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Efficacy of cyclosporine eye drops in managing post-cataract surgery dry eye symptoms: A randomized controlled trial

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Abstract: Many patients develop dry eye symptoms or further exacerbation post-cataract surgery. The aim is to analyse the efficacy of cyclosporine A (CsA) eye drops on the dry eye symptoms post-cataract surgery (DEPC). 100 DEPC patients admitted to First Affiliated Hospital of Gannan Medical University from August 2022 to August 2024 were randomly divided into control group (n=50) and study group (n=50): The control group was treated with sodium vitrate eye drops, the study group was treated with CsA eye drops. The primary assessments were the ocular surface disease index questionnaire (OSDI): tear break-up time (TBUT) and schirmer I test (SIT). Secondary outcomes included visual acuity, tear inflammatory factors, clinical efficacy and adverse reaction incidence. Before medication, no remarkable difference of the both groups. TBUT, SIT and visual acuity were obviously improved, and the OSDI score and inflammatory factors were markedly decreased in the both groups after medication 1 week, 2 weeks and 1 month (P<0.05). The study group were superior to the control group (P<0.05). The study group's clinical efficacy was above the control group, the adverse reaction incidence was below the control group (P<0.05). This treatment is accurate in its efficacy and has high clinical value.

Keywords: Dry eye after cataract surgery; cyclosporine an eye drops; vision; ocular surface disease; inflammatory factors

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INTRODUCTION

Cataract is one of the more common blinding eye diseases, and the incidence of this disease is on an increasing trend as the population ages (Cicinelli *et al*., 2023). Although cataract surgery is constantly developing and advancing, at present, no matter which surgical procedure is used, it inevitably damages the structure or function of the ocular surfaces, causing changes in the osmolality of the tear film, decreased mucin expression and destabilisation of the tear film, which increases friction between the eyelid brush epithelial tissue, which is originally well adhered to the cornea, and the ocular surface, and the persistent friction in turn leads to eyelid brush epithelial pathology, which increases the friction between the brush epithelial tissue and the The vicious cycle of friction between the eyelid brush epithelial tissue and the ocular surface continues to cause and exacerbate the signs and symptoms of dry eye (Leffler *et al*., 2020). Dry eye is a chronic ocular surface disease, which is an abnormality resulting from insufficient tear secretion or excessive evaporation. Its causative factors are based on abnormalities in tear quality, quantity and hydrodynamics, accompanied by tissue damage and abnormalities in neurological function, which can easily lead to visual dysfunction and seriously affect the quality of life of patients (Almaina *et al*., 2023). Symptoms include dryness, redness, and tearing with signs of decreased tear film stability or imbalance in the ocular surface microenvironment, and tear film instability and corneal epithelial damage are associated with each other in a vicious circle of worsening conditions leading to a poor prognosis (Yu *et al*., 2021). In addition, preoperative disinfection and perioperative medication can burden the ocular surface, and in order to effectively disinfect and sterilise the eye and prevent postoperative endophthalmitis, the conjunctival sac is usually rinsed with povidone-iodine before cataract surgery after routine skin disinfection, which can act quickly and effectively on the skin and mucous membranes (Shimada and Nakashizuka, 2021). Compared to tincture of iodine, povidone-iodine does not require deiodination and is less irritating to the mucous membranes, but it is toxic to the cornea and can cloud the cornea. It has also been shown that repeated topical application of povidone iodine can result in increased blepharoplasty deficiency and significant dry eye symptoms (Naderi *et al*., 2020). Complete disinfection of the ocular surface should not be expected preoperatively for intraocular surgery, as no germicidal regimen has been found to consistently decontaminate the ocular surface throughout the perioperative period. Although topical antimicrobial agents such as povidone-iodine, which are considered to be the most effective, are available, postoperative complications are still unavoidable (Zaharia *et al*., 2021).

There are few targeted interventions for postoperative dry eye in patients undergoing cataract surgery in clinical care, which has led to the worsening of these complications, thus there is a great need for an in-depth study of the causes and influencing factors of dry eye symptoms post-cataract

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surgery (DEPC) and the abnormal changes in the ocular surface, and then targeted interventions that will contribute to the elimination of the patients' ocular discomfort and the improvement of their visual acuity, as well as the improvement of the quality of their survival (Miura *et al*., 2022). At present, the traditional and commonly used method for clinical treatment of dry eye is artificial tears, which can temporarily relieve the symptoms of dry eye, but artificial tears as a substitute for tears in the treatment of a number of problems, such as artificial tears are not convenient to use, the price is not cheap and most of them contain preservatives, which have an irritating and damaging effect on the cornea, so that its therapeutic effect is not satisfactory, limiting its application in the clinic (Agarwal *et al*., 2021). Sodium vitrate eye drops are a type of artificial tears that not only help relieve dry eye symptoms, but may also promote repair and regeneration of eye tissues, thereby accelerating the patient's recovery process(Kojima *et al*., 2020).

Cyclosporine A (CsA) is a cyclic polypeptide of fungal origin containing 11 amino acids. In recent years, topical CsA eye drops have been widely used in ocular applications both domestically and internationally, and have begun to be used in the clinical treatment of a variety of ocular surface disorders due to their high efficacy and lack of apparent toxicity (Daull *et al*., 2022; Patocka *et al*., 2021). Some studies have demonstrated that CsA acts as a potent disease modifier, improving the signs and symptoms of dry keratoconjunctivitis by reducing inflammation that interferes with tear production (Jerkins *et al*., 2020). The current primary mechanism of action of CsA is that it binds to a cytoplasmic procyclic protein, thereby interfering with interleukin production, down-regulating inflammatory factors and inhibiting apoptosis and suppressing local ocular immune-inflammatory responses, and the mechanism of improvement of ocular surface epithelial disease may be the inhibition of apoptosis (Han *et al*., 2022). It has been conducted a randomised, controlled trial with Significant improvements in tear production and clinical symptoms were observed in patients with moderate to severe dry eye using 0.05% CsA gel (Peng *et al*., 2023).

