· Clinical Research ·

Changes in ocular surface status and dry eye symptoms following femtosecond laser-assisted cataract surgery

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Abstract

● **AIM: To observe the changes in ocular surface and the dry eye symptoms following femtosecond laser-assisted cataract surgery (FLACS).**

● **METHODS: Patients with no eye signs or symptoms in Guangzhou Aier Eye Hospital between October 2017 and September 2018, who underwent FLACS and intraocular lens (IOL) implantation for age-related cataract were enrolled. Tear film stability assessed with OCULUS Keratograph 5M, Schirmer's I test (SIT), and corneal fluorescein staining (CFS) were evaluated before and after surgery at 1d, 1wk, 1, and 3mo in order. Ocular Surface Disease Index scores (OSDI) and Subjective Symptom Questionnaires (SSQs) were recorded at the same time point.**

● **RESULTS: Thirty-eight eyes of 38 patients were enrolled. The noninvasive tear film break-up time (first break-up time and average break-up time) decreased in a peak at the 1wk visit, and then increased to basic levels at 1mo. The tear meniscus height (TMH) increased transiently at 1d, and declined in the following 3mo visits. The SIT had a transient increase at 1d (*P*=0.357) and a decrease at 1wk and 1mo (both *P*<0.05) but returned to the preoperative levels at 3mo after surgery (*P*=0.062). CFS scores were significantly improved compared with those before surgery, and had a statistical difference (*P*<0.05). OSDI scores and SSQs after surgery were obviously higher, and had a statistical difference (*P*<0.001) but didn't return to the basic level by 3mo.**

● **CONCLUSION: Dry eye signs and symptoms can occur immediately following FLACS and have a peak severity on day 7 postoperatively. Most signs of dry eye can return to preoperative basic levels within 3mo postoperatively. However, all cases can not recover from CFS and dry eye symptoms at 3mo postoperatively.**

● **KEYWORDS:** ocular surface; dry eye; tear film; femtosecond laser-assisted cataract surgery

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INTRODUCTION

Dry eye is a multifactorial disease of the ocular surface, which is characterized with a loss of homeostasis of the tear film and accompanied by ocular symptoms. The most common etiological factors include hyperosmolarity and instability of tear film, inflammation and damage of ocular surface and abnormalities of neurosensory[1]. Dry eye disease is one of the most common manifestations of ocular surface dysfunction, which changes the tear film and overall integrity of the ocular surface. The normal quality and quantity of tear film lipid layer, aqueous layer and mucinous layer and normal tear kinetics play a most important role in the stability of normal ocular surface tear film. Various reasons result in abnormal tear secretion and tear film instability, can cause ocular surface changes, and then lead to dry eyes[2-3]. Intraoperative microscopic damage to the ocular surface is a widely accepted factor of dry eyes after cataract surgery, which can result in ocular discomfort[4]. Many patients underwent with cataract surgery always complain of dry eye and symptoms of irritations after the surgery such as dryness, pain, burning sensation, blurred vision and foreign body sensation[5-8].

In recent years, femtosecond laser has been successfully applied in cataract surgery and demonstrated safety and efficacy, such as improvements in anterior capsulotomy, phacofragmentation and corneal incision. However, the direct contact with the ocular surface and sustained vacuum pressure of suction and the extra laser procedure, which lead to prolonged exposure time, may potentially affect the stability of tear film and function of ocular surface. This study is aimed to observe the changes in ocular surface and the subjective dry eye symptoms following femtosecond laser-assisted cataract surgery (FLACS).

SUBJECTS AND METHODS

Ethical Approval This research was approved by the Ethics Committee of Guangzhou Aier Eye Hospital. All procedures were conducted according to the Declaration of Helsinki. All patients in the research were well-informed and written informed consent was obtained.

Subjects of Study Patients without dry eye signs or symptoms in Guangzhou Aier Eye Hospital between October 2017 and September 2018, who underwent FLACS and intraocular lens (IOL) implantation for age-related cataract were enrolled. Any factors with a potential effect on the tear film and ocular surface function were excluded. The exclusive criteria were: patients with severe hypertension, diabetes mellitus, heart, lung, renal insufficiency and thyroid diseases; patients with rheumatoid arthritis, gout, Stevens-Johnson syndrome, Sjögren disease, systemic lupus erythematosus, multiple sclerosis, *etc.*; patients with eye trauma, entropion or ectropion, uveitis, glaucoma, fundus ocular disease, and other eye diseases; patients used drugs that affect tear secretion or tear film stability within half a year; patients with a history of previous eye surgery within half a year; and patients with cognitive impairment, paranoia, and poor compliance were also excluded. Only one eye evaluation per patient in both groups was included in order to avoid possible influence of the dry eye. Patients experienced serious intraoperative and postoperative complications such as capsule rupture, vitreous loss, postoperative high intraocular pressure or endophthalmitis had also been excluded from the research.

