [3]Assistant Professor, Department of Anaesthesiology, Government Kilpauk Medical College, Chennai, Tamil Nadu, India, [4]Research Associate, Department of Clinical Research, Dr. Agarwal's Health Care Limited, Tirunelveli, Tamil Nadu, India

Abstract

Background: Hemodynamic responses of laryngoscopy, intubation, and pain are powerful noxious stimulus which should be attenuated by the appropriate premedication, smooth induction, and rapid intubation. Laryngoscopy and tracheal intubation are such a noxious stimuli causing intense sympathetic hemodynamic response.

Aim: The aim of this study to know about the efficacy of oral metoprolol and oral pregabalin in decreasing this stress response.

Methods: Prospective, randomized, double-blinded, placebo controlled study in which adult the American Society of Anesthesiology I and II patients undergoing elective surgery of both the sexes were divided into three groups. Group A received metoprolol 100 mg, Group B received oral pregabalin 150 mg, and Group C received placebo orally. Baseline heart rate (HR), systolic, diastolic blood pressure (BP), and mean arterial pressure and before induction, after induction, at the time of laryngoscopy and at the end of 0, 1, 3, 5 and 10 min were recorded.

Results: When compared to metoprolol and pregabalin, there was a significant increase in HR and BP in the control group after laryngoscopy and tracheal intubation.

Conclusion: Metoprolol is found to be better than pregabalin in blunting the cardiovascular stress response to laryngoscopy and intubation.

Key words: Hemodynamic response, Laryngoscopy, Metoprolol, Pregabalin, Tracheal intubation

INTRODUCTION

Laryngoscopy and tracheal intubation are essential in providing general anesthesia, but produce sympathetic over drive by catecholamine release resulting in hypertension and tachycardia.[1] This is usually tolerated by healthy individuals, but susceptible patients are likely to overreact to the hemodynamic fluctuations.[2] Left ventricular compromise, myocardial ischemia, and cerebral hemorrhage can be precipitated by this sudden rise in blood pressure (BP). Numerous attempts have been done previously and are continuing to find out the suitable drug or technique to attenuate this intubation response. This involves the use of opioids, volatile agents, lignocaine, beta blockers, vasodilators, and calcium channel blockers. Since none of these drugs prove to be the best choice for attenuating the pressor response, the quest continues. The most commonly used drugs are benzodiazepines and opioids. The effects like variability in patients response, respiratory complications and post-operative nausea and vomiting, delay in recovery of bowel function with benzodiazepines and opioids. It creates the need to find a much more suitable drug with limited side effects. Recently, an increasing emphasis has been made on the use of non-opioid drugs as a part of multimodal regimen for decreasing anxiety and the intubation response. Many recent studies show that drugs such as gabapentin and pregabalin are known to decrease

Access this article online

www.ijss-sn.com

Month of Submission : 05-2016
Month of Peer Review : 06-2016
Month of Acceptance : 07-2016
Month of Publishing : 07-2016

Corresponding Author: Dr. Valli Sathyamoorthy, Professor of Anaesthesiology, Government Kilpauk Medical College, Kilpauk, Chennai -10, Tamil Nadu, India. Phone: 9840182189, E-mail: valli_sathy@yahoo.com

stress response due to laryngoscopy and intubation. Only minimal evidence is available in our literature related to the cardiovascular properties of pregabalin in patients undergoing surgery.[3,4]

Aim

Laryngoscopy and tracheal intubation are such a noxious stimuli causing intense sympathetic hemodynamic response. This study aims to know about the efficacy of oral metoprolol and oral pregabalin in decreasing this stress response.

