

The clinical effects of sodium hyaluronate, polyethylene glycol, and dextran-70 eye drops in relieving dry eye after phacoemulsification

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Abstract

To compare the clinical efficacy of sodium hyaluronate eye drops, polyethylene glycol eye drops, and compound dextran eye drops in the treatment of dry eye after phacoemulsification of cataract.

A total of 99 patients with dry eye after cataract phacoemulsification combined with intraocular lens implantation were treated in our hospital. Patients were divided into group A (sodium hyaluronate eye drops), group B (polyethylene glycol eye drops), and group C (dextran-70 eye drops). The clinical effect, tear film breakup time, basic tear secretion, corneal staining score, dry eye symptom score, and the incidence of ocular irritation were assessed.

On the 3rd, 15th, 30th, and 60th day after operation, the tear film breakup time, corneal staining score, Schirmer I test, and dry eye symptom score in group A and group B were better than those in group C ($P < .05$). In addition, there were no significant differences in tear breakdown time, corneal staining score, Schirmer I test, and dry eye symptom score between group A and group B ($P > .05$). At 3 days to 60 days after operation, the incidence of dry eye in group A (12.12%) and group B (18.18%) was lower than that in group C (39.39%), and the incidence of dry eye in group A was significantly lower than that in group B ($P < .05$).

The effect of sodium hyaluronate eye drops elicited a greater beneficial impact as compared to polyethylene glycol eye drops and dextran-70 eye drops.

Abbreviations: BUT = breakup time, IOL = intraocular lens.

Keywords: cataract, dextran-70 eye drops, dry eye, phacoemulsification, polyethylene glycol eye drops, sodium hyaluronate eye drops

1. Introduction

Cataract is considered one of the leading cause of blindness in China, which mostly occurs in elderly patients. Currently, cataract phacoemulsification is the only effective treatment for patients with cataract, which has the advantages of less trauma

and quick recovery after operation, hence has been widely used in clinical practice.^[1] However, according to several previous studies,^[2–4] the cataract phacoemulsification can lead to negative impact on the structure of the ocular surface and the stability of the tear film, for example, dry eye.^[2–4] Severe cases are linked to abnormal sensation and blurred vision and other adverse symptoms. Dry eye symptom is a common complication after cataract phacoemulsification.^[5] In order to alleviate the dry eye and reduce the adverse reactions after cataract phacoemulsification, artificial tear replacement, anti-inflammation, and surgical treatment are often used, among which the most convenient and effective treatment is artificial tear replacement therapy.^[6] The current study aims to investigate the comparative effects of sodium hyaluronate eye drops, polyethylene glycol eye drops, and compound dextran eye drops in terms of relieving the dry eye after cataract phacoemulsification.

2. Methods and materials

2.1. General information

A total of 99 patients with dry eye after phacoemulsification combined with intraocular lens implantation in our hospital from November 2017 to July 2019 were divided into group A, group B, and group C based on different treatment methods. In group A, there involved 19 males and 14 females, aged 49 to 78 years, with an average age of (62.19 ± 3.98) years. In group B, there were 20 males and 11 females, aged 48 to 77 years, with an average age of (62.04 ± 4.02) years. In group C, there were 21 males and 12 females, aged 48 to 76 years, with an average age of $(61.83 \pm$

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The study protocol was approved by the Ethics Committee of Eyegood Ophthalmic Hospital. Written informed consent was obtained from all the study subjects before enrollment.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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4.12) years. There was no significant difference in age and other general data among the 3 groups ($P > .05$). This study met the requirements of the Helsinki Declaration and the informed consent of all patients, and approved by the Ethics Committee of our hospital.

2.2. Diagnostic criteria for dry eye

Based on the previous reference,^[3,4,7] the corneal fluorescein staining, tear secretion test (Schirmer I test) (no topical anesthetics), and tear film breakup time were used in this study; the temperature and humidity of the experiment were (21.03, 2.54)°C and (61.39, 15.63)% respectively. Two or 3 positive results of abovementioned test represented dry eye. The following experiments were performed sequentially:

- 1) the diagnosis can be made if Schirmer I test was 6 to 10 mm, tear film breakup time was 6 to 10 seconds, and corneal fluorescein staining was 4 to 10 points;
- 2) the diagnosis can be made if Schirmer I test was 2 to 5 mm, tear film breakup time was 2 to 5 seconds, and corneal fluorescein staining was 11 to 50 points.

