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Research Article

The effect of gabapentin premedication on pain and anxiety during cataract surgery under peribulbar block

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KEYWORDS

Peribulbar block;
Premedication;
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Abstract *Background:* The principal goal of sedation during eye surgery is to keep the patient calm and comfortable without depression of the protective airway reflexes or affecting the hemodynamics. The aim of the present study was to evaluate the effect of oral gabapentin premedication on anxiety and pain during cataract surgery done under peribulbar block.
Material and methods: In this double blinded placebo controlled study, 60 patients scheduled for cataract surgery under peribulbar block were randomly allocated into two groups. In the gabapentin group (n = 30), patients were premedicated 2 h before peribulbar block by 1200 mg oral gabapentin capsules. In the placebo group (n = 30), patients were premedicated 2 h before peribulbar block by oral placebo capsules. Verbal pain score (VPS), sedation score, verbal anxiety score (VAS), respiratory rate, oxygen saturation, heart rate, blood pressure and side effects were recorded.

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Results: VPS was low in the gabapentin group versus the placebo group after the block till discharge ($P < 0.01$). VAS for anxiety was low in the gabapentin group versus the placebo group 1 h after premedication till discharge ($P < 0.01$). The heart rate and blood pressure were high in the placebo group versus the gabapentin group from arrival to the operating room till discharge. No side effects were recorded.

Conclusion: Premedication with 1200 mg oral gabapentin reduces anxiety and pain during cataract surgery done under peribulbar block without producing side effects.

1. Introduction

Cataract extraction surgery is the most common ophthalmic surgery and commonly done under regional anesthesia [1]. Although regional anesthesia for ophthalmic operations provides clear immobile field with good patient and surgeon cooperation, appropriate sedation may be required to relieve the patient anxiety and pain on performing the block and during the operation [2].

The goal of sedation in conjunction with regional anesthesia is to achieve patient's comfort without depression of the protective airway reflexes and to maintain stable hemodynamics throughout the operation [3].

Intravenous sedation is commonly used for eye surgery but deep sedation, respiratory depression and hemodynamic instability are the drawbacks that should be avoided by careful dose titration and close monitoring of the vital signs and degree of sedation [4].

Gabapentin was first introduced into clinical practice in 1993 for the treatment of refractory seizure in conjunction with other antiepileptic drugs. Gabapentin was proven to have good role in management of chronic pain, postoperative pain management, preemptive analgesia, attenuation of the hemodynamic response to endotracheal intubation, reduction of postoperative nausea and vomiting, and in reduction of perioperative anxiety and postoperative delirium [5].

The aim of the present study was to evaluate the effect of oral gabapentin premedication on the anxiety and pain during cataract surgery done under peribulbar block.

