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Effect of pranoprofen, tobramycin and dexamethasone combination on recurrence prevention and tear inflammatory factors after pterygium surgery

Ling Xu[1]*, Li Wei[1], Renzhong Zhang[2], Jinyu Li[1] and Fei Xie[1]
[1]Ophthalmology Department, Qionglai Medical Center Hospital
[2]General Medicine, Wenjun Community Health Service Center, Qionglai City

Abstract: Pterygium, characterized by conjunctival overgrowth onto the cornea, poses recurrence risks post-surgery. This study evaluated the efficacy of pranoprofen + tobramycin/dexamethasone vs. tobramycin/dexamethasone alone in 108 patients (55 observation, 53 control) randomized post-pterygium surgery (March 2023–March 2024). Outcomes included ocular pain (VAS), tear inflammatory factors (IgE, IL-6, IL-8, TNF-α), tear stability (BUT, CESS, SIt), quality of life (OSDI), adverse events and recurrence at 1 day, 1 week and 4 weeks postoperatively. At 1 week, the observation group reported superior pain relief (P<0.05), with both groups achieving pain-free status by 4 weeks. Inflammatory markers and OSDI scores were significantly lower in the observation group at 1 and 4 weeks (P<0.05), alongside improved tear stability (P<0.05). No adverse events occurred. At 6-month follow-up, recurrence rates were comparable (1.85% vs. 9.43%, P>0.05), though the observation group trended lower. In conclusion, Pranoprofen + tobramycin/dexamethasone offers enhanced pain control, tear function and anti-inflammatory effects, with a potential recurrence-lowering benefit, supporting its clinical utility in pterygium management.

Keywords: Pterygium; pranoprofen; tobramycin and dexamethasone; tears; inflammatory factors.

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INTRODUCTION

Pterygium is a frequent ocular condition characterized by conjunctival tissue overgrowth, starting from the canthus and spreading into the cornea in a triangular shape, reminiscent of an insect's wing, which gives it its name (Shahraki *et al.*, 2021). Pterygium consists of the apex (the arcuate opaque area underlying the corneal epithelium at the leading edge of the pterygium), the head (the white fibrous tissue attached to the cornea) and the body (the triangular fibrovascular tissue with its base connected to the conjunctival tissue) (Kodavoor *et al.*, 2024). Current research suggests that the development of pterygium involves inflammation, neovascularization, abnormal proliferation and apoptosis, potentially associated with the condition include environmental exposures such as ultraviolet radiation, oxidative stress, inflammatory agents, climatic conditions and particulate matter (He and Wu, 2022). During the initial stages of the condition, patients frequently report sensations of an ocular foreign body, burning and tearing. As the disease progresses, the proliferating bulbar conjunctival tissue alters the refractive state of the corneal surface, causing varying degrees of corneal astigmatism and affecting vision. In advanced stages, the proliferating bulbar conjunctival tissue can cover the pupillary area, severely impairing vision (Martins, 2024). In some severe cases, pterygium may affect ocular motility (Doğan *et al.*, 2021).

Over recent years, there has been a rising prevalence of pterygium, highlighting the growing significance of surgical treatment as the primary therapeutic approach for this condition. A systematic review and meta-analysis investigated the global prevalence and risk factors of pterygium. The findings revealed that the global pooled prevalence of pterygium was 12%, with a higher prevalence observed in males compared to females. Additionally, the study identified an increasing trend in pterygium prevalence with advancing age and decreasing geographic latitude (Rezvan *et al.*, 2018). According to current research, "pterygium excision combined with autologous limbal stem cell transplantation" is considered one of the more effective surgical options for pterygium (Palewski *et al.*, 2022). However, surgical-induced ocular tissue damage often leads to significant ocular irritation symptoms and triggers ocular surface inflammatory responses, with the damaged ocular surface structure typically taking a full month to recover (Linaburg *et al.*, 2021). Current research suggests that the persistent inflammatory response on the ocular surface after surgery is a major factor contributing to the recurrence of pterygium and surgical failure (Soleimani *et al.*, 2020). The regrowth of pterygium after surgical excision is referred to as recurrent pterygium, which can cause complications such as symblepharon, conjunctival sac stenosis and restricted ocular motility, severely threatening patients' visual function (Kim *et al.*, 2023). Hence, ophthalmologists prioritize the reduction of pterygium recurrence rates following surgical intervention as a key

**Corresponding author:* e-mail: xuling5389@hotmail.com

area of concern. In response to the persistent ocular surface inflammation and high recurrence rate after pterygium surgery, extensive efforts have been made. Postoperative care is crucial for reducing the recurrence of pterygium and improving prognosis.

