•Surgically Induced Dry Eye•

Effect of an Absorbable Punctal Plug in the Treatment of Preoperative Dry Eye after LASIK

HONG Ying, XIA Ying-jie, ZHANG Yu, CHEN Yue-guo

【**Abstract**】 **Objective:** To evaluate the efficacy of using an absorbable punctal plug in the treatment of patients with preoperative dry eye after laser in situ keratomileusis (LASIK). **Methods:** This was a prospective, randomized, double-blind study. The LASIK procedure was selected for treatment. Forty-one patients with pre-existing mild to moderate dry eye symptoms were included. Absorbable punctal plugs were randomly implanted in one eye of each patient in combination with medication (the experimental group). The other eye was treated with medication only (the control group). The complications from the punctal plugs were recorded. Comparisons of fluorescent staining (FL), break-up time (BUT), Schirmer I test (SIT) and ocular surface disease index (OSDI) values grading were carried out before the LASIK procedure, as well as 1 week and 1, 3, and 6 months after the procedure. Data analysis was conducted through the non-parametric test method for two related samples. **Results:** No complications were observed except for plug extrusion in one case, one day after the procedure. One week after the procedure, the SIT value of the experimental group was higher then the control group, and the difference was statistically significant (Z=-2.005, P=0.045). One month after the procedure, the SIT values of both groups became consistent. The FL staining value was lower in the experimental group compared to the control group at 1 week, 1 month and 3 months (Z=-2.124, -2.009, -2.120, P<0.05) after the procedure. The differences of the OSDI and BUT values at the above stages were not statistically significant between the two groups. **Conclusion:** An absorbable punctal plug is a safe and effective method for treating patients with dry eye after LASIK.

【**Key words**】 Keratomileusis, laser in situ; xerophthalmia; punctal plug; treatment outcome; comparative study

Xerophthalmia is one of the most common ocular surface diseases [1] which is caused by the instability of tear film and ocular surface damage due to the abnormal quantity or quality of the tears. Discomfort of the eyes is the main symptom. With the application of computers and other video terminals, the incidence of xerophthalmia is increasing among young people year after year, who are also the main population of excimer laser keratorefractive surgery. For patients with preoperative dry eye, the symptoms may be worse 6 to 12 months after excimer laser surgery[2-3]. This will greatly affect the quality of life and surgery efficacy for these patients [4]. At present, local medication treatment is the main therapeutic method for dry eye syndrome, including the application of artificial tears, glucocorticoid and immunosuppressive agents. However, artificial tears cannot completely replace physiological tears, while the glucocorticoid and immunosuppressive agents used for these patients are subject to clinical limitations [2]. Therefore, we need a new method to deal with such diseases.

The punctal plug can be used to treat dry eye syndrome and alleviate the symptoms in a safe, effective and reversible way[5]. Relevant research has shown that the simple supplement of artificial tears cannot achieve ideal therapeutic effect, while the application of the punctal plug has been proven to be a feasible therapeutic method before and after refractive surgery[6], but no current comparative studies on the two eyes of the same patient are available. To explore the effects of an absorbable punctal plug in the treatment of preoperative dry eye after LASIK (laser in situ keratomileusis), we employed a prospective randomized double-blind controlled study on patients with mild to moderate dry eye before LASIK. One eye of each patient was treated with randomly implanted absorbable punctal plugs in combination with drug therapy; while the other eye of the patient was treated solely with drug therapy. The efficacy differences between the two eyes were observed.

1 **Subjects** and Methods

1.1 Research Subjects

DOI: 10.3760/cma.j.issn. 1674-845X.2012.04.004
Authors' Unit: 100191 Ophthalmology Department of Peking University Third Hospital
Corresponding author: CHEN Yue-guo,Email: chenyueguo@263.net

There were 82 eyes of 41 patients with mild to moderate preoperative dry eye before LASIK. All of these patients had been treated at the Excimer Laser Treatment Center in the Ophthalmology Department of Peking University's No. 3 Hospital from March 2009 to March 2010.

