

A Comparative study of oral Gabapentin, oral Alprazolam and intravenous dexmedetomidine on perioperative anxiety and pain during posterior segment eye surgery under peribulbar block: a randomized, double-blind study

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Abstract

Background and aims: The goal of sedation for eye surgery is to prepare the patients to stay calm during surgery. Several drugs such as propofol, opioids, benzodiazepines and dexmedetomidine have been used for sedation during this procedure. Gabapentin is well-tolerated drug that is associated with anxiolytic and antinociceptive properties. In this study, we compared the sedative effects of oral gabapentin, alprazolam and intravenous of dexmedetomidine on various parameters including Ramsay Sedation Scale, Hemodynamics and Verbal Pain Score. Methods: In a double blinded study, 45 patients aged 18-65 years, scheduled posterior segment eye surgery under peribulbar block were divided equally to receive either 0.25 mg oral Alprazolam or dexmedetomidine 0.25 μg/kg IV dose over 10 min or 600mg oral gabapentin. Vital parameters, level of sedation (Ramsay Sedation Scale 1-6) and Verbal Pain score assessed at regular intervals. Results: Gabapentin and Alprazolam groups had predominantly stable hemodynamics, level 2 sedation. Dexmedetomidine group had a higher incidence of bradycardia, hypotension, level 3 sedation (Ramsay Sedation Scale). Adequate Pain control with local anesthesia with no statistical significant difference between three groups. Conclusion: Preoperative oral medication with Gabapentin for sedation of patients undergoing posterior segment eye surgery under local anesthesia showed satisfactory anxiolytic properties with stable hemodynamics close to premedication with Alprazolam. While comparison to minimal dose of intravenous dexmedetomidine for mid aged patients undergoing eye surgery revealed less intraoperative depth of sedation than dexmedetomidine with no negative effect on patient satisfaction and more hemodynamic stability.

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Introduction

The goal of sedation for eye surgery is to prepare the patients to stay calm during surgery. Both insufficient sedation and deep sedation may lead to sudden movements by patients, which may potentially result in harmful complications during eye surgery. Several drugs such as propofol, opioids, and dexmedetomidine have been used for sedation during this procedure [1]. However, each of these drugs has its own limitations, leading to impairment of patient's cooperation during surgery. Therefore, the potential clinical advantages of newly-marketed therapeutic drugs should be thoroughly evaluated. [2]

Benzodiazepines are amongst the most popular preoperative medication to produce anxiolysis, amnesia, and sedation for the patients coming for surgery [3]. Benzodiazepines are reported to be paradoxically associated with the increased episodes of arousal during sleep, restlessness, and hangover effects [4]. Alprazolam, a benzodiazepine class of antipsychotic drugs, is more anxio-selective than the other premedicants of this group like midazolam, lorazepam, or diazepam [5]. It has also been reported to show arousal episodes and may cause psychomotor impairment which is a disadvantage to be used in elderly in general and in day case in particular [4,6].

Gabapentin is well-tolerated drug that is associated with anxiolytic and antinociceptive properties [2]. It is reported that gabapentin has anxiolytic [7] and antinociceptive effects [8,9]. In another study, it is claimed that this drug does not depress respiration with no effect on gastric mucosa, platelets, and renal function [9]. Moreover, gabapentin seems to be an anxiolytic without amnesic effects which is an important advantage for elderly patients. Leung and colleagues reported that delirium is significantly less in patients receiving gabapentin before spine surgery [10].

Dexmedetomidine, a highly selective $\alpha 2$ agonist, has been widely used as a sedative in a variety of clinical settings owing to its analgesic properties, minimal respiratory depression and easy arousability [11,12]. Hypotension and bradycardia, the most frequent side effects of dexmedetomidine [12], occur in a dose-related manner [13,14]. To avoid these side effects, a dose adjustment is required. For procedural sedation, a loading dose of 0.25µg/kg over 10 min followed by maintenance dose of 0.25µg/kg/h provides an adequate level of sedation, stable hemodynamics and better surgeon satisfaction [15].

