

Assessment of Ocular Neuropathic Pain Following Vitreoretinal Surgery using 23-gauge Sclerotomy

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Abstract

Purpose: To investigate the presence of persistent ocular pain after 23-gauge pars plana vitreoretinal surgery

Method: This is a prospective study including patients who underwent 23-gauge vitrectomy or silicone removal with local or general anesthesia. We evaluated the symptoms of ocular neuropathic pain before and two months after surgery using the Brief Pain Inventory (BPI) questionnaire, and the impact of reported ocular symptoms on quality of life. Correlation between ocular pain and factors such as patient demographics and underlying conditions were also assessed.

Result: Seventy-five patients with a mean age of 58.93 ± 12.05 years were evaluated. Forty-four (58.7%) were males. Sixty-seven (89.3%) patients underwent vitrectomy and eight had silicone removal surgery, all using 23-gauge instruments. There was an increasing trend in eye pain scores at two months after surgery which did not reach a statistical significance. However, the analgesic consumption increased from 4% before surgery to 17.3% two months after surgery. Patients who reported increased analgesic usage two months after surgery, scored worse in items of the quality-of-life questionnaire. In addition, patients who reported ocular and facial pain and photophobia before surgery had higher chances of analgesic consumption after surgery (p-value: 0.03, 0.003, and 0.001, respectively). Those who reported migraine headaches had higher chances of reporting eye symptoms, postoperatively (p-value: 0.041).

Conclusion: Surgeries involving 23-gauge incisions may not induce ocular neuropathic pain. However, increased use of analgesics after surgery was observed.

Introduction

According to International Association for the Study of Pain, pain is defined as an unpleasant sensory and emotional experience associated with or resembling that associated with, actual or potential tissue damage. [1] External painful stimuli such as trauma, surgery, or inflammation hurt nerve terminals and induce acute nociceptive pain which is the physiologic function of nociceptors. During a cornea or conjunctival surgery, an injury to the trigeminal nerve and its branches occurs. Also, the density of goblet cells in the conjunctiva will change.

This initial insult to the nerve may lead to a set of pathologic changes that cause an improper nerve signal and a sense of persistent pain in the absence of painful stimuli. Allodynia is defined as an experience of pain, foreign body sensation, tearing, or photophobia in response to normally benign stimuli such as blinking. [2] This ocular discomfort develops due to modification of the normal function of receptors and if continue for two months following surgery, can be considered as ocular neuropathic pain. It has several features that overlap with dry eye syndrome [3–6] In fact when ocular pain symptoms disproportionately outweigh the clinical signs, i.e. symptoms of pain, foreign body sensation, or irritation are present despite no or minimal objective signs of ocular surface defects or staining, and/or conjunctival injection, it is called ocular neuropathic pain.

Neuropathic ocular pain has sensory, psychic, cognitive, and behavioral elements. [2] Patients with genetic factors as well as fibromyalgia or psychiatric disease such as depression are more susceptible to develop persistent postoperative pain. [7, 8] Similar to dry eye, the prevalence increases with age and is more common in females. [4, 9]

In addition to laser refractive surgeries, other operations such as cataract surgery, lid surgery, botulinum toxin usage, and aesthetic surgery can also cause or aggravate symptoms of dry eye syndrome. [4] However, a few studies have been conducted on retinal surgeries.

In this study, we aimed to evaluate the frequency of symptoms of ocular neuropathic pain after vitreoretinal surgeries involving 23-gauge sclerotomy. We have also investigated the effect of different variables such as demographic factors and underlying conditions on post-operative symptoms.

Method

This study is a prospective observational case series conducted on patients who had surgeries involving 23-gauge (23G) sclerotomy incisions including pars plana deep vitrectomy and silicone removal from June 2019 until January 2020 in a tertiary educational hospital. In the operating room, for local anesthesia, a combination of 0.02 mg/kg Midazolam and 1 mcg/kg Fentanyl was administered for IV sedation; and after monitoring for blood pressure, peribulbar injection of Lidocaine 2% and Marcaine was performed. For general anesthesia, Midazolam 0.02 mg/kg, Fentanyl 2 mcg/kg, Atracurium 0.5 mg/kg and Propofol 2 mg/kg were employed. Two to three scleral incisions were placed 3 to 4mm posterior to the limbus, on inferotemporal, superonasal, and superotemporal locations. Vicryl 8 - 0 or 7 - 0 absorbable sutures were placed to close the sclerotomies, in occasional cases that were not watertight at the end of surgery. All surgeries were performed by two surgeons (NE or MI).