METHODS

Prospective, randomized, double-blind, placebo-controlled study was conducted in the Department of Anesthesiology, Government Kilpauk Medical College Hospital, and Government Royapettah Hospital. 90 normotensive patients of both sexes in the American Society of Anesthesiology I and II physical status, between the age group of 18 and 45 years, who were posted for elective surgery under general anesthesia, were included in this study. Institutional Ethical Committee approval and written informed consent were obtained. They were divided into three groups: Group A - metoprolol group, Group B - pregabalin group, and Group C - placebo group. Exclusion criteria are patient refusal, Mallampati score >3, those with morbid obesity, end stage liver/renal disease, asthma, chronic obstructive pulmonary disease, hypertension, diabetes mellitus, and epilepsy. The two drugs were compared in terms of their effects on heart rate (HR), systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP). All patients were assessed preoperatively by history, physical examination, routine laboratory tests, chest X-ray, and electrocardiogram. A pre-operative visit was made to allay the anxiety and to develop a good rapport. The patients were instructed to fast overnight and aspiration prophylaxis was advised. On the day of surgery, the patients were examined in the waiting room and the pulse rate, SBP, DBP, and MAP were recorded as the baseline value. An 18-gauge intravenous (IV) cannula was placed and the crystalloid infusion was started. All patients were premedicated with injection ranitidine 150 mg and injection ondansetron 4 mg IV Half an hour later patients were given injection glycopyrrolate 0.005 mg/kg IV, injection midazolam 0.05 mg/kg IV. On arrival in the operating room, the vitals parameters were monitored. All patients received fentanyl 0.02 mg/kg IV in the operating room. Then, induced with injection propofol 2 mg/kg IV and injection vecuronium 0.1 mg/kg was given to achieve muscle relaxation. Controlled positive pressure ventilation was done with 100% oxygen using bag and mask. A direct laryngoscopy was done 3 min after the injection of the muscle relaxant and the patients were intubated with appropriate size cuffed oral endotracheal tube. The patients who strained on laryngoscopy, duration of laryngoscopy took more than 15 s, when the second attempt was required and patients in whom the surgical procedure lasted for more than 3 h were excluded from the study. HR and BP (systolic, diastolic, MAP) were recorded at the 1st, 2nd, 3rd, 5th, and 10th min following intubation and were recorded as T0, T1, T3, T5, and T10, respectively. All patients were ventilated using oxygen and nitrous oxide mixture in the ratio of 40:60%. Muscle relaxation was maintained with additional doses of injection vecuronium 0.02 mg/kg. At the end of surgery, neuromuscular paralysis was reversed with injection neostigmine 0.04 mg/kg IV and injection glycopyrrolate 0.01 mg/kg IV. Patients were extubated after thorough oral suctioning. The patients were then shifted to the post-operative ward and observed for up to 24 h.

Statistical Methods

Descriptive and inferential statistical analysis have been performed in this study. Results on continuous measurements are presented on mean ± standard deviation (min-max) and results on categorical measurements are presented in number (%). The significance is assessed at 5% level of significance. Analysis of variance has been used to find the significance of study parameters between three groups of patients. Chi-square/Fisher's exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Statistical software: SPSS.

RESULTS

A total of 90 patients were inducted into the study. In this study, there is no rise in HR and BP with a single dose of 100 mg metoprolol (in Group A) for the expected hemodynamic response to laryngoscopy and intubation and the HR and MAP (T0, T1, T3, T5, T10) are all below the baseline values. In Group B, with single dose of 150 mg pregabalin, the rise in HR, and MAP are not significant and reached the baseline within 10 min of intubation. Thus, it indicates that both the drugs were effective in blunting the pressor response to laryngoscopy and intubation when compared with the control group where there is highly significant rise in HR, BP, and MAP which are well above the baseline parameters until 10th min after intubation.

At the time of induction and at each minute of monitoring, HR in Group A is less than that of Group B which is less than that of Group C. At 5th min, HR in Group A and B are below baseline, but there is a significant rise in Group C (Table 1).

At the time of induction, Group A has less MAP than Groups B and C. At each minute of monitoring, mean

arterial pressure maintained below baseline in Group A, whereas in Group B there is a rise from baseline but it's insignificant. In Group C, there is a significant rise from baseline values (Table 2).