In this study, we planned to compare the sedative effects of oral gabapentin, alprazolam and intravenous of dexmedetomidine on various parameters including anxiety, sedation and orientation. In our literature review, we could not find any study comparing the effect of gabapentin and alprazolam on anxiety, pain, sedation scores, satisfaction of surgeon, and hemodynamic parameters in posterior segment⁻ eye surgery under peribulbar block.

Subjects and Methods

This randomized double blinded study was conducted in Kasr-Al-Ainy hospital, Ophthalmology surgeries operation theatre, Cairo University, Cairo, Egypt.

After the approval of the research ethical committee (approval number MD-240-2019 & clinical trials number NCT04659732) obtaining written informed consent from every patient, 45 patients belonging to the American society of anesthesiologists (ASA) status I, II, aging from 45 to 65 years old, both genders, co-operative patients aware of the instructions, scheduled for posterior segment eye surgery under peribulbar block were enrolled for this randomized double blinded study.



However, patients with cognitive impairment or mental disorder, hypersensitivity to any of used drugs, having any conditions the contraindicating local anesthesia (e.g. Coagulation disorders), Chronic use of narcotics, barbiturate, psychotropic medications or claustrophobia, Body weight less than

40 kg or more than 100 kg and patients unable to lie supine for the time of surgery were excluded from the study.

Furthermore, patients having severe pulmonary disease e.g. (obstructive sleep apnea), Patients on medications can affect the removal of alprazolam from the body which may affect how alprazolam works examples include azole antifungals (such as itraconazole, ketoconazole), cimetidine, certain antidepressants (such as fluoxetine, fluvoxamine, nefazodone), drugs to treat HIV(delavirdine, protease inhibitors such as indinavir), macrolide antibiotics (such as erythromycin), rifamycins (such as rifabutin) and drugs used to treat seizures (such as phenytoin) , Patients with myasthenia gravis or myoclonus problems and patients with chronic renal, hepatic and cardiac disorder (e.g. chronic renal failure, heart failure) were also excluded from the study.

Patients were randomly allocated by а computer-generated table into one of the study groups; the randomization sequence was concealed in sealed opaque envelopes. Patients were subjected to systematic preoperative assessment including history taking, physical examination and review of the results of routine investigations (CBC, coagulation profile, liver function test, kidney function test and ECG). The anesthetist was blinded to the patient's group assignment, and the study data recorded by а blinded observer. No premedication was given except for the drugs predetermined by the study protocol. The envelope opened by a research assistant who was not involved in patient management nor assessment. According to the instructions in the envelope, the study drug prepared by the eISSN 1303-5150

research assistant and delivered to the patient. Patients were allocated into one of the 3 groups: Alprazolam (A group), Gabapentin (G group) and Dexmedetomidine (D group) as control group. Alprazolam group (n=15): patients in this group received 0.25 mg Alprazolam (2 tablets of Xanax 0.125 mg manufactured by Pfizer). Gabapentin group (n=15): patients in this group received 600mg Gabapentin (2 capsules of Neurontin 300 mg manufactured by Pfizer). D group (n=15): patients in this group received 2 tablets of multivitamin (Vita-max manufactured by GlaxoSmithKline S.A.E) as placebo to ensure blindness of the study. The study drug received 120 minutes before the operation. Patients monitored with electrocardiogram (ECG), noninvasive measurement of blood pressure (NIBP), and pulse oximetry (SPO2) at the operating room and the baseline readings recorded. Dexmedetomidine 0.25 µg/kg infused intravenously over 10 minutes through syringe pump before surgery (Prepared using Precedex 200mcg/2ml manufactured by Hospira Inc, Highway 301, Rocky Mount, NC 278001 USA) while the other two groups 20cm saline infused intravenously over 10 minutes. Peribulbar nerve block with 8ml of local anesthetic comprising 3 ml of 0.5% bupivacaine hydrochloride,5 ml of 2% lidocaine, and hyaluronidase 50:70 IU/ml as given after 10 min of starting IV sedation. Success of the block was assessed by globe bulge, loss of ocular movements and the eye was padded 5 to 10 minutes (with intermittent pressing 5 seconds and relieve the press for 10 seconds) to enhance spread of the anesthetic solution and prevent a rise in the intraocular pressure.

