Pain and Its Determinants in Photorefractive Keratectomy

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Purpose: To assess the determinants of early postoperative pain in photorefractive keratectomy.

Design: A prospective cross-sectional study.

Methods: One hundred four myopic-astigmatic patients undergoing bilateral standard photorefractive keratectomy were evaluated for early postoperative pain severity. On day 1 postoperatively, the level of pain experienced was reported by the patient on a visual analog scale of 0 to 10. At the preoperative interview, data were collected on clinical, demographic, and social characteristics to find potential pain determinants.

Results: The median reported pain level was 3. About 20% of subjects reported a pain score of 6 or higher, and 2.9% (6 eyes of 4 patients) reported the highest pain score. The presence of external eye inflammatory signs was associated with higher levels of pain (P < 0.001). Patients with a higher body mass index reported more severe pain (P = 0.006). An inverse association was found between pain and harmful lifestyle choices (P = 0.008). Demographic characteristics, history of contact lens wear, history of major operation, past experience of severe pain, knowledge about the operation's adverse effects, preoperative insomnia, preoperative anxiety, operative factors, and refractive indices were not related to the severity of pain experienced (all P > 0.05).

Conclusions: The association of pain with ocular surface inflammation suggests that inflammatory processes have a role in early postoperative pain, supporting the use of anti-inflammatory agents for pain management. Prescription of weight-adjusted dosages of analgesics is recommended on the basis of the association between severity of postoperative pain and body mass index.

Key Words: postoperative pain, photorefractive keratectomy, body mass index, ocular surface inflammation, harmful lifestyle choices


Photorefractive keratectomy (PRK) has been regaining popularity in recent years.\(^1\)\(^–\)\(^3\) Intense postoperative discomfort and pain and delayed visual recovery due to slow epithelial-stromal wound healing are the main disadvantages.\(^2\)\(^–\)\(^5\)

Patients generally experience moderate to severe eye pain in the first 24 to 48 hours following PRK.\(^1\)\(^,\)\(^6\) In this regard, various methods have been used for pain management: prescription of steroids\(^7\) and nonsteroidal anti-inflammatory drugs,\(^2\)\(^,\)\(^8\)\(^–\)\(^9\) eye irrigation with cooled balanced saline solution at the conclusion of the surgery,\(^1\)\(^0\)\(^–\)\(^1\)\(^2\) and even administration of diluted topical anesthetics.\(^1\)\(^3\) Recently, conflicting reports on the ameliorating effects of antineuralgic-anticonvulsant agents for postoperative pain have been published.\(^1\)\(^2\)\(^,\)\(^1\)\(^3\)

Postoperative pain has been attributed to ocular surface inflammation,\(^3\)\(^,\)\(^1\)\(^4\) disruption of the corneal epithelial layer,\(^1\)\(^4\) and exposure of the stromal nerve endings.\(^3\)\(^,\)\(^1\)\(^5\) Previous studies have shown an interplay between the severity of postoperative pain and some demographic and individual characteristics.\(^1\)\(^6\)\(^–\)\(^2\)\(^4\)

In the current study, we aimed to comprehensively evaluate potential determinants of early postoperative pain, including demographic characteristics, postoperative external eye signs, operative factors, and refractive indices in myopic-astigmatic PRK candidates.

MATERIALS AND METHODS

One hundred four candidates for standard PRK (208 eyes) at Farabi Eye Hospital—the largest eye center in Iran's capital, Tehran—were consecutively included in the study. Photorefractive keratectomy candidates were selected following preoperative ophthalmic examination, which included slit-lamp microscopy, keratometry and topography, manifest refraction, Schirmer test, tonometry, and fundus examination. Patients with diabetes mellitus, candidates for unilateral refractive surgery, those with astigmatism of more than 4 diopters (D), and those who failed to attend the first postoperative visit or who did not follow the planned medication regimen were excluded from the study. A comprehensive survey of clinical and nonclinical characteristics of the studied population was carried out. Preoperatively, patients were questioned about their demographic characteristics, history of contact lens wear, history of major operation, past experience of severe pain, knowledge about the operation's adverse effects, preoperative insomnia, and preoperative anxiety. It should be noted that this list was drawn from an extensive literature review on the subject of postsurgical pain.\(^1\)\(^6\)\(^–\)\(^2\)\(^4\)

