Comparison of Pregabalin and Placebo Effects in Treating Eye Pain Following Cataract Surgery by Phacoemulsification Method

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Abstract- Cataract surgery sometimes is associated with adverse effects, such as dryness, burning, and patient discomfort. This study evaluates the treatment of dry eye syndrome and pain caused by corneal damage following cataract surgery with pregabalin compared to placebo. In our double-blind clinical trial, a total of 60 cases were divided into two groups. The pain score was assessed by the Numeric Rating Scale (NRS), and the impact of pain and dryness on the patient's performance was evaluated by the Brief Pain Inventory (BPI). The patient's pain score was evaluated postoperatively and followed for six weeks after the procedure. After the sixth week of the study, NRS, BPI, and photophobia in the pregabalin group were significantly different from the placebo group. Pregabalin can significantly reduce chronic and resistant eye pain after cataract surgery.

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Keywords: Pregabalin; Eye pain; Cataract surgery

Introduction

Localized and immediate damage that activates the peripheral sensory nerve is the most common cause of eye pain after cataract surgery. This process of stimulation is called nociception, and its receptors are called nociceptors. Dry eye syndrome (DES) is a disturbance to the integrity of the eye surface, and sometimes patients experience persistent pain postoperatively (1-3). It has been shown that in case of injury to the surface of the eye, central sensitization will occur over time due to the activation of the inflammatory cascade, which will be followed by increasing sensitivity and led to neuropathic eye pain (4). Cataract surgery, conducted in a group of patients to correct refractive errors, is associated with adverse effects, such as dryness, burning, and patient discomfort (5-6). These symptoms can be considered part of dry eye syndrome. According to Roberts' research, at least 47% of new patients who were referred to the eye injury department and 94% of those who completed the questionnaires had symptoms of dry eye after cataract surgery (7). Symptoms of ocular neuropathic pain include allodynia, photophobia, dysesthesia, and hyperalgesia (4). Since ophthalmologists have so far failed to reach an agreement on the symptoms of corneal surgery to be nociceptive or neuropathic, there is only a topical treatment to alleviate the symptoms of DES, which is sometimes ineffective. As a result, considering the seriousness of the problem and its multifaceted effects on the quality of life of patients, we conducted a comparative study on the treatment of dry eye syndrome and pain caused by corneal damage following cataract surgery with pregabalin compared to placebo.

Materials and Methods

This double-blind clinical trial study was approved by the appropriate Institutional Review Board (IRB) with ethics certificate number IR.TUMS.VCR.REC.1397.185 and written informed consent were obtained from all subjects. Patients with evidence of symptom-based dry eye syndrome, lack of dryness or eye or face pain before

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corneal surgery, absence of concomitant diseases that are mistaken for eye pain, and patients undergoing cataract surgery without concomitant procedures were included in this study. The exclusion criteria were lack of cooperation of the patient during the study, discontinuation of the drug due to complications or discontinuation of follow-up for more than two weeks, and Gastrointestinal, hepatic or renal complication throughout the study. Patients were referred by a corneal ophthalmologist and entered the study based on prolonged dry eye and pain for two months after surgery and non-response to local treatments. A total of 60 cases were included in this study (30 in each group) and randomly divided into two groups. After entering the study, patients were given an envelope containing the drug pregabalin or placebo. Placebo capsules that look exactly like pregabalin were used for placebo. Group A was initially given 50 mg of pregabalin before sleep and after one week every 12 hours daily, and group B received similar placebo capsules. Neither the physician nor the patient was aware of the envelope's contents, and the envelope was delivered by a third person who was aware of the envelope's contents. All patients were operated on by the same surgeon. The pain score was defined for the patient and assessed by the Numeric Rating Scale (NRS), and the impact of pain and dryness on the patient's performance with the Brief Pain Inventory (BPI), and patients were questioned for the photophobia. The patient's pain was assessed after the procedure and documented each week for up to 6 weeks. If the patient fails to continue care during care for any reason, or whether there are any side effects or the patient fails to continue medication, the treatment will be stopped, and the patient will be removed from the research. Local ophthalmic medications, such as artificial tear drops, twice a day in each eye in each drop was administered by an ophthalmologist for both groups. Our variables were analyzed by using Minitab 17 software (8).

Results

This study compared 60 patients in each group, placebo, and pregabalin, which included 30 patients in each group. The demographic characteristics of patients in the two groups are compared in Table 1. The average age, weight and gender, and duration of surgery were similar in both groups. The pain score, photophobia, and BPI score were not statistically significant between both groups at the start of the study and indicate that group randomization was appropriate in our study (Table 2) (Figure 1). At the end of the sixth week, the pain scores and BPI scores in the pregabalin group were significantly different from the placebo group (Table3) (Figure 2). The difference in photophobia was significant between the two groups at the end of the sixth week (Figure 3).

