Original Article Effect of microincisional cataract surgery on inflammatory indicators in tears and corneal endothelial cells in cataract patients

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Abstract: Objective: To analyze the effect of microincisional cataract surgery on inflammation in tears and corneal endothelial cells in cataract patients. Methods: A total of 103 patients with cataracts in our hospital were enrolled and randomly divided into group A (n=52) and group B (n=51) by a random double-blind lottery. Group A received 1.8 mm coaxial microincision cataract surgery (C-MICS) while group B received 3.0 mm C-MICS, and the efficacy was compared between the two groups. Results: Average ultrasound energy (AVG), accumulative phaco time (APT), and effective phaco time (EPT) did not differ between groups (P > 0.05). Group A exhibited higher interleukin-2 (IL-2) levels at 5 days postoperatively and lower interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α), and tumor necrosis factor- β 1 (TNF- β 1) levels than group B (P < 0.05). The density of corneal endothelial cells, coefficient of variation, and percentage of hexagonal cells showed no significant difference in both groups at 5 days postoperatively (P > 0.05). Group A had higher visual acuity and lower visual acuity loss, visual fatigue, foreign body sensation, tingling, and photophobia scores than group B at 7, 14, and 28 days postoperatively (P < 0.05). The tear film break-up time (TBUT) in group A was longer than that in group B at 7, 14, and 28 days postoperatively, and the tear secretion length (in mm) on the strip in group A was longer than that in group B at 14 and 28 days postoperatively (P < 0.05). Conclusion: Compared with other types of similar surgery, C-MICS can significantly control inflammation levels, with less effect on corneal endothelial cells, improve postoperative visual acuity, delay tear film break-up, increase tear secretion, and improve dry eye syndrome.

Keywords: Cataract, microincisional cataract surgery, tears, inflammatory indicators, corneal endothelial cells, effects

Introduction

Cataract surgery is performed using phacoemulsification techniques, and a more clinically used procedure is the microincision cataract surgery (MICS) with an incision size between 2.8-3.0, which is also the most mature procedure currently [1]. However, with the continuous improvement of techniques, the goals of surgery have gradually shifted from restoring sight and preventing blindness to enhancing visual quality [2]. Therefore, the current surgical treatment regarding cataract can be performed with minimal tissue damage, high safety, and rapid efficacy to improve visual quality [3].

Therefore, a new clinical procedure of MICS was proposed, with an incision of \leq 2.0 mm,

which is the biggest difference from standard surgery [4]. MICS had been successfully performed with a 0.9 mm incision [5]. Microincision cataract surgery initially was performed using bimanual microincision phacoemulsification. Coaxial microincision cataract surgery (C-MICS) was proposed with the accumulation of surgical experience and advances in ultrasound emulsification equipment [6]. Compared with MICS, bimanual microincision phacoemulsification can reduce the incision, reduce posterior segment complications, and accelerate the recovery of visual quality. However, there is a higher risk of incisional thermal burns and perfusion outflow due to the absence of a trocar for the ultrasound needle, which can affect the stability of the anterior chamber [7]. MICS is more effective and safer than the former, and the

incision after IOL implantation is only 1.8 mm, which avoids possible adverse complications and is more widely applicable [8].

However, 1.8 mm MICS has not been applied for a long time in China, and the accumulated clinical experience of the procedure is insufficient. Some scholars believe that improper operation will seriously affect the safety of the procedure [9], and other scholars believe that too small of an incision leads to a significantly reduced operating range, which will affect the accuracy of the operation [10]. Studies have found that phacoemulsification can cause a significant inflammatory response, which is specifically manifested as a decrease in interleukin-2 (IL-2) levels and an increase in interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α) and tumor necrosis factor- β 1 (TNF-\beta1) levels, and the changes in inflammatory levels may cause physiological instability and affect the safety of patients. Therefore, it is of great significance to control the levels of inflammatory factors. Since the value of this approach in cataract surgery has not been widely recognized, in order to further investigate the value of MICS in cataracts, 103 patients with cataracts in our hospital were selected in this study to compare the efficacy of 1.8 mm and 3.0 mm MICS.