Surgical Procedure

All patients underwent bilateral PRK, and the right eye was operated on first in every case. The epithelium was manually scraped following 20% alcohol exposure for 20 seconds; the alcohol excess was blotted away with a Weck-Cel cellulose sponge (Beaver-Visitec International Inc, Waltham, Mass). Then the eye was rinsed with a fixed volume of balanced salt solution so that the epithelium around the operation zone would not be disturbed. The loose epithelium was removed with a hockey knife. Stromal ablation of the cornea was done using a Nidek EC-5000 excimer laser set to an intended optical zone of 6.0 mm. Eyes with a cylinder of more than 1 D and/or an absolute spherical equivalent of 2.5 D or more were treated with 0.02% mitomycin C solution for about 15 seconds, which was followed by copious salt solution irrigation.

Finally, a bandage contact lens (ActiFresh 400; CooperVision, New York, NY) was placed. Antibiotic (chloramphenicol),

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The authors have no conflicts of interest to declare.

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Pain Measurement

On day 1 postoperatively, patients were inquired about significant ocular discomfort in terms of tearing, burning, photophobia, and foreign body sensation. In addition, ocular inflammatory signs including lid edema and conjunctival injection were recorded.

Statistical Analysis

We defined harmful lifestyle choices as any or all of the habits of alcohol consumption, cigarette smoking, and drug abuse (see Discussion). The aforementioned ocular discomfort symptoms (tearing, burning, photophobia, and foreign body sensation) were summed up, and an ocular discomfort scale (ODS) ranging from 0 to 4 was obtained. Also, we defined a scale of external eye inflammatory signs (inflammation score [IS]): 0, no significant conjunctival injection or lid edema; 1, either significant conjunctival injection or lid edema; and 2, significant conjunctival injection and lid edema.

Analysis was done with SPSS version 15 (SPSS, Inc, Chicago, Ill). All statistical tests were 2-sided, and \( P < 0.05 \) was considered as significant. The reported levels of pain in fellow eyes were significantly correlated (correlation coefficient = 0.71; \( P < 0.001 \), Spearman \( \rho \) test), and we used the average as the subjects’ ocular pain (Fig. 2). Because of the skewed distribution of pain (Kolmogorov-Smirnov test, \( P < 0.014 \), nonparametric tests were used for evaluating possible associations. Associations of pain with sex, harmful lifestyle choices, and recent habitual contact lens wear were evaluated with the Mann-Whitney \( U \) test. The Kruskal-Wallis \( H \) test was used to evaluate the relationship between pain and IS. Associations between pain and body mass index (BMI), age, and spherical equivalent (delivered energy) were assessed by linear regression. Variables with associations of 0.2 or less significance were entered into a linear regression model. Backward procedure was applied for variable selection, and the final model included the independent factors that were significant at \( P < 0.05 \).

RESULTS

Of 104 patients, 61% were female. The age range of the studied population was 19 to 45 years, with mean of 27 (SD, 5.26) years. The preoperative spherical equivalent by manifest refraction ranged from −1.25 to −7.00 D (mean, −3.6 D).

The median level of reported pain was 3, and the mean was 3.11 (SD, 2.86). About a quarter of patients were free of pain on day 1 postoperatively (VAS = 0), whereas just 2.9% scored their pain as the most severe they had ever experienced (VAS = 10). About 20% reported a pain score of 6 or higher. Figure 2 illustrates the distribution of postoperative pain. The median of ordinal ODS was 2 (ranging from 0 to 4). Of the whole studied eyes, 20% of them were symptom free (ie, ODS: 0). Foreign body sensation and tearing were the most common complaints of the patients, affecting 52% and 50% of the eyes, respectively. It is apparent in Figure 3 that the patients who had reported a more severe pain had more symptoms as well, and vice versa.

