Original Research Article

A comparative study of effectiveness of gabapentin, alprazolam and pregabalin in general anaesthesia

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Abstract

Background: Hemodynamic pressor response to airway instrumentation is commonly seen with general anaesthesia. Gabapentin, Alprazolam and Pregabalin are important premedications given in general anaesthesia. **Aim and objective:** To compare and evaluate the effectiveness of gabapentin, alprazolam and pregabalin for Attenuation of hemodynamic response to laryngoscopy, tracheal intubation and any adverse effects. **Methodology:** A prospective randomized study comparing gabapentin, alprazolam and pregabalin as premedicant was carried out in patients who were to undergo laparoscopic cholecystectomy under general anaesthesia. The study included 90 patients in the age group of 20 to 60 years belonging to ASA grade I and II. These patients were randomly assigned into 3 equal groups of 30 patients each. In each group hemodynamic responses to larynogoscopy, tracheal intubaion and adverse effects were noted. **Results and discussion:** All the three groups were found comparable at all the time intervals except heart rate at one minute for gabapentin group. Gabapentin and Pregabalin offer significant advantage in terms of no added side effects.
Key Word: gabapentin, alprazolam and pregabalin.

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INTRODUCTION

Endotracheal intubation is an integral part of anaesthesiologist armamentarium to patient care. Hemodynamic pressor response to airway instrumentation (direct laryngoscopy and tracheal intubation) is commonly seen with general anaesthesia that may lead to myocardial ischemia, left ventricular failure, and cerebral haemorrhage especially in high risk patients. The mechanisms of the responses to laryngoscopy and tracheal intubation are proposed to be by somato-visceral reflexes.[1] So, prevention and attenuation of cardiovascular response remains an important clinical goal during laryngoscopy and intubation. Good and effective preoperative management including counselling and various preoperative medications have traditionally been used to eliminate or to suppress the stress response to laryngoscopy and intubation. General aim of premedication is to relieve anxiety, produce amnesia, facilitate induction, prevent nausea, vomiting, suppress undesirable autonomic reflexes, reduce secretions and postoperative analgesic requirements. Alleviation of anxiety in general is the single most important target of premedication. Ideal premedication should be able to produce anxiolysis, amnesia and sedation. Undesired

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effects such as respiratory depression, restlessness, vomiting, and autonomic reflexes should be absent.

Benzodiazepines are one of the most commonly used drugs for premedication and among them alprazolam is most frequently used in our institution. Alprazolam possesses anxiolytic, sedative, hypnotic, skeletal muscle relaxant, anticonvulsant, amnestic, and antidepressant properties. [2-4] Gabapentin provides analgesia by binding to the α2-δ subunit of voltage-gated calcium channels, decreasing the release of glutamate, norepinephrine, and substance-P from presynaptic afferent neurons. It is generally safe and has no clinically important drug interactions. The main dose limiting side effects are somnolence and dizziness. [5] Pregabalin has similar pharmacological activity, but not identical with, that of gabapentin, it is pharmacologically superior due to higher bioavailability (90% versus 33%–66%), rapid absorption (peak plasma level: 1 hour versus 3-4 hours) and linear increase in plasma concentration when its dose is increased. Lower pregabalin doses have a similar analgesic effect. [6-8]

MATERIAL AND METHODOLOGY

Present study was a prospective study carried out in the Department of Anaesthesiology, Indira Gandhi Medical College, Shimla, Himachal Pradesh. Study population was 90 patients in the age group of 20 to 60 years belonging to ASA grade I and II. These patients were randomly assigned into 3 equal groups of 30 patients each.

Group G (n=30) received gabapentin 300 mg at bed time and gabapentin 300 mg in the morning. Group A (n=30) received alprazolam 0.25mg at bed time and alprazolam 0.25 mg in the morning. Group P (n =30) received pregabalin 75 mg at bed time and pregabalin 75 mg in the morning.

Inclusion criteria: 1.Patients within the age group of 20-60 years. 2.Patients of both genders were taken. 3. Patients who were to undergo laparoscopic cholecystectomy under general anaesthesia. 4.Willingness to participate in the study.

