Original Article

Comparing the Effect of Autologous Serum versus Preservative-Free Artificial Tears after Photorefractive Keratectomy: A Contralateral-Eye Clinical Trial

Mandana Ahmadi *[1], MD; Zhale Rajavi [1], MS; Hossein Mohammad Rebie [2], MD

1- Negah Aref Ophthalmic Reseach Center, Negah Eye Hospital, Tehran, Iran.
2- Department of Ophthalmology, Torfeh Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

***Corresponding Author:** Mandana Ahmadi
E-mail: ahmadisurgen@gmail.com

Abstract

Purpose: To compare 20 % autologous serum (AS) with preservative-free artificial tears (PFAT) for epithelial healing and early outcomes after photorefractive keratectomy (PRK).
Patients and Methods: This was a prospective, contralateral-eye clinical trial including 60 myopic patients (120 eyes). In each patient, one randomly assigned eye received 20 % AS and the fellow eye PFAT post-PRK. Primary outcome was time to complete epithelial closure. Secondary outcomes included day-by-day postoperative pain, epithelial defect (ED) size, corneal haze, and uncorrected visual acuity (UCVA).
Results: Epithelial closure time did not differ between groups (AS 3.00 ± 0.33 vs. PFAT 3.03 ± 0.21 days; P=0.655). Mean Day-1 pain was numerically lower with AS overall (AS 3.28 ± 1.75 vs. PFAT 3.60 ± 1.83), and significantly lower among women (AS 3.39 ± 1.96 vs. PFAT 4.11 ± 2.05; P = 0.003). Pain declined to near-zero by Day-2 in both groups (AS 0.07 ± 0.31 vs. PFAT 0.08 ± 0.38). ED size was similar on Day-1 (AS 5.50 ± 0.73 vs. PFAT 5.56 ± 0.73) and Day-2 (AS 3.33 ± 0.60 vs. PFAT 3.47 ± 0.79). No eye developed haze. UCVA at 12 weeks was excellent in both groups (AS 9.93 ± 0.31 vs. PFAT 9.95 ± 0.22; P=0.705). One transient sub-epithelial infiltration (AS eye) resolved after stopping AS.
Conclusion: After PRK, 20 % AS and PFAT yield comparable epithelial closure (~3 days) and 12-week visual outcomes. AS may reduce early postoperative pain, particularly in women, warranting larger paired-eye trials to confirm this signal.

Keywords: Autologous Serum; Photorefractive Keratectomy; Artificial Tears; Epithelium; Healing; Pain; Postoperative; Mitomycin-C.

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Introduction

Over the past three decades, excimer laser refractive surgery has been widely implemented, primarily through photorefractive keratectomy (PRK), LASEK, and femtosecond laser–assisted in situ keratomileusis (FemtoLASIK). In all approaches, a corneal flap or epithelial layer is lifted and a controlled amount of stromal tissue is ablated to alter corneal curvature. Surface ablation techniques such as PRK and LASEK involve removal of a thinner epithelial layer, whereas FemtoLASIK creates a deeper flap that includes stromal tissue. FemtoLASIK has become the most popular refractive procedure, largely because it offers rapid visual recovery and greater postoperative comfort. Nonetheless, FemtoLASIK carries potential complications, including flap-related problems and postoperative ectasia.

For patients with thin corneas, PRK and LASEK remain the preferred options. However, the main disadvantages of surface ablation are significant postoperative pain during the first few days and slower visual rehabilitation. Postoperative management is therefore essential to control inflammation and promote epithelial healing, and typically includes topical steroids, preservative-free artificial tears, and therapeutic bandage contact lenses [1,2].

Autologous serum eye drops have recently emerged as a promising therapy for various ocular surface disorders. Prepared from the patient's own blood, autologous serum closely mimics the biochemical composition of natural tears and contains bioactive substances such as fibronectin, vitamin A, epidermal growth factor (EGF), transforming growth factor-β, platelet-derived growth factor, neuropeptides (e.g., substance P), and insulin-like growth factor-1. These components have epitheliotrophic and anti-apoptotic effects and accelerate epithelial cell migration and regeneration [3-5]. In addition, autologous serum has a pH and osmolarity comparable to natural tears, provides lubrication and nutritional support, and has bactericidal properties that reduce the risk of infection [6].

Clinical studies have demonstrated favorable outcomes with autologous serum in conditions such as dry eye disease and recurrent corneal erosions, with symptomatic improvement often commencing within the first 48 hours of treatment [6-8]. Because of its structural similarity to natural tears and its high concentration of growth factors, autologous serum has been proposed as an effective alternative to preservative-free artificial tears in accelerating epithelial healing after surface ablation procedures.