The pain score was directly associated with IS (\( P < 0.001 \)) and higher BMI (\( P = 0.006 \)). However, harmful lifestyle choices were found to be inversely associated with pain (\( P = 0.008 \); Table 1). Characteristics such as age, sex, marital status, and level of education did not show significant relationships with pain (\( P = 0.745, 0.883, 0.492, \) and 0.559, respectively). Preoperative factors, such as knowledge about the operation’s risks, preoperative insomnia, preoperative anxiety, a history of major surgery, experience of severe pain, and recent habitual contact lens wear, were not correlated with early postoperative pain (\( P = 0.478, 0.699, 0.465, 0.619, \) and 0.914, respectively).

Pain was not significantly associated with surgical factors such as spherical equivalent (ie, ablation depth or total delivered laser energy), a toric ablation profile, or mitomycin C use (\( P = 0.888, 0.408, \) and 0.917 respectively).

FIGURE 1. The template of VAS used to ascertain the level of pain.

FIGURE 2. Pain score distribution on day 1 after PRK in the operated eyes of 104 myopic-astigmatic patients using VAS (because of averaging, results are nonintegers as well).
Practically, this failed, so we resorted to defining a collective social history of the aforementioned variables. Girdler et al\textsuperscript{18} and Fertig et al\textsuperscript{17} reported a protective effect of smoking on pain, whereas Wee and Hopman\textsuperscript{28} showed that exposure to cigarette smoke is significantly related to higher reported levels of pain experienced in response to electrical stimulation. However, Shiffman and Jarvik\textsuperscript{29} reported no effect of smoking on pain thresholds. Likewise, 2 systematic reviews suggest contradictory associations between smoking and pain,\textsuperscript{30,31} and the debate remained unresolved.

Social habits of alcohol consumption and drug abuse are more common among smokers, and these may complicate any association of pain with smoking. It could be hypothesized that the inverse association could be due to better access of such patients to narcotics. We cannot assess this interaction, and in any future study, the investigators should put their best efforts to individually assess the effects and explore such interactions.

Habitual contact lens wear induces partial hypoesthesia.\textsuperscript{7}

We hypothesized that postoperative pain is lower in such candidates, but in the current study, we could not prove such an association. This can be attributed to the poor quantifiability of contact lens wear history. Objective baseline corneal sensation measurements with anesthesiometer are recommended for future studies.

An association of age with pain is controversial. McCarty et al\textsuperscript{3} reported no association, similar to our findings, but Payse et al\textsuperscript{2} reported a direct association in PRK patients. Henzler et al\textsuperscript{16} reported that women expressed more pain, an association that we failed to replicate.

We did our best to standardize the postoperative care medication through giving the patients a strict instruction on the use of analgesic/sedative (medications were included in the discharge package). However, the patients might have taken additional painkillers (see the discussion about social habits above).

The analysis of 2-eye data is notoriously troublesome in ophthalmic research. However, we adopted the least controversial approach, that is, used average of the pain score of fellow eyes for investigating associations and reporting pain distribution.\textsuperscript{34}

In conclusion, we demonstrated direct association between early post-PRK pain and BMI and ocular surface inflammation. This evidence supports the use of anti-inflammatory agents for pain control and prescription of higher doses of analgesics for obese patients.

| TABLE 1. Determinants of Early Postoperative Eye Pain Following PRK |
|-----------------|---------------------|------------------|
| **Determinants** | **Simple Regression** | **Multiple Regression** |
| | **Magnitude/Pain** | **Median** | **P** | **Coefficient (B)** | **P** |
| BMIs | $R^2 = 0.073$ | 0.006 | 0.284 | 0.001 |
| Harmful lifestyle choices | Positive | 1.5/10 | 0.008 | -0.244 | 0.006 |
| | Negative | 3.5/10 | 0.001 | 0.147 | 0.001 |
| Inflammatory signs | Positive | 4.5/10 | <0.001 | 0.417 | <0.001 |
| | Negative | 1.5/10 | 0.001 | 0.343 | model significance: <0.001 |

*Adjusted $R^2 = 0.343$, model significance: <0.001.
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