Cell Damage and Repair after Phacoemulsification

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Abstract
To investigate the characteristics of corneal endothelial cell injury and repair after phacoemulsification for cataract patients. The 120 patients (120 eyes) who underwent phacoemulsification in ophthalmology department of our hospital were selected as the research objects. According to whether corneal edema occurred one day after phacoemulsification and intraocular lens implantation, the degree of corneal edema and the time of its disappearance were observed and recorded before operation. The changes of corneal cell density and corneal morphology 1 week, 1 month and 3 months after operation. Among 120 cases, 54 cases (observation group) had edema, 66 cases (control group) had no edema, and the time of corneal edema subsidence at all levels had statistical significance (F-88.946, P < 0.05). There were significant differences in corneal edema grade between the observation group and the control group (P < 0.05). The higher the edema grade, the lower the corneal cell density and the higher the loss rate of corneal cells. The corneal cell density of the observation group was significantly different from that of the control group in 1 week, 1 month and 3 months after the operation (P < 0.05). In clinical practice, recovery measures and appropriate recovery time can be formulated according to different levels of corneal edema. Patients with grade 1 edema and no edema after surgery can basically recover to endothelial cell repair in about 3 months.

Key words: Phacoemulsification, Endothelium, Corneal Cells, Corneal Edema.

1. Introduction
All kinds of reasons, such as aging, genetic, local nutritional disorders, immune and metabolic abnormalities, trauma, poisoning, radiation and so on which can cause lens metabolic disorders, leading to lens protein degeneration and opacity, known as cataract, when light is obstructed by opaque lens cannot be projected on the retina, leading to blurred vision. Most of them are over 40 years old and the incidence increases with age [1-3]. The disease can be divided into congenital and acquired nature. Congenital cataract, also known as developmental cataract, most of them exist before and after birth, mostly static, can be accompanied by...
hereditary diseases. There are endogenous and exogenous two types, endogenous and fetal developmental
disorders related, exogenous is caused by maternal or fetal systemic lesions damage to the lens, congenital
cataract is divided into anterior polar cataract, posterior polar cataract, circumferential nuclear cataract and total
cataract [4].

Postnatal lens opacity due to systemic or local eye diseases, abnormal nutritional metabolism, poisoning,
degeneration and trauma can be divided into six categories [5-7]:

1) Age-related cataract, the most common, also known as age-related cataract, is more common than 40
years old, and increases with age. It is related to many factors, such as slow metabolic degeneration in the
elderly, long-term exposure to sunlight, endocrine disorders, metabolic disorders and other factors. According
to the location of initial turbidity, it can be divided into two categories: nuclear and cortical; 2) Complicated
cataract (concurrent with other eye diseases); 3) Traumatic cataract; 4) Metabolic cataract; 5) Radioactive
cataract; 6) Drugs and toxic cataracts.

The most obvious feature of cataract patients is lens protein degeneration and opacity which is shown in
Figure 1. Corneal endothelial cells are monolayer hexagonal cells which are close to the elastic layer behind the
cornea. They are located in the innermost layer of the cornea and contact with aqueous humor. They have the
function of "pump". By participating in the control of corneal hydration, the corneal endothelial cells can keep
the cornea in a relatively dehydrated state with constant water content, so as to maintain the corneal
transparency. Endothelial cells are very vulnerable to injury and the number of cells decreases with age. Human
corneal endothelial cells can not regenerate after birth. After death, they can only be expanded and migrated by
adjacent cells. The damage of endothelial cells exceeds a certain limit. The adjacent cells can not fill the defect
area. There will be corneal edema and bullous keratopathy, leading to visual impairment or even blindness. The
minimum number of endothelial cells to maintain corneal transparency has not been determined yet. If the
density of corneal endothelial cells is greater than 400-500/mm², the body will maintain the dehydration of
corneal endothelial cells, which may lead to corneal decompensation [8]. Therefore, it is particularly important
to avoid corneal endothelial damage in various ophthalmological treatments and operations. The anatomical and
physiological map of corneal endothelial cells is shown in Fig. 2.