1.2 Research Methods

1.2.1 Inclusion criteria (1) Those patients who had planned to receive LASIK surgery with -2.00~-12.00D spherical equivalent degree and an astigmatic degree of <6 D. (2) Compliance with the dry eye diagnostic criteria. According to the reference diagnostic criteria of dry eye in China proposed by Liu Zu-guo in 2002[7]:① chronic symptoms (one or more positive symptoms): visual fatigue, dryness, foreign body sensation, burning sensation, photophobia, pains, lacrimation and redness; ②FL (fluorescent staining): a reflection of the corneal epithelial defects. The evaluation method involves dividing the cornea into four quadrants, the staining of each quadrant is further divided into four degrees (none, light, moderate and severe) corresponding respectively to 0~3 scores, and therefore the FL staining score for the entire cornea equals a score of 0~12. ③ BUT (break-up time): positive BUT ≤ 10s (strong positive ≤ 5 s); ④SIT (Schirmer I test): SIT value ≤ 10mm/5min (strong positive: ≤ 5 mm/5min). The syndrome can be diagnosed as xerophthalmia with positive dry eye symptoms and any two positive symptoms or one strong positive symptom among the ②, ③ and ④ three inspection items. Rating: dry eye symptoms can be divided into mild, moderate and severe symptoms based on the severity. Mild dry eye is characterized by relevant signs without visible symptoms under the slit lamp; moderate dry eye is characterized by relevant signs with ocular surface symptoms (which can be eliminated after treatment) under the slit lamp; severe dry eye is characterized by relevant signs with ocular surface symptoms (which cannot be completely eliminated after treatment) under the slit lamp[8]. (3) The patient was free of any major eye diseases (e.g., uveitis and retinal detachment), any immune diseases (e.g., rheumatoid arthritis) or any diseases of the endocrine system (e.g., hyperthyroidism and diabetes).

1.2.2 Dry eye evaluation method The symptoms were evaluated each time before the surgery, one week after the surgery and 1, 3, 6 months later. The range of evaluation covers the signs, symptoms and all the dry eye detection indices. (1) Evaluation of dry eye symptoms: With the application of OSDI (ocular surface disease index) for each inspection, a questionnaire survey was conducted among the patients enquiring about the existence of foreign body sensation, photophobia, eye pains, etc., as well as the effects on daily life and reactions to surrounding environment. The relevant results were used to evaluate the patient's subjective symptoms. (2) SIT: Schirmer (Schirmer test strips, Tianjin Jingming New Technological Development Co. .Ltd.) under the condition of topical anesthesia: SIT ≤ 5 mm/5min indicated abnormal phenomena. (3) Cornea FL: the cornea was divided into four quadrants, the staining of each quadrant was further divided into four degrees corresponding respectively to 0~3 scores, i.e., none/light degree (staining points existed, staining points<5), moderate degree (staining points≥5) and severe degree (staining points≥5, filamentous or massive staining existed); the FL staining score for the entire cornea equaled 0~12 scores. (4) BUT: inspection of tear film stability: BUT ≤ 10 s indicated that there were abnormal phenomena.

1.3 Grouping for the experiment

A prospective randomized double-blind comparative study was adopted in this research, the patients were randomly grouped in accordance with the single digit of their birthdate (if the single digit of the patient's birthdate was an odd number, his left eye was chosen for the test group, if the single digit of the patient's birthdate was an even number, then his right eye was chosen for the test group). All the research methods involved are in line with the principles of medical ethics and approved by the Ethics Committee of Peking University Third Hospital. All the patients participated in this research had expressed the informed consent and signed the informed consent agreement.