Examination Methods Tear meniscus height (TMH) and noninvasive tear film break-up time (BUT) were assessed with OCULUS Keratograph 5M (Oculus Optikgerate GmbH, Wetzlar, German) corneal topography, which is the first non-invasive, automated and objective instrument for evaluating the state of the ocular surface[9-10].

The Schirmer's I test (SIT) was carried out under natural light. A 5 mm×35 mm Schirmer test strip (Tianjin Jingming New Technology Co., Ltd., Tianjin, China) was placed in the middle and outer 1/3 junction of the lower conjunctival sac of the affected eye without anesthesia. The patient was asked to close eyes gently. After 5min, the strip was removed and the wet length of the strip was measured. Values less than 5 mm are indicators for dry eye syndrome. SIT was measured only once at every time point.

Corneal fluorescein staining (CFS) was used to assess ocular surface damage with sterile sodium fluorescein strips (Tianjin Jingming New Technology Development Co., Ltd., Tianjin, China) and observed by a slit lamp microscope under a wide cobalt blue illumination. The presence of fluorescein staining in each quadrant (superior temporal, inferior temporal, superior nasal and inferior nasal) was observed and recorded. No dying point in each quadrant, 0 points; the dying points scattered≤5, 1 point; the dying points scattered >5 but not in the fusion, 2 points; the dying points are merged into a line or a piece, 3 points. The entire CFS scores was added by the score of each quadrant, with a total score of 0-12[11].

Ocular surface disease index (OSDI) is a widely accepted questionnaire on subjective symptoms in patients with dry eyes[12]. It consisted of 12 questions on eye-related symptoms, vision-related function, and environment-related symptoms. Each question is evaluated according to the frequency of occurrence: never, 0 point; occasionally, 1 point; often, 2 points; most of the time, 3 points; all the time, 4 points. Not all the 12 questions needed to be answered. If the question is that the patient didn't participate in the activity or the environment that would not be in the case, it would not be answered and scored. The final score is calculated according to the formula: OSDI values=(sum of all survey items)×100/(answered survey items)×4.

Subjective Symptom Questionnaires (SSQs) is another widely used subjective dry eye questionnaire. It was used to evaluate the dry eye symptoms, including foreign body sensation, photophobia, itching, pain, dryness, heaviness, blurring, eye fatigue, eye discomfort, eye secretions and tears. A total of 11 items were graded as follows: 3 points, persistent; 2 points, intermittent mild; 1 point, occasional and 0 point, never. The higher scores, the greater severity[13].

The examinations were performed within 1wk before surgery (the basic level) and at the same time interval of 1, 7, 30 and 90d after surgery sequently: the questionnaires and tear-film assessments. After at least 15min, the SIT was performed and the fluorescein staining was conducted finally. All examinations were performed by the same person (Ju RH) in the same room, with constant temperature and humidity.

The diagnostic criteria for dry eye was adopted in this study according to Chinese Medical Association Ophthalmology Group in 2013[11]. The patient had one of the following symptoms: irritation, discomfort, and vision fluctuations, and at the same time, BUT <5s or SIT <5 mm/5min; or the patient had one of the above symptoms and 5s<BUT<10s or 5 mm/5min<SIT <10 mm/5min and positive CFS.

Surgical Procedures All operations are performed by the same skilled cataract specialist (Wu ZM) into two steps. Firstly, the femtosecond laser (LenSx; Alcon Laboratories, TX, USA) was used to perform capsulorhexis (4.8 to 5.2 mm), chop nucleus (energy parameter, 10 μJ) and make clear corneal incisions (2.5 mm and 1.1 mm). Secondly, phaco was performed (Centurion Vision System with Active Fluidics, Alcon Laboratories, TX, USA) and posterior chamber IOL was implanted. After surgery, tobradex eye ointments (Alcon, TX, USA) were used and the operative eyes were bandaged.

Table 1 Mean values of ocular surface parameters measured preoperatively and at 1d, 1wk, 1, and 3mo after FLACS

