Efficacy of corneal cooling on postoperative pain management after photorefractive keratectomy: A contralateral eye randomized clinical trial

Siamak Zarei-Ghanavati a,*, Nastaran Nosrata, Negar Morovatdar b, Mojtaba Abrishamic, Pardis Eghbali a

a Eye Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
b Clinical Research Unit, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
c Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran

Received 19 December 2016; revised 19 April 2017; accepted 21 April 2017

Abstract

Purpose: To compare chilled and room temperature balanced salt solution (BSS) and bandage Contact Lens (BCL) on post photorefractive keratectomy (PRK) pain.

Methods: In a prospective, single-masked, controlled eye study, one hundred eyes of fifty patients were divided into two groups which received room temperature or chilled BSS and BCL in each eye, and compared for post-PRK pain. Three different pain evaluation systems were used to evaluate pain between the groups at 1 and 6 h and days 1, 2, 3, 5, and 7, postoperatively.

Results: 15 subjects were male (30%), and 35 were female (70%). The mean age was 29 ± 5 (20–40) y/o. The mean spherical equivalent (SE) of preoperative refractive error in both groups was not statistically significantly different (−4.18 ± 1.5 in chilled and −4.19 ± 1.7 in room-temperature groups, respectively; P = 0.94). The mean time of epithelial healing was 6.16 ± 1.7 (3–13) days in the chilled and 6.10 ± 1.59 (3–12) in the room temperature group (P = 0.32). Best corrected visual acuity (BCVA) at 1 month was 0.013 ± 0.03 (0–0.22) logMAR in the chilled group and 0.014 ± 0.04 (0–0.22) logMAR in the room temperature group, postoperatively (P = 0.84). No statistically significant difference was found between the two groups by any of the three pain scoring systems. No clinically important corneal haziness was found in the groups during follow-up.

Conclusion: Chilled BSS and BCL do not seem to be superior to room temperature in reducing post-PRK pain.

Keywords: Photorefractive keratectomy; PRK; Balanced salt solution; Bandage contact lens; Cooling; Pain

Introduction

For more than two decades, excimer lasers have been used for change of the corneal shape. In 1985 in Berlin, Theo Seilor treated corneal astigmatism in the first case of human eye with linear incisions which were created by an excimer laser. The first photorefractive keratectomy (PRK) was performed by Marguerite McDonald in 1988.¹ Surface ablation technique is one of the most common procedures for refractive error correction by excimer laser, especially in the range of mild to moderate myopia. Although photorefractive keratectomy (PRK) is the oldest of the surface ablation technique, with
advances in laser technology, its results have improved, so that it is still a strong arm for refractive surgeon for ametropia correction. The advantage of PRK to LASIK is that there is no need for a flap creation and subsequent complication of flap, but pain that is the main limitation of PRK still exists.

The main cause of pain after PRK is baring of the corneal nerve after epithelial debridement, and it remains until epithelial repair occurs. For decreasing pain after PRK, various medical and surgical methods were suggested including: using bandage contact lens (BCL), dilute-tetracaine eye drops, non-steroidal anti-inflammatory drugs (NSAIDs), topical morphine, trans-epithelial all surface laser ablation, flap-off EPI-LASIK, and LASEK.

It is suggested that irrigation of the corneal surface with chilled solution diminishes pain by decreasing the thermal effect of the excimer laser. This effect of cooling may be due to decreasing prostaglandins and other inflammatory mediators. Furthermore, it has been shown that irrigation of the ocular surface with chilled solution after PRK for high myopia may diminish corneal haziness and regression of myopia. However, these early studies were performed using older generation excimer lasers and postoperative regimen. Now, new excimer machines and effective pain medications are available. By using small flying laser spot, the temperature does not increase significantly during the ablation; therefore, inflammatory mediators might be released less in comparison with older laser machines. In this study, we evaluated the effect of chilled and room temperature balanced salt solution (BSS) and BCL on postoperative pain.

**Methods**

Patients with myopia and myopic astigmatism who presented to our Eye Hospital for refractive surgery were enrolled in this study. Inclusion criteria were age between 20 and 40 years, spherical equivalent (SE) refraction between −1.00 and −8.00 diopters (D) with 3.00 D or less astigmatic error, stable refraction for at least 1 year, and preoperative best corrected visual acuity (BCVA) of 10/10 or better.

Exclusion criteria for this study included the presence of any ocular pathologic condition impairing visual function, any corneal dystrophies or abnormalities, keratoconus or keratoconus suspect, any previous ocular surgery, glaucoma or glaucoma suspect, diabetes mellitus, auto-immune diseases, pregnancy, breast feeding, and moderate-to-severe dry eye. All patients discontinued contact lens wear at least one month and then fluorometholone 0.1% eye drop was started every 6 h and gradually tapered over 2 months. Preservative-free artificial tears were prescribed frequently in the first month and then tapered based on the ocular surface condition.