We assessed persistent pain in patients using the Persian version of the standardized brief pain inventory (BPI) questionnaire [10], immediately before surgery and two months after surgery. The items evaluated include frequency of deep eye pain, irritation, photophobia, tearing, foreign body sensation, deep head and facial pain, and numbness. All these symptoms were measured on an 11-point numeric rating scale (NRS). The average of all items, defined as overall eye symptoms, was calculated to evaluate the correlation of ocular manifestations with demographic characteristics and systemic conditions. All patients have also undergone slit-lamp examination and intraocular pressure measurement on day one, week one, month one, and month 2 after the surgery.

The effect of demographic characteristics (such as patient's age, sex, level of education), as well as background systemic conditions (such as diabetes mellitus (DM), hypertension (HTN), chronic back pain, musculoskeletal pain, migraine headaches, depression), and type of surgery, method of anesthesia on reported ocular symptoms and quality of life were investigated. Items that were questioned for this purpose were whether any disturbance has happened in general activity, mood, relationships, sleep, enjoyment of life, the ability of walking, the ability of performing normal work both outside and inside the home, and the patients rated them via an 11-point numeric scale.

Patients with difficulty in communication, history of psychiatric, cerebrovascular, or neurologic disease, alcohol consumption, or using illicit drugs, analgesics or opioids within the last 48 hours of the surgery were excluded from the study.

Written consent was obtained from patients who wish to participate. The collected data was analyzed using SPSS software. To evaluate the difference of mean between two independent groups, the Mann-Whitney U test and for comparison of more than two groups, the Kruskal-Wallis test was used. Correlation between quantitative variables was analyzed by the Spearman correlation test. To evaluate the association of a covariate with a dichotomous dependent variable, logistic regression was used. The significance level of the test was considered as 0.05.

Results

A total of 75 patients were enrolled in this study. Forty-four (59%) were male. The mean age of participants was 58.93 ± 12.05 (range: 35–82) years. Sixty-seven (89.3%) underwent 23G vitrectomy and 8 (10.7%) patients had 23G silicone removal surgery. Sixty (80%) patients received regional anesthesia (sub-tenon or retrobulbar block), and 15 (20%) received general anesthesia.

The level of education of participants was classified as illiterate (8%), not completed high school (29.3%), with a high school diploma (29.3%), and with a college degree (9.3%). The underlying condition at baseline included DM (37.3%), HTN (40%), musculoskeletal pain (38.7%), chronic back pain (38.7%), migraine headache (14.7%), and depression (4%).

No postoperative complications such as uveitis, corneal epithelial defect, punctate epithelial erosion, significant ocular surface inflammation, or conjunctival injection were observed during follow-up examinations.

Table 1 demonstrates the prevalence and intensity of pain-related symptoms pre- and post-operatively. Although the frequency of some symptoms such as deep eye pain, photophobia, and facial numbness increased after surgery, the difference was not statistically significant.

Table 2 demonstrates the quality-of-life scores at baseline and two months following surgery which did not show a significant alteration.

Preoperative scores for eye symptoms were correlated with postoperative scores including eye pain ($r:0.505$, $p\text{-value} < 0.001$), foreign body sensation ($r:0.419$, $p\text{-value} < 0.001$), tearing ($r:0.336$, $p\text{-value}: 0.003$), facial pain ($r:0.406$, $p\text{-value} < 0.001$). This positive correlation was not observed with photophobia ($r:0.214$, $p\text{-value}: 0.06$) and facial numbness ($r: -0.019$, $p\text{-value}: 0.870$).

Using systemic analgesics like non-steroidal anti-inflammatory drugs (NSAIDs) for eye symptoms increased from 4% at baseline to 17.33%, two months after surgery ($p\text{-value} = 0.004$). We found a positive correlation between post-operative analgesic usage and pre-operative eye pain score (OR: 1.24, CI95%:1.02–1.51, $p\text{-value}: 0.030$), photophobia (OR: 1.35, CI95%: 1.12–1.62, $p\text{-value}: 0.001$), and face

pain (OR: 1.28, CI95%: 1.08–1.52, p-value: 0.003), but such significance was not found with foreign body sensation (OR: 1.17, CI95%: 0.96–1.42, p-value: 0.112), and tearing (OR: 1.07, CI95%: 0.85–1.33, p-value: 0.537). (figure-1)

In a subgroup analysis, it was found that patients with analgesic consumption two months after surgery scored significantly worse in items of quality-of-life questionnaire such as disturbance in general activity (1.92 ± 0.84 vs 0.15 ± 0.75 , p-value: 0.021), mood (3.69 ± 4.35 vs 0.16 ± 0.77 , p-value < 0.001), normal work (2.23 ± 3.83 vs 0.10 ± 0.47 , p-value: 0.002), relationship with others (2.92 ± 4.13 vs 0.00 ± 0.00 , p-value < 0.001), sleep (2.46 ± 4.10 vs 0.15 ± 0.74 , p-value: 0.002), and life enjoyment (2.92 ± 4.11 vs 0.10 ± 0.65 , p-value < 0.001), postoperatively.

