Volume-4, Issue-12, Dec-2015 • ISSN No 2277 - 8160

Research Paper medical sciences

Effect of Oral Pregabalin As Adjuvant to Standard Premedication for Attenuation of Hemodynamic Responses in Laparoscopic Surgeries.

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ABSTRACT

Hemodynamic pressor response to the airway instrumentation and surgical stimulation is a hazardous complication of General Anaesthesia.. The aim of present study is to evaluate efficacy of oral pregabalin 150 mg as adjuvant to standard premedication for attenuation of haemodynamic responses to surgical stimulation and compare it with placebo for patients undergoing laparascopic surgeries.A total of 50 adult consented patients aged 18–65 years, ASA grade I and II, of both gender were randomized into two treatment groups of 25 patients each. Group I received ora pregabalin 150 mg and Group II oral placebo 1 h prior to induction. Anaesthetic technique was standardized and all groups were assessed for pre-operative sedation, haemodynamic changes after the premedication, after laryngoscopy and intubation, along with intraoperative haemodynamic stability and post-operative analgesia and side-effects.Pre-operative sedation levels were higher with pregabalin premedication.Statistically significant attenuation of heart rate and mean arterial pressure was seen in Group I while significant increase in heart rate and mean arterial pressure was observed in Group II after airway instrumentation and also intraoperatively and post operatively. Oral pregabalin 150 mg premedication has adequately sedated the patients with effective attenuation of haemodynamic pressor response of airway instrumentation. The premedicated patients were haemodynamically stable perioperatively without prolongation of recovery time and notable side-effects

KEYWORDS : Haemodynamic pressor response, intubation, laryngoscopy, pregabalin, sedation

INTRODUCTION

Hemodynamic pressor response to the airway instrumentation and surgical stimulation is a hazardous complication of General Anaesthesia.[1]Laryngoscopy and intubation are associated with cardiovascular changes such as hypertension, tachycardia, dysrhythmias, myocardial ischaemia and increased circulating catecholamines. Several techniques have been proposed to prevent or attenuate the haemodynamic responses following laryngoscopy and intubation, such as pretreatment with vasodilators such as nitroglycerin,beta-blockers, calcium channel blockers, opioids and alpha 2 agonists.[2] Studies have reported usefulness of pregabalin as a premedicant to attenuate the hemodynamic responses to laryngoscopy and intubation.[3,4]

Pregabalin is a structural analogue of gamma amino butyric acid,which shares some characterstics with its predecessor,gabapentin.It's mechanism of action is probably the same as gabapentin but it has a superior pharmacokinetic profile. Pregabalin is a potent ligand for the alpha-2-delta subunit of voltage-gated calcium channels in the central nervous system that exhibits potent anticonvulsant, analgesic and anxiolytic activity and for amelioration of perioperative anxiety.[7]

The aim of present study is to evaluate efficacy of oral pregabalin 150 mg as adjuvant to standard premedication for attenuation of haemodynamic responses to surgical stimulation and post-operative analgesia and compare it with placebo for patients undergoing laparascopic surgeries.

MATERIAL AND METHODS

After approval by institutional ethics committee, informed written consent for anesthesia was taken. '50' patients with ASA grade I or II in age group (18yr-65yr) were enrolled for the study

Group I (Study Grp.) :25 patients will receive Tab. Pregabalin 150mg 1 hour prior to induction of anaesthesia in preoperative room.
Group II(Control Grp.) :25 Patients will receive placebo 1 hour prior to induction of anaesthesia in preoperative room.

INCLUSION CRITERIA:Age between 18-65years.ASA physical status classI-II.Presenting for elective laparoscopic surgeries requiring general anaesthesia.

EXCLUSION CRITERIA:Patient's refusal.ASA physical status class III or more. Allergy to the drugs to be used.Difficult airway.Patients on medication with sedatives, hypnotics, antidepressants or drugs effecting central nervous system.