Three pain assessment systems were completed for each patient, including:

1. Visual Analogue Scale (VAS), consisting of a horizontal line, 10 cm in length, with a number from 0 to 10 in which, 0 is the lack of pain and 10 the most severe pain the patient experienced. The patient is asked to place a mark on the line that corresponds to the intensity of the pain he or she is experiencing.
2. Verbal Rating Scale (VRS), consisting of a series of words commonly used to describe pain (0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain, 4: disabling pain). The patient reads the words and chooses the one that best describes the pain he or she is experiencing. A score is then assigned to each word and used to measure pain levels.

3. Short-Form McGill Pain Questionnaire (SF-MPQ). The scale contains 4 subscales evaluating the sensory, affective and evaluative, and miscellaneous aspects of pain, responses to which comprise the Pain Rating Index, and a 5-point pain intensity scale.

Each pain questionnaire was separately completed for each eye by every patient, at 1 h, 6 h, day 1, day 2, day 3, day 5, and day 7 after surgery. In each visit before the examination, the pain questionnaires were completed via interview by the physician. Time of epithelial healing and BCVA after 1 month were recorded for each patient.

Statistical analysis

For statistical analysis, Snellen acuities were converted to logarithm of the minimum angle of resolution (logMAR) equivalent values. Statistical testing was performed with the Statistical Package for the Social Sciences, Windows version 16 (SPSS, Inc., Chicago, IL). Variables were expressed as mean ± standard deviation (range). Paired-T Test was used to compare mean SE between chilled and room-temperature groups. If pain scoring systems data did not have normal distribution (Kolmogorov-Smirnov test), then we used non parametric statistical tests. Wilcoxon Signed Rank test was used to compare the groups by each type of pain scoring systems. We used power analysis by PASS software. Our study power was 65%.

Results

Fifty patients were enrolled in the study (15 male and 35 female). The mean age was 29 ± 5 (range: 20–40) years old. Mean SE of preoperative refractive error in the chilled group was −4.18 ± 1.5 (−2D to −8.12D) diopters and −4.19 ± 1.7 (−2D to −8.25D) diopters in the room temperature group. There was no statistically significant difference between the two groups (p = 0.94) (Table 1).

The mean time of epithelial healing was 6.16 ± 1.7 (3–14) days in the chilled and 6.10 ± 1.59 (3–13) days in the room temperature group with no statistically difference between the two groups (p = 0.32). The mean BCVA one month after PRK were 0.013 ± 0.03 (0–0.22) logMAR and 0.014 ± 0.03 (0–0.22) logMAR in the chilled and room temperature groups, respectively, with no statistically significant difference between the groups (p = 0.84) (Table 2).

With regard to all three pain scoring systems, there was no statistically significant difference in pain between the groups at different times, while within the chilled and room temperature groups, a significant difference in pain intensity was observed in repeated time measurement (Table 3 and Figs. 1–3).

Discussion

Pain after PRK is unpleasant for patients and is one of the limitations of this type of laser refractive surgery. Thus, control of pain after surgery is crucial for patient satisfaction. Moreover, the side effect of PRK seems to be due to overproduction of tissue mediators such as collagen type III and heat shock protein-70. In this situation, increased temperature could have a significant role. To reduce postoperative pain, some surgeons believe that cooling the cornea with chilled BSS reduces postoperative pain. This kind of treatment that is named chilling or cooling therapy is used for decreasing pain and swelling after trauma to musculoskeletal system for decades, but can be annoying for patients. Some studies that show the role of chilling in other fields of medicine. It was shown that cooling the wound after burn decreases the intensity of tissue destruction. In addition, there is experimental evidence that shows after trauma, hypothermia decreases other pathophysio logic sequence such as ischemia, apoptosis, oxidative stress, inflammation, and edema. The advantage of chilling is controversial. Kitazawa et al showed that chilling decreased postoperative pain one day after PRK. Another study showed cooling PRK effectively reduced postoperative pain after PRK without any
Table 3
Repeated measurements of pain scoring systems in the chilled and room temperature groups.