Preoperatively, there was no significant correlation between overall eye symptoms with patients' age (r: -0.45, p-value: 0.703), sex (male: 1.17 ± 2.12 versus female: 1.09 ± 1.55 , p-value: 0.799), and level of education (unlettered: 0.67 ± 0.57 , not completed high school: 1.53 ± 2.36 , high school diploma: 1.43 ± 2.24 , college degree: 0.29 ± 0.40 , p-value: 0.665). Similarly, overall eye symptoms at two months after surgery was not correlated with age (r: -0.142, p-value: 0.225) and sex (male: 1.10 ± 1.82 versus female: 1.30 ± 1.67 , p-value: 0.373), but significantly varied among different levels of education (unlettered: 0.92 ± 0.74 , not completed high school: 1.40 ± 1.36 , high school diploma: 1.63 ± 2.58 , college degree: 0.17 ± 0.44 , p-value: 0.044).

Patients' overall eye symptoms at baseline did not differ with the presence of systemic diseases such as diabetes and hypertension (0.84 ± 1.29 vs 1.90 ± 2.83 , p-value: 0.396). Similarly, two months after surgery, such association was not observed (1.17 ± 1.86 vs 1.21 ± 1.46 , p-value: 0.566).

The presence of musculoskeletal pain, migraine headache, and depression did not affect the overall eye scores in the preoperative period. Similarly, these factors except migraine headache (OR: 1.39, CI95%: 1.014–1.918; p-value: 0.041) were not correlated with overall eye scores, postoperatively.

The method of anesthesia (local or general) and type of surgery (vitrectomy or silicone oil removal surgery) did not affect eye symptoms two months after surgery (p-value > 0.05).

Table 1

Prevalence and intensity of eye symptoms, mean and SD of patient-reported pain score, and other symptoms before and after surgery.

Symptoms		Total %	Mild ^c %	Moderate ^d %	Severe ^e %	Mean score (0–10) (± SD)	P-value (Pre & post)
Eye pain	Pre-OP ^a	25.4	14.7	4	6.7	1.12 (± 2.5)	0.257
	Post-OP ^b	33.3	17.3	10.7	5.3	1.34 (± 2.55)	
Photophobia	Pre-OP	28	13.3	5.3	9.4	1.42 (± 2.97)	0.816
	Post-OP	30.7	13.3	8	9.4	1.45 (± 2.76)	
Eye irritation and foreign body sensation	Pre-OP	36	21.3	6.7	8	1.52 (± 2.65)	0.967
	Post-OP	34.7	20	5.3	9.4	1.52 (± 2.75)	
Tearing	Pre-OP	29.3	13.3	10.7	5.3	1.3 (± 2.47)	0.637
	Post-OP	29.3	13.3	8	8	1.33 (± 2.53)	
Deep head and face pain	Pre-OP	20	5.3	4	10.7	1.3 (± 3.03)	0.930
	Post-OP	20	4	5.3	10.7	1.26 (± 2.9)	
Facial numbness	Pre-OP	13.3	0	0	13.3	0.13 (± 1.15)	0.785
	Post-OP	26.7	13.35	0	13.35	0.17 (± 1.2)	
<p>a = Pre-OP: Before the surgery, b = Post-OP: Two months after the surgery <i>Eye symptoms = c: Mild = 1–3, d: Moderate = 4–6, e: Severe = 7–10</i></p>							

Table 2
Scores of quality-of-life at baseline and 2 months after surgery

Disturbance in items of quality of life	Pre-operative	Post-operative	P-value
	Mean score (0–10) ± SD	Mean score (0–10) ± SD	
General activity	0.48 ± 1.67	0.45 ± 1.81	0.833
Mood	0.96 ± 2.29	0.77 ± 2.31	0.369
Walking ability	0.22 ± 0.86	0.21 ± 1.22	0.832
Normal daily work	0.49 ± 1.64	0.46 ± 1.79	0.789
Relationship	0.61 ± 1.82	0.50 ± 2.00	0.634
Sleep	0.60 ± 1.77	0.54 ± 1.98	0.654
Enjoyment of life	0.81 ± 2.12	0.58 ± 2.06	0.377

Discussion

In the present study, we showed that following 23-gauge sclerotomies, ocular pain scores did not alter significantly. However, we observed a significant increase in analgesics consumption during two months following surgery. In addition, patients using analgesics after surgery have reported worse quality-of-life-related items. Patients who reported ocular and facial pain as well as photophobia before surgery had a higher chance of analgesic consumption after surgery.

