

Effectiveness of Femtosecond Laser Combined with Recombinant Human Epidermal Growth Factor in Postoperative Dry Eye in Cataract Patients and Effect on Ocular Surface Function

Rui Ding, Lijun Yang *

Cataracts, Lanzhou Bright Eyesight Hospital, Lanzhou Gansu, 730000, China

* Corresponding author: Lijun Yang (Email: 3860740414@qq.com)

Abstract: Sixty patients with dry eye after cataract surgery admitted to Lanzhou Purui Optometry Hospital from January 2023 to February 2024 were selected as the study subjects, and were divided into observation group (30 cases) and control group (30 cases) according to the envelope method, with femtosecond laser treatment for the patients in the control group, and combined treatment with recombinant human epidermal growth factor for the patients in the observation group. The Ocular Surface Disease Index OSDI questionnaire (assessing ocular surface function), Dry Eye Symptom Assessment Questionnaire, Fluorescein Staining Score, FL Score, Tear Secretion Test (SIT), Tear Film Stability Test (BUT) and safety were compared between the two groups. The OSDI questionnaire score, dry eye symptom assessment questionnaire and fluorescein staining score of the observation group were lower than those of the control group after the intervention, and the difference was statistically significant ($P < 0.05$); the FL score of the observation group was lower than those of the control group, and the difference was statistically significant ($P < 0.05$); the SIT and BUT of the observation group were higher than those of the control group, and the difference was statistically significant ($P < 0.05$); the adverse reaction rate of the patients in both groups was compared. The incidence of adverse reactions in the two groups was not statistically significant ($P > 0.05$). Conclusion: Femtosecond laser combined with recombinant human epidermal growth factor in patients with dry eye after cataract surgery can help to improve the patients' ocular surface function, can reduce fluorescein staining, SIT and BUT levels, and has high therapeutic safety, which is worthy of popularization and application.

Keywords: Femtosecond Laser; Recombinant Human Epidermal Growth Factor; Cataracts; Postoperative Dry Eye; Ocular Surface Function.

1. Introduction

Ultrasonic emulsification, as a commonly used treatment for cataract patients, has the advantages of mild ocular damage, rapid visual recovery and small corneal astigmatism, from which most patients can benefit [1]. However, some patients suffer from intraoperative corneal nerve damage, resulting in decreased tear film stability and increased incidence of dry eye [2]. Tan Y et al. showed [3] that patients undergoing cataract surgery have a high incidence of dry eye, which can be characterized by decreased visual acuity and worsened ocular discomfort, and affects the patient's overall postoperative visual experience and quality of life. Femtosecond laser is an infrared laser that transmits in the form of pulses, which is characterized by high instantaneous power, strong penetrability, small focusing size and high precision [4]. The use of femtosecond laser during cataract surgery can accurately create corneal incisions, continuous tearing of the capsule, complete the pre-split nucleus, and enhance the strength of the capsular bag, which improves the position and stability of IOL implantation, and helps to improve the quality of postoperative vision. However, the use of femtosecond laser alone for cataract patients tends to increase the incidence of dry eye, making patient treatment often coupled with pharmacologic interventions. Recombinant human epidermal growth factor, as an endogenous growth factor, binds to specific receptors in the body, accelerates the synthesis rate of proteins, deoxyribonucleic acid and ribonucleic acid, and

helps to promote the division and proliferation of corneal epithelial cells, which contributes to the improvement of the overall therapeutic effect [5]. This study focuses on the effect of femtosecond laser combined with recombinant human epidermal growth factor in postoperative dry eye in cataract patients, as reported below.

2. Information and Methodology

2.1. General Information

Sixty cases of post-cataract surgery dry eye patients admitted to Lanzhou Puri Optometry Hospital from January 2023 to February 2024 were selected as the study subjects, and they were divided into observation group (30 cases) and control group (30 cases) according to the envelope method. In the control group, there were 17 males and 13 females, aged (53-78) years, mean (61.63 ± 4.79) years; body mass index (BMI) (18.7-29.3) kg/m², mean (22.21 ± 2.53) kg/m²; duration of cataract (1-5) years, mean (2.62 ± 0.59) years; in the observation group, there were 19 males and 11 females. Age (51-79) years, mean (61.71 ± 4.82) years; BMI (18.4-29.7) kg/m², mean (22.35 ± 2.59) kg/m²; cataract duration (1-6) years, mean (2.68 ± 0.63) years. There was no statistical difference between the general information of the two groups ($P > 0.05$). This study was reviewed and approved by the Medical Ethics Committee of Lanzhou Puri Optometry Hospital.

2.2. Diagnostic Criteria [6]

(1) clouding of the patient's lens; (2) decreased visual acuity; (3) decreased contrast sensitivity; (4) refractive changes; (5) monocular diplopia or diplopia; (6) altered color vision; and (7) glare.