DISCUSSION

Although the patients are well anesthetized before performing laryngoscopy and tracheal intubation, reflex cardiovascular response to this noxious stimuli arises as described by Reid and Brace.[1] Orotracheal intubation with the use of laryngoscope normally needs elevation of epiglottis, thereby exposing the glottic opening. This maneuver causes sympathetic activation leading to tachycardia and hypertension. The increase in pulse pressure of around 10 mmHg is associated with 20% or more risk of any events occurring in the renal, cardiovascular, and central nervous systems in both hypertensive and normotensive individuals.[2] Many anesthetic techniques and different drugs such as opioids (fentanyl, remifentanil,[3] alfentanil), beta blockers (esmolol, labetalol, metoprolol, earlier bunitrolol, propranolol), calcium channel blockers (verapamil, diltiazem, nicardipine), vasodilators (nitroglycerin, sodium nitroprusside), IV lignocaine, and newer drugs like gabapentin,[6] pregabalin with various doses were tried to blunt this reflex pressor response, but none proved to attenuate this reflex fully. Many drugs used in the past to reduce this response is associated with some adverse effects.

Table 1: HR response

HR	Group A	Group B	Group C	*P* value
Pre-operative	79.9±4.84	88.7±11.4	84.8±11.5	0.004*
Pre-induction	79.9±4.84	88.7±11.4	84.8±11.5	0.004*
T0 (scopy)	80.5±8.05	98.16±9.80	106.4±14.4	<0.0001**
T1	83.4±6.6	100.6±10.25	109.7±10.77	<0.0001**
T3	80.1±5.82	96.46±11.5	104.66±11.49	<0.0001**
T5	76.0±6.65	88.1±8.57	96.2±9.15	<0.0001**
T10	73.86±5.90	84.8±7.04	86.6±10.47	<0.0001**

Data were expressed as mean±SD. *Means there was a significant difference in HR between the three groups (P<0.05). **Means there was a highly significant difference in HR between three groups (P<0.01). HR: Heart rate, SD: Standard deviation

Table 2: MAP

MAP	Group A	Group B	Group C	*P* value
Pre-operative	94.2±4.69	94.46±10.8	87±6.81	<0.0001**
Pre-induction	82.6±8.73	83.3±6.30	92.7±7.00	0.000**
T0 (scopy)	83.7±10.5	91.4±14.74	93.8±17.56	0.024*
T1	84.6±9.7	95.1±10.10	113.2±10.98	<0.0001**
T3	81.7±9.65	87.1±9.27	104.06±11.31	<0.0001**
T5	82.9±8.3	85.3±8.76	93.5±12.8	<0.0001**
T10	82.4±6.28	87.7±8.12	88.4±7.74	0.004*

Data were expressed as mean±SD. *Means there was a significant difference in HR between the three groups (P<0.05). **Means there was a highly significant difference in HR between three groups (P<0.01). MAP: Mean arterial pressure, SD: Standard deviation, HR: Heart rate