Based on this study, CsA eye drops were used to treat DEPC patients with sodium vitrate eye drops as a control, and the ocular surface disease index questionnaire (OSDI): tear break-up time (TBUT) and schirmer I test (SIT) were monitored dynamically to investigate the treatment of DEPC with the changes of inflammatory factors in the tears, visual acuity, and the clinical efficacy of the CsA eye drops, so as to provide the basis for the treatment of related diseases.

MATERIALS AND METHODS

Research design

This study is a systematic evaluation and integration aimed at analysing the use and efficacy of CsA eye drops in DEPC. The design of this study was a randomised controlled trial design conducted in multiple clinical centres. The 100 patients with DEPC admitted to the Department of Ophthalmology of the First Affiliated Hospital of Gannan Medical Universityfrom August 2022 to August 2024 were selected, and were categorised in two groups depending on the different treatment protocols, with 50 patients in the control group and 50 patients in the study group. The basic clinical data of the patients were collected, in which the age range of the patients was 40-75 years. Fig. 1. is the flow chart showing that after recruiting the patients in this study and passing through the inclusion and exclusion criteria, the patients were randomly divided into the study group and the control group according to the treatment methods, and the changes in the indexes were observed after the treatment, and finally statistically analyzed.

Randomization and Blinding

A total of 100 patients with DEPC were enrolled in the clinical diagnostic trial and assigned to the study and control groups according to a computer programme-generated random allocation table. Randomisation was carried out by an independent member of staff to minimise the risk of allocation concealment. The specific task was to place each allocation in a separate envelope, a process that was opaque to participants. Whereas the intervention could not be blinded to patients and treating physicians, study outcome assessors were blinded to treatment allocation.

Participants

This study was a randomised controlled clinical trial conducted at the First Affiliated Hospital of Gannan Medical University and the study protocol was reviewed and ethically approved by the Institutional Review Board. Each participant in this study was informed and signed a consent to participate form.

Inclusion Criteria: (1) matching the diagnostic criteria related to cataract and dry eye, as well as cataract surgery performed in our hospital (Biela *et al*., 2023); (2) the whole surgical procedure progressed smoothly, with no other postoperative complications; (3) able to come to the hospital for follow-up at the specified time; (4) if one eye matched the diagnostic criteria and the inclusion criteria, only the affected eye was enrolled, while both eyes were enrolled if both eyes matched the diagnostic criteria and the inclusion criteria. Exclusion criteria: (1) combination of ocular surface and external eye diseases such as keratoconjunctivitis, conjunctivitis, pterygium, tear duct obstruction, impaction, history of ocular surgery, history of ocular trauma; (2) combination of lens dislocation, glaucoma, retinal detachment, and other serious ocular diseases; (3) combination of diabetes mellitus, autoimmune diseases, or serious diseases of the heart, lungs, brain, kidneys, and other systems; (4) history of allergy to the drugs used in the study; (5) severe mental

illness or other conditions that prevent cooperation; (6) Serious adverse reactions during treatment, including, but not limited to, severe excessive tearing, severe burning sensation, severe eye stinging, and severe conjunctival congestion; (7) Other circumstances affecting indicators of follow-up observations.

Interventions

● The patients were ensuing divided into a control group and an study group, both of which underwent cataract surgery according to conventional surgical methods, and were given routine anti-inflammatory drug interventions in the postoperative period, treated with tobramycin dexamethasone eye drops (Specification: 5mL; Approval No.: H20150119; Manufacturer: s.a. Alcon-Couvreurn.v.). The tobramycin dexamethasone eye drops are compounded and formulated to contain tobramycin 15 mg and dexamethasone 5 mg per 5 mL. Drops every 4-6 h, 1 drop/times (approximately 0.04-0.05 mL).

● The control group was given sodium vitrate eye drops (Specification: 5 mL; Approval No.: H20173248; Manufacturer: Sentian Pharmaceuticals (China) Co. Ltd.). Drops every 4-5 h, 1 drop/times (approximately 0.04-0.05 mL): and the concentration of sodium vitrate eye drops is 0.3%. The duration of the pharmacological intervention was 1 month.

● The study group was treated with CsA eye drops (Specification: 5 mL: 150 mg; Approval No.: J20180008; Manufacturer: Santen Pharmaceutical (China) Co. Ltd.). Drops every 4 h, 1 drop/times (approximately 0.04-0.05 mL): and the concentration of CsA eye drops is 3%. The duration of the pharmacological intervention was 1 month.

Therapeutic effect observation

The relevant indicators were observed and recorded in detail before the administration of the drug, 1 week, 2 weeks and 1 month respectively.

● ***OSDI***: This questionnaire assesses the subjective symptoms of dry eye affecting patients in 3 dimensions: environment, visual function, and symptoms, including 12 items such as dry eyes, itchy eyes, pain, swelling, foreign body sensation, burning sensation, photophobia, poorly sustained vision, bloodshot eyes, easy fatigue and increased discharge (Yang *et al*., 2022). Based on the degree and frequency of occurrence, each symptom was classified into the following five scales: 0 for never occurring; 1 for occasional; 2 for occurring roughly 50% of the time; 3 for occurring from time to time; and 4 for persistent. The total score is equal to the total value of the ratings of all the questions on the questionnaire multiplied by 25 divided by the number of questionnaire questions answered, with higher ratings indicating greater severity.

● ***TBUT***: TBUT was analysed in both groups of patients (Sędzikowska *et al*., 2021). When examining this index, approximately 2 μL of 1% fluorescein sodium was first dropped into the conjunctival sac of the patient's lower eyelid. The patients were then asked to blink three times in a row and allowed to open their eyes normally. The tear film was observed using cobalt blue light from a slit lamp, and timing was started after the last transient opening of the eyes, and the observation ended when the first dry spot appeared on the surface of the tear film stained with fluorescein.

● ***SIT***: First, the patient was seated in a dark room, and the examiner placed a standard filter paper strip (5 mm × 35 mm): with the tip folded inward, into the conjunctival sac (without anaesthetic) in the middle and outer third of the patient's lower eyelid, with the tail end of the strip hanging outside the eyelid. The patient was told to close the eyes slightly, look upward, and not to restrict blinking. After 5 min, the lower eyelid was gently pulled to remove the strip of filter paper, and the length of the strip of filter paper wetted was examined and recorded (Zhao *et al*., 2023). SIT>10 mm was considered normal, and the corresponding values for low secretion and dry eyes were below 10 mm and 5 mm, respectively.

