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Original research

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

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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 patients 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) logarithm of the minimum angle of resolution (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) on human 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 PRK is the oldest of the surface ablation technique, with advances in laser technology,

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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,[1] non-steroidal anti-inflammatory drugs (NSAIDs),[2,3] homatropine eye drops,[4] topical morphine,[5] transepithelial all surface laser ablation,[6] flap-off EPI-LASIK,[7] and LASEK.[8]

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.[9] 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 before refraction, topography, and aberrometric evaluation. We also excluded patients with a minimum corneal thickness less than 450 μm, calculated residual thickness less than 400 μm, and high-order wavefront root mean square (RMS) more than 0.50 μm in a 6 mm optical zone.

The study followed the tenets of the Declaration of Helsinki. All patients were appropriately informed before their participation in this study, and after a complete ophthalmic examination and a thorough discussion of the risks and benefits of the surgery, all participants gave written informed consent. We obtained full approval from the Ethics Committee of Mashhad University of Medical Sciences.

Before surgery, a detailed ocular examination was performed, including uncorrected visual acuity (UCVA), BCVA, slit-lamp examination, applanation Goldmann tonometry, indirect funduscopy, manifest refraction, cycloplegic refraction, keratometry (Topcon KR8800Auto-kerato-refractometer, Tokyo, Japan), TMS-4 Topography (Tomey, USA), scanning slit corneal tomography (Orbscan IIz − Bausch & Lomb, Irvine, CA). Snellen acuity charts were used to measure UCVA and BCVA. The visual acuities were converted to logarithm of the minimum angle of resolution (logMAR) for analysis.

One surgeon performed all surgeries using a flying-spot 193-nm excimer laser (Technolas217z, Bausch & Lomb, Irvine, CA) with a fixed pulse repetition rate of 100 Hz and a spot diameter of 1−2 mm. After sterile draping, the cornea was anesthetized with tetracaine 1% eye drops, and an eyelid speculum was placed. Ethyl alcohol 20% was then applied in a 9 mm well for 20 s, and the epithelium was removed with a hockey stick spatula.

Multidimensional rotational eye tracking was used during the ablation. The minimum optical zone was 6 mm, and equal optical zone was selected for both eyes of each patient. In all patients, a sponge soaked with mitomycin C 0.02% was applied over the ablated area for 5 s per each diopter of treatment. A BCL was placed following copious BSS irrigation of the ocular surface. The patients were randomly divided into two groups: one consisted of twenty-four and other was 26 patients. In the first group, BSS and BCL at room temperature (usually 21−23 °C) was applied to the right eye and chilled BSS and BCL (2−5 °C) to the left eye. In the other group, treatment was applied vice versa. Surgeons were unaware of the randomization. Then the ocular surface was irrigated with 30 cc BSS (chilled or room temperature). Finally, a drop of ciprofloxacin and a BCL (chilled or room temperature) were applied to the cornea, and speculum was removed.

Postoperatively, the patients were given levofloxacin (Oftaquix, Santen Pharmaceutical, Japan) for ten days and betamethasone 0.1% (Betasonate, Sina Daru, Iran) eye drops every 6 h. After complete re-epithelialization (usually on the fifth day), the BCL was removed. Betamethasone was used for 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 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 percent to detect a difference between two groups. Friedman test was used to compare repeated measures of pain scoring systems. Differences were considered statistically significant at a *P*-value of $\leq$0.05. Bonferroni correction was used for multiple comparisons for pain score systems, and *P*-value of less than 0.008 was considered statistically significance.

Table 1
Demographic characteristics of the patients.

Variable	Group (number)	Mean (SD)/%
Age	50	29 (5)
Gender	Female (35)	(70%)
	Male (15)	(30%)

SD: Standard deviation.

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 (−2 D to −8.12 D) diopters and −4.19 ± 1.7 (−2 D to −8.25 D) 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[3–12] 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.[1] 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.[9,10] 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.[11] There are 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.[12] In addition, there is experimental evidence that shows after trauma, hypothermia decreases other pathophysiologic sequence such as ischemia, apoptosis, oxidative stress, inflammation, and edema.[13,14] The advantage of chilling is controversial. Kitazawa et al showed that chilling decreased postoperative pain one day after PRK.[15] Another study showed cooling PRK effectively reduced postoperative pain after PRK without any

Table 2
Comparison of preoperative spherical equivalent (SE), one-month postoperative best corrected visual acuity (BCVA) and epithelial repair time in the chilled and room temperature groups.

	Chilled group (N = 50)	Room-temperature group (N = 50)	*P*-value
Preoperative spherical equivalent (Diopter) mean (SD)	−4.18 (1.5)	−4.19 (1.7)	0.94
Postoperative BCVA (logMAR) mean (SD)	0.013 (0.03)	0.014 (0.03)	0.84
Epithelial repair time mean (SD)	6.16 (1.7)	6.10 (1.59)	0.32

BCVA: best corrected visual acuity; SD: Standard deviation; logMAR: Logarithm of the minimum angle of resolution.

Table 3
Repeated measurements of pain scoring systems in the chilled and room temperature groups.

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

VAS: Visual analog scale; VRS: Verbal rating scale; MPQ: McGill Pain Questionnaire.
[a] Friedman Test.
[b] Paired T test or Wilcoxon Signed Rank test.