Despite its potential, limited data exist comparing autologous serum to conventional preservative-free artificial tears in patients undergoing PRK. Therefore, the present study aimed to evaluate the effect of autologous serum versus preservative-free artificial tear drops on epithelial defect healing in patients who underwent PRK surgery at Negah Ophthalmology Hospital.

Patients and Methods

This study is a controlled clinical trial conducted on sixty patients (120 eyes) who were candidates for PRK surgery at Negah Ophthalmology Hospital during 2021-2022. This study was approved by the Ethics Committee of the Islamic Azad University of Medical Sciences with the code (IR.IAU.TMU.REC.1399.029). Informed consent was obtained from all patients before entering the study.

Inclusion criteria included: age over 18 years, stable refractive error for at least six

months, spherical equivalent difference of fewer than two diopters between the two eyes, normal curvature of the cornea in Orbscan and topography, central corneal thickness above 480 microns, and absence of ocular and systemic diseases that prohibit refractive surgery (such as diabetes, autoimmune diseases, and uncontrolled thyroid diseases). Patients with dry eye, blepharitis, corneal diseases, glaucoma, and symptoms of keratoconus were excluded from the study.

Pre-operative examinations included medication records and complete ophthalmological examinations, uncorrected and corrected visual acuity, slit-lamp examination, eye pressure check, fundoscopy, and Tear Break-Up Time (TBUT). The Schirmer test was performed if TBUT was disturbed (less than 10 seconds). Corneal topography (Orbscan) and aberrometry were performed.

Before surgery, 20 cc of the patient's blood was taken and centrifuged; the serum was separated under completely sterile conditions and diluted with artificial tears (Sina Daru Tearlose) to a concentration of 20 %, and was given to the patient with dry ice after surgery.

Reporting followed CONSORT guidelines, and a flowchart of patient recruitment, allocation, follow-up, and analysis is presented in figure 1.

Surgical Technique

On the day of surgery, both eyes were anesthetized with one drop of tetracaine and

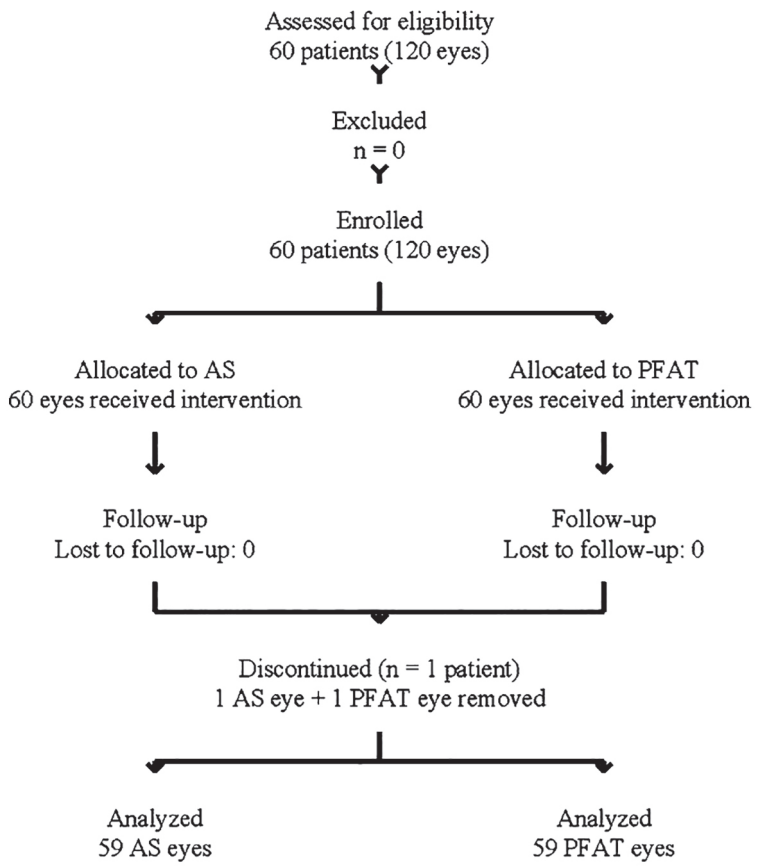

Figure 1: CONSORT flowchart of patient screening, enrollment, allocation, follow-up, and analysis