![Figure 1. The lens protein degeneration and opacity](image1)

![Figure 2. The anatomical and physiological map of corneal endothelial cells](image2)

Extracapsular cataract extraction (ECCE) is a major cause of corneal endothelial damage, including trauma,
repeated instrumentation in the anterior chamber, and intraocular lens implantation when the lens nucleus is
delivered and the anterior chamber disappears. Studies have shown that extracapsular cataract extraction is more
harmful to corneal endothelial cells than phacoemulsification [9]. Liu Jianwei’s results showed that there was no significant difference between extracapsular cataract extraction and phacoemulsification in corneal endothelial cell damage [10]. The reasons for the difference may be related to the proficiency of the operator, the energy and time of phacoemulsification during operation, and the nursing after operation. Cataract is a kind of ophthalmic disease characterized by degeneration of lens protein in the eyes. The etiology of cataract is diverse. It can be induced by heredity, local immunity and metabolic disorders, trauma, radiation and poisoning.

Phacoemulsification cataract extraction is one of the most commonly used cataract treatment methods in clinic. It is effective in improving the vision and quality of life of patients. However, after phacoemulsification, patients often suffer from corneal endothelial cell damage, and when the damage accumulates to a certain extent, the corneal endothelial function of patients will lose compensation, which may lead to bullous keratopathy and eventually blindness [11]. Therefore, how to improve and control corneal endothelial cell damage after phacoemulsification cataract extraction has become an important part of clinical research. 120 cases of cataract patients admitted to our Ophthalmic Center from February 2017 to October 2018 were selected as the research objects to observe the characteristics of corneal endothelial cell injury and repair after phacoemulsification cataract extraction.

2. Materials and Methods

2.1. General Information

The 120 cataract patients were divided into observation group (54 eyes with edema) and control group (66 eyes without edema) according to whether corneal edema occurred one day after phacoemulsification and intraocular lens implantation. Observation group: 21 males and 33 females, aged 54-76 (63.6±11.4) years; control group: 27 males and 39 females, aged 51-78 (64.2±12.4) years. There was no significant difference in age and gender between the two groups (P > 0.05).

2.2. Inclusion Criteria and Exclusion Criteria

Inclusion criteria: 1) Cataract patients diagnosed by doctors’ clinical examination and related auxiliary examinations; 2) All patients are suitable for the operation method of this study and willing to accept follow-up observation after operation; 3) All patients begin this study after signing the informed consent.

Exclusion criteria: 1) Exclusion of patients complicated with glaucoma, uveitis, Fuchs corneal endothelial dystrophy, diabetes and other diseases affecting corneal endothelial cells; 2) Exclusion of patients unwilling to receive follow-up observation.

2.3. Methods

Phacoemulsification and intraocular lens implantation: The operation was performed by three medical staff. After anesthesia, eyelid opener was used to open the eyelid. A scleral tunnel approach was established at 12 o’clock and an auxiliary approach was established at 3 o’clock. After injecting viscoelastic agent into the anterior chamber of the affected eye and routinely performing continuous circular capsulorhexis and water separation of the lens nucleus, the Universal II phacoemulsifier produced by Aicon Company of the United States was selected to perform phacoemulsification, remove the nucleus of the lens, suck out the residual lens cortex with an automatic suction head, implant the intraocular lens, and finish the operation after removing the viscoelastic agent.

2.4. Observation Index

The degree of corneal edema and the time of disappearance were observed. The changes of corneal cell density and corneal morphology were observed and recorded before, 1 week, 1 month and 3 months after operation. Observation of corneal edema: The degree of corneal edema was observed by slit lamp microscope after operation, and the time of edema subsidence was recorded. Corneal edema was divided into four grades.

- **Grade 0**: no edema at all;
- **Grade 1**: localized corneal edema, smooth corneal endothelial surface and visible iris texture;
- **Grade 2**: light grey corneal edema, rough corneal endothelium, blurred iris texture;
- **Grade 3**: diffuse grey corneal edema, tortoise-shaped corneal endothelial surface, invisible iris texture;
- **Grade 4**: milky white corneal edema, intraocular structure is not visible. The density and morphology of corneal endothelial cells were examined by Tomey EM-1000 contact corneal endothelial microscopy before operation, 1 week after operation, 1 month and 3 months after operation, and printed and counted.
2.4. Statistical method

SPSS 18.0 software was used for statistical analysis. \( \chi^2 \) test was used for counting data and t test was used for measuring data. Quantitative data were expressed by mean (±standard deviation) (\( \bar{x} \pm s \)). The comparison of mean between groups was performed by t-test of independent samples. \( P \leq 0.05 \) can be considered statistically significant.