Materials and methods

General data

A total of 103 cataract patients admitted to our hospital from January 2019 to December 2019 were enrolled as study subjects. Inclusion criteria: age > 18 years, good compliance with all examinations; nuclear grades of I to IV; astigmatism < 1.5 D; normal communication ability; cataract etiology determined to be age-related. All subjects signed the informed consent form, and this study passed the ethical approval of the First People's Hospital of Fuyang District. Exclusion criteria: comorbid with ocular trauma, keratitis or conjunctivitis; retinopathy; glaucoma; previous treatment with eye surgery; high myopia.

Materials and methods

Instruments and equipment required for the procedure: Stellaris ultrasound emulsifier; Pentacam 3-dimensional diagnostic system for anterior segment; Topcon SP-2000P specular

microscopy for corneal endothelial cell count; Anterior segment optical coherence tomography (AS-OCT); AKreos AO M160 lens (group A), AKreos AO lens (group B).

Group A: The pupils were dilated by eye drops before surgery. After surface anesthesia, a clear corneal tunnel incision was made at the limbus at 12 o'clock, with a length of 1.8 mm, and the viscoelastic agent was injected into the anterior chamber. A clear cornea incision was made at 2 o'clock position using a 15° side cutter, followed by 4-5 mm continuous curvilinear capsulorhexis, hydrodelineation, hydrodissection and nuclear rotation. The phacoemulsification was performed with Stellaris PC platform. After aspirating the lens nucleus, the remaining part of the cortex was aspirated with a perfusion/aspiration needle, and the posterior capsule was polished. The viscoelastic agent was injected into the anterior chamber and capsular bag, and the AKreos AO M160 lenses were implanted into the capsular bag through a bolus device. The position of the intraocular lens was adjusted reasonably, and the viscoelastic agent was absorbed. After the anterior chamber was refilled with BBS, the incision closes naturally.

Group B: The surgery was basically the same as in group A, but a 3.0-mm-long corneal incision was made at the 12 o'clock position, and the AKreos AO lenses were selected for implantation. In addition, the ultrasound emulsification needle, perfusion/aspiration needle, and irrigation cannula used were all standard coaxial small-incision surgical instruments with a slightly larger tube diameter than in group A.

The height of the perfusion bottle was controlled at 1 m, the flow rate was controlled at 35 mL/min, the negative pressure was controlled at 300 mmHg and the ultrasound energy was controlled at less than 30% in both groups during the ultrasonic emulsification.

Outcome measurements

Ultrasonic emulsification: average ultrasound energy (AVG), accumulative phaco time (APT), and the effective phaco time (EPT) were compared between the two groups.

Inflammatory indicators in tears: IL-2, IL-6, IL-8, TNF- α , and TNF- β 1 were measured in both groups before and at 5 days after surgery,

Data		Group A (n=52)	Group B (n=51)	t/X^2	Р
Gender	Male	28 (53.85)	29 (56.86)	0.095	0.758
	Female	24 (46.15)	22 (43.14)		
Mean age (years)		60.45±19.62	61.37±20.15	0.235	0.815
Mean eye axis (mm)		24.68±1.79	24.81±1.85	0.362	0.718
Mean corneal endothelial count (pcs)		2676.85±385.49	2705.46±389.51	0.375	0.709
Crystalline Nucleus Grading	Grade I	12 (23.08)	10 (19.61)	0.629	0.182
	Grade II	20 (38.46)	21 (41.18)		
	Grade III	17 (32.69)	18 (35.29)		
	Grade IV	3 (5.77)	2 (3.92)		

Table 1. Comparison of baseline data between the two groups $(\bar{x} \pm s)/[n (\%)]$

respectively. A total of 15 μ L of tear samples from the operated eyes of the two groups were collected using 10 μ L capillary tube. A radioimmunoassay was performed according to the kit instructions.