1.4 Treatment in Surgery and Perioperative Period

(1) 3~7 days before the surgery, 0.5% levofloxacin eye drops and 0.1% sodium hyaluronate eye drops were applied four times every day. (2) Surgery methods: use 0.4% oxybuprocaine hydrochloride eye drops were used twice to reach the state of topical anesthesia. The M2 90 microlamellar incision knife (Moria Inc., France) was operated to manipulate the corneal flap above, then the corneal flap was turned over to expose the corneal stromal bed. After the determination of counterpoint of the eyeball, the Allegretto Wave Eye-Q excimer laser machine (WaveLight Inc., Germany) was started to ablate the cornea with an optical zone of 6 mm or 6.5 mm and an ablation depth of 39 ~17μm. The flap under BSS was flushed, then we reset the corneal flap. After the surgery, we dropped in 1 droplet of tobramycin and dexamethasone compound, 2 droplets of carboxymethyl cellulose

into the conjunctival sac, then properly arranged the eyeshade. (3) Before the preparation of corneal flap for LASIK, punctal plugs shall be applied upward and downward to the inspected eye. This research has adopted the absorbable punctal plugs (OPAQUE Herrick Lacrimal Plug, Lacrinmedics Inc., USA) with a diameter of 0.4 mm, the average degradation period is 180 days. Place one punctal plug separately for the up and down lacrimal point. (4) 1 day after the surgery, the eyeshade can be removed upon the return visit. Use the following eye drops: 0.5% levofloxacin and 0.1% fluorometholone, 4 times /day, two weeks in total; 0.1% sodium hyaluronate, 4 times /day;1% carboxymethyl cellulose, once per night, 4 weeks in total.

1.5 Postoperative Follow-up and Inspection Items

Return visits were made 1 day, 1 week, 1, 3, 6 months respectively after the surgery. The detailed slit lamp examinations were carried out during each return visit. Detections of the SIT, FL, BUT, and OSDI values were carried out 1 week, 1, 3, 6 months respectively after the surgery with relevant records were made.

1.6 Statistical Methods

With SPSS 14.0 statistical software, the data were analyzed with non-parametric test method for two related samples. P <0.05 indicated statistically significant differences.

2 Results

Forty-one patients were selected for this research and there was plug extrusion in one case one day after surgery. The research was completed with 80 eyes of 40 patients, including 5 male patients and 35 female patients. The ages of these patients ranged from 19 to 39 years old with an average age of (29.8 ± 5.0) years old. The average preoperative spherical equivalent was (-5.60 ± 2.40) D.

The spherical equivalent degree of both test group and control group, SIT, FL, BUT and OSDI values did not meet the requirements of normal distribution. Therefore, the median value (median, M), the 25th percentile and 75th percentile (P_{25}, P_{75}) were chosen to describe the centralized location and degree of dispersion of the statistical data. The patients' test results before surgery were as follows: the Schirmer test value was 1~6 mm, corneal fluorescein staining was a score of 0~5, break-up time was 3~10s, and the OSDI score was 0~1.4. According to the symptoms observed in this group, these patients were diagnosed as patients with light and moderate dry eye.

There were no statistically significant differences between the two groups in terms of spherical equivalents for each time point before and after surgery (Table 1). There were no statistically significant differences between two groups of preoperative SIT values. One week after LASIK, the SIT values in the test group were obviously higher than those in the control group, there were statistically significant differences (Z = -2.005, P = 0.045). The differences disappeared one month later (Table 2). There were no statistically significant differences between the two groups of preoperative FL values. 1 week,1 month and 3 months after LASIK, the FL values in the test group were obviously lower than those in the control group, there were statistically significant differences (Z = -2.124, -2.009, -2.120, and all of the P values were <0.05). There were no statistically significant differences between the two groups 6 months after LASIK (Table 3).There were no statistically significant differences between the BUT values of the two groups for each time point before and after the surgery (Table 4). There were no statistically significant differences between the OSDI values of the two groups for each time point before and after the surgery (Table 5).