Pranoprofen, a non-steroidal anti-inflammatory agent, exerts its antipyretic, analgesic and anti-inflammatory actions through the inhibition of cyclooxygenase (COX) activity, thereby decreasing prostaglandin synthesis (Yin and Wu, 2024). Pranoprofen eye drops are used for the symptomatic treatment of external ocular and anterior segment inflammatory diseases, such as blepharitis, conjunctivitis, keratitis, scleritis, episcleritis, iris cyclitis, postoperative inflammation and so on (Larsson *et al.*, 2024). Tobramycin and dexamethasone belong to the class of glucocorticoid drugs, which have powerful anti-inflammatory, anti-allergic, immunosuppressive and anti-fibrotic effects, effectively inhibiting postoperative inflammatory responses and tissue proliferation (Xiao *et al.*, 2024). Tobramycin and dexamethasone eye drops, a compound preparation consisting of tobramycin and dexamethasone, are utilized in the management of ocular inflammatory conditions, including allergic inflammation, iris cyclitis, traumatic ophthalmia and serve as therapeutic and prophylactic agents against ocular infections (Gu *et al.*, 2025). A prospective, randomized trial demonstrated that the application of 0.1% pranoprofen topically can decrease the expression levels of VEGF and COX-2 in primary pterygium, suggesting its potential therapeutic benefit in lowering postoperative recurrence rates among patients with this condition (Yao *et al.*, 2021). Studies have shown that the application of tobramycin and dexamethasone eye ointment after pterygium surgery has a good therapeutic effect (Mu and Fan, 2022). Xie X *et al*. applied pranoprofen combined with tobramycin and dexamethasone in the treatment of middle-aged and elderly patients after cataract surgery and found that, compared with tobramycin and dexamethasone alone, the combination significantly improved ocular symptoms, signs, inflammatory marker levels, anterior chamber flare values, central macular thickness, corneal edema and posterior capsule opacification of the lens. It also aided in restoring intraocular pressure and visual acuity, with a lower incidence of adverse reactions and remarkable clinical efficacy (Xie *et al.*, 2024). However, there is a paucity of clinical research on the use of pranoprofen combined with tobramycin and dexamethasone in preventing postoperative recurrence of pterygium. In light of this, the present study conducts an in-depth analysis and discussion, aiming to provide a more effective postoperative management plan for clinical practice.

MATERIALS AND METHODS

Information and methods

Study design

This study is a retrospective clinical controlled study conducted at the clinical diagnosis and treatment center of our hospital. The designed operational flow is shown in fig. 1. A total of 130 pterygium patients from March 2023 to March 2024 were selected, among which 108 patients underwent pterygium surgery and met the inclusion and exclusion criteria. The patients were categorized into two groups: the observation group (n=55) receiving tobramycin and dexamethasone eye drops combined with pranoprofen postoperatively and the control group (n=53) receiving only tobramycin and dexamethasone eye drops. All patients were followed up. Outcome assessors for subjective measures (such as VAS, OSDI) were blinded to treatment allocation, while surgeons were not due to the nature of the intervention.

Clinical data

Disease diagnostic criteria: The lesion is a fibrovascular-like proliferative tissue on the surface of the eyeball, originating from the conjunctiva in the palpebral fissure area (commonly seen near the inner canthus) and gradually invading the corneal surface, which can cause ocular discomfort, decreased visual acuity and other symptoms. In severe cases, it may cause ocular movement disorders due to the traction of the pterygium. Inclusion criteria: (1) Age over 18 years; (2) Initial onset of pterygium; (3) Primary pterygium; (4) Pterygium invading more than 3 mm into the corneal limbus without invading the pupillary zone of the cornea, undergoing monocular surgery; (5) The lesion is located near the inner canthus. Exclusion criteria: (1) Accompanied by ocular cellular abnormalities caused by systemic tumors, immune system disorders, etc.; (2) Accompanied by related corneal and conjunctival diseases such as conjunctivitis and keratitis; (3) Accompanied by inflammatory eye diseases such as scleritis, iritis and blepharitis; (4) The observed eye has a history of surgery; (5) Intolerance or allergic reaction to the medications used in this study.

Grouping criteria

The observation group included 55 patients who received pranoprofen eye drops in addition to tobramycin and dexamethasone eye drops postoperatively. The control group included 53 patients who received only tobramycin and dexamethasone eye drops.