2. Material and methods

The present study is a randomized double blinded placebo controlled study. After approval of the ethical committee of El Menoufiya University hospital, 60 different patients of both sexes, American Society Of Anaesthesiologists (ASA) I and II physical status, their age between 20 and 70 years and scheduled for cataract extraction under peribulbar block were included in the study. A written informed consent was taken from all patients. Patients excluded from the study were those with hepatic or renal impairment, coagulation disorders, chronic psychotropic medications, morbid obese patients and with the history of allergy to the study drug or local anesthetics used. Patients were randomly allocated into two groups, 30 patients in each. Randomization was done using closed envelope method and the patient was asked to choose one envelope. In the gabapentin group patients were premedicated by 1200 mg oral gabapentin (Gaptin 400 mg/capsule. Deltapharm, Co., Egypt) 2 h before surgery. In the placebo group (control group) patients were premedicated by placebo capsules 2 h before surgery. Placebo capsules were prepared by evacuating the capsule of gabapentin and filling it with sugar to achieve the blindness of the nurse or the observer about the drug used in both groups. No sedation was given to any patient in the study. All patients were monitored for heart rate, non invasive blood pressure, oxygen saturation and respiratory rate (Nihon Khoden, Japan) and recorded before premedication, 1 h after premedication, on arrival to the operating room (OR), 1 min after performing the block, intraoperatively, every 5 min from the start of the operation and at discharge of the patient from the recovery room. Peribulbar block was performed by a single ophthalmologist blinded to the group allocation. Local anesthetic drops were instilled into the eye to be operated on. Under strict sterilization, a 23-G, 25 mm long needle (Mascomid, Egypt) was inserted through the conjunctiva as far laterally as possible in the inferotemporal quadrant, between the middle and lateral third of the lower orbital rim. Once the needle is under the globe, it was directed along the orbital floor, passing the globe equator to a depth controlled by observing the needle hub junction reach the plane of the iris. 5 mL of local anesthetic was injected slowly. Local anesthetic injected was a mixture of 1:1 solution of 2% lidocaine (Sigma pharmaceuticals, Egypt) and 0.5% bupivacaine (Al-Debeiky pharma, Egypt). Firm intermittent pressure was applied for 15 min for equal distribution of the anesthetic agent and to prevent retrobulbar hemorrhage. Pain, anxiety and sedation were assessed at the following intervals: before premedication, 1 h after premedication, on arrival to OR, 1 min after peribulbar block then every 5 min intraoperativelly from the start of the surgery and at discharge of the patient from the recovery room. Pain was assessed by verbal pain score (VPS) where 0 = no pain, 100 = the worst pain imaginable. Anxiety was assessed by verbal anxiety score (VAS) where 0 = not at all anxious, 100 = extremely anxious [6]. Sedation was assessed by a scale from 1–5, 1 = completely awake, 2 = awake but drowsy, 3 = asleep but responsive to verbal commands, 4 = asleep but responsive to tactile stimulus, 5 = asleep and not responsive to any stimulus [7]. The patient cooperation during performing the block was assessed according the following scale: 0 = movement of limbs, head and trunk, 1 = slight movement of the arms, 2 = slight painful facial expression, 3 = completely calm. If the patient cannot tolerate the block fentanyl 0.5 ug kg^{-1} was given and recorded. At the end of surgery, the surgeon was asked about his satisfaction about the patient's condition during performing the block and during the operation according to the following scale: 0 = very bad, 1 = moderate, 2 = good. The overall patient satisfaction was recorded using verbal rating score (VRS) from 0 to 100 with 0 = not satisfied at all and 100 = completely satisfied. Side effects in the form of ataxia, confusion, respiratory

depression (respiratory rate < 8), deep sedation (sedation score = 5) and dizziness were recorded.

2.1. Power analysis

A power analysis was performed using a power of 90% and an α value 0.05. We assumed that the VAS for anxiety would be 40% in the gabapentin group after premedication and 60% in the placebo group after premedication with a standard deviation 20. The sample size was calculated to be 27 patients so we decided to include 30 patients in each group in the study. We used Graphpad Instat statistics program for power analysis.

2.2. Statistical analysis

Statistical analysis was done using SPSS program version 10. Patient characteristics operation data, heart rate and mean blood pressure comparisons between groups were done by the unpaired student *t*-test and data presented as mean ± SD. VPS,VAS, sedation score, patient satisfaction and cooperation scores and surgeon satisfaction scores were analyzed using the Mann–Whitney *U* test and data presented as median (25–75 inter-quartile range). Sex distribution, ASA status and incidence of patients required fentanyl were analyzed by chi square χ^2 test. *P*-value of <0.05 was considered statistically significant while *P*-value <0.01 was considered highly significant.

3. Results

The patient characteristics and operation data were presented in Table 1 with no significant differences between groups. The heart rate and mean arterial blood pressure (MABP) were significantly high from arrival to OR till patient discharge in the placebo group compared to the gabapentin group ($P < 0.01$) with no significant difference between the two groups in other periods of measurement (Table 2). The respiratory rate and oxygen saturation showed no statistically significant difference between the two groups at any time of measurement. As shown in (Table 3) The VPS was comparable between the two groups before premedication, 1 h after premedication and on arrival to OR ($P > 0.05$). VPS was high in the placebo group, 1 min after the block, in the intraoperative period and at the time of discharge compared to the gabapentin group ($P < 0.01$).VAS for anxiety was not significant before premedication between the two groups but it was statistically low in the gabapentin group compared to the placebo group, 1 h after premedication thereafter till the time of discharge from the recovery room (Table 3). Sedation scores, before premedication, showed no significant difference in both groups but in the gabapentin group, sedation scores were statistically high ($P < 0.01$) 1 h after premedication till the time of patient discharge compared to the placebo group (Table 4). Scores for patient cooperation during performing the block were 2(2–3) in the gabapentin group versus 1(0–2) in the placebo group with $P < 0.05$. Number of patients requiring fentanyl during performing the block was three patients in the gabapentin group ($n = 30$) and 12 patients in the placebo group ($n = 30$) with $P < 0.05$. Surgeon satisfaction scores during performing the block and during the operation were 2(1–2) in the gabapentin group versus 1(0–1) in the placebo group with $P < 0.05$. Overall patient satisfaction scores were 90(70–100) in the gabapentin group versus 60(40–70) in the placebo group ($P < 0.05$). No side effects were recorded in the present study.