Table 1 Comparison of the two groups in terms of spherical equivalents for each time point before and after LASIK (D, M[P_{25}, P_{75}],n=40)

Time	Experimental group	Control group	Z value	P value
Preoperative period	-5.50[3.75,7.50]	-5.50[3.75,7.50]	0.584	0.559
1 week after LASIK	-0.25[0.25,0.75]	-0.25[0.25,0.63]	-0.362	0.717
1 Month after LASIK	-0.50[0.125,0.75]	-0.25[0.25,0.751	-0.115	0.908
3 Months after LASIK	-0.50[0.25,0.63]	-0.50[0.25,0.75]	-0.064	0.949
6 Months after LASIK	-0.25[0.25,0.75]	-0.50[0.25,0.75]	-0.500	0.617

Table 2 Comparison of the two groups in terms of Schirmer test values for each time point before and after LASIK (mm, M[P_{25}, P_{75}], n=40)

Time	Experimental group	Control group	Z value	P value
Preoperative period	3[2.00,4.00]	3[2.00,4.00]	-0.350	0.726
1 week after LASIK	3[1.75,4.25]	2[1.00,3.00]	-2.005	0.045
1 Month after LASIK	4[2.00,7.00]	3[2.00,6.00]	-1.614	0.107
3 Months after LASIK	4.5[3.00,7.00]	4[3.00,6.00]	-0.713	0.476
6 Months after LASIK	4.5[3.00,6.00]	3[3.00,6.75]	0.000	1.000

Table 3 Comparison of the two groups in terms of FL values (M[P_{25}, P_{75}], n=40)

Time	Experimental group	Control group	Z values	P values
Preoperative period	2[0.00,3.00]	2[0.00,3.00]	-1.514	0.130
1 week after LASIK	1[0.00,2.00]	1.5[0.00,3.00]	-2.124	0.034
1 Month after LASIK	1[0.00,2.00]	2[0.00,3.00]	-2.009	0.045
3 Months after LASIK	1[0.00,2.00]	1[0.00,3.00]	-2.120	0.034
6 Months after LASIK	1.5[0.00,2.00]	2[0.00,3.50]	-1.480	0.139

Table 4 Comparison of the two groups in terms of BUT for each time point before and after LASIK (s, M[P_{25}, P_{75}], n=40)

Time	Experimental group	Control group	Z values	P values
Preoperative period	5[4.00,7.00]	6[4.00,8.00]	-0.670	0.503
1 week after LASIK	3[2.00,8.00]	3[2.00,6.00]	-0.531	0.596
1 Month after LASIK	4[2.25,5.00]	4[3.00,5.00]	-0.115	0.908
3 Months after LASIK	4[2.50,5.50]	4[3.00,6.00]	-0.202	0.840
6 Months after LASIK	5[3.00,6.00]	4[2.00,6.00]	-0.179	0.858

Table 5 Comparison of the two groups in terms of OSDI values for each time point before and after LASIK (M[P_{25}, P_{75}], n=40)

Time	Experimental group	Control group	Z values	P values
Preoperative period	0.3[0.00,0.50]	0.2[0.00,0.50]	-1.000	0.317
1 week after LASIK	0.3[0.18,0.50]	0.3[0.10,0.50]	-1.611	0.107

1 Month after LASIK	0.2[0.05,0.35]	0.2[0.00,0.35]	-1.000	0.317
3 Months after LASIK	0.2[0.10,0.35]	0.3[0.20,0.30]	-1.342	0.180
6 Months after LASIK	0.1[0.00,0.45]	0.3[0.00,0.50]	-1.342	0.180

3 Discussion

Xerophthalmia is one of the most common complications after excimer laser keratorefractive surgery[9]. The corresponding incidence rates 1 week, 1 month and 6 months after the surgery are about 50%, 40% and 20~40%[10-11]. The exacerbation of xerophthalmia after LASIK is mainly due to the cutting off of many corneal sensory nerve fibers during the preparation process of corneal flap, resulting in the abnormal reactions of lacrimal gland-ocular surface functional units and reduction of reflexively secreted tears[12]. At present, local medication treatment is the main therapeutic method for such patients, including the application of artificial tears, glucocorticoid and immunosuppressive agents. However, artificial tears lack the electrolytes and immune components contained in physiological tears [13], while the long-term application of glucocorticoids and immunosuppressive agents will result in certain side effects [2].