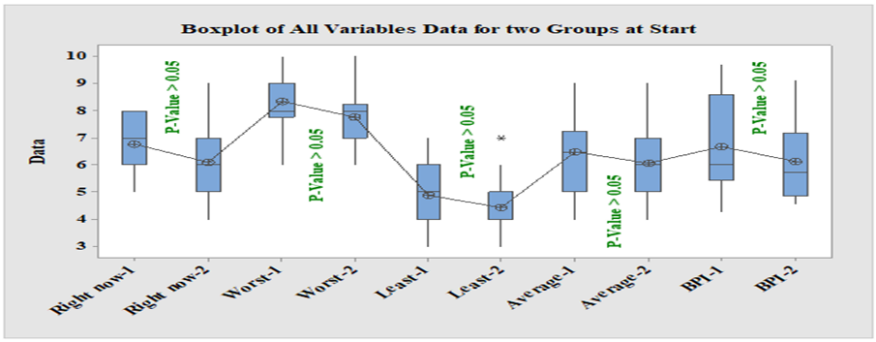
Table 1. Comparison of demographic variables and surgical time of the two groups

Variable	Group pregabalin	Group placebo	*P*
Age (year)	3.7±61.2	3.9±59.4	0.592
Gender (M / F)	(12 / 18)	(13 / 17)	0.90
Weigh (kg)	2 ± 73.4	1.7 ±73	0.702
Operation time(sec)	0.2 ± 14.4	0.2 ± 14.3	0.409

Table 2. Comparison of the variables of the two study groups at the start of the study

Variable	Group pregabalin	Group placebo	*P*
Right now, pain NRS	0.34 ±6.77	0.42 ± 6.10	0.065
Worst pain NRS	0.37 ± 8.33	0.38 ± 7.77	0.081
Least painNRS	0.32 ± 4.90	0.33 ±4.43	0.100
Average pain NRS	0.41 ± 6.50	0.42 ± 6.07	0.214
BPI Average	0.50 ± 6.69	0.44 ± 6.12	0.155

NRS: numerical rating scale, BPI: brief pain inventory



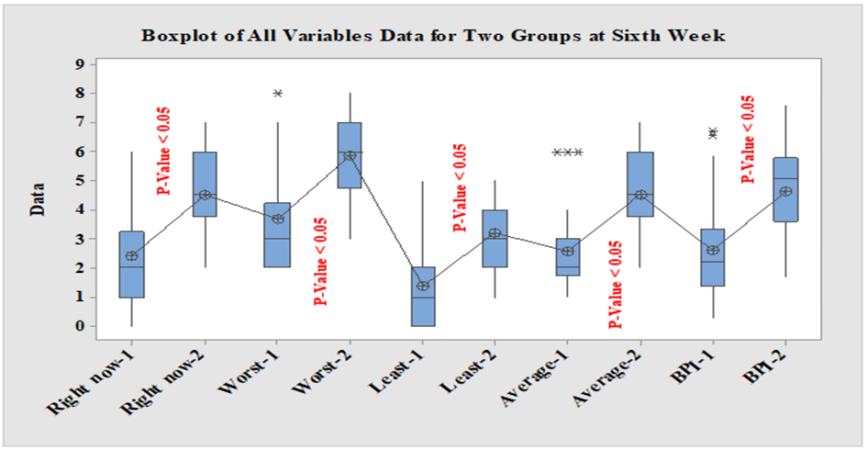
(One-Way Analysis of Variance & Paired t for the Mean by Minitab 17)

Figure 1. Box plot of NRS and BPI for two groups (1 and 2 means pregabalin and placebo group respectively) at the start at the confidence level % 95

Table 3. Comparison of the variables of the two study groups after the sixth week

Variable	Group pregabalin	Group placebo	*P*
Right now, pain NRS	0.47 ± 2.40	0.41 ± 4.53	000,0
Worst pain NRS	0.49 ± 3.67	0.47 ± 5.87	000,0
Least pain NRS	0.44 ± 1.37	0.37 ± 3.20	000,0
Average pain NRS	0.45 ± 2.57	0.40 ± 4.50	000,0
BPI Average	0.50 ± 2.91	0.49 ± 4.63	000,0

NRS: numerical rating scale, BPI: brief pain inventory



(One-Way Analysis of Variance & Paired t for the Mean by Minitab 17)

Figure 2. Box plot of NRS and BPI of two groups (1 and 2 means pregabalin and placebo group respectively) at 6th week at the confidence level % 95