Table 1 Patient characteristics and operation data.

	Placebo group $N = 30$	Gabapentin group $N = 30$	P value
Age (years)	61.32 ± 5.45	63.21 ± 4.78	0.97
Weight (kg)	66.40 ± 9.54	68.20 ± 8.89	0.98
Height (cm)	170.34 ± 10.45	169.56 ± 11.57	0.96
Sex (female/male)	9/21	8/22	0.72
ASA I/II	12/18	10/20	0.52
Duration of surgery (min)	20.42 ± 4.58	19.58 ± 3.83	0.66

4. Discussion

The present study showed significantly lower VAP scores after peribulbar block till discharge and lower VAS, 1 h after premedication and thereafter till discharge in the gabapentin group compared to the placebo group. Also lower heart rates and mean arterial blood pressure in the gabapentin group than in the placebo group from arrival to OR till discharge. No difference in respiratory rate between the two groups and no case of respiratory depression recorded. Surgeon satisfaction scores and patient satisfaction and cooperation scores were better in the gabapentin group compared to the placebo group. No side effects were recorded in the present study.

The mechanism of action of gabapentin is still unclear but its antihyperalgesic action is thought to be produced through its binding to $GABA_B$ receptor (gama amino butyric acid) [8]. Other mechanisms include: enhancement of N methyl D-aspartate current at GABAergic interneurons [9], blocking AMPA (a-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) recep tors in the spinal cord [10], activation of ATP (adenosine triphosphate) sensitive potassium channels leading to hyperpolarization [11] and binding to the $\alpha_2\delta$ subunit of voltage activated calcium channels [12].

In a metanalysis study done by Rachael and colleagues, on studying the effect of premedication using gabapentin on postoperative analgesia, they reported that, patients who received preoperative gabapentin showed lower pain scores during rest and movement and reduced total analgesic consumption. Also they concluded that, a dose of 1200 mg gabapentin was more effective in reducing the total analgesic consumption than 300 mg or 400 mg gabapentin [13]. In the Rachael and colleagues metanalysis study and in all studies they reviewed, general anesthesia was conducted either alone or with regional block and pain and anxiety were recorded in the postoperative period but in the present study the goal is to give regional anesthesia and to monitor intraoperative pain and anxiety without giving the patient general anesthesia. In the present study a dose of 1200 mg gabapentin was used which was reported in the Rachael and colleagues study to produce the most effective results in most studies.

Gabapentin is proved to be an effective anxiolytic drug in patients with psychiatric disorders [14,15]. De-Paris and colleagues reported that gabapentin reduced anxiety induced by simulated public speaking in human volunteers [16] in agreement to the present study results, Ménigaux and colleagues studied the effects of preoperative 1200 mg oral gabapentin on pain and anxiety after knee surgery and they reported,

Table 2 The heart rate and MABP changes in both groups. Data presented as Mean ± SD and compared by unpaired *t*-test.

Time	Placebo group $N = 30$		Gabapentin N = 30		P1	P2
	Heart rate	MABP	Heart rate	MABP		
Before premedication	88.33 ± 5.7	72.19 ± 9.60	85.44 ± 7.34	74.39 ± 8.88	0.08	0.36
1 h after premedication	86.89 ± 6.76	75.4 ± 6.05	85.32 ± 7.12	73.84 ± 7.67	0.38	0.38
On arrival to the OR	87.43 ± 9.67	80.59 ± 9.80	76.78 ± 8.45[a]	74.98 ± 8.90[a]	< 0.01	< 0.01
1 min after the block	90.36 ± 7.24	86.24 ± 5.56	78.54 ± 6.74[a]	76.54 ± 7.45[a]	< 0.01	< 0.01
5 min after start of surgery	85.53 ± 9.38	84.46 ± 7.38	74.18 ± 8.59[a]	75.93 ± 8.12[a]	< 0.01	< 0.01
10 min after start of surgery	83.19 ± 4.56	82.49 ± 5.87	72.56 ± 6.120[a]	76.71 ± 6.32[a]	< 0.01	< 0.01
15 min after start of surgery	82.20 ± 4.45	81.33 ± 5.63	73.23 ± 5.55[a]	74.78 ± 6.76[a]	< 0.01	< 0.01
At discharge	80.82 ± 3.47	81.47 ± 4.84	71.53 ± 4.23[a]	75.61 ± 5.42[a]	< 0.01	< 0.01