Exclusion criteria: 1. Patients with Known cases of hypertension, diabetes, thyroid, asthma, renal and liver diseases. 2. Patient with anticipated difficult airway. 3. Patient with known psychiatric disorder. 4. Pregnancy and lactation. 5. Patients already on pregabalin or gabapentin. 6. Patients with Morbid obesity. 7. Patient who was developed any intra operative complications was excluded from the study. Study was approved by ethical committee of the institute. A valid written consent was taken from the patients after explaining study to them. Data was collected with pretested questionnaire. Data include detailed history, general examination and investigations day prior to surgery. Routine investigations were done. Anxiety of the patient was assessed after counselling them privately and explaining that it was normal to have fear and anxiety about anaesthesia and surgery. Anxiety, pain and sedation was assessed according to VAS-A, VAS-P and Ramsay sedation scores. Anxiety was assessed at the time of pre-anaesthetic check-up then before wheeling the patient to operation theatre and finally just before induction. On arrival in the operating room, intravenous line was secured. Monitoring of non-invasive blood pressure, heart rate, electrocardiogram and arterial oxygen saturation were done and basal readings noted. Anxiety was assessed just before induction according to Visual Analogue Scale for anxiety (VAS-A). A uniform anaesthetic technique was used in all the study groups. Anaesthesia was induced with fentanyl at a dose of 2 g/kg followed by pre oxygenation for 3 minutes with 100% oxygen. Injection propofol 2 mg/kg was given slowly for induction and followed by inj. succinylcholine 2mg/kg intravenously. Airway was secured by a person who has minimum three years of experience in anaesthesia with an appropriate size endotracheal tube followed by injection atracurium at a dose of 0.5 mg/kg for muscle relaxation. Anaesthesia was maintained with oxygen 33%, nitrous oxide 66% and halothane 0.5% - 1%. Vital parameters were monitored throughout intraoperative period. Tracheal extubation performed after residual neuromuscular blockade was reversed with intravenous injection of neostigmine and glycopyrrolate. In the recovery room patients were monitored for vitals and assessed for any adverse effect. Data was analysed using statistical software Epi Info version 7.2.0.1 and SPSS 16.

RESULTS

The mean age (in years) in Group G was 40.93 ± 9.47, in Group A was 42.0 ± 10.53 and in Group P was 39.70 ± 9.73. Majority of the patients in our study group were females. The ratios of female versus male in Group G was 26:4, in Group A and Group P was 22:8, which was statistically not significant with p value 0.36. The demographic profile of the patients in terms of age, body weight and female: male ratios were comparable in all the three study groups. There was no significant difference found among them (p>0.05). Patient's baseline vitals (HR, MAP, SpO2) were recorded before induction and after intubation at 1 min, 2 min, 3 min, 4 min, 5 min, 10 min and 15 min. As most of our surgeries lasted <30 min so time period beyond 30 min was not taken for statistical analysis. Heart Rate at 1 min in Group G, Group A and Group P was 97.20 ± 13.07, vs. 88.40 ± 15.09, vs. 93.90 ± 15.19, (p>0.05). In the intergroup comparison of HR a significant difference was found in variation of HR at 1 min post intubation between Group G and Group A with a p value of 0.02. The baseline MAP was similar in all the three groups (p>0.05). In the intergroup comparison of MAP no

significant difference was found in variation of MAP at any time interval post intubation in all the groups with a p value of >0.05. No significant difference in SpO2 was observed at any time interval between the three study groups with p value >0.05. The baseline sedation score before premedication was comparable in all the three groups (p>0.05). The sedation score was recorded post-operatively in all the three groups when the patients were extubated and shifted to the recovery room. Between Group G and Group A and Group A and Group P significant difference was observed only at 6 hrs postoperatively with p value of 0.006 and 0.02, respectively. There was significant reduction in requirement of total analgesic dose (Inj. Diclofenac sodium) within 12hrs in both the Group G and Group P, p value < 0.0001. In Group G, 12 patients (40.0%) required no analgesic in first 12hrs, 16 patients (53.3%) required 1 dose and only 2 patients (6.7%) required 2 doses. In Group A, 4 patients (13.3%) required no analgesic in first 12hrs, 6 patients (20.0%) required 1 dose, and 20 patients (66.7%) required 2 doses. In Group P, 12 patients (40.0%) required no analgesic in first 12hrs, 13 patients (43.3%) required 1 dose, and 5 patients (16.6%) required 2 doses. A significant difference was found in total analgesics requirement in all the 3 groups, between Group G and Group A and Group A and Group P a highly significant difference was found with p value <0.0001. Total analgesic requirement was lowest in Group G in comparison to Group P and Group A. The main adverse effects noticed postoperatively in our study were nausea and vomiting. In Group G, 6 patients complained of having nausea and vomiting, in Group A, around 4 patients reported the similar complaints while in Group P, around 5 patients reported similar complaints. There was no significant difference found between all the three groups.