All experiments were measured by 3 experimenters who had been trained before the experiment. The suspected dry eye needs to be further determined if there was only 1 positive result of the abovementioned tests. The lactoferrin content in tear was determined by radioimmunoassay, and the lactoferrin concentration of samples was determined by standard curve strictly following the kit instructions (Xinfan, Shanghai, China). And patients should be diagnosed with dry eye if the lacrimal lactoferrin level was <100 mg/L. Further, eye surface disease index algorithm: each subject's symptoms were evaluated by objective indicators given by the Ocular Surface Disease Index Scale (OSDI), which includes 3 aspects: eye symptoms, visual-related functions, environmental stimulants. The scale has a total of 12 items, and the corresponding scores of each item are 0 to 4 points, including 3 items of eye symptoms, 6 items of vision-related functions, and 3 items of environmental stimulus factors. The calculated score of the scale depends on the response to each question on the scale. The OSDI score ranges from 0 to 100, and the higher the score, the greater its clinical significance. The total score of OSDI was calculated by Schiffman^[8]: $OSDI = (\text{total score of answering all questions} \times 100) / (\text{total number of answering questions} \times 4) = \text{total score} \times 25 / \text{total number of answering questions}$.

2.3. Selection criteria

To be included in the current study, the following inclusion criteria should be met:

- 1) patients with age-related cataract;
- 2) patients were diagnosed in accordance with the above diagnostic criteria of dry eye after phacoemulsification;
- 3) complete clinical data;
- 4) patients with normal mental statement and good compliance;
- 5) there was no history of other ophthalmic diseases and eye surgery;
- 6) patients with binocular diseases;
- 7) OSDI score in accordance with the degree of dry eye;
- 8) patients with aqueous deficient dry eye.

Exclusion criteria were as follows:

- 1) patients with previous history of ocular surface surgery;

- 2) patients with monocular disease;
- 3) patients with autoimmune diseases, diabetes, hypertension, and other systemic diseases;
- 4) patients receiving long-term local administration;
- 5) patients combined with glaucoma, uveitis, retinopathy, and other eye diseases;
- 6) patients with mental abnormality and poor compliance;
- 7) incomplete clinical data;
- 8) patients were allergic to the experimental drug;
- 9) patients with previous dehydration dry eye or evaporation dry eye;
- 10) patients with evaporative dry eye.

2.4. Treatment

Three groups were treated with cataract phacoemulsification combined with intraocular lens implantation. After explaining in detail the nature and possible consequences of the study and informing all patients of the need for attention after surgery, all participants had obtained informed consent. All patients were submitted to routine phacoemulsification (Infinity, Alcon) and posterior chamber foldable intraocular lens implantation with coaxial microincision. All operations were performed by 2 experienced surgeons in the same group. All patients were asked to use a combined eye drop of tobramycin/dexamethasone (Alcon Couvreur NV, Belgium) for 4 weeks; tropicamide eye drops (Yongguang Pharmaceutical Co., Ltd.) for 2 weeks. Tobramycin-dexamethasone eye drops reduce edema and inflammation; compound tropicamide eye drops are used to regulate paralysis after surgery. Additionally, patients in group A were given sodium hyaluronate eye drops (trade name: sodium hyaluronate eye drops; specification: 5 mg: 5 mL; manufacturer: Cantian Pharmaceutical [China] Co., Ltd.; approval number: H20063950), 4 times a day at initial stage, decreased once per week, with a total of 4 weeks for treatment; patients in group B were given polyethylene glycol eye drops (trade name: polyethylene glycol eye drops; specification: 1.5 mL; manufacturer: Alcon Laboratories, Inc.; approval number: H20110412), 4 times a day for 30 days; patients in group C were given compound dextran eye drops (trade name: compound dextran 70 eye drops; specification: 8 mL; manufacturer: Jiangxi Heshimeikang Pharmaceutical Limited Company; approval number: 20073639), 3 times a day for 30 days. Sodium hyaluronate eye drops are mainly composed of sodium hyaluronate. The main components of polyethylene glycol eye drops are polyethylene glycol and propylene glycol; and the main component of dextran 70 eye drops is dextran 70. Dry eye were examined at 3 days, 15 days, 30 days, and 60 days after operation, including 10 items of ocular symptoms: dry eyes, itching, fear of light, blurred vision, eye fatigue, eye secretions, tears, abnormal sensation, eye pain, eye heaviness, etc. The score was ranged from 0 to 3, in which 0 represented for no obvious discomfort; 1 for occasional slight discomfort; 3 for often feel obvious discomfort. The higher the score, the more obvious the symptoms.

