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Research Article

Postoperative Effect of Short-Term Treatment with Fluorometholone Combined with Pranoprofen on LASEK

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Abstract

Objective: To compare the effect of fluoromethalone combined with pranoprofen eye drops in short and long term after excimer laser subepithelial keratomileusis (LASEK) and to probe its impact on the postoperative effect. **Method：** We selected myopia patients who underwent laser subepithelial keratomileusis (LASEK) in the Department of Laser Ophthalmology, the First Affiliated Hospital of Yangtze University. According to the length of using fluorometholone eye drops after LASEK divided into control and experimental group, the patients who were used for four months (long course of treatment) from March 2008 to March 2010 as the control group, and those were used for one month (short course of treatment) from October 2012 to December 2012 were set as the experimental group, thus， to compare the differences of uncorrected visual acuity, diopter, intraocular pressure, slit-lamp examination and the occurrence of corneal haze with different medication time points. **Result:** There was no statistically significant difference in the postoperative uncorrected visual acuity (UCVA) and postoperative refractive power between the two groups at each time points within 1 year and 5 years. The difference of intraocular pressure between the two groups at 2 months, 3 months, and 4 months were statistically significant compared with expected intraocular pressure of postoperative. Comparing the incidence of increased intraocular pressure> 3 mmHg, the control groups and experimental groups' incidences were 12% and 2.5%, respectively. The incidence of haze was 8% and 11.25%, respectively, the experimental group showed mild evidence higher than the control groups, but there is no statistically significant. **Conclusions：** The short-term treatment of fluorometholone combined with pranoprofen eye drops and the long-term treatment group was equally effective in maintaining postoperative uncorrected visual acuity and postoperative diopter stability. But, the short-term group was better at preventing elevated intraocular pressure, and the incidence was lower than the long-term

group. There was no difference between the two groups in preventing and reducing the incidence of haze. The postoperative safety, efficacy and stability between the two groups makes no difference, which is worthy of popularization in clinical practice.

Key words: myopia, LASEK, NSAIDs, glucocorticoids, haze.

Introduction

Corneal excimer laser keratorefractive surgery has made significant progress among myopia patients in the whole world since the early 20th century. In general, corneal excimer laser refractive surgery can be divided into two types: corneal stromal layer surgery, which was represented by (laser-assisted in situ keratomileuses, LASIK) corneal surface layer surgery, which were represented by (photorefractive keratectomy, PRK) and (Laser-assisted sub-epithelial keratectomy, LASEK) (1). LASEK combines the advantages of LASIK and PRK, which avoids intraoperative and postoperative corneal flap-related complications. Since the operation does not need to make a corneal flap, it broadens the indications of excimer laser surgery. It has been demonstrated that LASEK provides more stable corneal biomechanical properties (2-3). Compared with other corneal refractive surgery, LASEK has superior postoperative effect, predictability and safety (4). In contrast with our expected, the shortages of LASEK were corneal irritation the longer vision recovery period after the surgery and a higher incidence of haze (4-5).

Haze is the dominating issue after LASEK surgery. The main mechanisms of haze include corneal epithelial cell apoptosis, corneal epithelial repair, excessive proliferation of epithelial cells, stimulation of stromal cell expression, stromal layer remodelling, contraction, and the formation of adhesion with surrounding tissues eventually formed haze (6-7). Glucocorticoids combined with nonsteroidal anti-inflammatory drugs (NSAIDs) have been demonstrated to alleviate corneal discomfort, promote the recovery of patients' vision and visual quality, and reduce haze after postoperative (8-9). What's more, studies have shown (8,10,11) that the patients with low to moderate myopia who underwent LASEK, have fewer fluctuations in intraocular pressure and slightly higher the incidence of haze with NSAIDs, compared with the routine use of fluorometholone. Even though there was no difference in subjective sensation, postoperative vision and diopter between the two groups, NSAIDs can reduce corneal irritation symptoms and prevent haze after LASEK. But the inhibitory effect of NSAIDs is not as good as glucocorticoids. Therefore, the combination uses of glucocorticoids and NSAIDs have become a routine treatment after LASEK.

In recent years, scientists have found (8,12,13) that fluorometholone eye drops combined with pranoprofen can significantly alleviate LASEK's postoperative inflammatory response. This method can also reduce postoperative symptoms of corneal irritation in the earlier time and prevent the occurrence of haze.

As representative of NSAIDs, pranoprofen eye drops in the long-term use can partially replace the role of glucocorticoids without increasing intraocular pressure (14-15). However, glucocorticoids have been the first-line treatment and prevention of the occurrence of haze, which is better than pranoprofen (16). And, the combination of glucocorticoids and pranoprofen effectively prevents and controls the event of haze after LASEK (8). However, some patients with hormone glaucoma still need surgical treatment, or even worse.