Table 1: Variation of heart rate in all groups intra operatively

Group	Pulse	P value inter group	P value
Heart rate before induction			
G	92.53±15.69	Group G Vs Group A=0.25	0.37
A	87.70±17.07	Group G Vs Group P=0.19	
P	87.13±16.43	Group A Vs Group P=0.89	
Heart rate 1 min after Intubation			
G	97.20±13.07	Group G Vs Group A=0.02*	0.06
A	88.40±15.09	Group G Vs Group P=0.37	
P	93.90±15.19	Group A Vs Group P=0.16	
Heart rate 2 min after Intubation			
G	89.60±12.45	Group G Vs Group A=0.89	0.98
A	89.13±14.96	Group G Vs Group P=0.87	
P	89.03±15.48	Group A Vs Group P=0.97	
Heart rate 3 min after Intubation			
G	88.03±12.85	Group G Vs Group A=0.63	0.75
A	89.76±15.50	Group G Vs Group P=0.76	
P	86.83±17.28	Group A Vs Group P=0.49	
Heart rate 4 min after Intubation			
G	84.86±12.99	Group G Vs Group A=0.36	0.54
A	88.30±15.84	Group G Vs Group P=0.89	
P	84.36±16.14	Group A Vs Group P=0.34	
Heart rate 5 min after Intubation)			
G	82.76±13.53	Group G Vs Group A=0.24	0.30
A	87.26±16.07	Group G Vs Group P=0.73	
P	81.50±15.46	Group A Vs Group P=0.16	
Heart rate 10 min after Intubation			
G	81.86±14.34	Group G Vs Group A=0.57	0.20
A	83.96±14.71	Group G Vs Group P=0.22	
P	77.23±15.18	Group A Vs Group P=0.08	
Heart rate 15 min after Intubation			
G	80.43±12.69	Group G Vs Group A=0.52	0.33
A	82.40±10.97	Group G Vs Group P=0.40	
P	82.40±10.97	Group A Vs Group P=0.14	

Table 2: Variation of Mean Arterial Pressure in all groups intra operatively

Group	Mean Arterial Pressure	P value inter group	P value
	Mean Arterial Pressure before induction		
G	99.23±13.49	Group G Vs Group A=0.68	0.30
A	97.93±11.54	Group G Vs Group P=0.28	
P	102.60±10.68	Group A Vs Group P=0.10	
	Mean Arterial Pressure 1 min after Intubation		
G	93.80±18.85	Group G Vs Group A=0.23	0.40
A	99.80±19.94	Group G Vs Group P=0.24	
P	100.03±22.18	Group A Vs Group P=0.96	
	Mean Arterial Pressure 2 min after Intubation		
G	88.93±16.72	Group G Vs Group A=0.24	0.34
A	94.26±18.59	Group G Vs Group P=0.85	
P	88.10±17.92	Group A Vs Group P=0.19	
	Mean Arterial Pressure 3 min after Intubation		
G	86.70±19.06	Group G Vs Group A=0.29	0.26
A	91.56±16.36	Group G Vs Group P=0.62	
P	84.43±16.19	Group A Vs Group P=0.09	
	Mean Arterial Pressure 4 min after Intubation		
G	86.30±19.52	Group G Vs Group A=0.34	0.51
A	90.50±14.60	Group G Vs Group P=0.93	
P	85.90±16.39	Group A Vs Group P=0.25	
	Mean Arterial Pressure 5 min after Intubation		
G	84.83±15.10	Group G Vs Group A=0.27	0.40
A	89.30±16.46	Group G Vs Group P=0.21	
P	90.00±16.81	Group A Vs Group P=0.87	
	Mean Arterial Pressure 10 min after Intubation		
G	95.03±15.60	Group G Vs Group A=0.65	0.64
A	93.36±13.31	Group G Vs Group P=0.36	
P	91.60±13.62	Group A Vs Group P=0.61	
	Mean Arterial Pressure 15 min after Intubation		
G	93.46±11.33	Group G Vs Group A=0.45	0.74
A	95.90±13.38	Group G Vs Group P=0.70	
P	94.60±11.88	Group A Vs Group P=0.69	