Parameters	Preoperative	1d	1wk	1mo	3mo	Preop. *vs* 1d	Preop. *vs* 1wk	Preop. *vs* 1mo	Preop. *vs* 3mo
fBUT (s)	10.69±1.21	8.11±1.23	7.00±1.72	10.36±1.46	11.10±2.08	<0.001[a]	<0.001[a]	0.267[a]	0.306[a]
avBUT (s)	11.57±0.95	9.44±0.98	8.54±0.86	11.28±0.82	11.34±0.94	<0.001[a]	<0.001[a]	0.088[a]	0.191[a]
TMH (mm)	0.32±0.11	0.41±0.13	0.31±0.07	0.30±0.09	0.29±0.07	<0.001[b]	0.501[a]	0.313[a]	0.224[a]
SIT (mm)	12.91±3.22	13.36±2.56	10.56±2.30	11.40±3.04	11.63±2.56	0.357[a]	0.001[a]	0.033[a]	0.062[b]
CFS	0.89±0.73	4.13±1.17	3.21±0.91	1.34±0.71	1.10±0.77	<0.001[b]	<0.001[b]	<0.001[b]	0.044[b]
OSDI	8.37±2.10	17.50±5.50	16.00±6.73	13.49±3.63	11.74±2.98	<0.001[b]	<0.001[b]	<0.001[a]	<0.001[a]
SSQ	2.76±1.30	4.08±1.00	4.82±0.98	3.76±1.03	3.58±1.00	<0.001[b]	<0.001[a]	<0.001[a]	<0.001[a]

fBUT: First tear film break-up time; avBUT: Average tear film break-up time; TMH: Tear meniscus height; SIT: Schirmer's I test; CFS: Corneal fluorescein staining; OSDI: Ocular surface disease index; SSQ: Subjective symptoms questionnaires. [a]Paired *t* test, [b]Mann-Whitney *U* test.

Before surgery, topical levofloxacin (Santen Pharmaceutical Co., Ltd., China) and diclofenac sodium eye drops (Shenyang Xingqi Pharmaceutical Co., Ltd., China) were prescribed *q.i.d.* for 3d. After surgery, topical tobradex eye drops (Alcon, TX, USA) was prescribed for each eye *q.i.d.* for 2wk, and pranoprofen (Yangtze River Pharmaceutical Group Co., Ltd., China) for 2wk.

Statistical Analysis For statistical analysis, SPSS software (version 23.0, Inc., Chicago, USA) was used. The data were expressed as the mean±standard deviation in continuous variables, and as number and percentage in categorical variables. Paired *t* test or Mann-Whitney *U* test was used to compare the data. A $P<0.05$ value was recognized statistically different.

RESULTS

A total of 70 eyes (one eye per patient) without dry eye disease who underwent uneventful FLACS were enrolled in the study at the beginning. Only 38 eyes' clinical tests and questionnaires were available after 3mo follow-up. Hence, 38 eyes of 38 patients (16 males and 22 females) were enrolled and analyzed. The age of the patients was 72.58±8.74y.

Changes in Ocular Surface

First tear film break-up time and average tear film break-up time In our research, the first BUT (fBUT) and average BUT (avBUT) after FLACS were instantly decreased and the decrease was largest at the 1wk visit. Compared with those before surgery, there were obviously significant differences ($P<0.05$), both BUTs gradually improved to the basic level at 1mo after surgery, and there were no statistically significant differences at 1 and 3mo after surgery compared with those before surgery ($P>0.05$; Table 1).

Tear meniscus height Before operation, TMH was 0.32±0.11 mm and increased significantly at 1d after surgery (0.41±0.13 mm; $P<0.05$); then it was declined in the following 3mo visits without statistically significant differences ($P>0.05$; Table 1).

Schirmer's I test Before surgery, SIT values were 12.91±3.22 mm, and there was a transient increase at 1d but without significant difference ($P=0.357$), which was 13.36±2.56 mm. Then the values had a significant decrease at 1wk and 1mo after surgery (10.56±2.30 mm and 11.40±3.04 mm, respectively). SIT values recovered to the basic levels at 3mo after surgery (11.63±2.56 mm, $P=0.062$; Table 1).

Corneal fluorescein staining scores CFS scores had a significant increase after surgery (all $P<0.05$). The scores had a peak at 1d postoperatively, and a gradual decrease in the following visits, but did not return to the basic levels at 3mo postoperatively (Table 1).

Changes in Dry Eye Symptoms

Ocular surface disease index scores Compared with that before surgery, OSDI scores after surgery were significantly higher (all $P<0.001$). The scores didn't return to the basic level at 3mo after surgery (Table 1).

Subjective symptoms questionnaires In this research, the symptoms became worse after FLACS, which was most obvious at 1wk, but didn't return to the basic level by 3mo. The three main complaints after surgery were foreign-body sensation (68.9%), ocular discomfort (54.7%) and dryness (48.3%), especially at 1d and 1wk follow-up.

DISCUSSION

FLACS is an epoch-making advancement in the development of cataract surgery, which has brought not only patients but also ophthalmologists' potential benefits. With the development of cataract surgery, patients not only want to see more clearly, but also to see more comfortably. However, some patients still complain with dry eye symptoms, even though the complete vision has been restored[14-15]. Hence, this study was undertaken to observe the changes in ocular surface and subjective dry eye symptoms after FLACS.