After adequate and complete muscle akinesia, the surgeon was allowed to start the operation.



Assessment of ocular motility after the local **2**. Secondary outcome(s) anesthetic injection:

Ocular movement was evaluated in all four directions (inferior, superior, medial, and lateral) using the three points scale. The patient was instructed to look in the primary position of gaze, then in the direction of the quadrant to be examined, and the extent of limbal excursion in that direction. Overall movement score was obtained by combining the scores of these four directions of movement. This score ranges from 0 (no movement) to 8 (complete movement) and was categorized into two groups, akinesia (score 0-4) and no akinesia (score 5-8). The motility was assessed every 2 minutes until akinesia was attained or up to 10 minutes. The serial measurement was terminated once akinesia was attained. If the block was inadequate for more than 10 minutes additional injection of 3ml of local anesthetic solution was given at medial canthus. Before surgery, the effectiveness of the block was assessed by the surgeon and deemed satisfactory only if minimal ocular mobility or orbicularis function remained.

The OR was equipped with emergency equipment and drugs. All the equipment necessary for transformation to general anesthesia if needed at any point were also present including (analgesic, hypnotic, muscle relaxant, laryngoscope, different endotracheal tube sizes a supraglottic device, and a wellfunctioning anesthesia machine). This transformation would have been needed if a safety end point was reached.

1. Primary outcome

The sedation level of patients using Ramsay sedation scale (RSS) during surgery assessed every 5 min for the first 15 min (5, 10, 15), every 15 min until the end of surgery and every 30 min for 2 h in the post-operative ward.

The verbal pain score (VPS) ranging from 0 to10 (0 = no pain and 10 = worst pain imaginable) was fully explained to patients. The score evaluated every 5 min for the first 15 min (5, 10, 15), every 15 min until the end of surgery and every 30 min for 2 h in the post-operative ward. Vital signs: Blood Pressure (BP), Mean arterial blood pressure (MAP) and the heart rate (HR) at every 5 min for the first 15 min (5, 10, 15), every 15 min until the end of surgery and every 30 min for 2 h in the post-operative ward

Statistical methods:

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for normally distributed quantitative variables or median and interquartile range for non-normally distributed quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test in normally distributed quantitative variables while nonparametric Kruskal-Wallis test and Mann-Whitney test were used for non- normally distributed quantitative variables. For comparison of serial measurements within each group repeated measures ANOVA was used. For comparing categorical data, Chi square (22) test was performed. Exact test was used instead when the expected frequency is less than 5 Pvalues less than 0.05 were considered as statistically significant.



Results

45 patients were enrolled in the study, 15 in each of the three compared groups (Alprazolam, Gabapentin and Dexmedetomidine). The groups were compared regarding: demographic data of the patients including age in years, sex, ASA classifications, duration of operation, hemodynamic parameters (at baseline before **The demographic data:**

medications, zero at local anesthesia, 5 minutes intervals during first 15 mins, then every 15 mins intraoperative and finally every 30 mins postoperative for 2 hours) including systolic, diastolic and mean arterial blood pressures, heart rate, intraoperative and postoperative level of sedation according to Ramsay's sedation scale and verbal pain score intra and post- operative.

		Gre	oup A	Gre	oup G	Group D		Develope
		Count	%	Count	%	Count	%	P value
Sex	male	7	46.7%	9	60.0%	8	53.3%	0.765
	female	8	53.3%	6	40.0%	7	46.7%	0.765
ASA	1	3	20.0%	4	26.7%	4	26.7%	4
	2	12	80.0%	11	73.3%	11	73.3%	I

Table (1): Demographic data between groups A, G and D

	Group A		Gr	Group G		oup D	
	Mean	SD	Mean	SD	Mean	SD	P value
Age	53.53	9.54	49.67	12.22	52.00	9.05	0.593
operation duration	74.00	13.65	79.33	10.83	77.00	11.46	0.484

Numerical data are presented as Mean \pm SD (Range). SD: standard deviation, categorical data are presented as frequency (%). p \leq 0.05 is statistically significant.