How to effectively and suitably use glucocorticoids to treat the patients while ensuring the intraocular pressure is controlled within the

normal range after surgery, but also can also reduce the incidence of haze and the severity of its occurrence. In this study, we did not change the patients' dosage and period of pranoprofen eye drops. The long-course treatment using fluorometholone eye drops (4 months) was set as the control group, and the short-course treatment using fluorometholone eye drops (one month) was selected as the experimental group. After that, we compared the postoperative effects of between two groups from the following aspects: uncorrected vision acuity, refractive power, intraocular pressure, slit-lamp examination and observation of the occurrence of haze.

1. Materials and Methods

1.1 Research objects

The object of this study was a case-control study. We enrolled the myopia patients who underwent laser epithelial keratomileusis (LASEK) in our department. 63 controls (125 eyes) and 40 cases (80 eyes) were selected from 2008.03 to 2010.03 and 2012.10 to 2012.12, respectively. There were 25 males with 50 eyes in the control groups and 38 females with 75 eyes, 18-46 years, with an average age (24.89 ± 7.13). The case group had 15 males with 30 eyes and 25 females with 50 eyes, with the age range of 18-40 years, with an average age (24.95 ± 6.15). In the control group, the preoperative equivalent sphere is - 1.625-8.50D (average - 5.56 ± 1.66); the best-corrected visual acuity is 0.6-1.0 (0.95 ± 0.09); Intraocular pressure is 8-20 mmHg (average 13.39 ± 2.17); the central corneal thickness is 450-607μm (average 517.94 ± 35.72). The preoperative equivalent sphere in the experimental group is -1.25 ~ -8.50D (average -5.56 ± 1.80); the best-corrected visual acuity is 0.8 ~ 1.0 (0.93 ± 0.09); intraocular pressure is 9 ~ 19mmHg (average 13.39 ± 2.23); the central cornea thickness is 453 ~ 584μm (average 520.60 ± 26.98). Admission criteria: All subjects were following LASEK's indications for surgery. The diopter was stable in the past two years. The patients stopped wearing hard contact lenses for more than three months and stopped wearing soft contact lenses for more than two weeks. Exclusion criteria: Pregnant and lactating women, patients with mental illness, active eye disease, diabetes, hyperthyroidism or systemic immune diseases and other systemic diseases that can cause eye changes, keratoconus and occult keratoconus. All the selected patients had no contraindications and could be followed up regularly after the operation. Before the study, all participants were informed of the nature of the study and signed an informed consent form before entering the study cohort under the guidance of relevant researchers. The medical ethics committee has approved the experiment of the hospital, and all patients have informed consent. The same experienced surgeon performed all operations.

1.2 Surgical methods

Patients had to follow the doctor's instructions for topical antibiotic eye drops for at least 3 days before surgery, rinsed the conjunctival sac with 0.9% sodium chloride plus gentamicin, and 0.4% oxybuprocaine hydrochloride eye drops (Benoxil, Santen, Inc, Japan) were used for anaesthetize three times with an interval of 5 minutes. The laser subepithelial keratomileusis (LASEK) was performed with the Bausch and Lomb company's TECHNOLAS 217z100 excimer laser therapeutic instrument. Operate according to the routine procedure of LASEK myopia correction operation: disinfect and spread the drape, open the eyelid with the eyelid opener, and wash the conjunctival sac again during the operation, the corneal epithelium scraper is perpendicular to the corneal surface, and scrapes the corneal epithelium from the outside to the inside with a proper depth and even shape, which is a regular round shape with smooth edge, gently wipe the residual epithelial debris with disposable medical sterile sponge, and expose the laser cutting area, activate the three-dimensional eyeball tracking system, and position the focus of the three beams of the patient's gaze light, focusing light and aiming light on the corneal surface is

aligned with the center of the pupil and scanned with a 193nm laser flying spot generated by a mixture of fluorine and argon (ArF) for laser cutting; after that, infiltrate with 0.02% Mitomycin C (MMC) (The specific situation depends on the diopter. The higher the degree, the longer the infiltration time, and vice versa.) After the operation, BSS rinses the cutting surface, absorbs the overflowing water with a sponge, and wears a high oxygen permeability corneal contact lens (AOSYS, Johnson & Johnson, USA).

1.3 Observation index

Regular re-examinations were performed at 1 week, 3 weeks, 2 months, 3 months, 4 months, 6 months, 1 year, and 5 years after the operation. The inspection items included uncorrected vision acuity, best-corrected vision acuity, diopter, intraocular pressure, slit lamp and fundus examination.

1.3.1 Vision measurement

The international standard visual acuity chart was used for measurement, and the recording methods were 0.1-1.0, 1.0-2.0. Check the right eye first, then the left eye; Check the uncorrected vision acuity first, then check the best-corrected visual acuity. The best-corrected visual acuity of adults ≥ 0.8 is expected. All the patients who underwent the operation are based on the best-corrected visual acuity before the procedure. Still, the decline of the best-corrected visual acuity of high myopia patients after the process is not excluded. The corrected vision acuity fluctuated up and down one line after the operation was regular.