● ***Visual acuity***: Tested by a standard logarithmic visual acuity chart.

● ***Inflammatory factors***: Tear fluid was collected from both groups of patients, and the specimens were uniformly tested by ELISA method by our laboratory department, and the levels of inflammatory factors of the patients were recorded separately (Lu *et al*., 2021). Tear fluid interleukin-6 (IL-6): interleukin-1β (IL-1β) and tumour necrosis factor-α (TNF-α) levels were analysed by human IL-6 ELISA kit (PI330, Shanghai Beyotime Biotechnology Co., Ltd.): human IL-1β ELISA kit (PI305, Shanghai Beyotime Biotechnology Co., Ltd.) and human TNF-α ELISA kit (97072ES96, Shanghai Yeasen Biotechnology Co., Ltd.): respectively.

● ***Efficacy judgement***: Cured: all clinical symptoms disappeared, such as dry eyes, red eyes, foreign body sensation, etc., no positive signs were seen in slit lamp examination, SIT>10 mm /5 min, and fluorescein staining was negative. Significant effect: the above symptoms were greatly reduced compared with those before the intervention, the slit lamp examination was basically normal, the SIT was in the range of 5-10 mm, and the fluorescein staining was negative. Effective: patients with a reduction of the above symptoms compared with the pre-intervention period, SIT <5 mm /5 min, positive fluorescein staining. Ineffective: patients did not see a significant reduction in the above symptoms, or even became more severe, SIT <5 mm /5 min, and fluorescein staining was strongly positive. The overall efficiency was determined based on the sum of the first three.

● ***Incidence of adverse reactions****:* Count the number of patients who experienced dizziness and headache, blurred vision and drowsiness during treatment and analyse the incidence of adverse reactions.

Sample size calculation

A power analysis was conducted in this study using G*Power 3.1.9.7 software to determine the sample size required to detect statistically significant differences. The sample size was calculated based on the primary outcome of the OSDI score. With an α level of 0.05 and 80% power analysis, the findings showed that a sample size of 42 patients per group was required. The sample size selected for this study was 50 patients in each group, and in combination with the patients' ocular treatments, there were a total of 69 eyes in the study group and 67 eyes in the control group. Therefore, we considered the sample size of the present study to be able to draw reliable conclusions.

Ethical Approval

This study was a randomised controlled clinical trial conducted at the First Affiliated Hospital of Gannan Medical University and the study protocol was reviewed and ethically approved by the Institutional Review Board. The ethical approval number is: GN2091-20153.

STATISTICAL ANALYSIS

Data were analyzed using SPSS 27.0 statistical software. Measurements data conformed to normal distribution were ($\bar{x}$±s): and comparisons among groups was made using independent samples *t*-test, and count data were expressed as rate (%) using x^2 test, with $P<0.05$ meaning the discrepancy was statistically significance.

RESULTS

Baseline information

The baseline demographic characteristics and baseline status of patients randomly assigned to the control and study groups are shown in Table 1. There were no significant differences between the two groups in terms of demographic variables/instruments/status ($P>0.05$). Thus, the randomisation process achieved the important goal of evenly assigning participants to the two groups, which were comparable at the pre-treatment level, and the confounding of demographic/clinical factors did not affect the analysis of treatment outcomes.

OSDI

The results of OSDI scores analysed for both groups are demonstrated in Table 2, with no remarkable discrepancy in scores among the both groups before medication ($P>0.05$). After one week of medication, the scores of patients in both groups declined remarkably, and the degree of decrease became more pronounced over time, with scores at 1 month of medication markedly below the 2 weeks of medication, 1 week of medication, and before medication ($P<0.001$). Between groups, the OSDI scores of patients in the study group were remarkably below the control group from 1 week of dosing to 1 month of dosing ($P<0.001$). This result suggests that the occurrence of subjective symptoms of dry eye was markedly reduced in both groups after medication, and the patients in the study group had better symptom relief.

TBUT

The results of TBUT analysis of the both groups of patients are demonstrated in Table 3, and no discrepancy was found in TBUT results of the both groups of patients before medication ($P>0.05$). After 1 week of medication, the TBUT results of the both groups of patients were markedly elevated, and with the increasing time of medication, the TBUT results subsequently increased remarkably, and the TBUT results of 1 month of medication were the highest, which was remarkably above the 2 weeks of medication, the 1 week of medication, and the pre-medication ($P<0.001$). In the study group, the increase in TBUT was more marked in the 1 week, 2 weeks and 1 month medication in comparison with the control group ($P<0.001$). This indicates that tear film instability was remarkably improved in both groups, and the improvement was better in the study group.

SIT

The results of SIT analysis for the both groups of patients are demonstrated in Table 4, and no remarkable difference was found among the SIT results of the both groups of patients before the medication ($P>0.05$). After medication, the SIT results of patients in both groups increased remarkably, and the increasing of SIT was more remarkable the more time of medication, and the highest SIT result was found in 1 month of medication, remarkably above the 2 weeks, 1 week and pre-medication ($P<0.001$). Between groups, the SIT results of patients in the study group were markedly above the control group from 1 week to 1 month of medication ($P<0.001$). This result indicated that tear secretion was markedly improved in both groups after medication, and the improvement in the degree of tear secretion was better in the patients in the study group.

Visual acuity

The results of visual acuity analyses of the both groups of patients are presented in Table 5, and no remarkable discrepancy was found among the results of visual acuity of the both groups of patients before medication ($P>0.05$). After 1 week of medication, the visual acuity of patients in both groups improved remarkably, and the visual acuity improved markedly at 2 weeks and 1 month comparing with that before medication, and the improvement of visual acuity was most obvious at 1 month of medication ($P<0.001$). In the study group, the improvement of visual acuity was more obvious after 1 week, 2 weeks and 1

month versus the control group (P<0.001). This indicates that the visual acuity of the patients in both groups improved remarkably after medication, and the visual acuity of the patients in the study group improved to a more marked degree.