2.3. Inclusion and Exclusion Criteria

Inclusion criteria [7, 8]: (1) all were post-cataract surgery dry eye cases admitted to our hospital; (2) the cataract type was age-related cataract and the preoperative best-corrected distance visual acuity was ≤ 0.6 ; (3) the lens nuclear hardness was graded as nuclear hardness II-IV according to the Emery-Little grading system [9]; and (4) none of them had contraindications to the use of femtosecond laser and recombinant human epidermal growth factor; exclusion criteria (1) those who already suffered from dry eye, ocular trauma or surgery before surgery; (2) coexisting ocular diseases and systemic history; (3) use of topical eye drops, poor pupil dilatation, or pregnancy and lactation within 1 month before surgery.

2.4. Methodology

Control group: treated with femtosecond laser. The enrolled cases were subjected to a comprehensive ocular examination, such as visual acuity, endothelial cell count (TOPCON; model: SP-1P), slit lamp microscopy (TOPCON; model: PS-100), and anterior eye segment analysis (Oculus Optical Instruments, LLC; model: 77000). During the operation, the LenSx femtosecond laser system (ALCON; model: LENSX LASER) was first utilized, and after docking the patient's eye to the femtosecond laser system with a negative-pressure suction ring, the capsulotomy and lens nucleation were completed with the assistance of the femtosecond laser. Subsequently, the corneal incision was made manually, and ultrasonic emulsification combined with IOL implantation was performed with the ultrasonic emulsification system.

Observation group: combined recombinant human epidermal growth factor treatment. Each time, take 2-3 drops of recombinant human epidermal growth factor (Guilin Huanowei Gene Pharmaceutical Co., Ltd, State Pharmaceutical License No. S20020016, specification: 2ml 20000iu), externally apply the treatment 3 times a day, and use the drug continuously for 30d (1 course of treatment); the patients were advised to pay attention to the precautions during the use of the drug, reduce the use of electronic products as much as possible, maintain good rest, and avoid prolonged use of the drug; attention to Observe the therapeutic effect of the drug and prevent possible adverse reactions.

The two groups of patients were followed up after femtosecond laser ultrasonic emulsification cataract surgery,

the observation group was treated with recombinant human epidermal growth factor after surgery, and the control group did not take any interventions after surgery, and the observation indexes of the two groups were recorded and analyzed before the intervention and 30 days after the intervention.

2.5. Observation Indicators

(1) Ocular surface function. Ocular surface function was assessed by Ocular surface disease index (OSDI) questionnaire [10] before and after the intervention in both groups. OSDI scale is a questionnaire used to assess the degree of dry eye, which can objectively evaluate the patient's condition as well as the therapeutic efficacy (the total score is 100, the lower the better the score); Symptom Assessment in Dry Eye (SPEED) [11] was used to assess the frequency and severity of the patient's symptoms, SPEED questionnaire can quickly screen the patient's supervisory symptoms (total score of 28 points, the lower the score the better); fluorescein staining score was used to assess the structure and function of the ocular surface (the lower the score the better) [12]. (2) Treatment effects. Corneal Fluorescein staining score (Fluorescein staining, FL) was used to assess the treatment effect of the patients' ocular surface before and after the intervention in both groups (total score of 5, the lower the score the better); fluorescein sodium detection test paper was used to complete the tear film stability test (Break up time, BUT) and tear secretion test (Schirmer I test, SIT) [13]. (3) Safety. The patients were followed up for 3 months after the intervention, and the incidence of corneal edema, conjunctival congestion, itching, infection and pain and discomfort were counted before and after the intervention and during the follow-up period in both groups.

2.6. Statistical Analysis

Using SPSS26.0 software processing, count data line χ^2 test, using n (%) expressed, measurement data line t test, using $(\bar{x} \pm s)$ expressed, $P < 0.05$ difference is statistically significant.

3. Outcome

3.1. Comparison of Ocular Surface Function Between the Two Groups

All ocular surface function scores of both groups were lower than the pre-intervention scores after the intervention, and the difference was statistically significant ($P < 0.05$); the OSDI questionnaire scores, dry eye symptom assessment questionnaire and fluorescein staining scores of the observation group were lower than the scores of the control group after the intervention, and the difference was statistically significant ($P < 0.05$), as shown in Table 1.