3. Results

3.1. Edema after Phacoemulsification and Its Subsidence Time in Observation Group

There were 34 cases of grade 1 edema, 14 cases of grade 2 edema, 3 cases of grade 3 edema and 3 cases of grade 4 edema in the observation group. The average edema of grade 1 was (2.1±0.5) days, and that of grade 2 was (5.5±0.9) days. The average edema of grade 3 was (22±6.5) days. The average edema of grade 4 was (133±18.5) days. There was a significant difference in the regression time of corneal edema at all levels (\( F= 88.946, P < 0.001 \)).

3.2. Comparison of Corneal Cell Density before and After Surgery in Two Groups

There was no significant difference in corneal cell density between the observation group and the control group before operation (\( F=12.147, P > 0.05 \)); there was significant difference in corneal edema grade between the observation group and the control group at 1 week, 1 month and 3 months after operation (\( P < 0.05 \)). The higher the edema grade, the lower the corneal cell density after operation, the higher the loss rate of corneal cells in the observation group at all levels. The corneal cell density at 1 week, 1 month and 3 months after operation was significantly different from that before operation (\( P < 0.05 \)). The corneal cell density in the control group returned to normal at 3 months after operation, but there was no significant difference compared with that before operation (\( P > 0.05 \)) which is shown in Table 1.

Table 1. Comparison of corneal cell density before and after surgery in two groups (\( \bar{x} \pm s \))

<table>
<thead>
<tr>
<th>Time</th>
<th>Observation group (54 eyes)</th>
<th>Control group (66)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1 edema (34 cases)</td>
<td>Grade 2 edema (14 cases)</td>
</tr>
<tr>
<td>Preoperative</td>
<td>2898.8±294.8</td>
<td>2890.7±285.2</td>
</tr>
<tr>
<td>1 weeks after</td>
<td>2436.1±242.1</td>
<td>2137.4±251.7</td>
</tr>
<tr>
<td>operation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One month after</td>
<td>2654.3±273.3</td>
<td>2310.3±287.4</td>
</tr>
<tr>
<td>operation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three months after</td>
<td>2751.1±285.7</td>
<td>2510.4±288.3</td>
</tr>
<tr>
<td>operation</td>
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</tbody>
</table>

3.3. Comparison of Corneal Endothelial Cell Diameter between Two Groups Before and after Surgery

There was no significant difference in corneal endothelial cell diameter between the observation group and the control group (\( F = 1.941, P > 0.05 \)). The corneal endothelial cell diameter in the first week, one month and three months after operation was compared with that before operation. Only the patients with corneal endothelial cell grade 1 edema in the control group and observation group recovered to the preoperative level in the third month after operation, and there was no significant difference compared with that before operation (\( P > 0.05 \)). There were significant differences in the diameter of corneal endothelial cells between the patients with grade 2, grade 3 and grade 4 edema in the first week, one month and three months after operation (\( P < 0.05 \)). It showed that the recovery of endothelial cells in the patients with grade 2, grade 3 and grade 4 edema after operation was slow, as shown in Table 2. The corneal endothelial cell diagram of the patient after surgery is shown in Figure 3.
Figure 3. The corneal endothelial cell diagram of the patient after surgery

Table 2. Comparison of corneal endothelial cell diameter between two groups before and after surgery (x ± s)

<table>
<thead>
<tr>
<th>Time</th>
<th>Observation group (54 eyes)</th>
<th>Control group (66 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1 edema (34 cases)</td>
<td>Grade 2 edema (14 cases)</td>
</tr>
<tr>
<td>Preoperative</td>
<td>69.8±3.2</td>
<td>68.4±2.8</td>
</tr>
<tr>
<td>1 weeks after operation</td>
<td>81.3±3.7</td>
<td>81.6±3.4</td>
</tr>
<tr>
<td>One month after operation</td>
<td>75.8±3.1</td>
<td>76.2±3.1</td>
</tr>
<tr>
<td>Three months after operation</td>
<td>69.9±2.9</td>
<td>71.3±3.1</td>
</tr>
</tbody>
</table>