Inflammatory factors

The results of the analysis of inflammatory factors of IL-6, IL-1β and TNF-α in the tear fluid of the both groups of patients are demonstrated in Table 6, and no remarkable discrepancy was found in the concentration of inflammatory factors in the tear fluid before medication (P>0.05). After medication, the levels of inflammatory factors in both groups decreased remarkably, and the lowest levels of inflammatory factors were observed in 1 month of medication, which were remarkably below the 2 weeks, 1 week and pre-medication (P<0.05). Compared among the groups, from 1 week to 1 month of medication, the levels of inflammatory factors of patients in the study group were markedly below the control group (P<0.05). This indicates that the level of inflammatory factors in the tear fluid of patients in both groups was markedly reduced after medication, and the effect of the reduction of tear fluid inflammatory reaction was better in the study group.

Determination of therapeutic efficacy

The results of the clinical efficacy analysis of the both groups of patients are demonstrated in Table 7, the total effective rate of treatment in the control group was 86.00% (43/50): and the study group was 96.00% (48/50): which was remarkably above the control group, and the the discrepancy was remarkable (P<0.05): indicating that the patients in the study group showed a better therapeutic efficacy.

Incidence of adverse reactions

Adverse reactions such as dizziness headache and blurred vision occurred during the medication period in the both groups as presented in Table 8, the adverse incidence of control group was 12.00% (6/50): and the adverse incidence of the study group was 4.00% (2/50): indicating that the adverse incidence of the patients in the study group was markedly below the control group (P<0.05).

DISCUSSION

There is no specific treatment for DEPC, and it is often treated with medications such as anti-inflammatory and antibacterial drugs and artificial tear substitutes or non-pharmacological treatments such as eyelid margin cleansing and blepharoplasty (Borowska Waniak *et al*., 2023; Rák and Csutak, 2024). Anti-inflammatory and antimicrobial medications may provide temporary relief, but long-term efficacy is uncertain and recurrence rates are high, possibly due to increased blepharospasmalacia from repeated topical antibiotic use, and preservatives such as benzalkonium chloride, contained in anti-inflammatory medications and drops, are corneal epithelial toxicity, which can destabilize the tear film(Nguyen *et al*., 2023; Vernhardsdottir *et al*., 2022). Manipulations such as topical physiotherapy during the postoperative recovery period also increase the risk of postoperative infection and delay incision recovery(F. Guo *et al*., 2022; Nieć *et al*., 2024). Artificial tears are medicinal agents that mimic normal tears, and have characteristics such as mucus and water absorption, which can moist the surface of the eye to protect the eye and improve the symptom of dryness and astigmatism when applied to the surface of the eye (Sun *et al*., 2024). However, the disadvantages of artificial tear replacement therapy are obvious. Artificial tears need to be used several times for a long period of time, which causes some inconvenience to the patients' life (Kathuria *et al*., 2021). Artificial tears are after all only a substitute, their composition is hardly close to that of real physiological tears and most of them contain preservatives that do not alleviate the inflammatory conditions of the eye, so they are often ineffective and difficult to provide patients with a high quality of life and visual quality (Semp *et al*., 2023). Therefore, finding efficient and less toxic therapeutic measures to treat DEPC is an urgent task.

CsA is a cyclic hydrophobic peptide isolated from the metabolites of *Aspergillus polysporus* and *Aspergillus columnaris*, and it can inhibit T-cell proliferation, antibody production, and cytokine secretion through selective inhibition of calcium-dependent phosphatases, thus exerting immunosuppressive effects (Periman *et al*., 2020). The immunosuppressive effects of CsA are highly targeted, reversible, and non-myelotoxic, and have been progressively used to inhibit rejection in organ transplantation, and in the treatment of aplastic anaemia, glomerulonephritis, and autoimmune diseases (Lee *et al*., 2023; Liddicoat and Lavelle, 2019; Zhu *et al*., 2023). Subsequently, it has been demonstrated that CsA suppresses localised inflammation in the eye by reducing T-lymphocyte infiltration and down-regulating the secretion of inflammatory factors (van Geffen *et al*., 2022). At the same time, the drug has been shown to increase tear production in patients while exerting an immunosuppressive effect (Liu *et al*., 2025). In recent years, CsA has begun to be widely used in the treatments of dry eye caused by various factors in ophthalmology.

Usually, CsA is used as an immunosuppressant by oral administration or direct injection (Patel and Wairkar, 2019). And when CsA is applied ocularly, its application is hampered by the difficulty in entering the eye due to factors such as the blood-eye barrier. The ocular formulations of CsA reported so far are: aqueous solvent, oil solvent, liposome, collagen mask and implant (Biswas *et al*., 2024). Whereas, we chose liposomal eye drops, whose liposomes are enclosed vesicles consisting of one or more lipid-like bilayers, which can contain drugs in or between their bilayers.

Table 1: Baseline characteristics of patients in each group

Parameter	Control group (*n*=50)	Study group (*n*=50)	t/x^2	*P*
Age (years)	58.46±9.47	58.74±10.18	0.142	0.887
Gender (Male/Female)	27/23	26/24	0.040	0.841
Body mass index (kg/m^2)	24.33±2.25	24.27±2.93	-0.115	0.909
Variable (single/double)	33/17	31/19	0.174	0.677

Table 2: Analysis of OSDI scores

Medication duration	Control group	Study group	*t*	*P*
Pre-medication	25.61±2.07	25.52±2.08	-0.217	0.829
1 week	22.18±2.25*	17.90±1.51*	-11.169	<0.001
2 weeks	19.90±2.07^{*a}	16.94±2.12^{*a}	-7.064	<0.001
1 month	17.51±1.80^{*ab}	14.04±2.18^{*ab}	-8.679	<0.001

Note: '*' indicates remarkable differences from pre-dose, 'a' indicates remarkable differences from 1 week, and 'b' indicates remarkable differences from 2 weeks.