Treatment method

All patients underwent surgery (limbal stem cell transplantation) performed by the same surgeon. Surgical method: After routine disinfection of the eye, local infiltration anesthesia was administered around the pterygium. The conjunctival tissue at the neck of the pterygium was cut open and the conjunctiva and subconjunctival tissues were appropriately separated. The proliferative tissue on the surface of the sclera and cornea was excised. An appropriately sized graft (containing limbal stem cells) was taken from the inferior bulbar conjunctiva and transplanted to the exposed scleral area

after pterygium excision (with the end containing limbal stem cells aligned with the nasal corneal limbus). The free end of the inferior donor bulbar conjunctiva was pulled upwards and approximated to the inferior corneal limbus and the bulbar conjunctiva was sutured intermittently and fixed to the superficial sclera, ensuring that the entire scleral surface in the surgical area was covered by conjunctival tissue. Starting from the first day after surgery, the two groups received different eye drop treatment regimens: the control group received tobramycin and dexamethasone eye drops (specification: 5 ml, containing tobramycin 15 mg and dexamethasone 5 mg; approval number: National Medicine Permit HJ20150119; manufacturer: s.a. Alcon-Couvreur n.v.), while the observation group received pranoprofen eye drops in combination with tobramycin and dexamethasone eye drops (specification: 5 ml : 5 mg; import drug registration certificate number: H20130682; manufacturer: Senju Pharmaceutical Co., Ltd.). Both medications were used 1-2 drops at a time, 4 times a day (morning, noon, evening and before bedtime), for 4 consecutive weeks. Patients assigned to the observation group were directed to use tobramycin and dexamethasone eye drops first, followed by pranoprofen eye drops 5 minutes later to ensure adequate absorption of the medications.

Observation indicators

(1) Observation time points: 1 day postoperatively, 1 week postoperatively and 4 weeks postoperatively.

(2) The Visual Analog Scale (VAS) (He *et al.*, 2022) was employed to evaluate the intensity of ocular pain in patients, scored on a scale from 0 to 10, where 0 represents the absence of pain and 10 signifies the utmost severity of pain.

(3) Tear detection: Tear samples were collected for the measurement of tear IgE and inflammatory cytokine concentrations (Jiao *et al.*, 2024). Tear sample collection was performed without surface anesthesia and completed between 8:00 and 10:00 AM on the day of collection. Eye drop treatment was temporarily withheld before tear sample collection. The concentrations of IgE, IL-6, IL-8 and TNF-α in the tear samples were measured using a chemiluminescence assay.

(4) Postoperative observation and recording of the tear film break-up time (BUT) (Yazdani *et al.*, 2021) for patients in both groups. Fluorescein was added to the tear film and patients were instructed to blink completely several times to ensure even distribution of the fluorescein on the ocular surface. Under cobalt blue light with a slit-lamp, observations of the tear film were conducted, while an electronic stopwatch was utilized to measure the interval between the patient's final blink and the emergence of the initial dry spot on the tear film. This procedure was replicated three times and the BUT was determined as the average of all recorded durations.

(5) Postoperative observation and recording of the Corneal Epithelial Status Score (CESS) (Amparo *et al.*, 2018). Observe the staining of the corneal epithelium: 0 points for no significant staining, 1 point for only a few scattered punctate stainings, 2 points for moderate punctate staining or with some staining fusion and 3 points for dense punctate staining with staining fusion. The cornea is divided into four quadrants: superonasal, inferonasal, superotemporal and inferotemporal. Each quadrant is scored separately based on its staining condition and the final aggregate score is derived by summing the individual scores assigned to each of the four quadrants.

(6) Schirmer I test (SIt) (Zhang *et al.*, 2024): Place a Schirmer tear secretion test strip in the outer one-third of the conjunctival sac of the patient's operated eye's lower lid, instruct the patient to close their eyes and observe the length wetted by tears after 5 minutes. A length of <10 mm indicates reduced tear secretion.

(7) The Ocular Surface Disease Index (OSDI) (Martin and Emo Research, 2023) was employed to assess the influence of ocular conditions on patients' daily life quality, encompassing three dimensions: "ocular symptoms," "visual function," and "environmental trigger factors," with a total of 12 items, each scored from 0 to 4. Ocular symptoms include five indicators: photophobia, grittiness, eye pain, fluctuating vision and poor vision; visual function includes the impact on reading, night driving, using electronic devices and watching television; environmental trigger factors include three situations: windy weather, very dry environments and air-conditioned rooms. The scoring system is as follows: 0 points indicate "never," 1 point for "some of the time," 2 points for "half of the time," 3 points for "most of the time," and 4 points for "all of the time." The cumulative score can range from 0 to 48, with increasing scores reflecting greater severity of dysfunction.

(8) Record any adverse reactions in patients, including ocular irritation, increased intraocular pressure, ocular infections, allergic reactions, etc. During medication use, closely monitor patients' symptoms and discontinue the medication promptly if any discomfort occurs.