*P*1 = *P* value for heart rate comparison and *P*2 = *P* value for MABP comparison.
[a] High statistical significance $P < 0.01$.

Table 3 VAP scores for pain and VAS for anxiety. Data presented as median (25–75 inter-quartile range) and compared by Mann–Whitney *U* test.

Time	Placebo group $N = 30$		Gabapentin group $N = 30$		P1	P2
	VAP	VAS	VAP	VAS		
Before premedication	20 (20–30)	70 (60–80)	20 (20–30)	70 (60–80)	0.85	0.73
1 h after premedication	30 (20–32.5)	70 (50–80)	20 (10–30)	40 (30–50)[a]	0.14	< 0.01
On arrival to the OR	30 (20–32.5)	70 (60–90)	20 (10–30)	50 (40–60)[a]	0.17	< 0.01
1 min after the block	80 (60–80)	90(70–90)	40 (30–60)[a]	40 (40–60)[a]	< 0.01	< 0.01
5 min after start of surgery	70 (50–80)	80 (60–90)	40 (20–60)[a]	40 (30–50)[a]	< 0.01	< 0.01
10 min after start of surgery	70 (50–80)	80 (70–90)	40 (30–50)[a]	40 (30–50)[a]	< 0.01	< 0.01
15 min after start of surgery	70 (60–80)	80 (50–90)	30 (20–50)[a]	50 (40–80)[a]	< 0.01	< 0.01
At discharge	70 (70–80)	80 (60–80)	30 (30–50)[a]	50 (30–80)[a]	< 0.01	< 0.01

*P*1 = *P* value for VAP comparison, *P*2 = *P* value for VAS comparison.
[a] High statistical significance $P < 0.01$.

Table 4 Sedation scores presented as median (25–75 inter-quartile range) and compared by Mann–Whitney U test.

Time	Placebo group $N = 30$	Gabapentin group $N = 30$	*P* value
Before premedication	1 (1–1)	1 (1–1)	1.0
1 h after premedication	1 (1–1)	2 (1–2)[a]	< 0.01
On arrival to the OR	1 (1–1)	3 (1–3)[a]	< 0.01
1 min after the block	1 (1–1)	2 (1–2)[a]	< 0.01
5 min start of surgery	1 (1–1)	3 (2–3)[a]	< 0.01
10 min after start of surgery	1 (1–1)	3 (2–3)[a]	< 0.01
15 min after start of surgery	1 (1–1)	3 (1–3)[a]	< 0.01
At discharge	1 (1–1)	2 (1–2)[a]	< 0.01

[a] High statistical significance $P < 0.01$.

decreased pain scores, anxiety scores, total analgesic consumption and early functional recovery after knee surgery [17].

In contrast to the present study, Adam and colleagues studied the effects of a single dose of 800 mg oral gabapentin premedication before interscalene brachial plexus block for shoulder arthroscopy on the postoperative pain and reported that this single dose has no effect on postoperative pain or total postoperative analgesic requirements [18] but they used a smaller dose than that used in the present study.

In the present study sedation produced was mild and no case of deep sedation was recorded. These results proved the safety of the used dose of gabapentin.

Experimental studies and human studies showed that gabapentin had no direct effect on the cardiovascular system [19,20]. In the present study, the lower heart rate and blood pressure in the gabapentin group compared to the placebo group would be explained by an indirect effect of gabapentin through reducing pain and anxiety and consequently the accompanying hemodynamic response.

As regards side effects of gabapentin, no side effects are reported in the present study.

In conclusion, premedication with 1200 mg oral gabapentin reduces anxiety and pain during cataract surgery done under peribulbar block without producing side effects.

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