Severing the enriched nerve plexus in surgeries involving corneal incisions has been shown to induce ocular neuropathic pain and dry eye symptoms. However, few studies exist that investigate ocular pain following surgeries involving solely scleral incisions. [11, 12]

The prevalence of chronic eye pain following cataract surgery has been reported as high as 34%. [13] Similarly, ocular neuropathic pain after refractive surgery is a well-known complication. [14–17] One study [17] reported that 20% of patients who underwent laser-assisted in-situ keratomileusis (LASIK) had symptoms of dry eye six months after surgery.

Compared with the cornea which has the highest nerve density in the body, the sclera is 100 times less sensitive due to its lower nerve density and the less exposed nerves which are located far from the surface. [18] The anterior sclera is innervated by two long posterior ciliary nerves which are branches of the ophthalmic division of the trigeminal nerve. [19] These nerves pierce the sclera adjacent to the optic nerve and travel anteriorly to around the ciliary body. The small gauge sclerotomies can injure these nerve endings. Additionally, conjunctival manipulation, desiccation, exposure to microscope light, and toxicity of povidone iodine or postoperative topical drugs can induce ocular surface abnormalities. A study

conducted in 2013, investigated ocular pain after conventional 20-gauge pars plana vitrectomy and reported that the frequency of ocular pain increased from 4.6% before surgery to 49.4% the day after surgery which then gradually decreased. In this study, 12.6% of patients reported persistent ocular pain at the final report which was 2 months after surgery. Symptoms of dry eye and foreign body sensation were found in 25% of patients. [11] The insignificance alteration of pain scores in our study may be related to the use of a smaller gauge device to pierce the sclera with induction of fewer nerve endings destruction. Interestingly, a retrospective study comparing 20-gauge vs 23-gauge vitrectomy, showed less pain and sleep disturbance, and fewer analgesics consumption in 23-gauge vitrectomy group one week after surgery. [12]

Although ocular pain scores did not alter significantly after surgery, a significant proportion of our patients used analgesics afterward. This subset of patients scored worse in the items of the quality-of-life questionnaire. In fact, analgesic consumption may have masked the ocular pain symptoms, in exchange for a decrease in quality-of-life. Previous studies have shown that the use of oral analgesics is an independent predictor of lower scores of quality-of-life [20]. Using NSAIDs is associated with fatigue, anxiety, and depression in patients with rheumatoid arthritis [21]. Based on our findings, higher scores of ocular and facial pain, as well as photophobia before surgery herald higher odds of analgesic use after surgery. Detection of risk factors and appropriate management of postoperative ophthalmic pain may reduce the number of analgesic-dependent patients and may result in a more satisfactory outcome.

Although it is reported that the presence of underlying conditions such as DM, HTN, musculoskeletal pain, and depression may affect the rate of reported pain symptoms [7, 8, 22], we did not find any correlation between baseline and postoperative eye pain in this regard. The only underlying factor that could be considered as a predictive factor for postoperative eye pain was found to be migraine headaches. It is known that in neuropathic pain syndromes, social, and psychiatric issues play a significant role in the perception of pain by the patients. [23]

Our study has several limitations. First, the sample size is relatively small. Second, we did not record the dose and frequency of analgesic used after surgery. Also, although the type of surgery was not associated with post-operative pain, it would be helpful to collect and analyze the data of intraoperative surgical steps such as endolaser photocoagulation or scleral indentation in future studies.

To date, many studies investigated postoperative pain in different anterior segment surgeries, but reports focusing on pain after retinal surgery are quite a few. In this study, we evaluated ocular neuropathic pain in retina surgeries involving 23-gauge sclerotomies. Although the increasing trend of ocular pain at two months after scleral incisions was not significant, an increase in analgesic consumption after surgery was observed which affects the quality-of-life scores in this subset of patients.

Declarations

Funding:

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Conflicts of interest:

The authors have no conflicts of interest to declare that are relevant to the content of this article.

Availability of data and material:

Raw data of this study are available on request from the corresponding author.