There was no statistically significant difference between three groups.

According to the primary outcome Ramsay Sedation Scale (RSS) in comparison between three

groups A, G and D.

The comparison between 3 groups at the same time interval showed statistically significant ($p \le 0.05$) at 9 readings (zero ,5 ,10,15 mins, intraoperative 1,2,3, post-operative 90 and 120 mins).





Figure 1: RSS in comparison between three groups

It showed deeper RSS with dexmedetomidine all through the operation. According to systolic blood pressure (SBP) readings in mmhg at the same time interval compared between three groups.

The comparison between 3 groups at the same time interval showed statistically significant ($p \le 0.05$) at 10 readings (5 ,10,15 mins, intraoperative 1,2,3, postoperative 30,60,90 and 120 mins).



Figure 2: SBP readings in mmhg between three groups

It showed lower SBP with dexmedetomidine at all readings.

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According to Heart Rate beats per minute (HR) readings comparison between the groups:

The comparison between 3 groups at the same time interval showed statistically significant ($p \le 0.05$) at 8 readings (baseline, intraoperative 2,3, 30, 60, 90 and 120 mins postoperative).



Figure 3: HR beats per minute readings between three groups

It showed higher HR with dexmedetomidine at all readings in comparison to alprazolam and ¹⁰²⁴⁶ gabapentin while it shows lower HR within the dexmedetomidine group.

Mean Arterial blood Pressure (MAP):

Table (2): Group (A) MAP readings.

	Group A		P value compared
	Mean	SD	to baseline
MAP baseline	93.87	13.19	
MAP zero	96.73	6.40	0.472
MAP 5mins	97.67	9.13	0.407
MAP 10mins	96.00	9.90	0.635
MAP 15mins	94.87	9.67	0.841
MAP intraoperative 1	92.67	8.84	0.808
MAP intraoperative 2	93.53	7.57	0.945
MAP intraoperative 3	91.53	8.77	0.570



MAP intraoperative 4	96.40	7.91	0.584
MAP post 30 mins	94.73	9.15	0.849
MAP post 60mins	91.33	10.92	0.578
MAP post 90mins	90.93	12.06	0.497
MAP post 120mins	89.40	8.67	0.303

Numerical data are represented as mean \pm SD. SD: standard deviation, p \leq 0.05 is statistically significant.

The comparison in the same group at the same time interval was not statistically significant (P>0.05).

Heart Rate (HR):

Table (3): Group (A) HR readings.

	Group A		P value compared to
	Mean	SD	baseline
HR Base line	74.73	9.97	
HR zero	74.67	7.60	0.971
HR 5mins	75.40	9.69	0.705
HR 10 mins	73.27	9.82	0.421
HR 15mins	71.87	8.12	0.143
HR intraoperative 1	72.20	7.95	0.222
HR intraoperative 2	70.20	6.07	<mark>0.017</mark>
HR intraoperative 3	71.00	7.46	<mark>0.047</mark>
HR intraoperative 4	72.73	5.85	0.275
HR post 30mins	70.80	5.35	0.066
HR post 60mins	70.47	5.95	0.064
HR post 90mins	70.67	7.24	0.096
HR post 120mins	70.13	6.96	<mark>0.036</mark>

Numerical data are represented as mean \pm SD. SD: standard deviation, p \leq 0.05 is statistically significant.

The comparison in the same group showed statistically significant lower HR at intraoperative readings 2,3 and 120 mins postoperative.

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Ramsay Sedation Scale (RSS):

Table (4): Group (A) RSS readings

	Group A		P value compared to
	Mean	SD	baseline
RSS baseline	1.00	0.00	
RSS zero	1.47	0.64	<mark>0.014</mark>
RSS 5mins	1.80	0.41	<mark>< 0.001</mark>
RSS 10mins	1.93	0.26	<mark>< 0.001</mark>
RSS 15mins	1.93	0.26	<mark>< 0.001</mark>
RSS intraoperative 1	2.00	0.00	
RSS intraoperative 2	2.00	0.00	
RSS intraoperative 3	1.93	0.26	<mark>< 0.001</mark>
RSS intraoperative 4	2.00	0.00	
RSS post 30mins	2.07	0.26	<mark>< 0.001</mark>
RSS post 60 mins	2.27	0.46	<mark>< 0.001</mark>
RSS post 90mins	2.27	0.46	<mark>< 0.001</mark>
RSS post 120mins	2.27	0.46	<mark>< 0.001</mark>

Numerical data are represented as mean \pm SD. SD: standard deviation, p \leq 0.05 is statistically significant.