4. Discussion

All kinds of cataract extraction methods in cataract surgery will lead to different degrees of corneal endothelial injury. In severe cases, corneal turbidity is caused by the decompensation of endothelial function after operation, which leads to the failure of operation. At present, because drug therapy cannot effectively prevent or slow down the development of lens opacity, surgery is the main means of treatment of various cataracts, and phacoemulsification is the fastest growing and most commonly used surgical method in clinic in recent years. But the degree of corneal endothelial injury is the key to the effect of surgery. Studies have shown that cataract surgery causes endothelial cell loss, the loss rate is more than 5% to 30%. The mechanism of corneal endothelial injury caused by phacoemulsification surgery includes thermal burn, concussion injury, mechanical injury and chemical injury [12].

Relevant factors affecting corneal endothelium after phacoemulsification were as follows:
1) The lens nucleus hardness and phacoemulsification time: Hagashi and Piazzoli found that the most important factors causing corneal endothelial injury were nuclear grading and ultrasound time, i.e. the higher nuclear hardness and the longer ultrasound time, the more serious corneal endothelial injury.

2) Skilled degree of operation: The more skilled the surgeon is in phacoemulsification of cataract, the farther the phacoemulsification is from the corneal endothelium, the lighter the corneal endothelial injury is.

3) The performance of the ultrasonic emulsifier: According to the different suction devices, the ultrasonic emulsifier can be divided into two main types: Venturi pump and peristaltic pump. The former has the advantage of fast peak negative pressure and stable linear mode, while the disadvantage is that it is easy to produce anterior chamber surge when the control is not proper. The latter is easier to form stable anterior chamber, so the damage of corneal endothelial cells is less. At present, the appearance of cold ultrasound instrument, because of the operation process, the damage to eye tissue reduced to the lowest extent, almost no damage to corneal endothelium.

4) Intraoperative use of viscoelastic agents: Generally speaking, they can be divided into cohesive or diffuse types. Intraoperative use of diffuse viscoelastic agents such as Viscoat has a good protective effect on corneal endothelium [13].

5) Patients with high myopia: The endothelial cell density, cell area and proportion of hexagonal cells in patients with high myopia were lower than those in the same age group, and the rate of endothelial cell loss after phacoemulsification was higher than that in normal people, which indicated that high myopia could affect endothelial cells and was more sensitive to phacoemulsification injury.

6) Diabetic patients: In diabetic animals, the activity of Na⁺-K⁺-ATPase in corneal endothelium decreased by 69% to 176% [14], suggesting that the disorder of pump function of corneal endothelium dependent on Na⁺-K⁺-ATPase is the main cause of uncontrolled corneal hydration. Studies have shown that the corneal endothelium of type 2 diabetes mellitus is more sensitive to the damage caused by phacoemulsification than that of age-related patients.

Cataract is more common in people over 40 years old. The higher the age of patients, the higher the incidence of cataract. The symptoms of cataract are mostly mockery of lens opacity and blurred vision. With the development of the condition, the vision of cataract patients will gradually deteriorate and disappear, seriously affecting the quality of life of patients, so active treatment is extremely necessary. At present, the main treatment methods for cataract are drug therapy and surgical treatment. Glutathione, vitamin C, vitamin E, pearl-red eye drops and other drugs are mostly used in drug therapy. It is worth emphasizing that there is no definite clinical basis for the efficacy of drug treatment, so it is mostly used in assistant surgical treatment [15]. Surgical treatment is the most effective and commonly used treatment for cataract diseases. Extracapsular cataract extraction and phacoemulsification are commonly used.