The punctal plug can be used to treat dry eye symptoms in a safe, effective and reversible way as well as alleviate the syndromes through the preservation of physiological tears and artificial tears [5]. The clinical use of the punctal plug for dry eye can be traced back to 1975, and subsequent studies have shown that up to 77% of patients showed relief of symptoms and improvement [14]. Previous studies showed that the punctal plug can effectively improve dry eye symptoms after excimer laser keratorefractive surgery, improve the density of conjunctival goblet cells and reduce optical aberrations [15-16].

The application of the punctal plug is featured with high probability of success, reversibility and low probability of complications. Common clinical complications include plug extrusion, foreign body sensation, infection, epiphora, conjunctival erosion and pyogenic granuloma, etc.[17]. No complications were observed in this research except for plug extrusion in one case one day after surgery.

All the patients in this group were healthy young people aged from 19 to 39 years old without any systemic diseases (such as immune diseases and diseases of the endocrine system). Symptomatic diagnosis was based on corneal fluorescein staining, Schirmer test and BUT during the process of screening for excimer surgery, the subjects were diagnosed as patients with mild to moderate dry eye. OSDI was used to evaluate the patient's subjective symptoms. The self-control study was applied to this research in order to objectively evaluate the therapeutic effects of the punctal plug.

The results of this research showed that, after treatment using the punctal plug for patients with dry eye before LASIK, 1 week after the surgery the SIT values in the experimental group were obviously higher than those in the control group, and there were no statistically significant differences between the two groups 1, 3 and 6 months after surgery. 1 week, 1 month and 3 months after the surgery, the FL values in the test group were obviously lower than those in the control group, and there were no statistically significant differences between the two groups 6 months after the surgery. 1 week, 1, 3 and 6 months after the surgery, there were no statistically significant differences between spherical equivalents, BUT values and OSDI values in the two groups.

Through research, we found that the early postoperative Schirmer test results obtained from patients who had accepted punctal plug treatment were better than those obtained from the control group. The quantity of tears secreted in the early postoperative period was similar to that secreted before surgery. These quantities were obviously higher than those obtained from the control group. This was because punctal plug treatment can help retain tears and reduce the effects of LASIK on the lacrimal gland-ocular surface functional units. The punctal plugs were gradually absorbed with the passage of time, and therefore there were no statistically significant differences between the quantities of secreted tears of the two groups 1 month or more after surgery.

The results of this research show that for patients with mild to moderate dry eye before LASIK, the punctal plug treatment can help significantly reduce the corneal staining score 3 months after surgery. We considered that as the punctal plug can effectively retain secreted tears and extend the retention duration of pharmaceutical components within the conjunctival sac in combination with the application of artificial tears and glucocorticoid, therefore better control of postoperative inflammation, reduction of the effects of surgical trauma on the lacrimal gland-ocular surface functional unit and better recovery of corneal tissues can be realized. This is of great significance to the recovery of the ocular surface in the early postoperative period and prevention of complications (such as postoperative inflammation and infection).

For the patients with mild to moderate dry eye before LASIK, the punctal plug treatment in this research had no effects on the test results of postoperative spherical equivalent. Certain studies had pointed out that the application of the

punctal plug can improve postoperative refractive stability and help obtain smaller refractive deviations[16]; while the results of this research did not indicate such results. The relatively mild dry eye symptoms of the patients in this group and the replacement with standardized artificial tears for therapy in the control group would result in insignificant postoperative refractive differences.

BUT is the index for tear film stability which is correlated with the components of tear film and closely related to the shape of the cornea. The postoperative shape changes of the cornea would be the reason for sharp declines of BUT values compared with those obtained before the surgery[12], while the existence of punctal plugs had no significant effects on the BUT values.

There were no statistically significant differences between the two groups in terms of OSDI values. Previous reference research suggested that for patients with dry eye, the subjective symptoms may not be associated with the test indices of dry eye [12,18]. The results of this research also indicated that even if statistically significant differences existed between the objective test indices of the patient's two eyes, the patient's subjective scoring results may be the same. This may partly be due to the degradation of corneal sense perception during the early postoperative period. Therefore, whether dry eye symptoms existed or not after LASIK, equal attention should be paid to the postoperative conditions.