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The comparison in the same group showed statistically significant deep sedation at all readings (P \leq 0.05).

Group G:

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Table (5): Group (G) MAP readings.
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	(P value compared	
	Mean	SD	to baseline
MAP baseline	90.60	7.35	
MAP zero	102.13	11.34	<mark>0.002</mark>
MAP 5mins	97.67	8.10	<mark>0.011</mark>
MAP 10mins	94.07	8.92	0.153
MAP 15mins	94.13	9.65	0.287
MAP intraoperative 1	93.67	8.36	0.238
MAP intraoperative 2	93.87	10.31	0.240

MAP intraoperative 3	93.40	8.63	0.292
MAP post zero	95.33	10.60	0.054
MAP post 30 mins	90.33	10.05	0.930
MAP post 60mins	88.93	8.30	0.353
MAP post 90mins	86.20	9.83	0.077
MAP post 120mins	83.13	7.64	<mark>0.012</mark>

Numerical data are represented as mean \pm SD. SD: standard deviation, p \leq 0.05 is statistically significant.

The comparison in the same group at the same time interval showed statistically significant higher MAP At first two readings zero, 5 mins after local anesthesia while showed lower MAP at 120 mins postoperative

Heart Rate (HR):

Table (6): Group (G) HR readings.

	Gı	coup G	P value compared	
	Mean	SD		
HR Base line	73.60	12.24		
HR zero	74.80	9.29	0.681	
HR 5mins	74.33	11.26	0.787	
HR 10 mins	71.67	9.28	0.266	
HR 15mins	69.87	11.34	0.081	
HR intraoperative 1	68.40	9.83	0. <mark>012</mark>	
HR intraoperative 2	67.73	10.08	0. <mark>003</mark>	
HR intraoperative 3	67.33	8.99	0. <mark>003</mark>	
HR intraoperative 4	71.33	8.11	0.264	
HR post 30mins	66.67	7.91	0. <mark>003</mark>	
HR post 60mins	67.40	5.67	0. <mark>027</mark>	
HR post 90mins	65.47	6.28	0. <mark>003</mark>	
HR post 120mins	64.27	7.39	< <mark>0.001</mark>	

Numerical data are represented as mean \pm SD. SD: standard deviation, p \leq 0.05 is statistically significant.

The comparison in the same group at the same time interval showed statistically significant lower HR at seven readings intra-operative 1,2,3 and all postoperative readings.



Ramsay Sedation Scale (RSS):

Table (7): Group (G) RSS readings

	Group G		P value compared
	Mean	SD	to baseline
RSS baseline	1.00	0.00	
RSS zero	1.00	0.00	•
RSS 5mins	1.93	0.26	< 0.001
RSS 10mins	2.00	0.00	
RSS 15mins	2.00	0.00	•
RSS intraoperative 1	1.93	0.26	<mark>< 0.001</mark>
RSS intraoperative 2	1.93	0.26	<mark>< 0.001</mark>
RSS intraoperative 3	1.93	0.26	< 0.001
RSS intraoperative 4	1.87	0.35	< 0.001
RSS post 30mins	2.13	0.64	< 0.001
RSS post 60 mins	2.40	0.51	< 0.001
RSS post 90mins	2.53	0.52	< 0.001
RSS post 120mins	2.60	0.51	< 0.001

Numerical data are represented as mean \pm SD. SD: standard deviation, p \leq 0.05 is statistically significant.

The comparison in the same group at the same time interval showed statistically significant deeper 10250 sedation from 5 mins of local anesthesia to 2 hours postoperative.

Group D:

Table (8): Group (D) MAP readings.