(9) A six-month postoperative follow-up period was implemented to monitor the incidence of pterygium recurrence in both patient groups. The criteria for recurrence: under a slit-lamp, obvious dilated blood vessels invading towards the cornea can be observed on the scleral surface of the surgical area, accompanied by local fibrovascular tissue hyperplasia and elevation, or the proliferating fibrovascular tissue in the surgical area has broken through the corneal limbus and invaded the corneal surface.

Ethical approval

This study was approved by the Ethics Committee of the Qionglai Medical Center Hospital (Ethical Approval Code: 2023-1).

STATISTICAL ANALYSIS

Statistical analysis was conducted with SPSS 25.0. Normally distributed variables were reported as mean ± SD ($\bar{x} \pm s$), compared using the t-test. Non-normal variables were presented as [M (Q1, Q3)] and compared with the Mann-Whitney U test. Categorical data were given as n (%), with comparisons using χ^2 or Fisher's exact test as appropriate. All tests were two-sided and P<0.05 indicated significance.

RESULTS

Comparison of baseline characteristics

The χ^2 test was used for comparisons of gender, education level and lesion location between the control group and the observation group. Age and duration of illness were normally distributed and were compared using the independent samples t-test. No statistically significant disparities in baseline demographic features were observed between the two groups (P>0.05), thereby ensuring the comparability of subsequent intervention outcomes. See table 1.

The change in the degree of ocular pain over time after surgery

On the first day after surgery, a comparison of the degree of ocular pain between the two groups showed no statistically difference (P>0.05). One week after surgery, the ocular pain symptoms in the observation group were significantly alleviated and the improvement was significantly better than that in the control group (P<0.05). Over time, by four weeks after surgery, both groups of patients had no pain or only mild discomfort in their eyes. See table 2.

Changes in tear IgE and inflammatory cytokine concentrations over time

On the first day after surgery, a comparison of the concentrations of LgE, IL-6, IL-8 and TNF-α in the tears of the two groups of patients showed no statistically significant differences (P>0.05). However, at the one-week and four-week post-operative time points, with the continued use of medication, the concentrations of inflammatory cytokines in the tears of both groups showed a significant decreasing trend. Remarkably, the observation group exhibited significantly greater improvement compared to the control group, with a statistically significant difference between them (P<0.05). See table 3.

Changes in tear film stability over time after surgery

On the first day after surgery, a comparison of the BUT, CESS and SIt between the two groups revealed no statistically difference (P>0.05). One week and four weeks after surgery, the tear film stability of patients in the observation group underwent notable enhancement, with significantly superior improvements in BUT, CESS and SIt values compared to those in the control group (P<0.05). See table 4.

Changes in eye-related quality of daily life over time after surgery

One week and four weeks postoperatively, the observation group exhibited significant improvements in eye-related quality of daily life, as evidenced by notably lower OSDI scores compared to the control group. This was manifested by marked improvements in ocular symptoms, enhanced visual function and significantly reduced impact of environmental triggers on the eyes (P<0.05). See table 5.

Adverse effect

Adverse reactions (such as ocular irritation, infection) were monitored daily for the first postoperative week and weekly thereafter. No severe adverse events requiring discontinuation occurred. Mild irritation (n=3 in the control group, n=2 in the observation group) resolved without intervention. This positive result indicates that both pranoprofen and tobramycin dexamethasone performed well in terms of safety and did not have serious negative impacts on the overall health of the participants.

Postoperative recurrence of pterygium

At the six-month follow-up post-pterygium surgery, the observation group reported 1 recurrence among 55 patients, yielding a recurrence rate of 1.85%, whereas the control group had 5 recurrences among 53 patients, resulting in a recurrence rate of 9.43%. However, no statistically significant difference was observed between the two groups in terms of recurrence rates (P>0.05). See table 6.

DISCUSSION

Clinical studies have shown that the recurrence rate after simple pterygium excision surgery ranges from 10% to 40%, which is a challenging problem in ophthalmic clinical practice. The mechanism involves the interaction of multiple factors such as inflammatory response, angiogenesis and oxidative stress (Akbari, 2022). While surgical advancements like combined amniotic membrane transplantation and limbal stem cell transplantation can somewhat decrease the risk of conjunctival abnormal proliferation recurrence, persistent postoperative inflammation continues to be a pivotal factor in recurrence (Gupta *et al.*, 2024; Paganelli *et al.*, 2023). Studies have demonstrated that surgical trauma and postoperative inflammatory response can activate residual fibroblasts and vascular cells, resulting in the accumulation of extracellular matrix proteins and the formation of fibrovascular structures, which is one of the main causes of recurrence (Wang *et al.*, 2021). Furthermore, recurrent pterygium exhibits significantly elevated expression levels of inflammatory cytokines, including interleukins and tumor necrosis factor, which play a crucial role in facilitating recurrence compared to primary pterygium (Wan *et al.*, 2022). This study innovatively adopted a dual-pathway anti-inflammatory strategy combining pranoprofen (a non-steroidal anti-inflammatory drug,

NSAID) with tobramycin dexamethasone (an antibiotic-glucocorticoid combination), which not only verified its effect on improving postoperative pain and tear function but also revealed the potential value of inflammatory microenvironment regulation in inhibiting recurrence.