The corneal endothelial cells of the patients were reserved as samples before and at 5 days after surgery, and were counted using a corneal endothelial cell microscope. The cell density, coefficient of variation, and percentage of hexagonal cells were examined.

Visual acuity was measured before surgery, and at 7, 14, and 28 days after surgery in both groups using Tumbling E' eye test chart at a distance of 3 m.

Dry eye symptoms were evaluated using the Ocular Surface Disease Index (OSDI) [11] rating scale, which is assessed on a scale of 0 to 100 on a 0-4 Likert scale in terms of vision loss, visual fatigue, foreign body sensation, tingling, photophobia (0: "none of the time", 1: "some of the time", 2: "half of the time", 3: "most of the time", and 4: "all the time"), with higher scores representing greater disability. They were evaluated before surgery, and at 7, 14, and 28 days after surgery, respectively.

The tear film break-up time: 1 drop of sodium fluorescein solution was injected into the patient's conjunctival sac, followed by 3-4 eye blinks. Tear film break-up time (TBUT) is the time taken for the appearance of the first dry spot on the cornea after complete blinking [12], with < 10 s indicating an unstable tear film, 10-15 s indicating a stable tear film, and 15-30 s indicating a normal tear film. They were evaluated before surgery, and at 7, 14, and 28 days after surgery, respectively.

Schirmer's test: a 5 mm × 35 mm sterile paper test strip refolded by 5 mm was placed in the lower eyelid pouch. The patient was instructed to close their eyes, and after 5 min, the paper test strip was removed and the wetting length which represented the tear volume [13]. A length of 10-15 mm was considered normal tear secretion, a length of 5-10 mm was low volume of tear secretion, and a length of less than 5 mm was dry. They were evaluated before surgery, and at 7, 14, and 28 days after surgery, respectively.

Statistical methods

Statistical analysis was performed using SPSS 23.0. Count data expressed as [n (%)] were examined by chi-squared test. Measurement data ($\bar{x} \pm s$) were examined by t test. Multipoint comparisons were performed with ANVOA with post hoc F-test. Graphs were drawn with GraphPad Prism 8. *P* < 0.05 indicated statistically significant differences.

Results

Baseline data

There was no significant difference in terms of baseline data, such as gender, mean age, mean eye axis, mean corneal endothelial count, and nucleus grading between the two groups (P > 0.05) (Table 1).

Ultrasonic emulsification

AVG, APT and EPT were $(17.56\pm0.38)\%$, (42.15 ± 7.95) s, and (7.23 ± 1.18) s, respectively in group A, and $(17.50\pm0.42)\%$, (41.18 ± 8.24) s, and (7.16 ± 1.23) s respectively in group B, which showed no statistical difference between the two groups (*P* > 0.05) (**Figure 1**).





Figure 1. Ultrasonic emulsification. AVG, APT, and EPT did not differ between the two groups (P > 0.05).

Inflammatory indicators in tears

There was no significant difference in the levels of IL-2, IL-6, IL-8, TNF- α , and TNF- β 1 between the two groups before surgery (P > 0.05). The level of IL-2 was decreased while the levels of IL-6, IL-8, TNF- α , and TNF- β 1 were increased after surgery, showing a significant difference (P < 0.05). The level of IL-2 in group A was higher while the levels of IL-6, IL-8, TNF- α , and TNF- β 1 in group A were lower than those in group B at 5 days after surgery, indicating a significant difference (P < 0.05) (**Figure 2**).

Corneal endothelial cells

There was no significant difference in corneal cell density, coefficient of variation, and hexagonal cell ratio between the two groups before and after surgery (P > 0.05). The corneal cell density and ratio of hexagonal cells were decreased while the coefficient of variation was increased in both groups at 5 days after surgery (P > 0.05) (**Figure 3**).

