Original Research Article

A study of evaluation of gabapentin, alprazolam and pregabalin in preoperative anxiety score and post operative sedation

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Abstract

Background: Postoperative pain is a function of various factors like site and size of surgical incision, extent of tissue trauma and movement of the operated part. Effective postoperative pain control is an essential component of post-surgical care. Present study included gabapentin, alprazolam and pregabalin for post operative sedation. **Aim and objective:** To compare and evaluate the effectiveness of gabapentin, alprazolam and pregabalin in Preoperative sedation and anxiety score. **Methodology:** In the present study we included 90 patients in total (30 patients in each group) of ASA I and II, divided in three groups (gabapentin, alprazolam and pregabalin). In terms of age, weight and gender all the three groups were comparable. Anxiety, pain and sedation was assessed according to VAS-A, VAS-P and Ramsay sedation scores. **Results:** All the three groups were comparable in anxiety scores and there was no statistical difference found ($p>0.05$). In sedation score also except at 6 hours. Postoperatively there were no significant differences found in all the three groups. Gabapentin and pregabalin both had significant sedation in comparison to alprazolam ($p<0.05$) postoperatively at 6 hours.
Key Word: gabapentin, alprazolam and pregabalin.

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INTRODUCTION

Anxiety is characterised by an unpleasant feeling that is typically associated with uneasiness, fear or worry. Anxiety is common before surgery and up to 80% prevalence is observed.[1-2] Preoperative anxiety remains a problem for many patients and common causes of these are fear of surgery, anaesthesia, pain, nausea and previous unpleasant experience related to anaesthesia or surgery or a predisposing personality trait.[3-6] Preoperative anxiety and postoperative pain are interrelated.[7]

Various methods have been used to measure anxiety. Mostly used questionnaires are; Spielberg's State-Trait Anxiety Inventory (STAI), Depression Anxiety and Stress Scale (DASS), Hospital Anxiety and Depression Scale (HADS) and Visual Analogue Scale (VAS).[8] However more recently the Amsterdam Preoperative Anxiety and Information Scale (APAIS) has been designed and validated specifically for preoperative anxiety and is currently used by many.[9,10] Alprazolam is a potent, short-acting benzodiazepine anxiolytic.[11] Alprazolam, like other benzodiazepines, binds to specific sites on the GABAA receptor. It possesses anxiolytic, sedative, hypnotic, skeletal muscle relaxant, anticonvulsant, amnestic, and antidepressant properties. Gabapentin is an anti-epileptic drug that has showed analgesic effect in neuropathic pain. Recently, it has been effectively used to reduce pain and

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opioid requirement during postoperative period of various kinds of surgery. 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. [12,13] Present study was conducted to evaluate the effectiveness of gabapentin, alprazolam and pregabalin for preoperative sedation and anxiety score.

To compare and evaluate the effectiveness of gabapentin, alprazolam and pregabalin in Preoperative sedation and anxiety.

MATERIAL AND METHODS

This study was conducted in the Department of Anaesthesiology, Indira Gandhi Medical College, Shimla, Himachal Pradesh with in the time period extending from September 2016 to August 2017.

This 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.

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. Pre-anaesthetic check-up included detailed history, general examination and investigations day prior to surgery. All patients were kept overnight fasting. The respective medication as revealed by the randomisation were prescribed by the anaesthesiologist and administered to the patient by the ward nurse (not involved in the study) at bedtime and in the morning according to the hospital protocol. In this study the individual drugs used as premedicant were of the same pharmaceutical company. 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. We have encouraged them not to be hesitant or ashamed to mark their level of anxiety. The patients were familiarised that Visual Analogue Scale (VAS-A and VAS-P) 1 to 10 would be used to assess anxiety and pain. 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. The level of anxiety was measured using Visual Analogue Scale for anxiety (VAS-A) as follows: (a) Grade I 0 to 5 cm = non anxious patients; (b) Grade II 5.1 to 6.9 cm = anxious patients; and (c) Grade III 7.0 to 10 cm = phobic patients.55 The level of sedation was measured using Ramsay sedation score (1=Anxious or agitated, 2=Co-operative, oriented and tranquil, 3=Responds to command, 4=Asleep with brisk response to stimuli, 5=Asleep with sluggish response to stimuli, 6=Asleep with no response). Sedation score was assessed before wheeling the patient to operation theatre and then 1hours, 2hours, 4hours and 6hours post-operatively. 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%. Parameters (heart rate / SPO2 / non-invasive blood pressure) were recorded post intubation for 15 minutes. Every 1 minute for first 5 minutes and then every 5 minutes for next 10 minutes. Intravenous injection of aqueous diclofenac 75 mg was given intraoperatively. Injection bupivacaine 0.25% around the incision was locally infiltrated after gall bladder was out.