	(Group D	P value compared
	Mean	SD	to baseline
MAP baseline	88.87	10.64	
MAP zero	90.40	12.35	0.140
MAP 5mins	85.07	10.89	<mark>0.029</mark>
MAP 10mins	83.00	8.21	<mark>0.001</mark>
MAP 15mins	80.60	10.83	<mark>0.001</mark>
MAP intraoperative 1	78.53	8.21	< 0.001
MAP intraoperative 2	83.07	13.18	<mark>0.010</mark>
MAP intraoperative 3	81.80	10.33	<mark>0.001</mark>
MAP intraoperative 4	83.20	9.35	<mark>0.002</mark>
MAP post 30 mins	84.27	10.81	0.101
MAP post 60mins	78.80	10.23	<mark>0.001</mark>
MAP post 90mins	76.87	10.78	< 0.001
MAP post 120mins	75.27	9.52	< 0.001

Numerical data are represented as mean±SD. SD: standard deviation, p≤0.05 is statistically significant.



The comparison in the same group at the same time interval showed statistically significant lower MAP at (5,10,15 mins, intraoperative1,2,3,4,60,90 and 120 mins postoperative readings).

Table (9): Group (D) HR readings

	(Group D	P value compared
	Mean	SD	to baseline
HR Base line	84.20	13.54	
HR zero	81.47	13.27	0.320
HR 5mins	78.60	8.81	<mark>0.019</mark>
HR 10 mins	75.33	7.88	<mark>0.002</mark>
HR 15mins	75.47	7.27	<mark>0.001</mark>
HR intraoperative 1	74.07	7.19	0.001
HR intraoperative 2	76.40	11.26	<mark>0.005</mark>
HR intraoperative 3	75.87	10.24	0.007
HR intraoperative 4	83.20	12.03	0.773
HR post 30mins	76.67	11.18	<mark>0.002</mark>
HR post 60mins	73.20	6.88	<mark>0.002</mark>
HR post 90mins	71.40	6.56	0.001
HR post 120mins	70.93	7.85	<mark>0.001</mark>

Numerical data are represented as mean±SD. SD: standard deviation, p≤0.05 is statistically significant.

The comparison in the same group at the same time interval showed statistically significant lower HR at (5,10,15 mins, intraoperative1,2,3,30,60,90 and 120 mins postoperative readings).

Table (10): Group (D) RSS readings.

	Group D		P value compared
	Mean	SD	to baseline
RSS baseline	1.00	0.00	
RSS zero	1.27	0.46	<mark>0.041</mark>
RSS 5mins	2.20	0.41	< 0.001
RSS 10mins	2.20	0.41	< 0.001
RSS 15mins	2.27	0.46	< 0.001
RSS intraoperative 1	2.47	0.52	< 0.001
RSS intraoperative 2	2.47	0.64	< 0.001
RSS intraoperative 3	2.47	0.52	< 0.001
RSS intraoperative 4	1.87	0.35	< 0.001
RSS post 30mins	2.00	0.38	< 0.001
RSS post 60 mins	2.60	0.51	< 0.001
RSS post 90mins	2.73	0.46	< 0.001
RSS post 120mins	2.80	0.41	< 0.001

Numerical data are represented as mean \pm SD. SD: standard deviation, p \leq 0.05 is statistically significant.

The comparison in the same group at the same time interval showed statistically significant deeper sedation at all readings.



Discussion

Ophthalmological procedures are commonly anesthesia. Patients done under local undergoing procedures under local anesthesia commonly experience perioperative anxiety and discomfort. The use of sedation is one method that can reduce incidence of anxiety and its unwanted outcome. Different drugs through different routes are commonly used for sedation. Among the most common used intravenous sedative drugs are benzodiazepines as midazolam, alpha 2 adrenergic receptor agonist dexmedetomidine, the non-barbiturate imidazole intravenous anesthetic propofol, opioids as fentanyl and remifentanil and the NMDA receptor antagonist ketamine (16).