Postoperative pain is a direct issue that patients face in the early postoperative period, which not only disrupts patients' physical comfort but also triggers adverse emotional states, including anxiety and depression at the psychological level, thereby affecting patients' rehabilitation compliance and overall recovery process. The findings of this study suggest that, one week after surgery, the ocular pain symptoms of patients in the observation group were significantly mitigated and the observed improvement was notably superior to that of the control group. From a pharmacological perspective, pranoprofen, as a non-steroidal anti-inflammatory drug, specifically acts on cyclooxygenase (COX) to inhibit its activity, thereby effectively blocking the synthesis pathway of prostaglandins (Yao, Wang, Zhao, Wang, Yue, Ding and Liu, 2021). Prostaglandins, as important inflammatory mediators, serve as crucial factors in the inflammatory response. Their excessive production can lead to vasodilation, tissue edema and increased sensitivity of pain receptors to other pain-causing substances, making pain signals more easily transmitted to the central nervous system (Gahbauer *et al.*, 2023). By reducing prostaglandin production, pranoprofen decreases the sensitivity of pain receptors at the source, exerting an analgesic effect (Gong *et al.*, 2024). During the inflammatory process, in addition to prostaglandins, there are other inflammatory mediators such as histamine and leukotrienes, which not only trigger inflammatory reactions but also stimulate nerve endings, enhancing the sensitivity of pain receptors and thereby causing pain (García-Fernández *et al.*, 2023). Tobramycin dexamethasone alleviates inflammatory responses by inhibiting the release and action of these inflammatory mediators, indirectly exerting an analgesic effect and relieving pain caused by inflammation (Rasheed *et al.*, 2022). The combination of the two drugs synergistically acts on different inflammatory pathways, effectively reducing the inflammatory cascade reaction induced by surgical trauma, thereby achieving effective relief of pain symptoms. By four weeks postoperatively, both groups of patients experienced no pain or only mild discomfort in their eyes, which not only reflects the body's powerful self-healing ability but also indirectly demonstrates the positive promoting effect of effective early inflammation control on subsequent rehabilitation.

Tears play an indispensable role in maintaining the moisture, nutrition and immune balance of the ocular surface. The levels of inflammatory factors in tears are important indicators reflecting the inflammatory status of the ocular surface. On the first day after surgery, a comparison of the concentrations of IgE, IL-6, IL-8 and TNF-α in the tears of the two patient groups showed no statistically significant differences, indicating that the tear inflammatory microenvironment immediately after surgery had not yet significantly differentiated due to different medications. However, at one week and four weeks postoperatively, with the continued use of medications, the concentrations of inflammatory factors in the tears of both groups showed a significant decreasing trend and the observation group demonstrated notably superior improvement compared to the control group, with statistically significant intergroup differences. This fully demonstrates the outstanding efficacy of combination therapy in inflammation regulation. The abnormal elevation of inflammatory factors such as IL-6, IL-8 and TNF-α during the inflammatory response can trigger immune imbalances in ocular surface tissues, leading to a series of pathological changes including cell damage, neovascularization and tissue fibrosis (Ashrafizadeh, 2024; Ren, 2024; Tang *et al.*, 2022). Pranoprofen has a certain regulatory effect on the function of inflammatory cells, reducing the chemotaxis and activation of these cells, thereby decreasing the number of immune cells that aggregate on the ocular surface. These immune cells are one of the main cellular sources of inflammatory factors and a reduction in their number and activity leads to a decrease in the secretion of inflammatory factors (Kowalski and Mack, 2020). Tobramycin dexamethasone has a broad inhibitory effect on various immune cells, such as macrophages and lymphocytes. It can inhibit the phagocytic and antigen-presenting functions of macrophages, reducing the release of inflammatory factors by macrophages. It can also induce lymphocyte apoptosis or suppress their function, decreasing the secretion of cytokines by T lymphocytes, including IL-6, IL-8, TNF-α, etc. Additionally, it inhibits the proliferation of B lymphocytes and the production of antibodies (such as IgE), thereby lowering the concentrations of these inflammatory factors in tears (Kim *et al.*, 2021; Urru *et al.*, 2020). It is noteworthy that no statistically significant difference was observed in inflammatory factors between the two groups in the early postoperative period (first day), possibly because the genomic effects of glucocorticoids take several hours or even days to fully take effect, while although pranoprofen can quickly inhibit COX activity, the accumulation of tissue penetration concentration requires time. This suggests that the first 24 hours after surgery may be a "therapeutic window for anti-inflammatory treatment," and the value of preoperative prophylactic administration in intervening in acute inflammatory responses can be explored in the future. Of particular concern is the significant decrease in IgE levels in the observation group after surgery. Considering the role of IgE-mediated type I hypersensitivity reactions in the pathogenesis of pterygium, the combination regimen may block the vicious cycle of "inflammation-angiogenesis" by inhibiting mast cell degranulation and Th2-type immune responses.