<table>
<thead>
<tr>
<th>Pain scoring system</th>
<th>Study group</th>
<th>Times</th>
<th>1 h (mean ± SD)</th>
<th>6 h (mean ± SD)</th>
<th>1 day (mean ± SD)</th>
<th>2 days (mean ± SD)</th>
<th>3 days (mean ± SD)</th>
<th>5 days (mean ± SD)</th>
<th>7 days (mean ± SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VAS mean (SD)</td>
<td>Chilled</td>
<td>5.32 (3.53)</td>
<td>4.10 (3.64)</td>
<td>1.70 (2.24)</td>
<td>2.34 (2.64)</td>
<td>1.16 (1.90)</td>
<td>0.64 (1.50)</td>
<td>0.18 (0.71)</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Room temperature</td>
<td>5.40 (3.46)</td>
<td>3.78 (3.42)</td>
<td>1.72 (2.13)</td>
<td>2.30 (2.71)</td>
<td>1.04 (1.66)</td>
<td>0.62 (1.39)</td>
<td>0.26 (0.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
<td></td>
<td>0.62</td>
<td>0.25</td>
<td>0.87</td>
<td>0.46</td>
<td>0.93</td>
<td>0.99</td>
<td>0.59</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VRS mean (SD)</td>
<td>Chilled</td>
<td>1.82 (1.15)</td>
<td>1.74 (1.19)</td>
<td>0.94 (0.91)</td>
<td>0.98 (0.86)</td>
<td>0.58 (0.78)</td>
<td>0.28 (0.53)</td>
<td>0.14 (0.40)</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Room temperature</td>
<td>1.94 (1.13)</td>
<td>1.66 (1.13)</td>
<td>1 (0.88)</td>
<td>0.96 (0.87)</td>
<td>0.56 (0.78)</td>
<td>0.28 (0.64)</td>
<td>0.16 (0.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
<td></td>
<td>0.24</td>
<td>0.3</td>
<td>0.42</td>
<td>0.65</td>
<td>0.76</td>
<td>0.99</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MPG mean (SD)</td>
<td>Chilled</td>
<td>2.12 (1.46)</td>
<td>1.70 (1.26)</td>
<td>0.82 (0.94)</td>
<td>0.96 (0.85)</td>
<td>0.50 (0.73)</td>
<td>0.20 (0.40)</td>
<td>0.12 (0.38)</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Room temperature</td>
<td>2.18 (1.45)</td>
<td>1.64 (1.22)</td>
<td>0.80 (0.83)</td>
<td>0.98 (0.89)</td>
<td>0.46 (0.67)</td>
<td>0.26 (0.63)</td>
<td>0.24 (0.59)</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
<td></td>
<td>0.65</td>
<td>0.38</td>
<td>0.73</td>
<td>0.7</td>
<td>0.52</td>
<td>0.33</td>
<td>0.08</td>
<td></td>
</tr>
</tbody>
</table>

VAS = visual analog scale; VRS = verbal rating scale; MPG = McGill Pain Questionnaire.

* Friedman Test.

b Paired T test or Wilcoxon Signed Rank test.

Fig. 1. Mean of visual analogue scale (VAS) scoring system during follow-up. There is no statistically significant difference between the groups at different time points.

Fig. 2. Mean of verbal rating scale (VRS) scoring system during follow-up. There is no statistically significant difference between the groups at different time points.

additional adverse effect. However, another study by Neuffer et al did not find significant differences in pain between the groups at any time point during the first five days after surgery.11

In this study, we compared chilled and room temperature BSS on postoperative pain with several pain scoring systems, and found no difference in pain reported by the patients. In addition, there was no difference in the BCVA after one-month postoperatively and time of epithelial healing between the two groups.

Although pain, especially severe pain, might create a widespread response in the brain, a contralateral design could have some limitation. However, we believe that the use of different pain scoring systems could help to detect real differences between the groups. In addition, as intensity of postoperative pain varies significantly between individuals, contralateral eye study design is very helpful to reduce inter-individuals’ variabilities. As we did not find any differences between the groups by using different pain scoring systems, we can conclude that chilling system has a minimal role in reducing pain after PRK.

Studies supporting the use of chilled saline irrigation in PRK to prevent pain and corneal haze are primarily from the 1990s and are based on outdated laser technology and surgical methods. Using new generations of excimer laser machines which induce less temperature rise benefiting small flying spot and sophisticated laser delivery algorithms might eliminate the need of cooling system during operation by applying chilled BSS and BCL.

This study has some limitations. Our study was a contralateral study, however, conducting a randomized clinical trial including both eyes of each patient in each study group, could be confirmatory for our results.

In this study, we did not find any significant difference between the chilled and room temperature groups in pain intensity evaluated by different scaling systems. Maximum pain was at 1 h postoperatively, and the pain decreased over time. There was no difference in corneal epithelial repair, corneal haziness, and BCVA between the groups.

References