Of course, punctal plug treatment is subject to certain limitations, as it can only help retain tears rather than alleviate postoperative ocular inflammation [6]. Certain previous studies suggest that the combined local application of cyclosporine with low concentration would help achieve better results [19], and this is possibly one of the future research directions.

In summary, for patients with mild to moderate dry eye before LASIK, the intraoperative application of temporal punctal plug treatment can help effectively retain tears and promote postoperative corneal epithelial recovery in combination with local application of artificial tears and glucocorticoid eye drops.

Bibliography:

[1] Wang Hua, Liu Zu-Guo, Peng Juan, et al. The Clinical Therapeutic Efficiency of Anethol Trithione on Dry Eye. Chinese Journal of Ophthalmology, 2009, 45：492-497.

[2] Quinto GG, Camacho W, Behrens A. Postrefractive surgery dry eye. Curr Opin Ophthalmol, 2008, 19：335-341.

[3] Schallhorn SC. Amesbury EC, Tanzer DJ. Avoidance, recognition, and management of LASIK complications. Am J Ophthalmol, 2006, 141:733-739.

[4] Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome：a Delphi approach to treatment recommendations. Cornea, 2006, 25：900-907.

[5] Baxter SA, Laibson PR. Punctal plugs in the management of dry eyes. Ocul Surf, 2004, 2: 255-265.

[6] Albietz JM, Lenton LM. Management of the ocular surface and tear film before, during, and after laser in situ keratomileusis. J Refract Surg, 2004, 20：62-71.

[7] Liu Zu-Guo. The Diagnosis of Dry Eye. Chinese Journal of Ophthalmology, 2002, 38： 318-320.

[8] Liu Zu-Guo, Peng Juan. Diagnosis and Treatment Guidelines of Dry Eye. Chinese Ophthalmic Research, 2008, 26: 161-164.

[9] Toda L LASIK and the ocular surface. Cornea, 2008, 27(Suppll)：S70-76.

[10] De Paiva CS, Chen Z, Koch DD. et al. The incidence and risk factors for developing dry eye after myopic LASIK. Am J Ophthalmol, 2006, 141：438-445.

[11] Shoja MR, Besharati MR. Dry eye after LASIK for myopia：incidence and risk factors. Eur J Ophthalmol, 2007, 17: 1-6.

[12] Ambrosio R. Jr., Tervo T. Wilson SE. LASIK-associated dry eye and neurotrophic epitheliopathy：pathophysiology and strategies for prevention and treatment. J Refract Surg, 2008, 24:396-407.

[13] Su Long, Zhao Shaozhen, Sun Huimin, et al. The Use of Silicone Puncture Plugs in the Treatment of Dr y Eye. Chinese Journal of Optometry and Ophthalmology, 2006, 8：393-395.

[14] Tai MC, Cosar CB, Cohen EJ, et al. The clinical efficacy of silicone punctal plug therapy. Cornea, 2002, 21:135-139.

[15] Albietz JM , McLennan SG, Lenton LM. Ocular surface management of photorefractive keratectomy and laser in situ keratomileusis. J Refract Surg, 2003, 19: 636-644.

[16] Huang B, Mirza MA, Qazi MA, et al. The effect of punctal occlusion on wavefront aberrations in dry eye patients after laser in situ keratomileusis. Am J Ophthalmol, 2004, 137：52-61.

[17] Khalil MB, Latkany RA, Speaker MC. et al. Effect of punctal plugs in patients with low refractive errors considering refractive surgery. J Refract Surg, 2007, 23：467-471.

[18] Dogru M, Stern ME, Smith JA, et al. Changing trends in the definition and diagnosis of dry eyes. Am J Ophthalmol, 2005, 140:507-508.

[19] Roberts CW, Carniglia PE, Brazzo BG. Comparison of topical cyclosporine, punctal occlusion, and a combination for the treatment of dry eye. Cornea, 2007, 26：805-809.

(Submission date：2011-01-06)
(Editor: Wu Bin)