Methodology

The patients were explained and written, informed, valid consent was taken.The patients were randomly divided into groups as designated above and demographic data were noted.The drug for ingestion was selected by an independent anaesthetist.Baseline vital parameters were noted.Tab.pregabalin/placebo was given 1 hr prior to surgery in preoperative room and monitored for vital parameters.On arrival to the operation theatre, an 18G intravenous cannula was placed, on the dorsum of the hand and Ringer's lactate infusion was started.Monitors were attached and baseline of heart rate and systolic ,diastolic and mean arterial blood pressure were recorded. Anesthesia, surgical techniques and intraoperative analgesia was standardized for all patients. All patients were premedicated with inj. glycopyrolate (0.004mg/kg),inj.midazolam (0.02mg/kg) and inj.pentezocine 0.6mg/kg.Anaesthesia was induced with inj.thiopentone sodium(5mg/kg). Direct laryngoscopy and intubation was facilitated with inj.succinylcholine(2mg/kg).Anaesthesia was maintained with nitrous oxide (60%) in oxygen and halothane.The supplemental neuromuscular blockade was achieved by inj.vecuronium (0.08mg/kg). After completion of surgery residual Neuromuscular blockade was antagonized with appropriate doses of inj.neostigmine(0.05mg/kg) and inj.glycopyrolate(0.008mg/kg).Heart rate, mean arterial BP, ECG,oxygen saturation were monitored and recorded before and after induction, immediately after intubation and 1,3,5,10,15,20 and 30 minutes and every 10 mins thereafter till end of surgery. Patients were observed for complications like hypertension, tachycardia, arrhythmias, hypoxemia, bronchospasm and post operative respiratory depression.The patients were transferred to post anesthesia care unit and pain will be monitored by visual analogue scale immediately postoperatively and every hourly till 12 hours post-operatively.The following parameters were monitored.Pre induction sedation score was assessed by using Ramsey sedation scale.

Haemodynamic parameters.Blood pressure and heart rate were monitored just before induction , at induction, and at 1,3,5,10, 15,20,25,30 mins and at the interval of 10mins thereafter till end of surgery.Post operatively patients were monitored every hourly till 12 hrs after the surgery. Complications (if any)- were noted and treated accordingly.

RESULTS

Of the total of 50 patients, 25 patients in each group were evaluated and compared. All the two groups were comparable with respect to the demographic and surgical factors. No significant differences were found among them with respect to age, sex, gender, ASA, weight, time between oral premedication of pregabalin weight, time between oral premedication of pregabalin administration to anaesthetic induction, type of surgical procedures, and anaesthesia. Sedation was significantly higher in the pregabalin 150 mg group at

the pre-induction stage as compared with the control group.

There was no significant difference in the heart rate and mean arterial pressure values among groups before and after premedication.

However there was a significant difference in spo2 before and after premedication. Clinically significant respiratory depression was not seen in any group of the study preoperatively.. A statistically significant fall in oxygen saturation was seen in the P group preoperatively. The pre-operative lowest recorded SpO2 values was 96% and 98% in the P group. Immediately after laryngoscopy and intubation, the heart rate increased in both groups, but the increase was least in P group (P150).

Maximum increase in heart rate from baseline was observed after 1 min of laryngoscopy, but statistically highly significant increase was observed at 3 min, with significant change seen at 5 min and 10 min. Statistically significant attenuation of heart rate was observed in the premedicated group and it remained stabilized as compared with the control group.

No significant difference was observed in the mean arterial pressure before and after premedication.but, after laryngoscopy and intubation, the attenuation of mean arterial blood pressure in the premedicated group was statistically significant as compared with the control group.Intraoperative heart rate and mean arterial blood pressure values were attenuated and remained stabilized to base values in the premedicated group. Vasoactive medication was not required in any patient. There was no significant differences in SPO2 (table 15)and ETCO2(table 16) intraoperatively with $p>0.05$.

In the postoperative period, significant difference was noted in postoperative PR.(table 10).SBP(table 12).DBP(14).cardiovascular parameters remained at a lower level in the pregabalin group than in the control group. There was a significant difference in the post operative respiratory rate(table 17)($p<0.01$).Postoperatively no Clinically significant respiratory depression was seen in group P. There was no fall in oxygen saturation seen in the post operative period .

Dizziness and somnolence were the only side effects noticed in group P, of whom 2 patients reported to have dizziness and two patients somnolence which was not significant(table 21). No other side effects such as nausea, vomiting, ataxia, vertigo, postoperative respiratory depression were observed in either group.