Table 3: Variation of Oxygen saturation (SPO_2) in all groups intra operatively

Group	Oxygen saturation	P value inter group	P value
	SpO_2 before induction		
G	94.33±1.98	Group G Vs Group A=0.06	0.12
A	95.40±2.38	Group G Vs Group P=0.10	
P	95.13±1.77	Group A Vs Group P=0.62	
	SpO_2 1 min after Intubation		
G	98.83±1.11	Group G Vs Group A=0.43	0.39
A	99.03±0.80	Group G Vs Group P=0.21	
P	99.16±0.91	Group A Vs Group P=0.55	
	SpO_2 2 min after Intubation		
G	98.73±1.14	Group G Vs Group A=0.34	0.37
A	95.90±16.26	Group G Vs Group P=0.45	
P	98.96±1.27	Group A Vs Group P=0.30	
	SpO_2 3 min after Intubation		
G	98.60±1.03	Group G Vs Group A=0.76	0.44
A	98.50±1.54	Group G Vs Group P=0.29	
P	98.90±1.15	Group A Vs Group P=0.26	
	SpO_2 4 min after Intubation		
G	98.53±1.07	Group G Vs Group A=0.67	0.53
A	98.40±1.37	Group G Vs Group P=0.46	
P	98.76±1.38	Group A Vs Group P=0.30	
	SpO_2 5 min after Intubation		

G	98.60±1.10	Group G Vs Group A=0.70	0.41
A	98.46±1.54	Group G Vs Group P=0.30	
P	98.90±1.15	Group A Vs Group P=0.22	
	SpO_2 10 min after Intubation		
G	98.13±1.67	Group G Vs Group A=0.75	0.71
A	98.26±1.61	Group G Vs Group P=0.40	
P	98.46±1.40	Group A Vs Group P=0.61	
	SpO_2 15 min after Intubation		
G	98.30±1.20	Group G Vs Group A=0.36	0.40
A	97.96±1.58	Group G Vs Group P=0.64	
P	98.46±1.54	Group A Vs Group P=0.22	

Table 4: Side effects observed in all groups

Group	Side effects	Number of patients experiencing side effects
G	Nausea and Vomiting	6
A	Nausea and Vomiting	4
P	Nausea and Vomiting	5

DISCUSSION

In our study, baseline hemodynamic variables (HR, MAP, SpO2) before induction were comparable in all the three groups (p>0.05). Same hemodynamic variables were again recorded after intubation at 1 min, 2 min, 3 min, 4 min, 5 min, 10 min and 15 min. The HR at 1 min was 97.20±13.07 in gabapentin group vs 88.40±15.09 in alprazolam group vs 93.90±15.19 in pregabalin group (p<0.05). There was no significant difference found in variation of MAP at any time interval post intubation in all the groups (p>0.05).In SpO2 also no significant difference was observed at any time interval between all the study groups (p>0.05).Thus, we can say that minimal intubation response in terms of hemodynamic variables was observed in all the groups. Waikar *et al.*[9] noted the effects of oral gabapentin (900mg), pregabalin (150mg), and clonidine (200µg) as premedication for anxiolysis, sedation, and attenuation of pressor response to endotracheal intubation posted for elective surgery under general anaesthesia. Mean arterial pressure was well attenuated by pregabalin in comparison to others, and mean heart rate following laryngoscopy and intubation was attenuated by clonidine group significantly (p<0.05) better than gabapentin and pregabalin. In our study, the effects on various hemodynamic variables of all the drugs were found statistically insignificant (p>0.05) except the heart rate at 1 min where it was significantly increased compared to baseline in gabapentin group. The reason for this may be the dose (300 mg) chosen by us was much lower than that used in this study. Gupta *et al.*[10] also observed the effect of oral pregabalin (150 mg) with placebo on hemodynamic variables when pregabalin was given 60–75 min before surgery. They found that pregabalin effectively attenuates hemodynamic response to laryngoscopy and intubation though found statistically insignificant (p>0.05). Memis *et al.*[11] studied two doses of oral gabapentin (800 mg and 400 mg) with placebo. They found that group receiving 800 mg had significant reduction in pressor response due to laryngoscopy and intubation as compared to other groups. This shows that our dose of gabapentin 300 mg was not adequate for suppression of pressor response. Marashi *et al.*[12] studied the effects of oral gabapentin (900 mg) with clonidine (0.2 mg) and placebo given 120 min before surgery for attenuation of the pressor response to oro-tracheal intubation. They found that gabapentin attenuates the response better than clonidine. In comparison to all these studies, in our study we had observed that the effects of all drugs under study was found to be statistically insignificant on various hemodynamic variables (p>0.05). The main adverse effects observed in all the three groups post operatively were nausea and vomiting. However, on comparison they were found statistically insignificant (p>0.05). Ghai *et al.*[13] observed that higher percentage of patients in pregabalin group (300 mg) complained of dizziness and somnolence than the gabapentin group (900 mg). However, no such adverse effects were found in our study. This could be because of higher dose of drugs used in the above study. Mishra *et al.*[14] observed sedation, nausea and vomiting, respiratory depression, and vertigo as main side effects in their study groups comparing pregabalin (150mg), gabapentin (900mg) and placebo. Though, no significant statistical difference in number of patients with side effects was found among all the three groups. Rajappa *et al.*[15] noticed that the pregabalin in doses of 150 mg had a better analgesic profile, but they noticed dizziness as main side effect. Thus, we can say that pregabalin 75 mg may be the desired pre-emptive dose.