1.3.2 Diopter measurement

The KR8900 computer refractometer from TOPCON Corporation of Japan measured patients' preoperative and postoperative diopter. Each eye was continuously measured three times. The clinical standard of emmetropia is -0.25D ~ + 0.50D. Myopia: mild myopia: within -3.00D; moderate myopia: -3.25D ~ -6.00D; high myopia: -6.25D ~ -10.00D; ultra-high myopia: above -10.00D.

1.3.3 Intraocular pressure measurement

Adopt the TX-F non-contact tonometer of CANON company in Japan to measure the intraocular pressure of patients before and after the operation, measure 3 times in succession, and the average value was taken. ① The normal intraocular pressure is 9-21mmHg. Postoperative estimated intraocular pressure =5.175+0.411* preoperative intraocular pressure-0.0205* cutting volume. Armley divides the increase in intraocular pressure caused by glucocorticoid drip in normal people into three categories: intraocular pressure rise < 6mmHg and peak value ≤ 20mmHg after 4-6 weeks of local use of glucocorticoid; ② Moderate sensitive: intraocular pressure rise 6-15mmhg and the peak value is 21-30mmhg after 4-6 weeks of local use of glucocorticoid; ③ High sensitive type: the intraocular pressure increased more than 15mmHg and the peak value was more than 31mmhg after 4-6 weeks of local use of glucocorticoid. However, when intraocular pressure exceeds the expected intraocular pressure value of 5 mmHg, drugs should be stopped, or other drugs should be selected for alternative treatment. We set the increase of expected intraocular pressure (IOP) to more than 3 mmHg as the intervention standard in our hospital.

1.3.4 Slit-lamp inspection

The Japanese TOPCAN SL-1E (NO. 615760) slit lamp was used to check the patient's cornea before and after the operation. Haze (graded according to the Fantes grading standard) Grade 0: The cornea is entirely transparent; Grade 0.5: Slightly spotted turbidity is found by oblique illumination under the slit lamp; Grade 1: The slight turbidity which can be found only by careful inspection under the slit lamp, but does not affect the iris texture observation; Grade 2: mild corneal opacity that is easier to find under the slit lamp, which slightly affects the iris texture; Grade 3: moderate turbidity and the fine structure of the

anterior chamber and iris cannot be seen; grade 4: severe corneal opacification, which cannot be seen into the eyes.

1.3.5 Fundus examination

The fundus examination was inspected by Suzhou Liuliu Vision Technology Co., Ltd. crane brand YZ6E ophthalmoscope.

1.4 Statistical analysis

The research data of this subject uses Spss20.0 statistical software for data analysis. The constituent ratio represents the enumeration data. The chi-square test was used to analyze the difference between groups; measurement data shall be tested for normality first, and subject to normalcy shall be expressed as mean ± standard deviation. Difference between groups was analyzed using two independent samples t-tests. Two paired samples t-test was used for the comparison of intra-group and predicted intraocular pressures of post operation, to analyze the changes of uncorrected vision acuity, diopter and intraocular pressure in different follow-up times after LASEK operation from March 2008 to March 2010 and from October 2012 to December 2012, and a line chart was drawn. The difference was statistically significant with $p < 0.05$.

2. Results

2.1 Postoperative UNVA

The visual acuity of the control and experimental groups reached the pre-operative BCVA at 2 months, and 3 weeks after the operation, respectively, and gradually stabilized (see Figure 1). UCVA of the two groups decreased slightly at 1 year after the procedure. The control group was close to 1.0; that of the experimental group was greater than 1.0, and there was no significant difference between the two groups (See Table 1).

2.2 Postoperative diopter

The diopter of the two groups in the early postoperative stage was in the state of mild hyperopia, peaked at 3 weeks after the operation, and gradually receded at 2 months until it returned to the emmetropia state at 1 year (see Table 2 and Figure 2 for the specific results). The difference was not statistically significant (see Table 2).