Injection ondansetron intravenously was administered to prevent postoperative nausea and vomiting. 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. Pain in the postoperative recovery room was assessed immediately after shifting then at 1 hour, 2

hour, 4 hour and 6 hour according to Visual Analogue Scale for pain (VAS-P). Patients were given analgesics whenever VAS-P score equals or crosses 4 and total requirement of analgesics in first 12 hours was noted. Intravenous injection of aqueous diclofenac 75 mg was given as rescue analgesic. 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 and p value using ANOVA was 0.66. 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.

Mean weight (Kgs) in Group G was 61.20 ± 7.96, in Group A was 61.93 ± 8.80 and in Group P was 59.46 ± 7.38 and p value using ANOVA was 0.48. The anxiety score at pre-anaesthetic check-up, before wheeling the patient to operation theatre and just before induction was noted and found comparable in all the three groups (p>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 hours postoperatively with p value of 0.006 and 0.02, respectively. Postoperative analgesia was assessed in terms of intensity of pain, which was measured on the basis of VAS-P. Rescue analgesic was given when patient had VAS-P score of 4 or more. VAS-P score was measured immediately post operatively in the recovery room then at 1, 2, 4 and 6 hours postoperatively. A highly significant difference was observed in VAS-P score in Group A and Group P immediately in recovery room then at time intervals 1, 2 and 4 hours post operatively with a p value (<0.05). A highly significant difference was also observed in VAS-P score in Group G and Group A at time intervals 1, 2 and 4 hours post operatively with a p value<0.05. It was observed that in Group G more patients had VAS-P score <4 thus the quality of analgesia requiring rescue analgesic was better in Group G. Thus, Group G had best post-operative analgesia among three study groups. Patients in Group A had statistically more pain than Group G and Group P. Time required for first rescue analgesic post operatively was also observed. A statistical significant difference for the first rescue analgesic requirement occurred between three groups with p value 0.0001. Between Group G and Group A, a statistical difference was found in first rescue analgesic requirement with p value of 0.0001. Results between Group A and Group P was also found significant with p value of 0.0001. Thus, the results showed that Group G and Group P had good post-operative analgesia than Group A, and in between Group G and P, Group G had good postoperative analgesia. In terms of average time required for first rescue analgesic in Group G was 13.2hours, in Group P was 12.7hours and in Group A was 5.6hours. So, prolongation of first rescue analgesic requirement occurred in both Group G and Group P with maximum prolongation in Group G. There was significant reduction in requirement of total analgesic dose (Inj. Diclofenac sodium) within 12hours in both the Group G and Group P, p value < 0.0001. In Group G, 12 patients (40.0%) required no analgesic in first 12hours, 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 12hours, 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 12hours, 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.

Table 1

Group	Grade I (0 to 5 cm)	Grade II (5.1 to 6.9 cm)	Grade III (7 to 10 cm)	P value inter group	P value
VAS-A at pre-anaesthetic check-up					
G	29	1	0	Group G Vs Group A=0.30	0.51
A	29	1	0	Group G Vs Group P=0.36	
P	29	1	0	Group A Vs Group P=0.85	
VAS-A before wheeling the patient to operation theatre					
G	30	0	0	Group G Vs Group A=0.80	0.45
A	30	0	0	Group G Vs Group P=0.30	
P	30	0	0	Group A Vs Group P=0.25	
VAS-A just before induction					
G	30	0	0	Group G Vs Group A=0.43	0.69
A	30	0	0	Group G Vs Group P=0.55	

P	30	0	0	Group A Vs Group P=0.78

Table 2

Group	Sedation score 1	Sedation score 2	Sedation score 3	Sedation score 4	Sedation score 5	Sedation score 6	P value inter group	P value
Sedation score before wheeling the patient to operation theatre								
G	0	4	13	11	2	0	Group G Vs Group A=0.74	0.86
A	0	4	14	11	1	0	Group G Vs Group P=0.86	
P	0	2	15	12	1	0	Group A Vs Group P=0.58	

Table 3

Group	Sedation score 1	Sedation score 2	Sedation score 3	Sedation score 4	Sedation score 5	Sedation score 6	P value inter group	P value
Sedation score 1 hour post-operatively								
G	0	0	5	20	5	0	Group G Vs Group A=0.11	0.14
A	0	1	13	14	2	0	Group G Vs Group P=0.51	
P	0	0	7	20	3	0	Group A Vs Group P=0.20	
Sedation score 2 hours post-operatively								
G	0	0	7	20	3	0	Group G Vs Group A=0.13	0.28
A	0	3	14	12	1	0	Group G Vs Group P=0.64	
P	0	0	8	19	3	0	Group A Vs Group P=0.27	
Sedation score 4 hours post-operatively								
G	0	0	15	13	2	0	Group G Vs Group A=0.28	0.47
A	0	2	16	12	0	0	Group G Vs Group P=1.0	
P	0	1	12	16	1	0	Group A Vs Group P=0.28	
Sedation score 6 hours post-operatively								
G	0	3	16	11	0	0	Group G Vs Group A=0.006*	0.01*
A	0	5	24	1	0	0	Group G Vs Group P=0.53	
P	0	3	19	8	0	0	Group A Vs Group P=0.02*	