Many previous literatures have studied the use of different sedatives with local anesthesia for patients undergoing different surgical procedures. In these studies drugs were compared to each other, to placebo or to different types of music in a trial to overcome anxiety. Intravenous sedation was given either by the anesthetist or by the patient him/herself in what is called patient controlled sedation (17).

In our study we compared preoperative sedation with Gabapentin, Alprazolam and Dexmedetomidine in patients undergoing posterior eye surgery procedure under local anesthesia. The comparison between the three groups was in terms of Ramsay Sedation Scale (RSS), hemodynamic parameters (SBP, DBP, MAP, HR) and Verbal Pain Score.

Regarding the intra and perioperative sedation in terms of RSS which was our primary outcome, the comparison showed statistically significant deeper sedation in Gabapentin group in comparison to baseline readings while in comparison with Alprazolam and Dexmedetomidine, gabapentin showed satisfactory sedation score (RSS level 2) close to alprazolam and less than dexmedetomidine

that showed level 3 sedation RSS especially in the first 15 mins intraoperative.

In consistency with our results, a study by Marzieh-Beigom Khezri , Mohammad-Reza Oladi and Ali Atlasbaf. who compared Effect of gabapentin on anxiety and pain associated with retrobulbar eye block for cataract surgery, found that The level of anxiety was significantly lower with gabapentin (18).

Also in consistency with our results , a study Shree Ramaswamy , B Parimala by Suman . who compared two different loading doses of dexmedetomidine with midazolam-fentanyl for sedation in vitreoretinal surgery under anesthesia. peribulbar found that dexmedetomidine 0.25 µg/kg loading dose over 10 min is an effective and provides controlled (level 3) sedation(15). Away from eye surgery, Mueen Ullah Khan et al. studied on 50 patients undergoing sleeve gastrectomy giving 1200 mg gabapentin or placebo 2 hours before operation. Preoperative anxiety and sedation were recorded at 2 hours interval after the drug administration through Visual Analogue Scale (VAS). The study found that oral gabapentin was effective in reducing preoperative anxiety in morbid obese patients undergone laparoscopic sleeve gastrectomy (18).

However, Against our study, a study by Tim Thomas Joseph et al. compared the effects of pre-operative oral gabapentin 600 mg, alprazolam 0.5 mg or a placebo on pre-operative anxiety using Visual analogue scale (VAS) on 75 patients scheduled for abdominal hysterectomy under general anesthesia and found that 600 mg Gabapentin did not have significant anxiolytic effect compared to alprazolam in the preoperative period(18).



Regarding the **hemodynamic parameters**:

Regarding the SBP: the comparison between the three groups was statistically significant lower SBP with dexmedetomidine than both alprazolam and gabapentin, however the comparison within the same group gabapentin and dexmedetomidine showed a statistically significant higher SBP at the time of local anesthesia.

As to the DBP: the comparison between the three groups was statistically significant lower DBP with dexmedetomidine than both alprazolam and gabapentin, however the comparison within the same group gabapentin and dexmedetomidine showed a statistically significant higher DBP at the time of local anesthesia.

As to the HR: the comparison between the three groups was statistically significant higher HR with dexmedetomidine than both alprazolam and gabapentin, however the comparison within the same group dexmedetomidine showed statistically significant lower HR in comparison to baseline readings.

However, in contrast to our results, the study by **Suman Shree Ramaswamy**, **B Parimala.** Found stable hemodynamics with low dose dexmedetomidine 0.25 μ g/kg loading dose over 10 min. Our results show marked decrease in

SBP, DPB and MAP which wasn't hazardous and didn't need any intervention (15)

Limitations

First of all, the study was conducted on patients undergoing posterior segment eye surgery only, and it is a minor procedure with minimal pain in the perioperative period. Secondly, the study was conducted on a specific age group (18-65), excluding pediatric and geriatric populations. Lastly, we used a single preoperative precalculated dose for alprazolam and gabapentin.

Conclusion

Preoperative oral medication with Gabapentin for sedation of patients undergoing posterior segment eye surgery under local anesthesia showed satisfactory anxiolytic properties RSS level 2 with stable hemodynamics close to premedication with Alprazolam. While comparison to minimal dose of intravenous dexmedetomidine for mid aged patients undergoing eye surgery revealed less depth intraoperative of sedation than dexmedetomidine with no negative effect on patient satisfaction and more hemodynamic stability.