2.3 Postoperative IOP

At each observation time point in the control and experimental groups, the intraocular pressure value was compared with the predicted intraocular pressure value postoperation. In the control group, the intraocular pressure began to increase at 2 months after the operation (see Table 3 and Figure 3), the intraocular pressure measured at 2 months, 3 months and 4 months after surgery was statistically significant compared with the predicted intraocular pressure (see Table 3), the difference between the remaining time points is not statistically significant. Compared with the expected intraocular pressure value at various time points after the operation in the experimental group, there was no statistically significant difference (see Table 4) and no significant upward trend (see Figure 4). The incidence of IOP elevation> 3 mmHg between the two groups was statistically significant (see Table 5). Comparison of the increase in intraocular pressure before and after the operation between the two groups, in the control group, there were 15 cases of new cases with intraocular pressure values exceeding the postoperative intraocular pressure value of 3 mmHg, accounting for 12%; of which 3 eyes (2.4%) in 3 weeks after operation, there were 6 eyes (4.8%) at 2 months postoperatively, 5 eyes (4.0%) at 3 months postoperatively, and 1 eye (0.8%) at 4 months postoperatively (see Table 6). However, only 2 eyes of the new cases in the experimental group had IOP value exceeding the expected IOP value of 3mmHg, accounting for 2.5%; 2 eyes (2.5%) had IOP value 3 weeks after the operation, and no new cases had IOP value exceeding the expected IOP value of 3mmHg in 2 months, 3 months and 4 months after the operation.

There was no intraocular pressure higher than the normal value of 21 mmHg in both groups.

2.4 Corneal epithelial haze and others

Comparison of the incidence of haze between the two groups: the haze of the control group and test groups' haze was 8% and 11.25%, respectively. The test group was higher than the control group, but the difference was not statistically significant (see Table 7).In the control group, grade 0.5-1 haze was found in 10 eyes (8%) of 125 eyes from 63 patients, among which grade 0.5 haze was seen in 1 eye (0.8%), and grade 1 haze was seen in 3 eyes (2.4%) after the second month of operation; grade 0.5 haze was seen in 4 eyes (3.2%) during the third month of operation; grade 0.5 haze was seen in 2 eyes (1.6%) after the fourth month of operation. In the experimental group, grade 1 haze was found in 9 eyes (11.25%) of 80 eyes from 40 patients, 4 eyes (5%) in the second month after the operation, 3 eyes (3.8%) in the third month after the operation , and 2 eyes (2.5%) in the fourth month after the operation. No haze was found in 6 months, 1 year and 5 years follow-up after operation.

Table 1. Comparison of postoperative uncorrected visual acuity at different time points between the two groups

Grouping	examples	Po-op 1w	Po-op 3w	Po-op 2m	Po-op 3m	Po-op 6m	Po-op 1y	Po-op 5y
The control group	125	0.77±0.18	0.91±0.15	0.97±0.13	1.01±0.13	1.04±0.10	1.05±0.14	1.02±0.16
The experimental group	80	0.81±0.17	0.94±0.17	0.99±0.14	1.03±0.11	1.05±0.12	1.07±0.13	1.05±0.14
t		1.648	1.569	1.168	1.441	1.219	0.994	1.374
p		0.101	0.118	0.244	0.151	0.224	0.321	0.171

p<0.05 means the difference was significantly different.

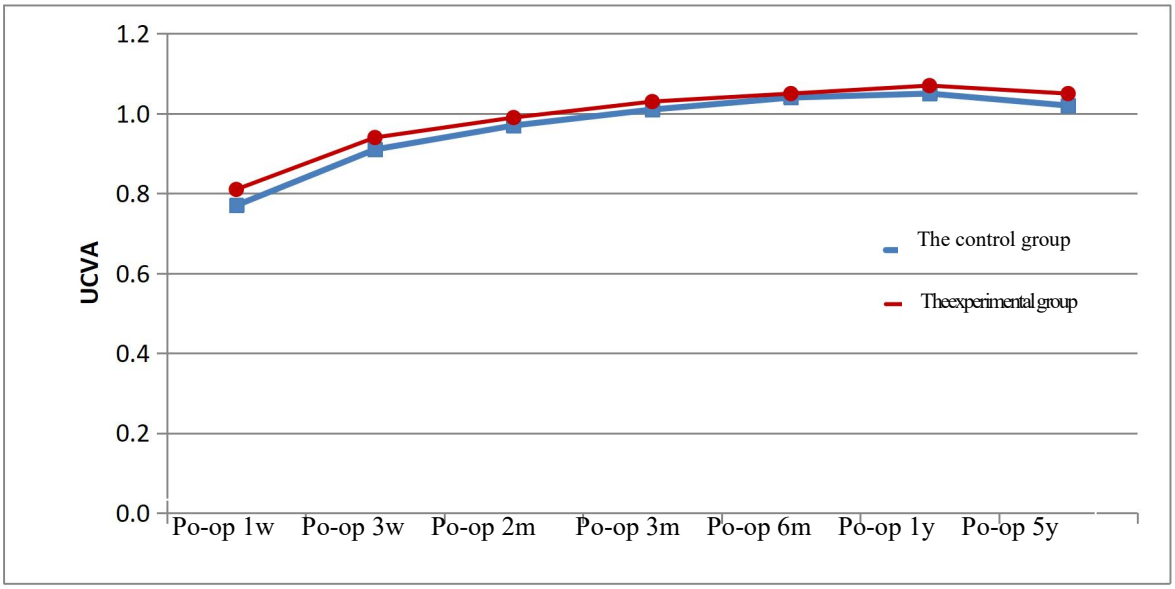

Figure 1. Uncorrected visual acuity trend at different time points after operation in the two groups.