Table 3: Analysis of TBUT results

Medication duration	Control group	Study group	*t*	*P*
Pre-medication	2.41±0.53	2.40±0.47	-0.100	0.921
1 week	3.11±0.40*	3.44±0.51*	3.600	<0.001
2 weeks	3.33±0.51^{*a}	3.75±0.51^{*a}	4.118	<0.001
1 month	3.70±0.49^{*ab}	4.05±0.50^{*ab}	3.535	<0.001

Note: '*' indicates remarkable differences from pre-dose, 'a' indicates remarkable differences from 1 week, and 'b' indicates remarkable differences from 2 weeks.

Table 4: Analysis of SIT results

Medication duration	Control group	Study group	*t*	*P*
Pre-medication	12.03±1.67	12.00±1.95	-0.0826	0.934
1 week	12.81±1.50*	16.89±1.71*	12.683	<0.001
2 weeks	13.50±1.69^{*a}	18.52±1.79^{*a}	14.419	<0.001
1 month	14.23±1.40^{*ab}	20.06±1.89^{*ab}	17.527	<0.001

Note: '*' indicates remarkable differences from pre-dose, 'a' indicates remarkable differences from 1 week, and 'b' indicates remarkable differences from 2 weeks.

Table 5: Comparison of visual acuity

Medication duration	Control group	Study group	*t*	*P*
Pre-medication	0.14±0.05	0.15±0.06	0.905	0.368
1 week	0.31±0.09*	0.39±0.10*	4.205	<0.001
2 weeks	0.39±0.10^{*a}	0.58±0.10^{*a}	9.500	<0.001
1 month	0.51±0.07^{*ab}	0.75±0.10^{*ab}	13.903	<0.001

Note: '*' indicates remarkable differences from pre-dose, 'a' indicates remarkable differences from 1 week, and 'b' indicates remarkable differences from 2 weeks.

Moreover, liposomal drug carriers have significant advantages such as slow-release potentiation, reduced drug toxicity, targeted release of drugs and increased corneal permeability of drugs (Y. X. Guo and He, 2024). Some research has reviewed showed that liposomes/microemulsions as a carrier for CsA delivery contribute to corneal uptake capacity of CsA (Wiącek *et al*., 2020).

Patients with DEPC may experience a wide range of uncomfortable ocular symptoms, the most common of which include dry eyes, foreign body sensation, and increased ocular discharge (Kato *et al*., 2019). The OSDI questionnaire was used to assess the severity of dry eye symptoms in conjunction with the frequency and severity of associated symptoms (Rodriguez Garcia *et al*., 2023). In addition, TBUT has the advantages of high reliability, easy and quick operation, and is an indispensable objective examination index for the diagnosis of ocular surface diseases (Gawash *et al*., 2024). SIT is also one of the most important indexes in the diagnosis of dry eye, and the filter paper strip method is simple, quick, and inexpensive, so it is still widely used (Yadav *et al*., 2024).

Table 6: Comparison of inflammatory factor indicators

	Medication duration	Control group	Study group	*t*	*P*
IL-6	Pre-medication	3.44±0.46	3.48±0.48	0.425	0.672
(pg/mL)	1 week	2.82±0.36*	2.56±0.38*	-3.512	<0.001
	2 weeks	2.56±0.40^{*a}	2.33±0.28^{*a}	-3.331	<0.001
	1 month	2.27±0.27^{*ab}	1.90±0.25^{*ab}	-7.110	<0.001
IL-1β	Pre-medication	14.55±4.32	14.28±4.04	0.836	0.748
(pg/mL)	1 week	12.12±2.99*	9.63±2.78*	4.313	<0.001
	2 weeks	10.05±2.71^{*a}	7.27±1.60^{*a}	-6.246	<0.001
	1 month	6.14±1.56^{*ab}	4.94±0.99^{*ab}	-4.593	<0.001
TNF-α	Pre-medication	33.49±6.38	33.70±5.37	0.178	0.859
(pg/ml)	1 week	30.27±3.77*	27.94±4.08*	-2.966	<0.05
	2 weeks	28.51±4.39^{*a}	25.18±4.31^{*a}	-3.827	<0.001
	1 month	23.07±2.99^{*ab}	20.88±3.33^{*ab}	-3.460	<0.001

Note: '*' indicates remarkable differences from pre-dose, 'a' indicates remarkable differences from 1 week, and 'b' indicates remarkable differences from 2 weeks.

Table 7: Clinical efficacy analysis

Group (*n*=50)	Cured (*n*)	Significant effect (*n*)	Effective (*n*)	Ineffective (*n*)	Overall effective rate (*n*, %)
Control group	16	18	9	7	43 (86.00)
Study group	18	20	10	2	48 (96.00)
x^2	6.105				
P	0.013				

Table 8: Occurrence of adverse reactions

Group (*n*=50)	Dizziness headache (*n*)	Blurred vision (*n*)	Drowsiness (*n*)	Overall incidence (*n*, %)
Control group	2	2	2	6 (12.0)
Study group	1	1	0	2 (4.00)
x^2	4.348			
P	0.037			