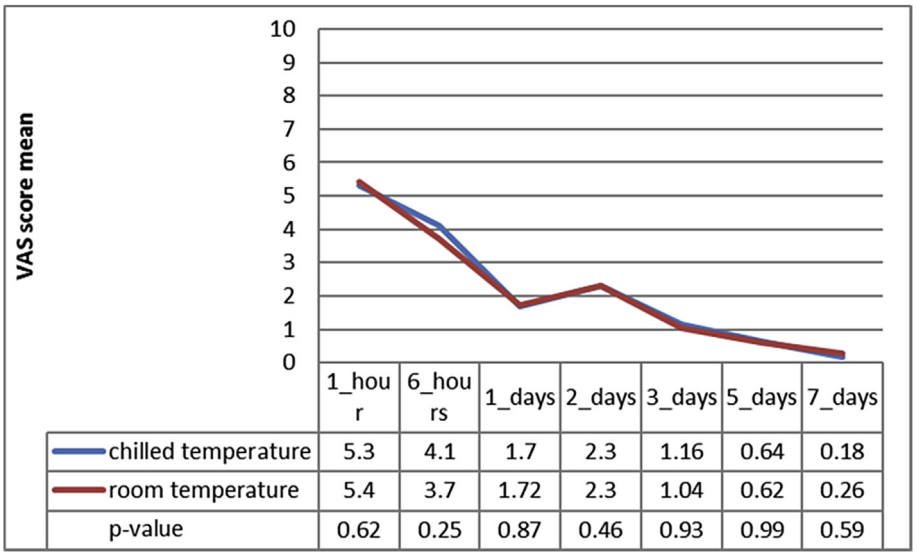


Fig. 1. Mean of visual analogue scale (VAS) scoring system during follow-up. There is no statistically significant difference between the groups at different time points.

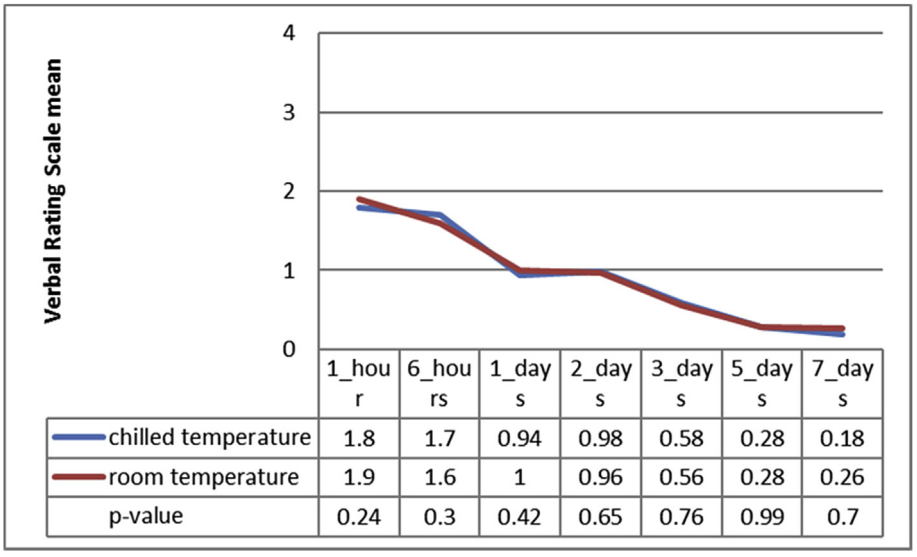
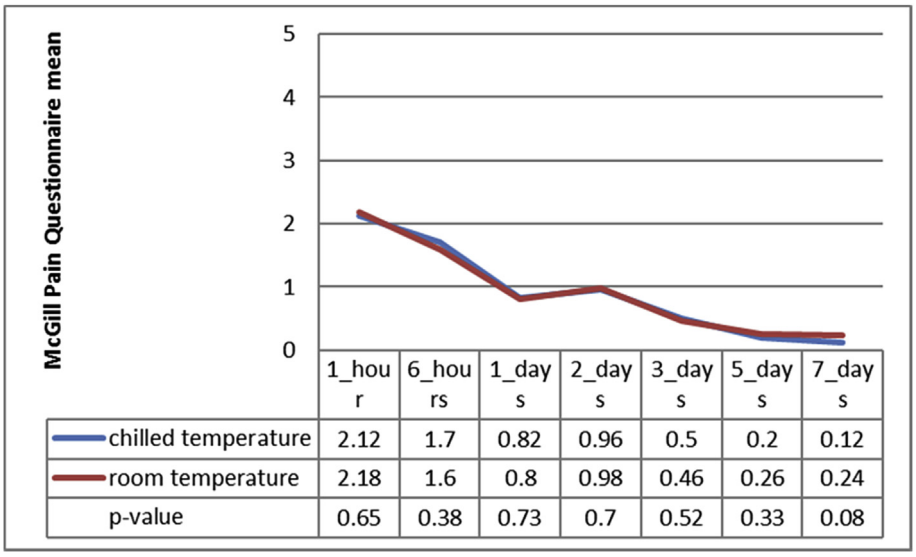


Fig. 2. Mean of verbal rating scale (VRS) scoring system during follow-up. There is no statistically significant difference between the groups at different time points.



	1_hour	6_hours	1_days	2_days	3_days	5_days	7_days
chilled temperature	2.12	1.7	0.82	0.96	0.5	0.2	0.12
room temperature	2.18	1.6	0.8	0.98	0.46	0.26	0.24
p-value	0.65	0.38	0.73	0.7	0.52	0.33	0.08

Fig. 3. Mean of McGill scoring system (MGS) during follow-up. There is no statistically significant difference between the groups at different time points.

additional adverse effect.[16] 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.

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