2.5. Observation index

The clinical curative effect, tear film breakup time, basic tear secretion test, corneal staining score, dry eye score, and the incidence of ocular irritation symptoms were observed.

The clinical effect was divided into 4 aspects: the Schirmer test was used to reflect the basic secretion of tear. The normal value of

Table 1**Comparison of clinical efficacy among the 3 groups (%).**

Group	Not effective	Effective	Markedly effective	Cured	Effective rate
Group A (n=33)	2 (0.06)	10 (30.30)	12 (36.36)	9 (27.27)	31 (93.94)*
Group B (n=33)	3 (9.09)	9 (27.27)	13 (39.39)	8 (24.24)	30 (90.91)*
Group C (n=33)	5 (15.15)	13 (39.39)	9 (27.27)	6 (18.18)	28 (84.85)

* Note: After treatment, compared with group C ($P < .05$).

tear test was ≥ 10 mm/5 minutes. If the result of tear test was ≥ 5 mm/5 minutes, but < 10 mm/5 minutes, it was called reduced tear secretion. If the tear secretion was < 5 mm/5 minutes, it indicated dry eye. Fluorescein staining was graded according to Korb,^[9] grade I: 0.5 to 1.0 (mild), grade 2: 1.25 to 2.0 (moderate), grade 3: 2.25 to 3.0 (severe). Analysis of treatment according to the above criteria:

- 1) Cured: Disappearance of dry eye symptoms; the Schirmer I test was ≥ 10 mm/5 minutes; the corneal fluorescein staining was 0, and the symptoms disappeared completely.
- 2) Markedly effective: 10 mm $>$ Schirmer I test ≥ 5 mm; corneal fluorescein staining score was 1 point, and the symptom relieved obviously.
- 3) Effective: Schirmer I test < 5 mm; corneal fluorescein staining score was 2 points, with alleviated symptoms.
- 4) Ineffective: Dry eye, Schirmer I test, and corneal fluorescein staining did not reach the effective standard, and the symptoms were not improved. Effective rate = cure rate + markedly effective rate + effective rate.

Tear film breakup time: 8 μ L sodium fluorescein solution was injected into the conjunctival sac at 3 days, 15 days, 30 days, and 60 days after operation, and the patient was told to blink. The wide slit light band of slit lamp was used to record the time from the last blink to the first dark spot in the cornea. Use the electronic stopwatch to calculate the time; in order to maintain the accuracy of the measurement, the measurement should be repeated 3 times, and the average value should be taken.

Corneal staining score: after the tear film breakup examination, the cornea was directly observed under slit lamp blue light and divided into upper, middle, and lower quadrants, which ranged from 0 to 9 points (0 points: without corneal fluorescence staining; 1 point: there were less than 30 fluorescent staining spots; 2 points: there were more than 30 fluorescent staining spots; 3 points: there were fluorescent staining spots, filamentous matter and fusion, etc).

Basic tear secretion test: 5 mm \times 35 mm filter paper was folded and placed in the conjunctival sac of the lower eyelid margin at 3 days, 15 days, 30 days, and 60 days after operation. The soaking range was recorded after 5 minutes, and the average value was taken after 3 times.

The incidence of ocular irritation symptoms: according to the patient's tolerance and eye irritation symptoms, the score ranged

from 0 to 3 (0 point: the eyes without any irritation symptoms; 1 point: patients with tolerable eye irritation symptoms; 2 points: patients could tolerate the irritation symptoms without affecting normal life; 3 points: patients could not tolerate the symptoms of eye irritation, which had a serious impact on their normal life). The incidence of ocular irritation symptoms = incidence of 1 point + 2 points + 3 points.