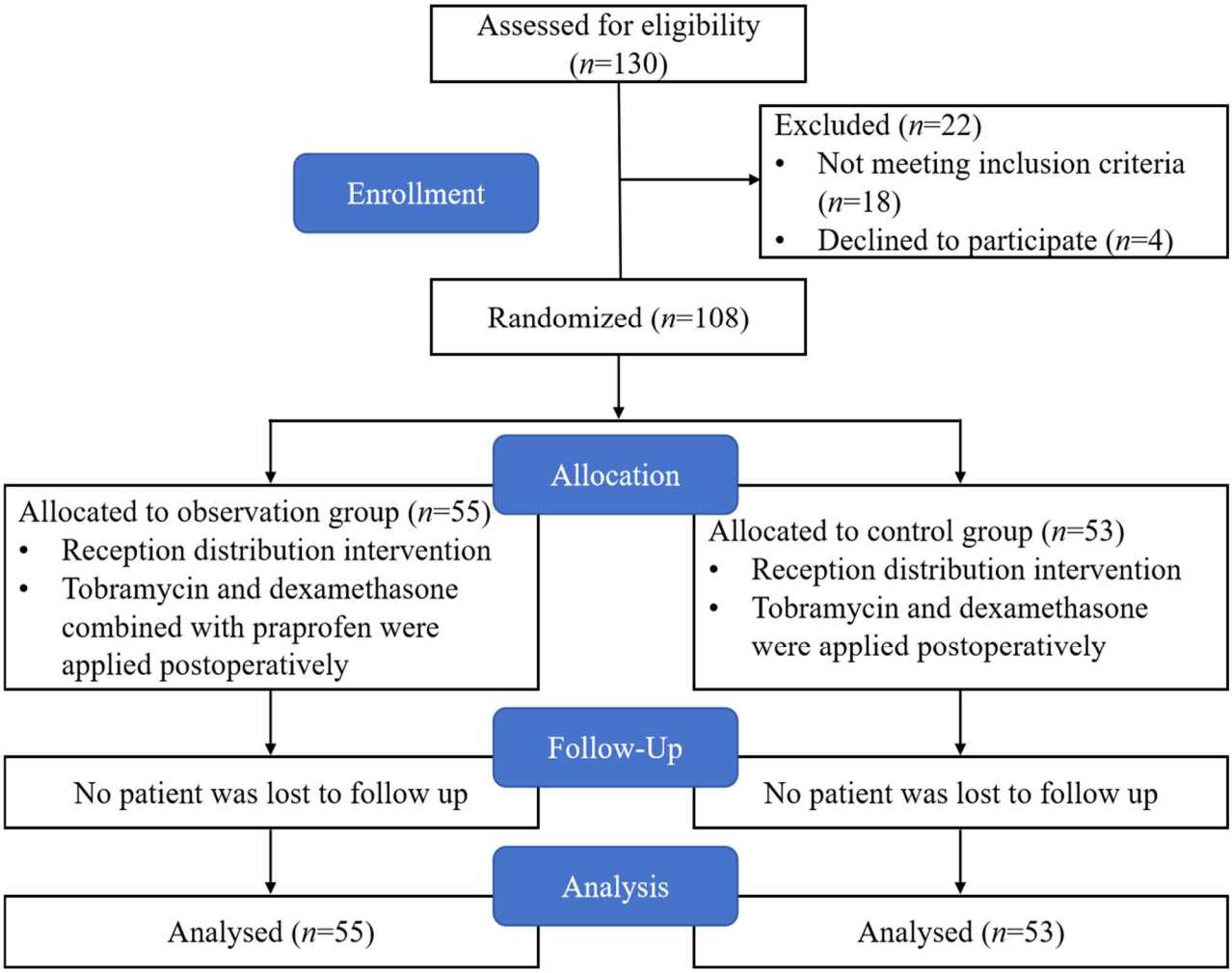

Fig. 1: Design operation process

Table 1: Comparison of Baseline Characteristics

Variables	Control group (*n*=53)	Observation group (*n*=55)	χ^2/t	*P*
sex (*n*,%)				
male	18 (33.96)	22 (40.00)	0.422	0.516
female	35 (66.04)	33 (60.00)		
age ($\overline{x}\pm s$, years)	52.42±7.31	51.56±6.53	0.639	0.524
education level (*n*,%)				
below high school	27 (50.94)	26 (47.27)	0.146	0.703
high school and above	26 (49.06)	29 (52.73)		
lesion location (*n*,%)				
left eye	28 (52.83)	32 (58.18)	0.313	0.576
right eye	25 (47.17)	23 (41.82)		
duration of illness ($\overline{x}\pm s$, year)	6.58±2.24	6.47±2.18	0.264	0.793

Table 2: VAS score comparison

Postoperative Time	Control group (*n*=53)	Observation group (*n*=55)	*Z*	*P*
Day 1	4 (3, 5)	4 (3, 5)	0.508	0.611
Week 1	3 (2, 4)	2 (1, 2)	5.688	0.000
Week 4	0 (0, 1)	0 (0, 0)	1.384	0.166

Table 3: Comparison of Inflammatory Factor Concentration

Variables	Postoperative Time	Control group (*n*=53)	Observation group (*n*=55)	*t*	*P*
LgE (ng/mL)	Day 1	382.14±42.33	387.52±40.21	0.679	0.499
	Week 1	225.76±35.75	184.33±32.44	6.310	<0.001
	Week 4	121.33±21.44	65.66±14.13	15.982	<0.001
IL-6 (pg/mL)	Day 1	42.15±16.78	40.19±16.46	0.616	0.539
	Week 1	22.48±5.44	18.66±5.77	3.539	<0.001
	Week 4	17.55±3.41	11.49±3.77	8.776	<0.001
IL-8 (pg/mL)	Day 1	158.44±34.36	150.82±35.66	1.130	0.261
	Week 1	125.66±29.44	82.74±21.44	8.684	<0.001
	Week 4	78.66±15.77	50.33±14.66	9.673	<0.001