Visual acuity

The visual acuity before surgery, and at 7, 14, and 28 days after surgery in group A were

(0.23±0.07), (0.66±0.09), (0.77±0.14), (0.88± 0.17), while the visual acuity of group B at the four time points were (0.22±0.05), (0.48±0.06), (0.62±0.10), (0.73±0.08), which showed no significant difference between the two groups (P > 0.05). The uncorrected visual acuity of group A was higher than that of group B at 7, 14 and 28 days after surgery, showing significant differences (P < 0.05) (**Figure 4**).

Dry eye symptoms

There was no significant difference in preoperative OSDI scores of vision loss, visual fatigue, foreign body sensation, stinging and photophobia between the two groups (P > 0.05). The OSDI scores of vision loss, visual fatigue, foreign body sensation, stinging and photophobia were decreased in both groups after surgery (P< 0.05), and were lower in group A than in group B (P < 0.05) (**Figure 5**).

TBUT

The preoperative TBUT was (10.25 ± 1.39) s in group A and (10.19 ± 1.42) s in group B. The TBUT were (9.85 ± 1.03) s, (11.86 ± 1.38) s, and (12.65 ± 1.52) s at 7, 14, and 28 days after surgery in group A and (7.24 ± 1.23) s, (8.19 ± 1.32)





Group A

Group B

Group A

Group B

s, and (10.28±1.67) s in group B. The preoperative TBUT had little significant difference between groups A and B (P > 0.05). The TBUT

was longer in group A than in group B at 7, 14, and 28 days after surgery, indicating a significant difference (P < 0.05) (Figure 6).







Figure 3. Corneal endothelial cells. Corneal cell density (A), coefficient of variation (B), and percentage of hexagonal cells (C). Compared with those before surgery within the group, the corneal cell density and the percentage of hexagonal cells were lower and the coefficient of variation was higher in group A and group B at 5 days postoperatively (P < 0.05). *indicates comparison with group B, P < 0.05.

fore surgery (P > 0.05). Group A had higher visual acuity at 7, 14, and 28 days postoperatively than group B (P < 0.05). *indicates comparison with group B, P < 0.05.

Schirmer's test results

The preoperative tear secretion length was (9.51 ± 1.35) mm in group A and (9.42 ± 1.43) mm in group B. The tear secretion length was (8.15 ± 1.76) mm, (11.69 ± 1.52) mm, and (12.27 ± 1.49) mm at 7, 14, and 28 days after surgery in group A and (8.91 ± 1.36) mm, (10.21 ± 1.39) mm, (10.82 ± 1.29) mm in group B. The preoperative tear secretion length was not significantly different between the two groups (P > 0.05). The preoperative tear secretion length was longer in group A than in group B at 7, 14, and 28 days after surgery, suggesting a significant difference (P < 0.05) (Figure 7).



Discussion

With the widespread success of the phacoemulsification technique regarding cataract treatment, techniques with better visual outcomes and less surgically induced astigmatism were explored to minimize complications [14]. MICS is a new procedure that meets these goals, and a large number of comparative studies have shown that C-MICS has greater advan-



Figure 6. Tear film break-up time. There was no significant difference in tear film break-up time between the two groups before surgery (P > 0.05). Group A had longer tear film break-up time at 7, 14, and 28 days postoperatively than group B (P < 0.05). *indicates comparison with group B, P < 0.05.

tages in terms of simplicity and ease of operation compared with bimanual microincisional cataract surgery [15, 16].

The incision stability was correlated with incision length and diameter, that is, a narrower incision ensures higher incision stability if the incision length is maintained [17]. The 1.8 mm C-MICS has a smaller surgical incision, allowing for narrowing of the channel between anterior chamber and outer during continuous curvilinear capsulorhexis, hydrodelineation, hydrodissection, thus effectively reducing the amount of viscoelastic spilling out of the anterior chamber via the incision, thereby eliminating the need for the surgeon to inject viscoelastic multiple times, enhancing the stability of the anterior chamber, and improving surgical efficiency and safety [18]. There was no significant difference in AVG, APT, and EPT between the two groups (P > 0.05), suggesting that there was no significant difference in the time of ultrasound emulsification and the energy used regardless of the width of the incision. The reason may be that two procedures were similar, and they differed only in terms of instruments used and the size of the incisions made, so there would be no significant effect on ultrasound emulsification.