Table 2. Comparison of postoperative diopter at different time points in the two groups

Grouping	examples	Po-op 1w	Po-op 1m	Po-op 2m	Po-op 3m	Po-op 6m	Po-op 1y	Po-op 5y
The control group	125	0.54±1.00	0.80±0.76	0.67±0.78	0.50±0.68	0.26±0.67	-0.04±0.61	-0.310±0.63
The experimental group	80	0.39±0.94	0.68±0.73	0.50±0.67	0.36±0.66	0.15±0.77	-0.05±0.71	-0.490±0.78
t		1.201	1.211	1.770	1.577	1.238	0.104	1.816
p		0.231	0.227	0.078	0.116	0.217	0.917	0.071

p<0.05 means the difference was significantly different.

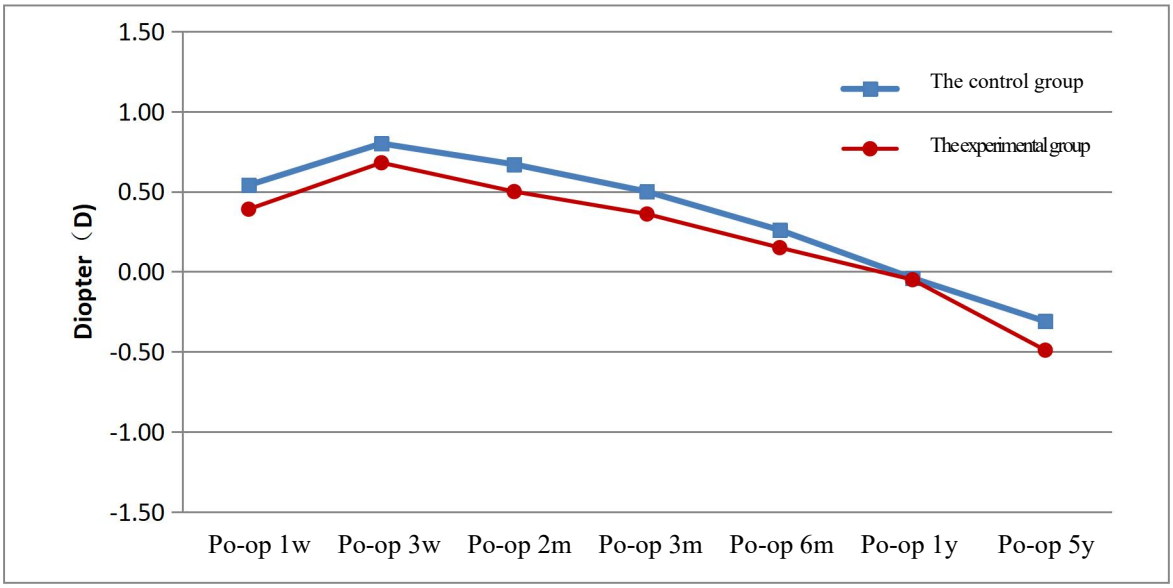

Figure 2 Diopter trend at different time points after operation in the two groups.

Table 3 Postoperative intraocular pressure in the control group

Grouping	Examples	Postoperative estimated IOP▲	Po-op 3w	Po-op 2m	Po-op 3m	Po-op 4m	Po-op 6m	Po-op 1y	Po-op 5y
The control group	125	9.52±0.96	9.93±1.71	12.13±1.89	11.21±1.93	10.93±1.90	9.87±1.69	9.98±1.58	10.28±1.83
t			1.534	12.43	9.078	3.608	1.315	1.764	1.927

			9					
P		0.127	<0.001*	<0.001*	<0.001*	0.190	0.079	0.056

Remark: ▲Postoperative estimated intraocular pressure value = 5.175 + 0.411 * preoperative intraocular pressure-0.0205 * cutting volume. *It indicates the comparison between the actual measured intraocular pressure value after operation and the postoperative estimated intraocular pressure value p <0.05. (p<0.05 means the difference was statistically significant).