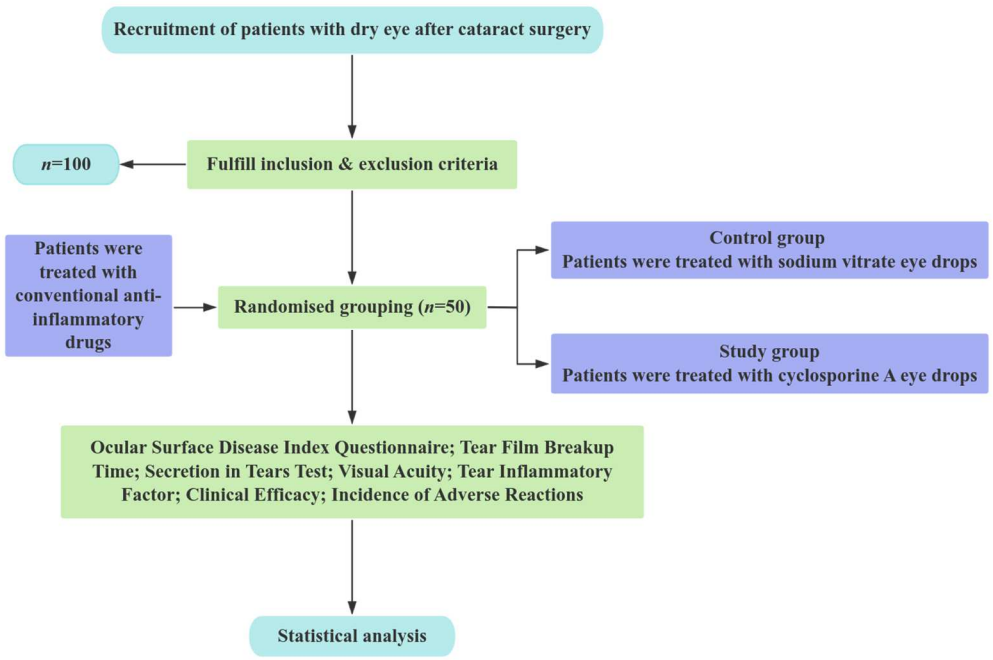

Fig. 1: Flow chart of the design of this study

In the present analysis of the results of the study, OSDI scores were remarkably reduced after medication while TBUT and SIT were remarkably improved in both the groups after 1 week, 2 weeks, and 1 month of medication as compared to the before medication (P<0.05). The study group showed better improvement than the control group during the medication period (P<0.05). Studies have been conducted using patient autologous serum eye drops for the treatment of dry eye and have reported significant reductions in OSDI scores and significant improvements in both SIT and TBUT scores in patients who received the treatment (He *et al*., 2024). A systematic evaluation and meta-analysis of the use of topical corticosteroids for the treatment of dry eye has been conducted and reported significant improvements in OSDI scores, SIT and TBUT scores after treatment (Prinz *et al*., 2022). These studies reported similar findings to the present study. The results of this study showed that the application of CsA eye drops improved subjective symptoms and tear film stability and increased tear production in DEPC patients. CsA eye drops were more effective than sodium vitrate eye drops when compared to the treatment results of both groups of patients.

Since cataract surgery can stimulate the body to produce pro-inflammatory factors, oxygen free radicals, etc., during operation, and because surgery damages the corneal nerves, affects the transient reflex, tear-stimulating reflexes and leads to a decrease in the production of tears and an increase in evaporation, increasing the osmotic pressure of the tear film, which can induce the inflammatory process, leading to the release of a variety of cytokines and chemokines, etc. (Pilotto *et al*., 2019). Therefore, inflammatory response is an important indicator in DEPC patients. The results of the study demonstrated that the levels of inflammatory factors of patients in both groups were markedly decreased after 1 week, 2 weeks, and 1 month of medication and before medication, and the lowest levels of inflammatory factors were observed in 1 month of medication, which were remarkably below 2 weeks of medication, 1 week of medication, and before medication (P<0.05). It indicated that DEPC patients had better tear inflammatory reaction reduction after applying CsA eye drops treatment. In addition, the outcomes of this study demonstrated that the visual acuity of both groups was remarkably improved after 1 week, 2 weeks, and 1 month of medication compared with the pre-medication period, and the visual acuity of the study group was markedly improved in comparison with the control group (P<0.05). This may be due to the fact that the CsA eye drops improved the severity of the patient's ocular symptoms, increased tear film stability, and reduced the inflammatory response, resulting in a favorable improvement in vision (Ogawa *et al*., 2021). Based on the results of the study, it can be concluded that after the CsA eye drops were applied to DEPC patients, the patients' visual acuity improved better.

Comparative in-depth analysis showed that patients treated with CsA eye drops had significant advantages over patients treated with sodium vitrate eye drops in terms of subjective and objective indicators, such as OSDI and TBUT, at three time points after the use of the medication, which may be attributed to the fact that CsA eye drops reduced the inflammatory response, thus better improving the clinical symptoms of the patients, which also proved the advantages and practical application value of CsA eye drops. Comparative analysis demonstrated that in terms of the total clinical effectiveness rate, the study group and the control group were 96.00% and 86.00%, respectively, with the former group remarkably above the later (P<0.05). In terms of the incidence of adverse reactions, the rate in the study group was 4.00%, which was remarkably below the 12.00% in the control group (P<0.05). Some studies have reported additional benefits of CsA drops over artificial tears, especially the potential for improving TBUT and its potential to improve tear film stability (Ahmadi *et al*., 2024). Results reported in a study of topical cyclosporine eye drops (II) for the treatment of dry eye associated with primary dry syndrome were similar to the findings of this study (Gao *et al*., 2023). All of the above confirms that CsA eye drops are superior to sodium vitrate eye drops in improving visual function, tear film stability, improving the inflammatory response and patients' subjective symptoms in DEPC patients.

There are some limitations to this study. The sample size is relatively small, such as the age range, which may lead to biased findings and affect the extrapolation and reliability of the conclusions. The study design was not double-blind, which may have led to instability in the results. Differences in patients' own underlying conditions and personal preferences, such as prior severe dry eye and poor compliance, which may affect the generalizability of the study results. Regarding adverse reactions, due to individual differences and subjective factors, we only considered whether they occurred, not how they occurred, their severity and frequency. This study was conducted under the premise of ensuring the safety and wishes of the patients themselves, and in the event of serious adverse reactions, we will immediately stop the study and carry out diagnosis and related treatment. Therefore, the results of the incidence of adverse reactions may have some unreliability. In addition, only the short-term treatment effect was observed, failing to assess the long-term efficacy of CsA eye drops in improving DEPC patients, while the long-term impact is crucial for a comprehensive understanding of the treatment effect and the development of scientific treatment strategies.

CONCLUSION

In this study, we analyzed the efficacy of CsA eye drops on the symptoms of DEPC, and the results showed that after the administration of the drug, TBUT, SIT and visual

acuity of the two groups improved significantly, and OSDI score and inflammatory factor decreased significantly. The study group was superior to the control group. The clinical efficacy of the study group was above the control group, and the incidence of adverse reactions was below the control group. It shows that the treatment of DEPC patients with CsA eye drops can reduce the inflammatory reaction and improve the clinical symptoms of the patients, and the efficacy of this method is accurate, which also provides a new reference method for the clinical treatment of the relevant dry eye patients. However, this study has a small sample size and the clinical medication course was only 1 month, which failed to observe the long-term effectiveness of CsA eye drops. Due to the limitation of conditions, more specific indexes such as others could not be added. Multi-center, large-sample, high-quality clinical studies can be carried out in the future for validation.