washed with 5 % diluted Betadine. Based on age, refractive error, astigmatism level, patient occupation, and corneal thickness, the laser profile was determined using the TENEO device (Technolas), and the Proscan and ZHT programs were used to perform the laser. The optical zone and the type of surgical program were selected the same for both eyes. Then, a speculum was placed, the epithelium was removed with a size of 8 to 8.5 mm, and excimer laser ablation was performed. Mitomycin 0.02 % was placed on the cornea for 10 to 40 seconds based on the refractive error and washed with 20 cc of cold BSS serum. A bandage lens (Bausch & Lomb) was placed on both eyes. One eye was randomly treated with autologous serum drops, and the opposite eye was treated with artificial tear drops (Artelac Advanced) and was registered in the patient's eye chart.

Autologous serum drops and artificial tears were administered as one drop every three hours for seven days, and then every six hours for fifteen days. Betamethasone drops (every eight hours for ten days), then Flucort (every twelve hours for fifteen days), and Chloramphenicol drops (every four hours for five days) were given to the patients. Patients were examined on the first, second, and third day, and in the first, third, and twelfth week, and the information was recorded. A pain ruler was used to record post-operative pain (0 = no pain, 10 = worst pain).

Statistical Analysis

SPSS version 26 software (IBM Corp., Armonk, N.Y., USA) was used for data analysis. Continuous variables were evaluated for normality. Paired t-tests (or Wilcoxon tests when non-normal) were used to compare outcomes between the two eyes. Categorical variables were analyzed using the chi-square test. A significance level of less than 5 % was considered.

Results

Sixty people participated in this study. The average age of the subjects was 19.28 ± 8.26 years. Among them, twenty-four (40 %) were male and thirty-six (60 %) were female. Twenty-nine right eyes (48.3 %) and thirty-one left eyes (51.7 %) received autologous serum as the intervention group; the fellow eyes were treated with preservative-free artificial tear drops as the control group. One patient developed mild, diffuse sub-epithelial infiltration in the eye treated with autologous serum on postoperative Day-2; autologous serum was discontinued, and complete recovery was achieved within two days. This patient was excluded from the study. So 59 eyes in AS group and 59 eyes in PFAT group were included in statistical analyses.

The average pre-operative refraction was -3.50 ± 1.72 D in the eyes receiving autologous serum and -3.54 ± 1.30 D in the eyes receiving artificial tears.

The average corrected myopia before surgery in the eye receiving autologous serum was -3.40 ± 1.75 D and -2.75 ± 1.61 D in the eye receiving artificial tears. The follow-up period was three to twelve months. All surgeries were completed without intraoperative complications. The average epithelial recovery time was 3.00 ± 0.33 days in the eyes treated with autologous serum and 3.03 ± 0.21 days in the eyes treated with artificial tears (Table 1), with no statistically significant difference (P = 0.655).

The average duration of mitomycin exposure was 29.17 ± 7.20 seconds in the autologous serum group and 28.33 ± 7.63 seconds in

Table 1: Comparison of lens removal time (recovery time) and visual acuity after treatment between intervention and control groups

Variable	Group	Mean ± SD	Difference (Mean ± SD)	P-value*
Recovery time (days)	AS	3.00 ± 0.33	0.03 ± 0.41	0.655
	PFAT	3.03 ± 0.21		
UCVA at 12 weeks (10-point)	AS	9.93 ± 0.31	0.02 ± 0.34	0.705
	PFAT	9.95 ± 0.22		

*Paired t-test

Table 2: Comparison of MMC exposure time between intervention and control groups

Variable	Group	Mean ± SD	Difference (Mean ± SD)	P-value*
MMC exposure time(seconds)	AS	29.1 ± 7.20	− 0.8 ± 3.34	0.059
	PFAT	28.33 ± 7.63		

*Paired t-test

the control group, which was not statistically significant (P = 0.059) (Table 2). The mean MMC exposure values did not differ significantly between the two groups (P > 0.05) (Table 2).

Across all eyes, Day-1 postoperative pain was numerically lower in the autologous serum group (3.28 ± 1.75) than in the artificial tear group (3.60 ± 1.83) (Table 3).

Postoperative pain trajectory: Pain peaked on Day-1 and declined rapidly by Day-2 in both groups (autologous serum 0.07 ± 0.31; artificial tears 0.08 ± 0.38), with minimal symptoms by Day-3. No patient reported pain from Day-4 onward.