Jakobsen *et al.* used 100 mg metoprolol for hysterectomy under general anesthesia and found it to be useful in reducing the cardiovascular stress response. Poupak rahimzadeh and coworkers used metoprolol specifically in nasal surgeries and found it to be effective not only in blunting the laryngoscopic and intubation response but also less bleeding and clear field for the surgeon to operate due to hypotension caused by metoprolol. They concluded that repetitive doses or large doses are needed to do such effect. Recently, gabapentin and pregabalin are being used along with preedicant drugs to blunt the cardiovascular stress response occuring to laryngoscopy and tracheal intubation but with different doses and conflicting results.[5-7] Bockrader *et al.* did a comparison of the pharmacokinetics and pharmacodynamics of gabapentin and pregabalin. They found pregabalin to be distinct with better pharmacodynamics. In another study by Bashyam *et al.* between 600 mg of gabapentin with 150 mg of pregabalin, it has been found pregabalin to be better than gabapentin in maintaining the hemodynamics, sedation and anxiolysis without significant adverse effects. Hence, we took pregabalin 150 mg as another drug and compared its effect in blunting the response to laryngoscopy and intubation metoprolol 100 mg. In our study, there was a significant rise in HR and BP following laryngoscopy and intubation in the Group C. This is consistent with the study done by Mullet *et al.* In our study, we found there is no rise in HR and BP with a single dose of 100 mg metoprolol (in Group A) for the expected hypertensive and tachycardic response to laryngoscopy and intubation and the HR and MAP are all below the baseline values. This is consistent with the study done by Saarnivaara *et al.* In Group B, with single dose of 150 mg pregabalin, the rise in HR and MAP is not significant and reached the baseline within 10 min of intubation. This result is consistent with the study done by Talikoti *et al.* Similarly, Rastogi *et al.* used two different doses of pregabalin to find out the clinically effective and safe dose during airway manipulation. The response is found to be dose-dependent and 150 mg pregabalin reduced the stress response significantly and maintained stable hemodynamics intraoperatively without any prolongation in the recovery time. The mechanism by how pregabalin blunts the cardiovascular effects to laryngoscopy and intubation is not clear till now but it has been postulated to be due to its action against nociceptive receptors. This mechanism most likely modifies the calcium current selectively by binding to the voltage-gated Ca^{2+} channels and act in the same way as calcium channel blockers in maintaining the cardiovascular hemodynamics. As beta blockers are known to reduce HR and BP even in the intraoperative period also, there is no occurrence of bradycardia or hypotension which necessitates treatment. Though pregabalin is known to have sedative effect,[3] there is no significant drowsiness in

patients who were given pregabalin. This is consistent with the study done by Gupta *et al.*

CONCLUSION

With this study, both metoprolol and pregabalin are found to be effective in attenuating the cardiovascular response to laryngoscopy and intubation when compared with the control group. The blunting of HR response is less with pregabalin than with metoprolol. Hence, we conclude that metoprolol is found to be better than pregabalin in blunting the cardiovascular stress to laryngoscopy and intubation.

REFERENCES

1. Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect upon heart. Surg Gynaec Obst 1940;70:157-62.
2. Gupta K, Sharma D, Gupta PK. Oral premedication with pregabalin or clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy: A comparative evaluation. Saudi J Anaesth 2011;5:179-84.
3. White PF, Tufanogullari B, Taylor J, Klein K. The effect of pregabalin on preoperative anxiety and sedation levels: A dose-ranging study. Anesth Analg 2009;108:1140-5.
4. Sundar AS, Kodali R, Sulaiman S, Ravullapalli H, Karthekeyan R, et al. The effects of preemptive pregabalin on attenuation of stress response to endotracheal intubation and opioid- sparing effect in patients undergoing off-pump coronary artery bypass grafting. Ann Car Anaesth 2012;15:18-25.
5. O'Hare R, McAtamney D, Mirakhur RK, Hughes D, Carabine U. Bolus dose remifentanil for control of haemodynamic response to tracheal intubation during rapid sequence induction of anaesthesia. Br J Anaesth 1999;82:283-5.
6. 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.
7. Rastogi B, Gupta K, Gupta PK, Agarwal S, Jain M, Chauhan H. Oral pregabalin premedication for attenuation of haemodynamic pressor response of airway instrumentation during general anaesthesia: A dose response study. Indian J Anaesth 2012;56:49-54.

How to cite this article: Sathyamoorthy V, Kumar N, Muthukrishnan B, Ali JM. Comparison of Oral Metoprolol and Oral Pregabalin for Suppression of Hemodynamic Responses to Laryngoscopy and Tracheal Intubation. Int J Sci Stud 2016;4(4):143-146.

Source of Support: Nil, **Conflict of Interest:** None declared.