In our research, we found many significant changes of the dry eye parameters and symptoms. Firstly, the dry eye parameters tended to be worse after FLACS, which occurred immediately at 1d, worst at 1wk, and gradually improved within 3mo postoperatively, which was consisted with a previous report[14]. Secondly, the ocular symptom scores had an obvious increase following FLACS.

The noninvasive tear film BUTs, both fBUT and avBUT had an immediate decrease after surgery, and achieved the lowest value after 1wk visit, and then increased to the basic levels at 1mo, which indicated the instability of tear film after FLACS. The TMH, reflecting tear film volume increased transiently at 1d, but declined in the following 3mo visits. Previous studies have found that the noninvasive tear film assessments was a simple screening method with high sensitivity, specificity and repeatability to find tear film stability, and noninvasive tear film BUT were more reliable, but TMH was less reliable in patients with dry eye diseases[9,16]. Yu *et al*[14] reported that TMH measured by the Keratograph had a good correlation and consistency with the SIT scores. Similarly, in this study, we found a transient increase in Schirmer's values at 1d and a significant decrease within 3mo postoperatively. The operation-induced pain and irritation may result in an artificially higher tear lake, which was a possible reason for this phenomena[14].

This instability of tear film indicates the changes in the status of ocular surface, and the reasons why FLACS can result in the instability are as follows: 1) the surgery procedure changes the smooth curvature of the corneal surface before surgery, causing damage to the limbal stem cells and conjunctival goblet cells; the transparent corneal incisions cause a damage to the trigeminal nerve of the cornea and a decrease in corneal sensation, leading to decreased tear secretion and tear film stability; the longer time of exposure to microscopic light during the surgery; 2) certain hyperemia and inflammatory edema after surgery, affecting the normal secretion of mucin, reducing the adhesion of mucin, would release a large number of lysosomal enzymes and leukocyte chemotaxis leading to dry eye, cornea damage; 3) postoperative routine application of a large number of eye drops containing preservatives based on benzalkonium chloride, have certain toxic effects on the eye, causing conjunctival hyperemia, follicular hyperplasia, severe conjunctival scars, corneal erosion and other phenomena, resulting in unstable tear film[8,17-20].

In our research, the corneal epithelial infiltration and fluorescence staining around the surgical incision could be observed in most patients after surgery. The CFS scores increased immediately after FLACS, and improved gradually at 3mo, but did not return to the basic levels at 3mo follow-up. We speculated two reasons for this: firstly, the peri-conjunctival injury caused by the suction ring used during femtosecond laser could contribute to a damage to the limbal stem cells and conjunctival goblet cells, similarly with laser-assisted *in situ* keratomileusis, which has been reported; secondly the surgical incisions changed the smooth curvature of the corneal surface before surgery, causing irregular corneal surface damage, is another important cause[8,21].

Our research demonstrated that the ocular symptom scores increased significantly after FLACS, and didn't return to the basic levels after 3mo. We speculated that the eyes could not recover from dry eye symptoms in the early postoperative period. Many researchers had the similar reports in the persistent dry eye symptoms following cataract surgery, especially during the first 3mo follow-up[22-23]. Choi *et al*[23] have concluded that a high OSDI score both at baseline and 1mo after surgery could predict persistent dry eye symptoms.

Pain is one symptom of dry eyes, which is associated with mechanical, chemical, and thermal heat stimulation of the ocular surface, and is mediated by trigeminal ganglion neurons. Inflammation after surgery and the transparent corneal incisions may cause a damage to the trigeminal nerve and a decrease in corneal sensation[1]. This could be the explainations for the pain after FLACS. The similar report of this has been reported in 2018. Iglesias *et al*[24] proposed persistent postsurgical pain (PPP) and evaluated the epidemiology of PPP after cataract surgery. They found that PPP could be manifested as dry eye symptoms and be presented in approximately 34% of patients during the 6mo follow-up. Therefore, these subjective dry eye symptoms should be considered carefully and treated effectively to improve dry eye symptoms and satisfaction.

The limitations of this research could not be ignored. Firstly, it was a small sample size and short follow-up study. Secondly, the intraoperative factors such as negative pressure suction time, laser energy, total operation time, *etc*., did not be taken into account in this research. Thirdly, the present study did not include meibomian gland dysfunction, which plays an important role in the ocular surface disease.

In conclusion, dry eye signs and symptoms can occur immediately following FLACS and have a peak severity on 7d postoperatively. Most signs of dry eye can return to preoperative basic levels within 3mo postoperatively. However, all cases cannot recover from CFS and dry eye symptoms at 3mo postoperatively. Given the limitations in our study, further researches with larger sample sizes and longer follow-up time focus on indicators such as symptom questionnaire scores and meibomian gland dysfunctions are required to reach a firmer conclusion.

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