Table 4

Group	VAS 0	VAS 1	VAS 2	VAS 3	VAS 4	VAS 5	VAS 6	P value inter group	P value
VAS-P Immediately post-operatively in recovery room									
G	3	9	15	2	0	0	1	Group G Vs Group A=0.14	0.09
A	1	6	14	5	3	0	1	Group G Vs Group P=0.50	
P	4	13	10	2	0	0	1	Group A Vs Group P=0.007*	
VAS-P 1 hour post-operatively									
G	1	8	17	3	1	0	0	Group G Vs Group A=0.003*	0.001*
A	0	3	13	10	3	1	0	Group G Vs Group P=0.9	
P	0	11	16	2	0	0	1	Group A Vs Group P=0.0009*	
VAS-P 2 hours post-operatively									
G	0	9	17	4	0	0	0	Group G Vs Group A=0.0001*	0.0001*
A	0	2	9	13	3	3	0	Group G Vs Group P=0.32	
P	0	8	15	6	0	1	0	Group A Vs Group P=0.001*	
VAS-P 4 hours post-operatively									
G	0	3	22	4	1	0	0	Group G Vs Group A=0.007*	0.01*
A	0	2	13	9	3	2	1	Group G Vs Group P=0.76	
P	0	9	11	7	2	1	0	Group A Vs Group P=0.02*	
VAS-P 6 hours post-operatively									
G	0	6	18	5	1	0	0	Group G Vs Group A=0.06	0.19
A	0	4	18	6	0	0	2	Group G Vs Group P=0.9	
P	0	4	19	5	0	2	0	Group A Vs Group P=0.05	

DISCUSSION

In our study, We measured the anxiety scores during pre-anaesthetic check-up, a day before surgery and found that anxiety levels were in grade I (0 to 5 cm) in 29 patients and one patient each in grade II (5.1 to 6.9 cm) among all the three groups. While before wheeling the patients to operation theatre and just before induction all the patients had anxiety levels in grade I (0 to 5 cm). Statistically anxiety scores were insignificant ($p>0.05$) when compared among three groups. The above findings were in coherence

with the study of Usama Ibrahim Abdalkarim Abotaleb [14] which was a comparative study of gabapentin, pregabalin. In their study both pregabalin and gabapentin had anxiolytic effect during preoperative period while preoperative VAS-A was significantly high in control group. VAS-A on 100mm scale was 29 ± 16 in gabapentin, 23 ± 15 in pregabalin, and 45 ± 22 in control group before operation. In our study, before wheeling the patient to operation theatre, VAS-A was 1.66 ± 0.88 in gabapentin, 1.43 ± 0.85 in pregabalin, and 1.73 ± 1.14 in alprazolam group which shows that all the three groups had lower anxiety scores. Pathak *et al.*. [15] in their study found that anxiety score to be significantly low in gabapentin group. They found that VAS-A score was 45.75 ± 30.27 in gabapentin group versus 68.13 ± 29.84 in placebo group on 100 mm scale just before induction of anaesthesia. In our study VAS-A was 1.66 ± 0.88 in gabapentin group on scale of 10 cm. Ghai *et al.*. [16] in their study found that the anxiety scores one hour after the drug administration were statistically significant from the baseline values in gabapentin group and pregabalin group but were comparable in placebo group ($p<0.05$). However, in our study anxiety scores were statistically nonsignificant in all the three groups at pre-anaesthetic check-up, before wheeling to operation theatre and just before induction. De Witte *et al.*.[17] observed the anxiety scores were decreased significantly at arrival in the operating room compared with their baseline scores in the alprazolam group. However, the decrease was greater ($p<0.05$) (to 19 ± 16 mm) in alprazolam group vs (to 23 ± 12 mm) in midazolam group vs (to 38 ± 18 mm) in placebo. In our study, VAS-A was also decreased but the difference was statistically insignificant in all the groups ($p>0.05$). Mishra *et al.* [18] found that sedation scores were comparable at 1 and 2 hours after surgery but were significant at 3 hours postoperatively. In our study, sedation score at 1 and 2 hours were comparable in all the groups ($p>0.05$) whereas were significant at 6 hours with both pregabalin and gabapentin having more sedation compared to alprazolam. Turan *et al.*.[19] while observing the safety and efficacy of gabapentin (1200mg) with placebo in rhinoplasty or endoscopic sinus surgery revealed that sedation score were similar in both gabapentin and placebo group ($p>0.05$). Pandey *et al.*. [20] in their study observed that gabapentin group reported a higher incidence of sedation (33.98%, $p < 0.05$) as compared to the other groups. These findings were similar to our study.

CONCLUSION

Premedication with 300mg gabapentin or 75mg pregabalin or 0.25mg alprazolam for control of preoperative anxiety was comparable, though gabapentin and pregabalin offer significant advantage in terms of postoperative pain control and reducing analgesic requirement with no added side effects.

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