2.6. Statistical analysis

In this study, the data were analyzed by SPSS18.0 software, tear film breakup time and corneal staining score were expressed by ($\bar{x} \pm s$), with the use of t test. The clinical efficacy and the incidence of ocular irritation symptoms were expressed by the number and percentage of cases, and were accurately tested by χ^2 test or Fisher. P value was corrected by Bonferoni, $P < .05$, indicating the difference was statistically significant.

3. Results

3.1. Comparison of clinical effects among the 3 groups

After treatment, the effective rate of group A was 93.94%, and that of group C was 84.85%. The clinical efficacy of group A was significantly higher than that of group C ($P = .045$); the effective rate of group B was 90.91%, which was also significantly higher than that of group C ($P = .048$); there was no significant difference between group A and group B ($P > .05$). See Table 1 for details.

3.2. Comparison of tear film breakup time among the 3 groups

On the 3rd, 15th, 30th, and 60th day after operation, the tear film rupture time of group A and group B was significantly better than that of group C ($P < .05$), and there was no statistical difference between group A and group B ($P > .05$) (Table 2).

3.3. Comparison of corneal staining scores among the 3 groups

On the 3rd, 15th, 30th, and 60th day after operation, the corneal staining scores in group A and group B were significantly better than those in group C ($P < .05$), and there was no significant

Table 2**Comparison of tear film breakup time among the 3 groups ($\bar{x} \pm s$).**

Group	3d after surgery (s)	15d after surgery(s)	30d after surgery(s)	60d after surgery(s)
Group A (n=33)	6.53 \pm 1.02*	8.31 \pm 1.26*	9.12 \pm 1.67*	11.87 \pm 2.01*
Group B (n=33)	6.37 \pm 1.11*	8.18 \pm 1.65*	9.08 \pm 1.71*	11.65 \pm 1.83*
Group C (n=33)	6.05 \pm 1.06	6.62 \pm 1.71	7.04 \pm 1.76	7.14 \pm 1.94

* Note: After treatment, compared with group C ($P < .05$).

Table 3**Comparison of corneal staining scores among the 3 groups ($\bar{x} \pm s$).**

Group	3 d after surgery	15 d after surgery	30 d after surgery	60 d after surgery
Group A (n=33)	3.11 ± 0.82*	2.18 ± 0.26*	1.43 ± 0.47*	1.41 ± 0.31*
Group B (n=33)	3.23 ± 0.11*	2.19 ± 0.35*	1.49 ± 0.71*	1.45 ± 0.33*
Group C (n=33)	3.05 ± 0.36	2.23 ± 0.71	1.61 ± 0.76	1.54 ± 0.54

* Note: After treatment, compared with group C ($P < .05$).**Table 4****Comparison of 3 groups of basic tear secretion tests ($\bar{x} \pm s$).**

Group	3 d after surgery	15 d after surgery	30 d after surgery	60 d after surgery
Group A (n=33)	8.27 ± 0.65*	9.34 ± 0.76*	10.45 ± 0.54*	11.41 ± 0.57*
Group B (n=33)	8.20 ± 0.56*	9.19 ± 0.68*	10.39 ± 0.71*	11.32 ± 0.49*
Group C (n=33)	8.07 ± 0.43	8.86 ± 0.51	9.41 ± 0.36	9.63 ± 0.54

* Note: After treatment, compared with group C ($P < .05$).

difference in corneal staining score between group A and group B ($P > .05$). See Table 3 for details.

3.4. Comparison of 3 groups of basic tear secretion test

On the 3rd, 15th, 30th, and 60th day after operation, the Schirmer I test in group A and group B was significantly better than that in group C ($P < .05$), and there was no significant difference in the Schirmer I test between group A and group B ($P > .05$). See Table 4 for details.

3.5. Comparison of dry eye symptom scores among the 3 groups

On the 3rd, 15th, 30th, and 60th day after operation, the dry eye symptom score of group A and group B was significantly better than that of group C ($P < .05$). In terms of dry eye score, there was no statistical difference between groups A and B ($P > .05$). See Table 5 for details.