DISCUSSION

The present study evaluated the safe and clinically effective dose of oral pregabalin premedication for its sedative effect and for attenuation of haemodynamic pressor response of airway instrumentation of direct laryngoscopy and intubation.

The significant attenuation of haemodynamic pressor response was observed by oral pregabalin premedication, with minimum effect on heart rate. The increase in haemodynamic values in the control group may be due to

Fassoulaki et al. Memis et al. have studied the effective attenuation of pressor response of laryngoscopy and intubation after oral premedication of gabapentin[17] .The haemodynamic results of our study were in agreement with recent results with gabapentin. Compared with gabapentin, pregabalin has a predictable and linear pharmacokinetic profile[16]. The haemodynamic pressor response during laryngoscopy and intubation, in the form of tachycardia and hypertension, occurs frequently.

Shribman et al. reported that laryngoscopy alone or with tracheal intubation increases the arterial blood pressure and catecholamine levels, while intubation significantly increases heart rate(18).These physiological changes are due to variation in the balance of sympathetic and parasympathetic outflow or receptor hypersensitivity. Specific measures should be taken to prevent these changes as hypertension may affect perioperative morbidity through the extent of end organ damage, like myocardial ischemia or cerebral haemorrhage.(3)

Many pharmacological techniques were introduced and evaluated either in the premedication or during induction to attenuate the haemodynamic pressor response to airway instrumentation, but results were controversial. More attention is given to the use of selective beta-adrenergic blockers to prevent the reflex sympatho-adrenal discharge-mediated tachycardia and hypertension during laryngoscopy and intubation. Hypotensive agents, including sodium nitroprusside, nitroglycerine, adreno receptor blockers, calcium channel blockers and opioids, have been used effectively to attenuate these haemodynamic responses(2).The intravenous lidocaine (1.5 mg/kg) prevented the increase in mean arterial pressure with no effect on heart rate.(24) Among opioids, remifentanil(1 µg/kg), alfentanil(10–20 µg/kg) or fentanyl (0.5–1 µg/kg) have been used successfully to attenuate haemodynamic pressor response to laryngoscopy and tracheal intubation, but these are associated with bradycardia, hypotension and post-operative respiratory depression(25). Helfman et al.reported that a 150 mg esmolol bolus was superior to intravenous high-dose lidocaine or low-dose fentanyl in preventing the tachycardia associated with intubation(2).

In our study, the 150 mg oral pregabalin has sedated the patients pre-operatively and effectively attenuated the laryngoscopy and intubation-induced haemodynamic pressor response intraoperatively. There was perioperative haemodynamic stability with no post-operative side-effects and respiratory inadequacy. When assessing techniques to lessen the haemodynamic pressor responses of airway instrumentation, the induction Post-operative nausea and vomiting were not recorded in any patient during study.

We studied patients up to 65 years as elderly patients more often take drugs such as antidepressants, hypnotics and antihypertensives with increased sensitivity to anaesthetic medications, and the safety and effectiveness of pregabalin in children and adolescents has not been established.

The attenuation of pressor response of airway instrumentation of direct laryngoscopy and intubation with near-stable haemodynamic variables and no post-operative complication during the present study was an indication of clinically effective and safe sedation with oral pregabalin (150 mg) premedication. We can say that the favourable pharmacokinetics of pregabalin make it a valuable premedicant for attenuation of haemodynamic pressor response of airway instrumentation during general anaesthesia.[22,23].The intraoperative haemodynamic stability may be beneficial in obese, hypertensive and cardiac compromised patients. The pregabalin may be used in asthmatic and airway-compromised patients as it does not cause post-operative respiratory depression.

Somnolence and dizziness are the two most common side effects associated with pregabalin. The incidence reported in present study is similar to earlier studies.(12) This is usually not disabling and provides good antianxiety effect.

Our study shows that pregabalin 150 mg, when given preoperatively is avaluable premedicant for attenuation of haemodynamic pressor response of airway instrumentation during general anaesthesia.

CONCLUSION

Pregabalin is an effective and safe drug as it leads to sedation and haemodynamic stability.A single, oral dose of 150 mg of pregabalin premedication seems to be effective in providing adequate preoperative sedation.It is useful in attenuating the haemodynamic response to orotracheal intubation after the first attempt.Is is useful in maintaining haemodynamic stability, intraoperatively and perioperatively. It has very few side effects.

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