Extracapsular cataract extraction (ECCE) is a routine cataract treatment in clinic. It is mainly performed by excreting diseased lens and intraocular lens implantation. However, this kind of operation requires high experience of operators and is difficult to further promote [16-20]. Cataract phacoemulsification is a relatively advanced new type of cataract treatment. It is mainly through high-energy acoustic wave to comminute the diseased lens and suck it out, then give the patient intraocular lens implantation operation. The injury in the operation is minimal, and because of the intervention of phacoemulsifier, the difficulty of operation is greatly reduced, which is conducive to promotion. Of course, cataract phacoemulsification also has some adverse reactions, such as corneal endothelial cell damage. Corneal endothelial cell injury is an unavoidable complication of phacoemulsification for cataract. Its pathogenesis may be related to intraoperative ultrasound oscillation, nucleus fragments and instrument damage to corneal cells. Some studies have shown that the degree of corneal endothelial cell damage after phacoemulsification is related to the hardness of the nucleus. The higher the hardness of the nucleus, the higher the intensity of the ultrasound, the greater the risk of corneal endothelial cell damage and the corresponding increase of the degree of damage. Clinical studies have shown that patients with corneal endothelial cell injury can gradually recover within a certain period of time, and the recovery process is mainly completed by the proliferation and extension of surrounding healthy cells. Some scholars have shown that the degree of endothelial cell damage in the upper, middle and lower corneas of cataract patients after phacoemulsification is different. The upper and middle corneas of cataract patients have the greatest damage, but they can basically recover in about 3 months, while the lower corneas can recover in 1 to 2 months. It is based on this difference in recovery time that the degree of corneal endothelial cell injury and recovery time are taken as important reference criteria for perioperative evaluation and surgical techniques of phacoemulsification.

In this study, there was no significant difference in corneal cell density between the observation group and the control group before operation (F=12.147, P > 0.05); there was significant difference in corneal edema grade between the observation group and the control group at 1 week, 1 month and 3 months after operation (P < 0.05). The higher the edema grade, the lower the corneal cell density and the loss of corneal cells after operation. The higher the rate was, and there were significant differences in corneal cell density between the
observation group and the preoperative group in 1 week, 1 month and 3 months after operation (P < 0.05). Only in the control group, corneal cell density returned to normal in the 3rd month after operation, but there was no significant difference between the observation group and the preoperative group (P > 0.05). It can be found that the corneal cell damage in the observation group is more serious, but it can recover within 3 months, which is like the similar studies mentioned above. In addition, there was no significant difference in corneal endothelial cell diameter between the observation group and the control group (F=1.941, P > 0.05). The corneal endothelial cell diameter at the 1st week, 1 month and 3 month after operation was compared with that before operation. Only in the control group and the observation group, the corneal endothelial cell grade 1 edema patients recovered to the preoperative level at the 3rd month, and the difference was not consistent with that before operation. Significance of the cell density between the observation group and the control group revealed significant differences between the observation group and the control group at all levels of corneal endothelial cell damage and dysfunction. Therefore, preoperative understanding of corneal endothelial cell status, according to the specific conditions of patients, formulate the most official operation time and program, the operation should be gentle, delicate, reduce the harassment of cornea, adopt various measures to reduce the damage to corneal endothelial cells. To sum up, in clinical practice, recovery measures and appropriate recovery time can be formulated according to different levels of corneal edema. Patients with grade 1 edema and no edema after surgery can basically recover to endothelial cell repair in about 3 months.

5. Conclusions

Among 120 cases, 54 cases (observation group) had edema, 66 cases (control group) had no edema, and the time of corneal edema subsidence at all levels had statistical significance (F=88.946, P < 0.05); there was no significant difference in corneal cell density between observation group and control group before operation (F=2.147, P > 0.05); one week after operation, one month after operation and three months after operation, there was no statistical significance (F=2.147, P > 0.05). There were significant differences in the diameter of corneal endothelial cells between the patients with grade 2, grade 3 and grade 4 edema in the first week, one month and three months after operation (P < 0.05). It indicated that the recovery of endothelial cells in the patients with grade 2, grade 3 and grade 4 edema of corneal endothelial cells was slow after operation. Cornea was an important part of refractive system and corneal endothelium was fine.

Normal cell density and morphology are essential for maintaining normal corneal thickness and transparency. The corneal endothelial cells with good function should be regular hexagonal, with clear outline and close arrangement of adjacent cells. After corneal endothelial cells are damaged, the regeneration ability is very low. Guilt, drugs, surgery and other factors can cause corneal endothelial cells damage and dysfunction. Therefore, preoperative understanding of corneal endothelial cell status, according to the specific conditions of patients, formulate the most official operation time and program, the operation should be gentle, delicate, reduce the harassment of cornea, adopt various measures to reduce the damage to corneal endothelial cells. To sum up, in clinical practice, recovery measures and appropriate recovery time can be formulated according to different levels of corneal edema. Patients with grade 1 edema and no edema after surgery can basically recover to endothelial cell repair in about 3 months.

References