3.6. Comparison of the incidence of ocular irritation symptoms among the 3 groups

On the 3rd, 15th, 30th, and 60th day after operation, the incidence of dry eye in group A and group B was significantly lower than that in group C ($P < .05$), and the incidence of dry eye in group A was significantly lower than that in group B ($P < .05$). See Table 6 for details.

4. Discussion

Dry eye syndrome is caused by ocular surface injury or abnormal tear quantity or hydrodynamics, followed by tear film instability, resulting in a series of symptoms such as dryness and itching of the eyes. It affects the life quality of patients and has become an urgent public health problem. Based on many studies,^[10,11] traumatic operations such as cataract phacoemulsification can lead to dry eye. Some of the dry eye occurred after operation, and there were no such symptoms before operation. The main reasons were as follows:

Table 5**Comparison of dry eye symptom scores among the 3 groups ($\bar{x} \pm s$).**

Group	3 d after surgery	15 d after surgery	30 d after surgery	60 d after surgery
Group A (n=33)	1.66 ± 0.32*	1.31 ± 0.29*	0.65 ± 0.16*	0.54 ± 0.09*
Group B (n=33)	1.78 ± 0.43*	1.39 ± 0.36*	0.69 ± 0.23*	0.59 ± 0.08*
Group C (n=33)	2.07 ± 0.45	1.77 ± 0.49	1.32 ± 0.36	1.21 ± 0.43

* Note: After treatment, compared with group C ($P < .05$).**Table 6****Comparison of the incidence of ocular irritation symptoms among the 3 groups (%).**

Group	0 point	1 point	2 points	3 points	Total
Group A (n=33)	87.88%	9.09%	3.03%	0	12.12%*†
Group B (n=33)	81.82%	12.12%	6.06%	0	18.18%
Group C (n=33)	60.61%	21.21%	12.12%	6.06%	39.39%

* Note: After treatment, compared with group B ($P < 0.05$).† Note: After treatment, compared with group C ($P < 0.05$).

The anesthetic drugs and eye drops used before operation stimulate the surface of cornea and conjunctiva. The mucin layer of lacrimal film was damaged to varying degrees:

- (1) the injury of corneal nerve fibers caused by surgical incision can reduce the corneal sensitivity, make the tear film on the ocular surface unevenly distributed and reduce its stability;
- (2) the ocular surface epithelial cells were directly damaged by intraoperative mechanical operation and ultrasonic energy;
- (3) the injury of ocular surface epithelial cells could be caused by washing with balanced salt solution after operation.

Artificial tear is a substitute for human tears, which is mainly composed of water/oil solution, gel, and ointment.^[5] Artificial tears have the effect of increasing ocular surface humidity and lubrication, alleviate the symptoms of dry eye discomfort after cataract phacoemulsification, and effectively improve the stability of tear film. Based on the study supported by You et al,^[12] phacoemulsification combined with artificial tear therapy can reduce the tear film injury and reduce postoperative eye discomfort. In this study, 3 different kinds of intraocular tears were used to treat patients with dry eyes after phacoemulsification combined with intraocular lens implantation. According to the results of the clinical effect, tear film breakup time, corneal staining score, the Schirmer I test and dry eye symptom score at 3 days, 15 days, 30 days, and 60 days after operation, the sodium hyaluronate eye drops group and polyethylene glycol eye drops group were better than those in dextran-70 eye drops group, and the incidence of ocular irritation symptoms in the sodium hyaluronate eye drops group and polyethylene glycol eye drops group was significantly lower than that in the dextran-70 eye drops group. Compared with the polyethylene glycol eye drops group, the clinical effect, tear film rupture time, corneal staining score, Schirmer I test, and dry eye symptom score of the sodium hyaluronate eye drops group had no significant difference at 3 days, 15 days, 30 days, and 60 days after surgery ($P > .05$), and the incidence of sodium hyaluronate dry eye disease was significantly lower than that of polyethylene glycol group ($P < .05$), which also suggested that the sodium hyaluronate eye drops were associated with the most significant effect among the 3 artificial tears. The results of this study are similar to those of Gao and Wang.^[13] There were several reasons that might contribute to the present results:

(1) Sodium hyaluronate eye drops:

- 1) Sodium hyaluronate eye drops are mainly sodium hyaluronate, and sodium hyaluronate is composed of a large number of carboxyl groups and hydroxyl groups, which is easy to combine with water molecules and adsorb a large number of water molecules, so that the water liquid layer can be stabilized, thus delaying the breakup time of lacrimal film. At the same time, its molecular structure is similar to that of mucin, with high viscosity, which has a protective effect on corneal epithelial cells, and can maintain its barrier function, and has the role of mucin layer and water layer in tears. This molecule can accelerate the repair of corneal epithelial cells and conjunctival cells. The principle is that the molecule has the same extensibility as physiological tears and can be extended to corneal epithelium, so as to promote the healing of corneal epithelium after operation.^[14,15]
- 2) Sodium hyaluronate eye drops can form a staggered reticular structure on the surface of the eyeball, which can fully lock the water, prolong the evaporation time of the water on the

surface of the tear film, and maintain the lubrication of the ocular surface tissue to the maximum extent.

- 3) Sodium hyaluronate eye drops without preservatives can reduce the time of tear film reconstruction after cataract surgery. Some clinical studies^[16] have suggested that most of the preservatives in artificial tears could cause damage to corneal epithelial cells, resulting in the adhesion of tear film to the eye surface and weaken the effective components of artificial tears. Therefore, sodium hyaluronate eye drops have the best effect among the 3 kinds of artificial tears.
- (2) Polyethylene glycol eye drops:
- 1) Polyethylene glycol eye drops are composed of polyethylene glycol, propylene glycol, HP-Guar, borate, sorbitol, and so on. HP-Guar is a kind of water-soluble polysaccharide with mannose as main chain and galactose as side chain. It has the effect of binding to damaged corneal epithelial cells to increase the retention time of polyethylene glycol and propylene glycol and protect the eye surface for a long time. In addition, HP-Guar has the same effect as mucin and is adsorbed in the damaged corneal epithelial area. It can not only moisturize the eye surface, but also repair the damaged corneal epithelial cells.^[15-18]
 - 2) Polyethylene glycol eye drops can promote the transformation of low viscosity fluid into viscoelastic gel, so that borate, sorbitol, and HP-Guar interact with each other to form an innovative release system and promote the reconstruction of viscoelastic reticular protective layer to prolong the time of eye surface lubrication for protection;
 - 3) After dextran 70 enters the conjunctival sac, the transitional transition of gel-water sample-gel is produced due to the instantaneous movement, which can effectively prolong its storage time in the eye, further improve the stability of the cells and prolong the cell rupture time. In addition, compound dextran 70 eye drops contain the preservative benzalkonium chloride, which can prevent microbial contamination. But benzalkonium chloride, compared with other preservatives, has a strong antimicrobial capacity and higher side effects.

In conclusion, compared with compound dextrose, 70 eye drops, polyethylene glycol eye drops, and sodium hyaluronate eye drops can prolong tear film rupture time, thereby improving dry eye. Sodium hyaluronate is preservative-free and safer for patients. The polyethylene glycol eye drops used in this study is made by Alcon Company of the United States, and Polyquad preservative is a new type of polyquaternary ammonium salt preservative, composed of tetramethyl-2-butene-1,4-diamine and 1,4-dichloro-2-2-butene under certain conditions for polymerization reaction, the terminal is synthesized with tri-β-hydroxyethylamine covering. Some clinical studies suggest that the preservative has the least toxicity and few patients have allergies. Therefore, the effect of polyethylene glycol eye drops elicited greater beneficial outcomes as compared to that of dextran-70 eye drops.^[19] In the current study, considering the limited time and the small sample size, more researches with larger sample size are warranted for further investigation.

5. Conclusion

Sodium hyaluronate eye drops, polyethylene glycol eye drops, and dextran-70 eye drops can relieve the symptoms of dry eye

after cataract phacoemulsification, in which sodium hyaluronate eye drops exerted best clinical effect, followed by polyethylene glycol eye drops.

Author contributions

Zhi-Hui Duan contributed to the conception and design of the study; Yi-Fei Tang performed the experiments, collected and analyzed data, and wrote the manuscript.

Conceptualization: Yi-Fei Tang.

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