Figure 7. Schirmer's test. There was no significant difference in tear secretion length between the two groups before surgery (P > 0.05). Group A had longer tear secretion length at 7, 14, and 28 days postoperatively than group B (P < 0.05). *indicates comparison with group B, P < 0.05.

Since the surgery is invasive, patients can experience an inflammatory response. When the inflammatory response occurs in the eye, it will cause abnormal inflammatory factor levels in tears, and the increase in inflammatory factor levels is positively correlated with the degree of inflammatory stress [19]. In this study, the level of IL-2 levels was higher and the levels of IL-6, IL-8, TNF- α , and TNF- β 1 were lower in group A than in group B at 5 days after surgery (P < 0.05), indicating that 1.8 mm C-MICS could more effectively control the level of inflammation in cataract patients, and the reduction in the degree of inflammation contributed to the improvement of clinical symptoms, which had positive significance for postoperative recovery. Evidence has also found that effective control of the inflammatory response is critical in the treatment of cataract and paves the road for a smooth postoperative recovery [20].

Surgeries tend to affect corneal endothelial cell counts which can slowly be restored over time, and the quality of recovery is closely related to the proliferation and growth of the adjacent healthy cells [21]. Cell density, coefficient of variation, and percentage of hexagonal cells are key indicators for cell proliferation and growth [22]. A study found that a greater cell density, a smaller coefficient of variation, and a greater percentage of hexagonal cells were indicative of better endothelial cell status in the cornea [23]. Some scholars have proposed that microincision cataract surgery results in less loss of corneal endothelial cells, with higher safety [24]. In this study, there was a decrease in corneal cell density and hexagonal cell percentage and an increase in the coefficient of variation in both groups at 5 days after surgery (P < 0.05), but there was no statistical difference between the two groups (P > 0.05), indicating that both two procedures were safe, which may be related to the small surgical incision and precise operation. By comparing conventional incision surgery with microincision type, the study showed that although there were changes in postoperative corneal cell density, hexagonal cell percentage, there was no significant difference in these indicators between the two groups, consistent with the results of this study. In this study, visual acuity in group A was higher than that in group B at 7, 14, and 28 days after surgery, and dry eye symptom scores in group A were lower than those in group B. Moreover, TBUT in group A was longer than that in group B, and wetting length in group A was longer than that in group B after surgery (P < 0.05). A study also found that TBUT at 1 month postoperatively and the wetting length were shorter in the conventional group [25], suggesting that 1.8 mm C-MICS resulted in better improvement in visual acuity in cataract patients compared to the standard 3.0 mm C-MICS. It also improved dry eye syndrome and improved tear film function. It was found that patients with more intact tear film function have a lower risk of postoperative dry eye symptoms [26]. Among the evaluation indices in this study, dry eye evaluation is subjective, but TUBT and wetting length are objective indices, which can reflect the function of tear film more accurately. Better tear film function suggests that patients have a better postoperative recovery, and the longer TBUT and wetting length in group A indicated that patients have better conditions for recovery and thus can achieve a higher quality of recovery.

In conclusion, C-MICS can more effectively control the level of tear inflammation, has less effect on corneal endothelial cells, improve postoperative visual acuity, delay tear film break-up, increase tear secretion, and improve dry eye. However, in this study, only two incision lengths, 3.0 mm and 1.8 mm, were compared, and it is not known whether the same results will be obtained for other incision lengths ranging 2.8-3.0 mm compared with the 1.8 mm. Meanwhile, the follow-up period was short and the occurrence of postoperative complications was not observed, which are the shortcomings of this study and need to be improved in the future studies.

Disclosure of conflict of interest

None.

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