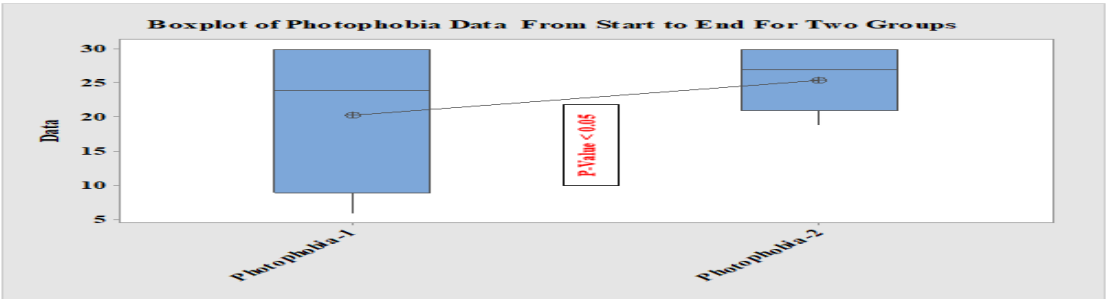


Figure 3. Display the photophobia box plot of the two groups studied from the beginning to the end of the research at the confidence level % 95

Discussion

There have been many studies on eye pain, especially those following surgery. Charles *et al*., used local anesthetics, pads, and bandages to control eye pain following superficial eye injuries and used Novocain for sphenopalatine ganglion block. They found that injections in sphenopalatine treated eye pain with the short onset and for the long time period, but it was not a safe method. By this method, blepharospasm and photophobia are eliminated, and the eye pain was reduced. They concluded that injections should be repeated every few weeks (3). Shah-Desai *et al*., indicated that uncontrollable eye pain could be relieved with local steroids, bandages, and contact lenses; however, these methods may be associated with an increased risk of eye infections. They also said that the procedure sometimes causes retrobulbar hematoma, conjunctival cysts, and eye pain, but this method could show pain relief for 6 to 15 weeks (9). Matsuura *et al*., believed that the pain that occurs after eye surgery does not improve with anti-inflammatory drugs, and the sphenopalatine block can be a good alternative and relieve eye pain for a long time (10). W H *et al*., believed that the use of diclofenac with or without topical steroids following LASIK could cause corneal damage (11). Hyung Cho *et al*., used non-steroidal anti-inflammatory (NSAIDs) drugs to treat postoperative eye pain and concluded that COX2 inhibitors were even more important than steroids in treating eye pain following eye surgery (12). Stephen Smith *et al*., Concluded that the use of Dfluprednate as a strong steroid solution is very effective in treating eye pain and postoperative inflammation and can be used 24 hours before surgery (13). In a pilot study, M Joshaghani concluded that homatropine as an eye drop was very effective in relieving postoperative pain (14). Galor *et al*., identified that anti-inflammatory drugs and topical or oral antibiotics could control dry eye syndrome, but the approach to it is very complicated due to its neuropathic potential (15,16). Moreover, Rajpal *et al*., showed that the use of topical anti-inflammatory drugs such as bromfenac eye solution could inhibit COX due to its penetration into the eye tissue and be useful in the treatment of postoperative eye pain (17). Aqdam *et al*., used homatropine and diclofenac eye solutions in the treatment of postoperative eye pain and concluded that diclofenac was much more effective in treating these pains than hemotropin (18). Levit *et al*., In their study, looked at the neuropathic role of eye pain and used antiepileptic drugs such as gabapentinoids in the treatment of central sensitization and control of these pains (4). Toruri *et al*., used cannabinoids in the treatment of eye pain and inflammation following PPK and concluded that these agents could play an important role in reducing postoperative eye pain (19). The study of Mcmonnies and colleagues showed that dry eye syndrome did not respond to treatment for tear secretion disorders, and this could confirm the role of neuropathic involvement (20). The use of pregabalin to control pain caused by surgery on the corneal surface was noticed because of reducing people's pain and decreeing the need to use other analgesics, increase in satisfaction, and the reduction in costs. Pregabalin is an analog of gamma-aminobutyric acid (GABA) and reduces neuropathic pain. The mechanism of action is a high synaptic attachment to the voltage gate-dependent calcium channels of the central nervous system, which inhibit the excess stimulation of neurons (21). Unlike traditional analgesics, which are nociceptive, gabapentoids like pregabalin and gabapentin decrease the stimulation of the posterior horn of spinal cord neurons caused by tissue damage compared to the period before afferent entry from tissue damage spot. On this basis, gabapentoids are recommended to relieve acute surgery pain. In recent years, pregabalin has been used as an adjuvant in order to manage postoperative pain. In our study, the severity of pain based on NRS and the effect of pain on individual performance based on BPI and photophobia rate based on questioning the patient in two groups over six weeks after cataract surgery were examined. It was concluded that pregabalin with 50 mg dose twice a day could play an important role in controlling long-term and resistant eye pain following cataract surgery. Fortunately, no specific drug side effects were observed during the study.

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