Conflict of interests

All authors disclose no relevant conflict of interests.

REFERENCES

Agarwal P, Craig JP and Rupenthal ID (2021). Formulation considerations for the management of dry eye disease. *Pharmaceutics,* **13**(2): 207.

Ahmadi H, Tahmasbian S, Janbazi M, Amiri A and Heidari Z (2024). Evaluation of cyclosporine 0.05% and artificial tears for the management of dry eye disease following cataract surgery: A randomized controlled trial. *Ann. Med. Surg,* **86**(4): 1983-1988.

Almaina APJ, Marzon M, Sangging PRA and Himayani R (2023). Xerophthalmia: Risk factors and prevention. *MEDULA,* **13**(4.1): 114-118.

Biela K, Winiarczyk M, Borowicz D and Mackiewicz J. (2023). Dry eye disease as a cause of refractive errors after cataract surgery – A systematic review. *Clin Ophthalmol.,* **17**: 1629-1638.

Biswas A, Kumar S, Choudhury A D, Bisen A C, Sanap S N, Agrawal S, Mishra A, Verma S K, Kumar M and Bhatta R S. (2024). Polymers and their engineered analogues for ocular drug delivery: Enhancing therapeutic precision. *Biopolymers,* **115**(4): e23578.

Borowska Waniak K, Łukaszczyk A, Opala A, Skorupińska K and Marcinkiewicz A (2023). Blepharoplasty--a practical approach to the selection of surgical techniques and wound dressing. *Leczenie Ran.,* **20**(4): 153-159.

Cicinelli M V, Buchan JC, Nicholson M, Varadaraj V and Khanna RC (2023). Cataracts. *The Lancet,* **401**(10374): 377-389.

Daull P, Baudouin C, Liang H, Feraille L, Barabino S and Garrigue JS (2022). Review of preclinical outcomes of a topical cationic emulsion of cyclosporine a for the treatment of ocular surface diseases. *Ocul. Immunol. Inflamm,* **30**(7-8): 1945-1955.

Gao M, Zhao L, Liang R, Zhu Q, Zhao Q and Kong X. (2023). Evaluation of the efficacy and safety of topical 0.05% cyclosporine eye drops (II) in the treatment of dry eye associated with primary sjogren's syndrome. *Ocul. Immunol. Inflamm,* **31**(8): 1662-1668.

Gawash A, Simonetti A, Lo DF, Shamilov DD, Kumar A and Wong JC (2024). Assessing the therapeutic role of trehalose and hyaluronic acid: implications for patient care. *Int. Ophthalmol,* **44**(1): 398.

Guo F, Song J, Wang L and Yu X (2022). Upper eyelid skin laxity in elderly patients: Correction surgery with eyelid marginal incision. *Ann Plast Surg,* **89**(6): 610-614.

Guo YX and He YX (2024). Nanoparticle-based drug delivery systems: An updated strategy for treating fungal keratitis. *Colloid Interface Sci. Commun,* **61**: 100794.

Han J, Lee MK, Jang Y, Cho WJ and Kim M (2022). Repurposing of cyclophilin A inhibitors as broad-spectrum antiviral agents. *Drug Discov. Today,* **27**(7): 1895-1912.

He C, Zeng Z, Liu J Q, Qiu Q and He Y (2024). Autologous serum eye drops for patients with dry eye disease: a systematic review and meta-analysis of randomized controlled trials. *Front. Med,* **11**: 1430785.

Jerkins GW, Pattar GR and Kannarr SR (2020). A review of topical cyclosporine A formulations—A disease-modifying agent for keratoconjunctivitis sicca. *Clin Ophthalmol,* **14**: 481-489.

Kathuria A, Shamloo K, Jhanji V and Sharma A (2021). Categorization of marketed artificial tear formulations based on their ingredients: A rational approach for their use. *J. Clin. Med,* **10**(6): 1289.

Kato K, Miyake K, Hirano K and Kondo M (2019). Management of postoperative inflammation and dry eye after cataract surgery. *Cornea,* **38**(Suppl 1): S25-S33.

Kojima T, Dogru M, Kawashima M, Nakamura S and Tsubota K (2020). Advances in the diagnosis and treatment of dry eye. *Progress in Retinal and Eye Research,* **78**: 100842.

Lee H, Myoung H and Kim SM (2023). Review of two immunosuppressants: tacrolimus and cyclosporine. *J Korean Assoc Oral Maxillofac Surg,* **49**(6): 311-323.

Leffler C T, Klebanov A, Samara W A and Grzybowski A (2020). The history of cataract surgery: From couching to phacoemulsification. *Ann Transl Med,* **8**(22): 1551.

Liddicoat AM and Lavelle EC (2019). Modulation of innate immunity by cyclosporine A. *Biochem. Pharmacol,* **163**: 472-480.

Liu Y, Wang M, Zhang F, Tang J, Han X and He Y (2025). Effect of 0.05% cyclosporine A eye drops on the healing process of corneal epithelial defects in rats. *Exp. Eye Res,* **251**: 110198.

Lu Q, Zhu Z, Tan C, Zhou H, Hu Y, Shen G, Zhu P, Yang G and Xie X (2021). Changes of serum IL-10, IL-1β, IL-6, MCP-1, TNF-α, IP-10 and IL-4 in COVID-19 patients. *Int. J. Clin. Pract,* **75**(9): e14462.

Miura M, Inomata T, Nakamura M, Sung J, Nagino K, Midorikawa-Inomata A, Zhu J, Fujimoto K, Okumura Y, Fujio K, Hirosawa K, Akasaki Y, Kuwahara M, Eguchi

A, Shokirova H and Murakami A (2022). Prevalence and characteristics of dry eye disease after cataract surgery: A systematic review and meta-analysis. *Ophthalmol Ther,* **11**(4): 1309-1332.