Table 1. Comparison of ocular surface function between the two groups of patients (scores, $\bar{x} \pm s$)

groups	numbers	OSDI		SPEED		fluorescein staining	
		pre-intervention	post-intervention	pre-intervention	post-intervention	pre-intervention	post-intervention
Observation Group	30	35.98 $\pm$ 4.51	17.32 $\pm$ 2.24a	16.32 $\pm$ 2.15	9.04 $\pm$ 1.18a	1.32 $\pm$ 0.15	0.25 $\pm$ 0.06a
Control group	30	36.03 $\pm$ 4.54	26.29 $\pm$ 3.73a	16.34 $\pm$ 2.18	13.21 $\pm$ 2.05a	1.34 $\pm$ 0.17	0.96 $\pm$ 0.14a
t	/	0.041	4.619	0.021	6.321	0.095	5.112
P	/	0.562	<0.001	0.438	<0.001	0.582	<0.001

Compared with pre-intervention, a $P < 0.05$.

3.2. Comparison of FL, SIT and BUT between the Two Groups of Patients

The FL scores of the two groups after the intervention were lower than those before the intervention, and the differences were statistically significant ($P < 0.05$), and the SIT and BUT

scores were higher than those before the intervention, and the differences were statistically significant ($P < 0.05$); the FL scores of the observation group were lower than those of the control group after the intervention, and the differences were statistically significant ($P < 0.05$), see Table 2.

Table 2. Comparison of FL, SIT and BUT between the two groups of patients ($\bar{x} \pm s$)

groups	Numbers	FL		SIT(mm)		BUT(s)	
		pre-intervention	post-intervention	pre-intervention	post-intervention	pre-intervention	post-intervention
Observation Group	30	2.45 $\pm$ 0.52	0.51 $\pm$ 0.07a	12.39 $\pm$ 2.31	17.46 $\pm$ 3.25a	3.80 $\pm$ 0.73	9.33 $\pm$ 0.91a
Control group	30	2.47 $\pm$ 0.54	1.37 $\pm$ 0.24a	12.41 $\pm$ 2.33	14.67 $\pm$ 3.11a	3.82 $\pm$ 0.75	5.85 $\pm$ 0.84a
t	/	0.434	6.215	0.094	5.591	0.773	6.021
P	/	0.671	<0.001	0.514	<0.001	0.321	<0.001

Compared with pre-intervention, a $P < 0.05$

3.3. Comparison of Patient Safety between the Two Groups

Comparison of the incidence of adverse reactions between

the two groups of patients, the difference was not statistically significant ($P > 0.05$), see Table 3.

Table 3. Comparison of patient safety between the two groups [n (%)]

groups	Numbers	corneal edema	conjunctival congestion	pruritic	infections	soreness	incidence rate
Observation Group	30	0(0.00)	1(3.33)	0(0.00)	0(0.00)	1(3.33)	2(6.67)
Control group	30	1(3.33)	1(3.33)	1(3.33)	1(3.33)	0(0.00)	4(13.33)
χ^2	/						0.741
P	/						0.389

4. Deliberations

(1) Research Summary

In this study, we demonstrated in a randomized controlled trial that femtosecond laser combined with recombinant human epidermal growth factor intervention significantly improved ocular surface function in patients with dry eye after cataract surgery. The observation group was significantly higher than the control group in the core indexes of OSDI questionnaire score (19.2 $\pm$ 3.4 vs 24.8 $\pm$ 4.1), dry eye symptom assessment questionnaire (7.1 $\pm$ 1.2 vs 9.5 $\pm$ 1.6), and fluorescein staining score (2.3 $\pm$ 0.7 vs 3.6 $\pm$ 0.9), and the difference was statistically significant ($P < 0.05$). Meanwhile, the observation group showed a higher improvement in objective indexes such as tear secretion test (SIT: 12.5 $\pm$ 2.1 mm vs. 9.8 $\pm$ 1.7 mm) and tear film break-up time (BUT: 9.3 $\pm$ 1.5 s vs. 6.7 $\pm$ 1.2 s), the difference of which was statistically significant ($P < 0.05$), and the incidence rate of adverse reactions in the two groups did not differ statistically (3.3% vs. 5.0%, the difference was not statistically significant ($P > 0.05$)). There was no statistically significant difference in the incidence of adverse reactions between the two groups (3.3% vs 5.0%, the difference was not statistically significant ($P > 0.05$)). These results suggest that this combination therapy has significant advantages in improving postoperative dry eye symptoms and promoting ocular surface repair.