References

 Alhashemi JA. Dexmedetomidinevs midazolamfor monitored anaesthesiacare during cataract surgery. BrJ Anaesth. 2006;96:722–6.

2. Kong VK, Irwin MG. Gabapentin: A multimodal perioperative drug? Br J Anaesth. 2007;99:775–86.

3. Moyers JR, Vincent CM. Preoperative medication. In: Barash PG, Cullen BF, Stoelting RK, editors. Clinical Anesthesia. 4th edition. Philadelphia, Pa, USA: Lippincott-Raven; 1997. pp. 551–563.

4.Dawson D, Encel N. Melatonin and sleep in humans. Journal of Pineal

Research. 1993;15(1):1-12.



5. Ansseau M, Doumont A, Diricq S. Methodology required to show clinical differences between benzodiazepines. Current Medical Research and Opinion. 1984;8(4):108–114.

6. De Witte JL, Alegret C, Sessler DI, Cammu G. Preoperative alprazolam reduces anxiety in ambulatory surgery patients: A comparison with oral midazolam. Anesth Analg. 2002;95:1601–6

7. de-Paris F, Sant'Anna MK, Vianna MR, Barichello T, Busnello JV, Kapczinski F, et al. Effects of gabapentin on anxiety induced by simulated public speaking. J Psychopharmacol. 2003;17:184–8.

8. Fassoulaki A, Triga A, A Melemeni A, Sarantopoulos C. Multimodal analgesia with gabapentin and local anesthetics prevents acute and chronic pain after breast surgery for cancer. AnesthAnalg. 2005;101:1427–32.

9. Turan A, Kaya G, Karamanlioglu B, Pamukcu Z, Apfel CC. Effect of oral gabapentin on postoperative epidural analgesia. Br J Anaesth. 2006;96:242–6. .

10. Leung JM, Sands LP, Rico M, Petersen KL, Rowbotham MC, Dahl JB, et al. Pilot clinical trial of gabapentin to decrease postoperative delirium in older patients. Neurology. 2006;67:1251–3.

11. Venn RM, Bradshaw CJ, Spencer R, Brealey D, Caudwell E, Naughton C, et al. Preliminary UK experience of dexmedetomidine, a novel agent for postoperativesedation in the

intensive care unit. Anaesthesia. 1999;54:1136–1142.

Carollo DS, Nossaman BD, Ramadhyani U.
Dexmedetomidine: a review of clinical applications. Curr Opin Anaesthesiol.
2008;21:457–461

 Bloor BC, Ward DS, Belleville JP, Maze M.
Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes.
Anesthesiology. 1992;77:1134–1142.

14. Kallio A, Scheinin M, Koulu M, Ponkilainen R, Ruskoaho H, Viinamaki O, et al. Effects of dexmedetomidine, a selective alpha 2-adrenoceptor agonist, on hemodynamic control mechanisms. Clin Pharmacol Ther. 1989;46:33–42.

15. Ramaswamy SS, Parimala B. Comparative evaluation of two different loading doses of dexmedetomidine with midazolam-fentanyl for sedation in vitreoretinal surgery under peribulbar anaesthesia. Indian J Anaesth. 2016;60:89–93.

16. Ferguson JA, Goldacre MJ, Henderson J, Bron AJ. Ophthalmology in the Oxford region: Analysis of time trends from linked statistics. Eye 1991; 5: 379–384.

17. Khezri MB, Oladi MR, Atlasbaf A. Effect of melatonin and gabapentin on anxiety and pain associated with retrobulbar eye block for cataract surgery: a randomized double-blind study. Indian J Pharmacol. 2013 Nov-Dec;45(6):581-6.

18. Joseph TT, Krishna HM, Kamath S. Premedication with gabapentin, alprazolam or a placebo for abdominal hysterectomy: Effect on pre- operative anxiety, post-operative pain and morphine consumption. Indian J Anaesth. 2014 Nov-Dec;58(6):693-9.