CONCLUSION

All the three groups were found comparable at all the time intervals except heart rate at one minute for gabapentin

group. This shows that gabapentin dose of 300 mg is not adequate for attenuation of hemodynamic response.

REFERENCES

1. Sarkar J, Anand T, Kamra SK, Hemodynamic response to endotracheal intubation using C-Trach assembly and direct laryngoscopy. Saudi J Anaesth 2015; 9:343-347.
2. Mandrioli R, Mercolini L, Raggi MA."Benzodiazepine Metabolism: An Analytical Perspective". Current Drug Metabolism.2008; 9(8):827–844.
3. Skelton KH, Nemeroff CB, Owens MJ."Spontaneous Withdrawal from the Triazolobenzodiazepine Alprazolam Increases Cortical Corticotropin-Releasing Factor mRNA Expression". Journal of Neuroscience.2004; 24(42):9303–9312.
4. Chouinard G."Issues in the Clinical Use of Benzodiazepines: Potency, Withdrawal, and Rebound". J of Clinical Psychiatry.2004; 65(Suppl 5):7–12.
5. Waikakula W, Chalachewaa T, Tantisirina N, Suranutkarina P, Saengpetch N. Combination of gabapentin and celecoxib for analgesia after major orthopedic surgery: a randomized, controlled trial. Asian Biomedicine.2011; 5(1):101-110.
6. Anand T Talikoti AT, Dinesh K , Nanda A, Kumar P, Somasekharam P. Optimizing the Dose of Preemptive Oral Pregabalin for Postoperative Pain Control after Abdominal Hysterectomy under Spinal Anaesthesia. J Clin Biomed Sci. 2013; 3(1):12-19.
7. Gajraj NM. Pregabalin: Its Pharmacology and Use in Pain Management. Anesth Analg. 2007; 105:1805–1815.
8. Ozgencil E, Yalcin S, Tuna H, Yorukoglu D, Kecik Y. Perioperative administration of gabapentin 1200 mg per day and pregabalin 300 mg per day for pain following lumbar laminectomy and discectomy: a randomised, double-blinded, placebo-controlled study. Singapore Med J. 2011; 52(12): 883-889.
9. Waikar C, Singh J, Gupta D, Agrawal A. Comparative Study of Oral Gabapentin, Pregabalin, and Clonidine as Premedication for Anxiolysis, Sedation, and Attenuation of Pressor Response to Endotracheal Intubation. Anesth Essays Res. 2017; 11(3): 558–560.
10. Gupta K, Bansal P, Gupta PK, Singh YP. Pregabalin premedication-A new treatment option for hemodynamic stability during general anaesthesia: A prospective study. Anesth Essays Res. 2011; 5:57–62.
11. Memis D, Turan A, Karamanlioglu B, Seker S, Türe M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol. 2006; 23:686–690.
12. Marashi SM, Ghafari MH, Saliminia A. Attenuation of hemodynamic responses following laryngoscopy and tracheal intubation - Comparative assessment of clonidine and gabapentin premedication. Middle East J Anaesthesiol. 2009; 20:233–237.
13. Ghai A, Gupta M, Rana N, Wadhera R. The effect of pregabalin and gabapentin on preoperative anxiety and sedation: a double blind study. Anaesth Pain and Intensive Care. 2012;16(3):257-261
14. Mishra R, Tripathi M, Chandola HC. Comparative clinical study of gabapentin and pregabalin for postoperative analgesia in laparoscopic cholecystectomy. Anesth Essays Res. 2016; 10(2):201–206.
15. Rajappa GC, Vig S, Bevanaguddaiah Y, Anadaswamy TC. Efficacy of Pregabalin as Premedication for Post-Operative Analgesia in Vaginal Hysterectomy. Anesth Pain Med. 2016; 6(3): e34591

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