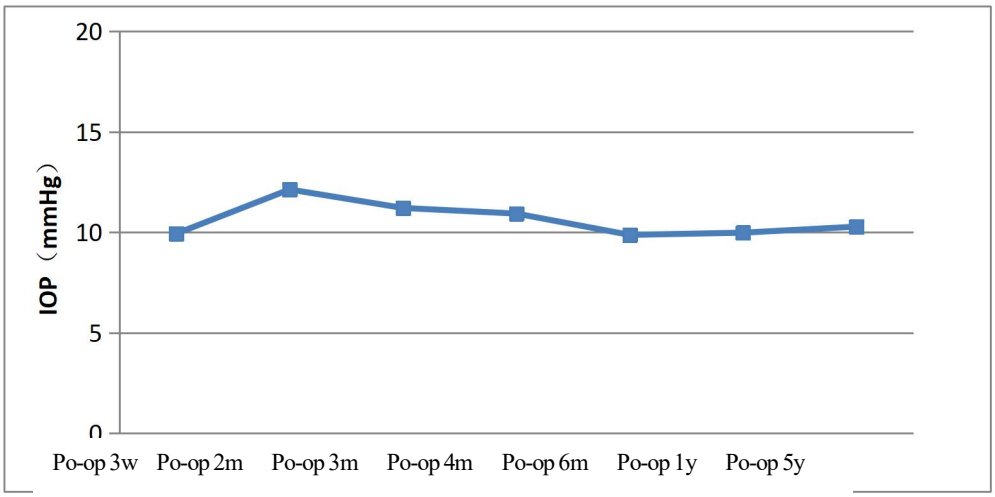

Figure 3 Postoperative intraocular pressure trend at different time points in the control group.

Table 4 Postoperative intraocular pressure in the experimental group

Grouping	Examples	Postoperative estimated IOP▲	Po-op 3w	Po-op 2m	Po-op 3m	Po-op 4m	Po-op 6m	Po-op 1y	Po-op 5y
The experimental group	80	9.46±1.03	9.74±1.45	9.90±1.82	9.97±1.96	9.73±1.91	9.50±1.38	9.80±1.23	10.08±1.89
t			1.408	1.899	1.911	1.392	0.208	1.896	1.904
P			0.161	0.063	0.053	0.168	0.836	0.060	0.057

Remark: ▲Postoperative estimated intraocular pressure value = 5.175 + 0.411 * preoperative intraocular pressure-0.0205 * cutting volume. (p<0.05 means the difference was statistically significant).

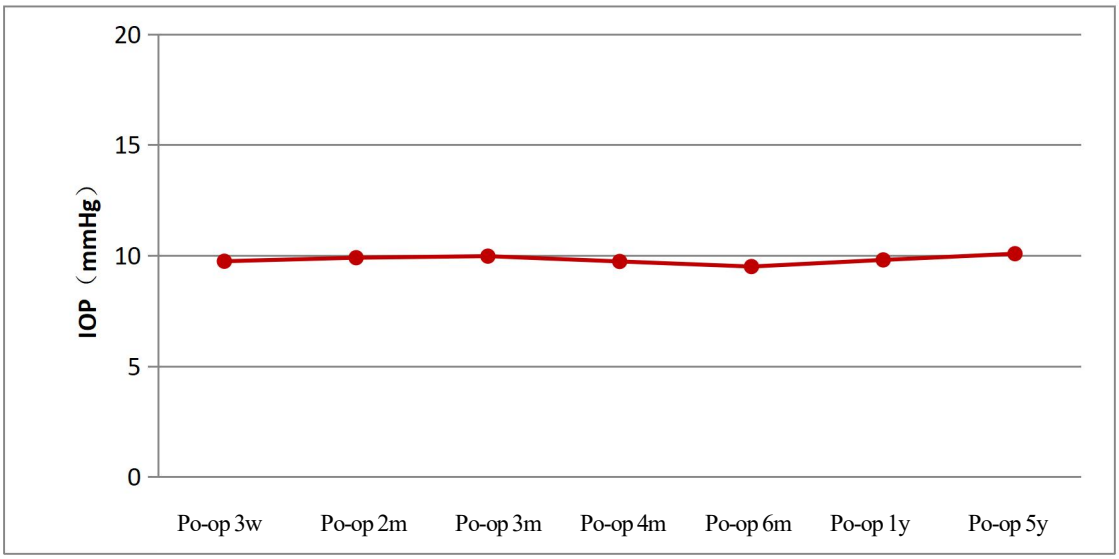

Figure 4 Postoperative intraocular pressure trend at different time points in the experimental group.

Table 5 Comparison of postoperative intraocular pressure in the two groups

Time	Grouping	examples	＜3mmHg	≥3, ＜21（mmHg）	＞21mmHg	χ^2	p
3 weeks	The control group	125	122（97.6）	3（2.4）	0（0.0）	0.000	1.000
	The experimental group	80	78（97.5）	2（2.5）	0（0.0）		
2 months	The control group	125	119（95.2）	6（4.8）	0（0.0）	2.447	0.118
	The experimental group	80	80（100.0）	0（0.0）	0（0.0）		
3 months	The control group	125	120（96.0）	5（4.0）	0（0.0）	1.814	0.178
	The experimental group	80	80（100.0）	0（0.0）	0（0.0）		
4 months	The control group	125	124（99.2）	1（0.8）	0（0.0）	0.000	1.000
	The experimental group	80	80（100.0）	0（0.0）	0（0.0）		
6 months	The control group	125	125（100.0）	0（0.0）	0（0.0）	-	-
	The experimental group	80	80（100.0）	0（0.0）	0（0.0）		

Table 6 Comparison of increased intraocular pressure in the two groups

Grouping	examples	＜3	≥3	χ^2	p
The control group	125	110（88%）	15（12%）	5.789	0.016 *
The experimental group	80	78（97.5）	2（2.5%）		

Remark: *It shows the number of patients in the control and experimental groups who measured intraocular pressure after operation compared with the number of patients expected to measure intraocular pressure increased after the operation. $P < 0.05$. ($p<0.05$ means the difference was statistically significant).