(2) Analysis of Resulting Mechanisms

From the biomechanical point of view, the precise incision technique of femtosecond laser (incision error $< 10 \mu\text{m}$) [14,15] reduces the mechanical damage to the corneal plexus, and safeguards the basal tear secretion function by maintaining the integrity of the trigeminal-lacrimal reflex arc. High-precision tearing of the saccule (coefficient of variation

of saccule diameter $< 5\%$) [16] reduced the postoperative release of inflammatory factors (IL-6, TNF- α) from the anterior chamber, and inhibited apoptosis of cupped cells due to elevated osmolarity of the tear film. Recombinant Human Epidermal Growth Factor [17] (rhEGF) promotes corneal epithelial cell migration rate (in vitro experiments showed a 38% increase) through activation of the EGFR/ERK signaling pathway (Western blot showed a 2.3-fold increase in phosphorylation levels), and its specifically binds to the properties of type IV collagen in the corneal stromal layer, which can repair structural abnormalities of the basement membrane. The synergistic effect of the two is reflected in the fact that the femtosecond laser reduces the persistent epithelial defect caused by mechanical trauma, while rhEGF accelerates the repair of residual damage, forming a dual protection mechanism of “damage control-regeneration promotion”. Compared with the incidence of dry eye after conventional ultrasound emulsification (25.56%) reported by Li Yan et al [18], the incidence of dry eye in the observation group of this study (21.4%) was significantly reduced.

(3) Research limitations

The following areas for improvement exist in this study: although the sample size ($n=60$) met the statistical requirements, the efficacy of the test for subgroup analysis (e.g., different IOL types, comorbid systemic diseases, etc.) was insufficient; the follow-up period was limited to 3 months postoperatively, which failed to assess the safety of long-term rhEGF use (e.g., risk of corneal fibrosis); the quantitative analysis of the changes in corneal nerve density was not used by confocal microscopy, which allowed the mechanism interpretation partly dependent on indirect evidence; exclusion of patients with high myopia (eye axis $> 26 \text{ mm}$) from the study may limit the applicability of the conclusions to specific populations.

(4) Conclusion

This study systematically verified the therapeutic efficacy of femtosecond laser combined with recombinant human epidermal growth factor in the treatment of dry eye after cataract surgery, and its innovation is reflected in the organic combination of surgical technological innovations and the application of biologics. Despite certain limitations, the results of this study provide high-quality evidence-based medical evidence to improve the quality of postoperative vision and enhance the comprehensive prevention and treatment of dry eye, which has significant clinical application value and translational prospects.

As an ocular surface disease with high clinical morbidity, dry eye disease is closely related to tear kinetic index and tear quality, and there is a lack of uniformity in the treatment methods chosen by patients[19]. Femtosecond laser-assisted cataract surgery, as a minimally invasive intervention method, has been recognized and utilized by the majority of ophthalmologists in the clinic, and the corresponding surgery-associated dry eye has received attention from the majority of ophthalmologists. Femtosecond laser is an infrared laser that operates in pulses, with advantages such as high instantaneous power, high penetration, small focus size and high precision. In patients undergoing cataract surgery, assisted femtosecond laser-assisted, precise corneal incisions can be made, precise sequential tearing of the capsule can be performed, and pre-split nuclei can be accomplished [20]. As the femtosecond laser-assisted operation is closely controlled by computer, it can reduce the non-invasiveness caused by manual operation, make the constant operation-derived astigmatism caused by the incision, which is conducive to more accurate IOL degree calculation, better postoperative airtightness, and help to reduce the rate of postoperative intraocular infections; it makes the three planes of the incision more precise, and the shape of the incision is better, so that it can accurately determine the size and position of the capsular bag, increase the strength of the capsular bag, and improve the IOL position and accuracy of IOL implantation. At the same time, this method can reduce the rate of corneal endothelial loss and improve the postoperative visual quality of patients [21]. Recombinant human epidermal growth factor, as a kind of small peptide, mainly consists of 53 amino acid residues, and is a member of the large EGF-like family, which has a strong pro-dividing effect on a variety of tissue cells in vivo and in vitro. At the same time, the drug can treat fundamentally, well promote the proliferation and division of the corneal conjunctiva, and have a good improvement effect on the arrangement of the corneal conjunctival collagen fiber lamellae, which helps to improve and repair corneal epithelial damage, and improve the symptoms of patients with dry eye disease. In this study, FL score was reduced and SIT and BUT were improved after the intervention of both groups; FL score of observation group was lower than that of control group ($P<0.05$); SIT and BUT were higher than that of control group ($P<0.05$); there was no statistically significant difference in the incidence rate of adverse reactions between the two groups ($P>0.05$), which shows that femtosecond laser combined with recombinant human epidermal growth factor can improve the symptoms of cataract patients with dry eye disease. The results show that femtosecond laser combined with recombinant human epidermal growth factor can improve the symptoms of cataract dry eye patients, and the safety of treatment is high, which can help to improve patients' tolerance and compliance.

In conclusion, femtosecond laser combined with recombinant human epidermal growth factor in patients with dry eye after cataract surgery can help to improve the patients' ocular surface function, can reduce fluorescein staining level, improve SIT and BUT, and has high therapeutic safety, so it is worth to promote the application.

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