Examination of visual acuity at twelve weeks showed a mean UCVA of 9.93 ± 0.31 in the autologous serum group and 9.95 ± 0.23 in

Table 3: Comparison of pain and ED size in ntervention and control groups on the first and second day

Variable	Time	Group	Mean ± SD	Difference (Mean ± SD)	P-value*
Pain (0–10)	Day-1	AS	3.28 ± 175	0.32 ± 1.75	0.035
		PFAT	3.60 ± 1.83		
Pain (0–10)	Day-2	AS	0.07 ± 0.31	0.02 ± 0.31	0.317
		PFAT	0.08 ± 0.38		
Epithelial defect (mm²)	Day-1	AS	5.50 ± 0.73	− 0.06 ± 0.73	0.493
		PFAT	5.56 ± 0.73		
Epithelial defect (mm²)	Day-2	AS	3.33 ± 0.60	− 0.14 ± 0.75	0.114
		PFAT	3.47 ± 0.79		

*Paired t-test

Table 4: Comparison of studied variables in two intervention and control groups based on gender

Sex	Outcome	AS (mean ± SD)	PFAT (mean ± SD)	• P
Male	Day-1 pain (0–10)	3.13 ± 1.39	2.83 ± 1.09	0.346
Male	Recovery time (days)	3.00 ± 0.00	3.00 ± 0.00	1.000
Male	UCVA at 12 weeks (10-point)	9.92 ± 0.28	9.88 ± 0.34	0.564
Female	Day-1 pain (0–10)	3.39 ± 1.96	4.11 ± 2.05	0.003
Female	Recovery time (days)	3.00 ± 0.00	3.06 ± 0.53	0.655
Female	UCVA at 12 weeks (10-point)	9.94 ± 0.33	10.00 ± 0.00	0.317

*Paired t-test

the artificial tear group, with no significant difference between the two groups (P = 0.705). In women, the average Day-1 pain in the intervention group was significantly lower than in the control group (3.39 ± 1.96 vs. 4.11 ± 2.05; P = 0.003) (Table 4). Corneal opacity was not observed in any patient.

Discussion

Surface ablation procedures such as PRK and LASEK are preferred in patients at risk for postoperative ectasia, particularly those with thinner corneas. Although visual outcomes are generally excellent, these techniques are associated with postoperative pain and slower epithelial healing compared with LASIK. Any strategy that can reduce early discomfort and shorten functional recovery has the potential to improve patient satisfaction.

Autologous serum contains fibronectin, vitamin A, epidermal growth factor, platelet-derived growth factor, and other epitheliotrophic mediators that support corneal epithelial cell proliferation, migration, and differentiation [8,9]. Previous studies have demonstrated its value in dry eye, recurrent corneal erosions, and postoperative tear-film instability after refractive surgery, including improvements in tear breakup time and reductions in rose bengal staining [10,11]. More recently, autologous serum has been associated with reduced postoperative pain in patients undergoing LASEK [12,13]. Animal studies have also suggested a role in minimizing postoperative corneal opacity [14].

In this randomized contralateral-eye study, 20 % autologous serum was compared directly with a preservative-free artificial tear (Artelac Advanced) in patients undergoing PRK. Surgical parameters were standardized: the epithelial removal size was the same in both eyes (8-8.5 mm), the difference in ablation depth was less than 20 µm, and mitomycin exposure was nearly identical. This design minimized inter-eye variability and reduced individual patient factors as potential confounders.

Epithelial recovery occurred at approximately three days in both groups, and no difference was detected in postoperative uncorrected visual acuity. However, patients consistently reported less Day-1 pain in the autologous serum eyes. This finding is consistent with the known trophic and anti-inflammatory effects of serum drops, and with prior studies suggesting a beneficial impact on postoperative comfort. No cases of infection or corneal opacity occurred, and standard sterile protocols for serum preparation and storage were maintained [6,15].

Patients with hyperopia or significant astigmatism were treated with FemtoLASIK and were not included in this analysis. Because haze risk is higher in higher refractive corrections, further studies are needed to determine whether autologous serum can reduce postoperative opacity in those settings. Similarly, exploring higher concentrations of autologous serum or platelet-rich plasma, both of which contain more growth factors, may clarify whether enhanced formulations can accelerate epithelial closure.

Conclusion

Twenty percent autologous serum and preservative-free artificial tears demonstrated similar epithelial healing and 12-week visual outcomes after PRK. The reduction in early postoperative pain observed with autologous serum, particularly in women, suggests a potential clinical benefit that warrants confirmation in larger contralateral-eye studies.

Authors ORCIDs

Mandana Ahmadi:
https://orcid.org/0009-0006-6059-3735

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.