Naderi K, Gormley J and O'Brart D (2020). Cataract surgery and dry eye disease: A review. *Eur. J. Ophthalmol,* **30**(5): 840-855.

Nguyen A, Kolluru A and Beglarian T (2023). Dry eye disease: A review of anti-inflammatory therapies. *Taiwan J. Ophthalmol,* **13**(1): 3-12.

Nieć M, Olejarz Z, Nowak K, Drygała Z, Wyrwał J, Zielińska Z, Słowik M, Gierlach K and Krasuska M (2024). Factors influencing the length of the recovery period after blepharoplasty: A review of the latest data. *J Educ. Health Sport,* **59**: 183-208.

Ogawa Y, Kawakami Y and Tsubota K (2021). Cascade of inflammatory, fibrotic processes, and stress-induced senescence in chronic gvhd-related dry eye disease. *Int. J. Mol. Sci,* **22**(11): 6114.

Patel D and Wairkar S. (2019). Recent advances in cyclosporine drug delivery: challenges and opportunities. *Drug Deliv. Transl. Res,* **9**(6): 1067-1081.

Patocka J, Nepovimova E, Kuca K and Wu W (2021). Cyclosporine A: chemistry and toxicity–a review. *Curr. Med. Chem,* **28**(20): 3925-3934.

Peng W, Jiang X, Zhu L, Li X, Zhou Q, Jie Y, You Z, Wu M, Jin X, Li X and Zhou S (2023). Cyclosporine a (0.05%) ophthalmic gel in the treatment of dry eye disease: A multicenter, randomized, double-masked, phase III, COSMO Trial. *Drug Des. Devel. Ther,* **16**: 3183-3194.

Periman L M, Mah F S and Karpecki P M (2020). A review of the mechanism of action of cyclosporine A: The role of cyclosporine a in dry eye disease and recent formulation developments. *Clini Ophthalmol,* **14**: 4187-4200.

Pilotto E, Leonardi F, Stefanon G, Longhin E, Torresin T, Deganello D, Cavarzeran F, Miglionico G, Parrozzani R and Midena EJB (2019). Early retinal and choroidal OCT and OCT angiography signs of inflammation after uncomplicated cataract surgery. *Br J Ophthalmol,* **103**(7): 1001-1007.

Prinz J, Maffulli N, Fuest M, Walter P, Bell A and Migliorini F (2022). Efficacy of topical administration of corticosteroids for the management of dry eye disease: Systematic review and meta-analysis. *Life,* **12**(11): 1932.

Rák T and Csutak A (2024). Exploring novel pharmacological trends: Natural compounds in dry eye disease management. *Acta Pharm,* **74**(3): 383-404.

Rodriguez Garcia A, Ruiz Lozano RE, Bustamante Arias A, Pantaleon Garcia J, Hernandez Quintela E and Navas A (2023). Correlation and level of agreement between the ocular surface disease index and the symptom assessment in dry eye questionnaires: A survey-based study. *Curr. Eye Res,* **48**(9): 788-798.

Sędzikowska A, Tarkowski W, Moneta-Wielgoś J, Grzyliński K, Tarkowski G and Młocicki D (2021). Effect of ocular demodicosis on the stability of the tear film and the tear break up time. *Sci. Rep,* **11**(1): 24296.

Semp DA, Beeson D, Sheppard AL, Dutta D and Wolffsohn JS (2023). Artificial Tears: A Systematic Review. *Clinical Optometry,* **15**: 9-27.

Shimada H and Nakashizuka H (2021). Cataract Surgery by Intraoperative Surface Irrigation with 0.25% Povidone–Iodine. *J. Clin. Med,* **10**(16): 3611.

Sun CC, Chan YH, Huang PW and Chen NN (2024). Evaluation of two artificial tears containing hyaluronic acid for post cataract surgery dry eye disease: A randomized controlled trial. *Ophthalmol Ther,* **13**(10): 2615-2627.

Van Geffen C, Heiss C, Deißler A and Kolahian S (2022). Pharmacological modulation of myeloid-derived suppressor cells to dampen inflammation. *Front. Immunol,* **13**: 933847.

Vernhardsdottir RR, Magno M S, Hynnekleiv L, Lagali N, Dartt DA, Vehof J, Jackson CJ and Utheim TP (2022). Antibiotic treatment for dry eye disease related to meibomian gland dysfunction and blepharitis–A review. *Ocul Surf,* **26**: 211-221.

Wiącek A E, Jurak M, Ładniak A, Przykaza K and Szafran K (2020). Cyclosporine CsA—The physicochemical characterization of liposomal and colloidal systems. *Colloids and Interfaces,* **4**(4): 46.

Yadav Y, Sharma V, Gupta R, Singh P, Mohapatra T and Kumar S (2024). Changes in ocular surface indices in myopia patients undergoing small incision lenticule extraction (SMILE) Surgery. *Clin. Experiment. Ophthalmol,* **15**(2): 974.

Yang J, Zhao W, Liao Y, Wu S, Li J, Jin L, Liu Q, Huang F and Liang L (2022). Ocular surface disease index questionnaire as a sensitive test for primary screening of chronic ocular graft-versus-host disease. *Ann Transl Med,* **10**(16): 855.

Yu K, Bunya V, Maguire M, Asbell P and Ying G (2021). Systemic conditions associated with severity of dry eye signs and symptoms in the dry eye assessment and management study. *Ophthalmology,* **128**(10): 1384-1392.

Zaharia A C, Dumitrescu O M, Rogoz R E, Dimirache A E and Zemba M (2021). Preoperative antisepsis in ophthalmic surgery (a review). *Rom J Ophthalmol,* **65**(2): 120-124.

Zhao X, Jia Q and Fu J (2023). Effectiveness of rb-bFGF eye drops for post-cataract surgery dry eye and observation of changes in tear secretion and corneal damage in patients. *Altern Ther Health Med,* **29**(8): 489.

Zhu W, Ma Y, Li X, Han T, Li L, Zhao Z and Yu Z (2023). Effect of Stanozolol combined with cyclosporine A on aplastic anemia. *Am J Transl Res,* **15**(11): 6660-6666.