TNF-α (pg/mL)	Day 1	75.77±19.14	70.55±18.77	1.428	0.156
	Week 1	58.67±11.42	42.56±14.72	6.341	<0.001
	Week 4	32.12±9.45	20.15±7.21	7.428	<0.001

Table 4: Comparison of tear film stability

Variables	Postoperative Time	Control group (*n*=53)	Observation group (*n*=55)	*Z/t*	*P*
BUT	Day 1	4.66±1.02	4.89±1.33	0.996	0.322
	Week 1	6.75±1.81	8.49±1.76	5.093	<0.001
	Week 4	9.11±2.01	11.28±2.33	5.186	<0.001
CESS	Day 1	8 (7, 8)	8 (7, 8)	1.423	0.155
	Week 1	5 (4, 6)	5 (4, 5)	2.079	0.038
	Week 4	1 (1, 2)	1 (0, 2)	-3.904	<0.001
SIt (mm)	Day 1	5 (4, 6)	5 (5, 6)	-1.869	0.062
	Week 1	6 (5, 7)	7 (7, 8)	-5.822	<0.001
	Week 4	9 (8, 10)	10 (9, 11)	-5.399	<0.001

Table 5: Comparison of OSDI scores

Variables	Postoperative Time	Control group (*n*=53)	Observation group (*n*=55)	*Z*	*P*
ocular symptoms	Week 1	9 (8, 10)	7 (6, 8)	7.760	<0.001
	Week 4	4 (3, 5)	2 (1, 3)	7.045	<0.001
visual function	Week 1	11 (10, 12)	9 (7.5, 11)	4.690	<0.001
	Week 4	5 (4, 6.5)	3 (2, 4)	6.625	<0.001
environmental trigger factors	Week 1	7 (7, 7)	5 (4, 5)	8.479	<0.001
	Week 4	4 (3, 5)	2 (2, 3)	7.553	<0.001

Table 6: Comparison of postoperative recurrence rates

Group	Number of recurrent cases (n)	Recurrence rate (%)
Control group (*n*=53)	5	9.43
Observation group (*n*=55)	1	1.85
χ^2	1.709	
P	0.191	

This finding provides new ideas for immunomodulatory treatment of pterygium, but further verification is needed through flow cytometry to detect changes in the ratio of Th1/Th2 cell subsets.