Table 7. Comparison of postoperative haze occurrence in different periods in both groups

Time	Grouping	Examples	Grades			
			0.5	1	2	3
3 Weeks	The control group	125	0（0.0）	0（0.0）	0（0.0）	0（0.0）
	The experimental group	80	0（0.0）	0（0.0）	0（0.0）	0（0.0）
2 Months	The control group	125	1（0.8）	3（2.4）	0（0.0）	0（0.0）
	The experimental group	80	0（0.0）	4（5.0）	0（0.0）	0（0.0）
3 Months	The control group	125	4（3.2）	0（0.0）	0（0.0）	0（0.0）
	The experimental group	80	0（0.0）	3（3.8）	0（0.0）	0（0.0）
4 Months	The control group	125	2（1.6）	0（0.0）	0（0.0）	0（0.0）
	The experimental group	80	0（0.0）	2（2.5）	0（0.0）	0（0.0）
6 Momths	The control group	125	0（0.0）	0（0.0）	0（0.0）	0（0.0）
	The experimental group	80	0（0.0）	0（0.0）	0（0.0）	0（0.0）
1 Year	The control group	125	0（0.0）	0（0.0）	0（0.0）	0（0.0）
	The experimental group	80	0（0.0）	0（0.0）	0（0.0）	0（0.0）

5 Years	The control group	125	0（0.0）	0（0.0）	0（0.0）	0（0.0）
	The experimental group	80	0（0.0）	0（0.0）	0（0.0）	0（0.0）

Table 8. Comparison of the occurrence of postoperative haze in both groups

Grouping	Examples	0.5	1	2	3	n（%）	χ^2	p
The control group	125	7	3	0	0	10（8%）	0.613	0.434
The experimental group	80	0	9	0	0	9（11.25%）		

$p<0.05$ means the difference was statistically significant.

3. Discussion

Refractive surgery, recognized as the safest and most favourable option for correcting myopia, has been used for more than 30 years.(17). The total refractive power of the eyeball is + 58.64D, and the cornea accounts for 70% of the total refractive power of the whole eye. Therefore, changing the cornea's refractive power can correct the refractive error, which is also a necessary surgery. Corneal refractive surgery is prevalent due to its minimally invasive or even "non-invasive" correction of refractive errors and good visual quality.

Excimer laser keratorefractive surgery promotes and implements personalized precision cutting according to patients' eye conditions, the same as the concept of precision medicine and evidence-based medicine. Nonetheless, its safety and effectiveness are still highly concerned (18-19). In particular, laser subepithelial keratomileusis (LASEK)combines the advantages of LASIK and PRK, has further expanded the indications of excimer laser surgery. However, the apparent corneal irritation, long vision recovery time, and haze are more likely than LASIK, hindered its development.

As a routine drug after corneal refractive surgery, glucocorticoid is mainly used to reduce the postoperative inflammatory response, inhibit haze production, and prevent refractive regression (20-22). However, the high intraocular pressure caused by the long-term use of glucocorticoids has become the most worrying problem of refractive surgeons. The degree and speed of intraocular pressure rise are related to drug type, dosage, duration, frequency and route of administration (23-25). Long-term high intraocular pressure will not only compress the optic nerve, causing vision loss, visual field defect, but also change the corneal biomechanical properties, and then cause severe ophthalmic diseases (23,26).

Increased intraocular pressure (IOP) is the leading risk factor for the development and progression of glaucoma (27-30). The initial response to steroids was reported by Armaly and Becker in the 1960s (31-33) and refers to patients with elevated intraocular pressure after steroid use, usually accounting for 18–36% of the total population. In most cases, intraocular pressure can be reduced to the baseline level 1-3 weeks after drug withdrawal (34). Long-term studies have found that after using glucocorticoids for 6 weeks in ordinary adults, about 1/3 of people have increased intraocular pressure of 6-15 mmHg (moderate responder), while 4%-6% of people have intraocular pressure increased by more than 15mmHg (high responders) (35-37). In addition, studies (38-39) have shown that patients with high

myopia are more susceptible to hormonal high intraocular pressure and glaucoma than moderate-to-low myopia; meantime, the incidence of hormonal high intraocular pressure and glaucoma may be higher due to changes in corneal biomechanics after corneal refractive surgery (40). This may be due to the thinning of the cornea after excimer laser keratorefractive surgery, which increases the permeability of drugs. Therefore, we should grasp the principle of small doses, fewer times and a short time to achieve a good effect. For patients with a family history of glaucoma and high myopia, intraocular pressure should be closely monitored.