Code availability:

Not applicable.

Ethics approval:

The questionnaire and methodology for this study were approved by the Human Research Ethics committee of Tehran University of Medical Sciences.

Consent to participate:

Informed consent was obtained from all individual participants included in the study.

Consent for publication:

Patients signed informed consent regarding publishing their data.

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Figures

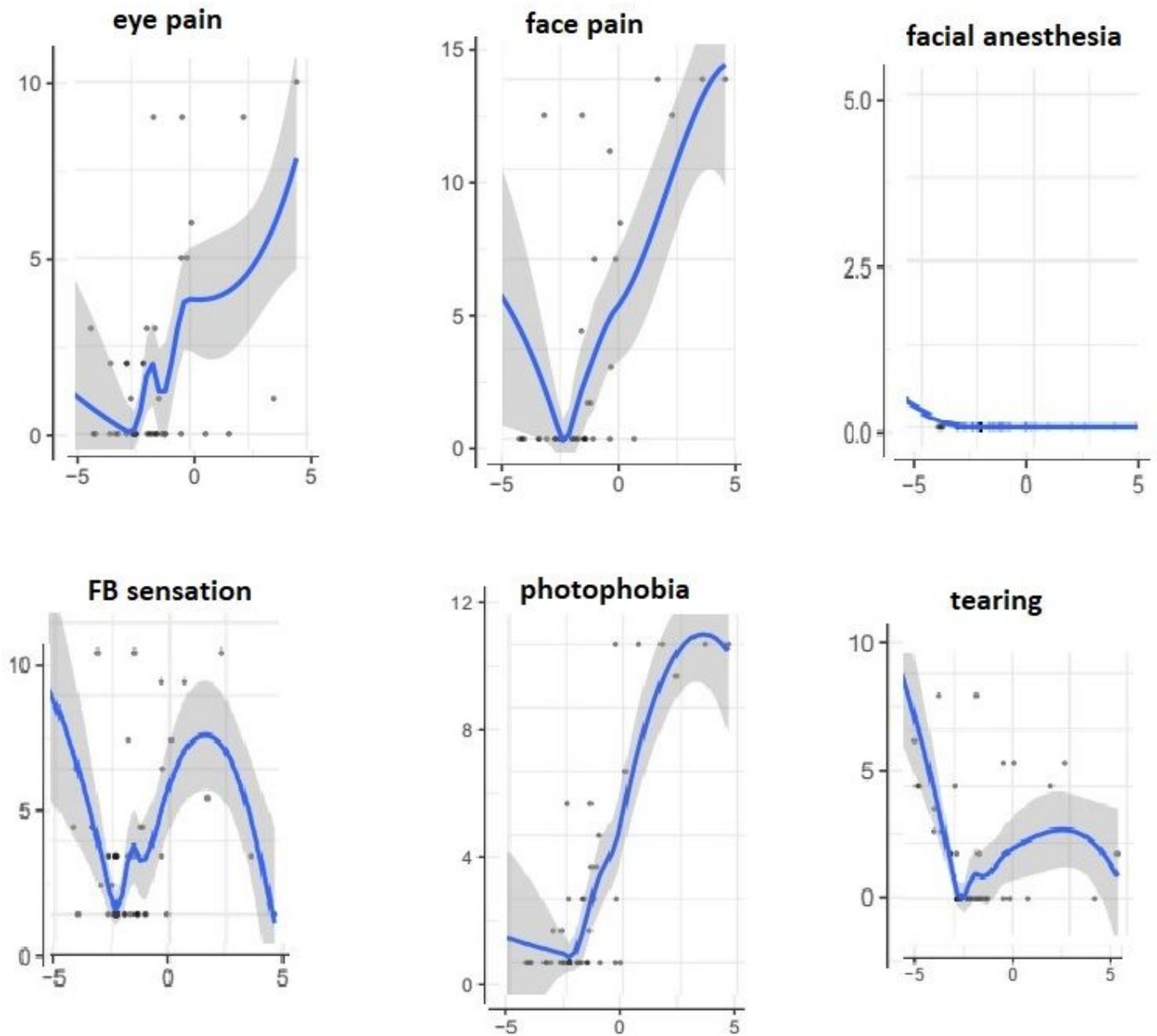


Figure 1

preoperative predictive factors of analgesics consumption in patients undergoing 23-gauge sclerotomy incision. The X-axis shows the logarithm of the odds of the outcome and the Y-axis shows the predictor value. It shows that factors including eye pain, face pain, and photophobia can predict analgesics consumption