Pranoprofen combined with tobramycin dexamethasone inhibits inflammatory signaling pathways through multiple targets and pathways, such as the NF-κB and MAPK key signaling pathways, effectively suppressing the expression of inflammatory factors, it facilitates the remodeling of the inflammatory microenvironment of tears, thereby establishing conducive conditions for ocular surface tissue repair and tear function restoration. On the first day after surgery, a comparison of the BUT, CESS and SIt between the two patient groups showed no statistically significant differences. This may be because the surgical trauma had just occurred and the inflammatory response was in its initial stage, with the medications not yet fully exerting their effects and not yet significantly impacting tear film-related indicators. However, one week and four weeks after surgery, the tear film stability of patients in the observation group significantly improved and the improvements in BUT, CESS and SIt were significantly better than those in the control group. This indicates that the combination

therapy gradually exerted its anti-inflammatory effects over time after surgery, improving tear film stability and ocular surface conditions. As the primary defensive barrier for the ocular surface, the tear film's stability is intimately linked to visual quality (Cornejo and Levano, 2022). Inflammatory responses have the potential to disrupt the structural integrity and functional capacity of the tear film's lipid, aqueous and mucin layers, resulting in accelerated tear evaporation, shortened tear film break-up time and ultimately manifesting in symptoms such as dry eye and decreased visual acuity (Devebacak *et al.*, 2023). The combination therapy, by reducing inflammation, minimizes damage to the components of the tear film, maintains the normal structure and function of the tear film and enhances its stability, providing patients with a clearer and more comfortable visual experience. This study shows that after surgery the OSDI scores of the observation group were better than those of the control group, suggesting that the combination therapy not only improves biological indicators but also enhances treatment benefits from the patients' subjective experience perspective. It is noteworthy that during the medication period, no serious adverse events occurred in either group, indicating that both pranoprofen and tobramycin dexamethasone performed well in terms of safety and had no substantial detrimental effects on the participants' overall health.

A six-month follow-up after pterygium surgery revealed that out of 55 cases in the observation group, only 1 case recurred, with a recurrence rate of 1.85%; whereas, out of 53 cases in the control group, 5 cases recurred, with a recurrence rate of 9.43%. However, while the combination therapy showed a trend toward lower recurrence rates, the difference was not statistically significant, suggesting that the claim of recurrence prevention requires further validation. The reoccurrence of pterygium encompasses a multifaceted pathological process that involves various factors and stages, characterized by precise regulatory imbalances among various cytokines, growth factors and the extracellular matrix (Martins, 2024). Persistent inflammatory stimulation activates fibroblasts, promoting their abnormal proliferation and migration, while also inducing angiogenesis, providing sufficient nutrition and material basis for the recurrence of pterygium (Meena *et al.*, 2024). The combined use of pranoprofen and tobramycin dexamethasone, through potent inhibition of inflammation, may to some extent block the critical steps of recurrence and reduce the risk of recurrence. However, it should be noted that this study was limited by its relatively modest sample size and the brief duration of follow-up, this potential advantage has not yet been fully verified. Future large-scale, long-term follow-up studies are needed to more accurately assess the true efficacy of combination therapy in preventing recurrence.

Limitations of the study

This study shows promising initial results but has significant limitations. It didn't explore the cellular or molecular mechanisms, such as receptor interactions or signaling pathways, limiting the understanding of how the treatment works. The study also didn't assess long-term visual outcomes or quality of life beyond six months, making it unclear if the ocular surface improvements have sustained benefits. Mild irritation occurred in some participants and potential long-term safety issues, like steroid-induced intraocular pressure increases, were not addressed. The numerically lower recurrence rate in the observation group (1.85%) compared to the control group (9.43%) at six months is intriguing but lacks statistical significance. This highlights the study's limited power to detect moderate-sized effects and emphasizes the necessity of larger-scale trials to validate any potential recurrence-preventive advantages. The single-center design and short follow-up also limit the generalizability. Future research should include multicenter trials, longer follow-up and mechanistic studies to better understand the treatment's effects and optimize its use for long-term ocular health. It is noteworthy that a patient's age may influence their drug metabolism capacity, treatment adherence and ocular physiological state, while different health statuses may also exert significant impacts on postoperative recovery and treatment efficacy. In the future, this study will categorize patients into more refined subgroups based on age, health status and other relevant factors to analyze the variations in treatment responses across different subgroups.

CONCLUSION

In conclusion, the combination of pranoprofen with tobramycin and dexamethasone significantly improves pain relief, tear function and inflammatory marker levels post-pterygium surgery compared to monotherapy. While the observed trend toward lower recurrence rates is encouraging, it does not reach statistical significance, necessitating further investigation. The therapy's safety profile is favorable, but long-term monitoring is recommended. Future studies should address the limitations of this work, including larger cohorts, longer follow-up and deeper mechanistic insights, to fully establish the clinical value of this combination therapy.

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Conflict of interest

There is no conflict of interest.

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