Sheppard et al. (41) defined an increase in intraocular pressure above the baseline of 6 mmHg as a significant IOP rise. In clinical work, our hospital sets the actual intraocular pressure to exceed the postoperative expected intraocular pressure value of 3mmHg as the intervention standard, to ensure the effect after refractive surgery and prevent the irreversible damage of vision, visual field and optic nerve caused by the increase of intraocular pressure, this intervention index is also different from other regions and various hospitals. Studies by Lane et al. (42-46) and Boynton et al. (47-49) showed that short-term and long-term glucocorticoids did not see clinically significant elevated intraocular pressure. Shokoohi et al.'s (25) research showed that using glucocorticoids after refractive surgery to prevent the occurrence of haze, fluorometholone has less impact on intraocular pressure than other drugs of the same type and is the safest glucocorticoid. Even so, to prevent the occurrence of hormonal glaucoma, the intraocular pressure should be closely monitored during medication.

Compared with the expected intraocular pressure value at 3 weeks after operation in the long-term treatment group of this experiment, there was no statistical difference; the intraocular pressure began to increase at 2 months after the operation, and the number of new cases reached the highest peak, suggesting that glucocorticoid is more likely to have a hormonal intraocular pressure increase when used for 2 months. Compared with the expected intraocular pressure value after operation in 2months, 3months and 4months, the difference was statistically significant, indicating that the increase in intraocular pressure was positively correlated with the use of glucocorticoids. Hormonal glaucoma is a highly harmful drug-induced disease. There is still controversy about whether glucocorticoids should be used for a long time after keratorefractive surgery, clinicians also attach great importance to this. Thanathanee and his colleagues (50) have shown that the intraocular pressure returned to normal within one month after discontinuation of glucocorticoids when the intraocular pressure rose more than 5 mmHg above the baseline, four times a day for one month after refractive surgery. Chang (51) believed that the long ocular axis was a risk factor for hormonal hypertension. Therefore, before using glucocorticoids, doctors should fully consider patients' susceptibility and drug factors; after using glucocorticoids, the intraocular pressure should be monitored closely and dynamically, and appropriate drugs should be added to reduce intraocular stress. Once the abnormality is found, it is vital to deal with it timely and effectively prevent and treat and all field damage caused by hormonal glaucoma.

Compared with intraocular pressure at each time point and the expected intraocular pressure in the short-term treatment group of this experiment after the operation, the difference was not statistically significant, and there was no considerable increase trend, indicating that in maintaining the stability of intraocular pressure, about the short-term treatment of fluorometholone combined with pranoprofen has apparent advantages. It is a feasible treatment in clinical practice.

Although the short course of treatment with fluorometholone effectively prevents IOP rise and improves patients' compliance, the short period of treatment is not as practical as the long course of treatment in preventing and controlling the occurrence and severity of haze. The long-term use

of fluorometholone has the potential risk of elevated intraocular pressure. Therefore, how to choose the appropriate dosage and duration of fluorometholone has become the focus to refractive physicians and has also become the focus of our research. Both groups of haze eventually subsided, which is consistent with the results of Karimian (52). Nguyen (53) and Seibold (54) have shown that NSAIDs have the same anti-inflammatory effects as steroid hormones, but there are no side effects in theory. Because the increase in intraocular pressure is positively related to the dosage and duration of glucocorticoid use, in future clinical work, we can consider appropriately extending the time of glucocorticoid use to ensure that the intraocular pressure is controlled within the normal range after surgery and to be able to reduce the incidence of haze and reduce the severity of its occurrence.

To sum up, this study's short course of fluorometholone combined with pranoprofen eye drops is equivalent to the extended course group in maintaining the stability of uncorrected vision acuity and diopter. There is no difference between the short treatment group and the extended treatment group in preventing and reducing the incidence of haze. Still, the data shows that the harsh treatment group has a slightly higher incidence of haze and heavier grades. Due to the small sample size of this experiment, a larger sample size will be needed to be confirmed.

Declarations

1) Consent to publication

We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement, and followed publication ethics.

2) Ethical approval and consent to participants

No applicable.

3) Disclosure of conflict of interests

We declare that no conflict of interest exists.

4) Funding

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5) Availability of data and material

We declare that the data supporting the results reported in the article are available in the published article.

6) Authors' contribution

Authors contributed to this paper with the design (LXQ), literature search (PF), drafting (PF), revision (LXQ), editing (PF) and final approval (LXQ).

7) Acknowledgement

None

8) Authors' biography

None.

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