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COMPARATIVE ASSESSMENT OF THE EFFICACY OF PRIMARY AND SECONDARY CORNEAL ENDOTHELIAL DYSTROPHY TREATMENT BY ISOLATED DESCEMETORHEXIS AND ACCELERATED COLLAGEN CROSSLINKING METHOD

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✧ The article examines the efficacy of the author's method of endothelial corneal dystrophy treatment, including descemetorhexis and accelerated collagen crosslinking. In primary endothelial dystrophy, corneal state improvement and restoration of its transparency were observed in 66.6% of cases (due to migration of endothelial cells from the periphery to the central zone). In secondary endothelial dystrophy, the treatment method described in the present article is ineffective, and the reasons for failures are not quite clear and require further investigation.

✧ ***Keywords:*** cornea; endothelial dystrophy; descemetorhexis; accelerated collagen crosslinking.

СРАВНИТЕЛЬНАЯ ОЦЕНКА ЭФФЕКТИВНОСТИ ЛЕЧЕНИЯ ПЕРВИЧНОЙ И ВТОРИЧНОЙ ЭНДОТЕЛИАЛЬНОЙ ДИСТРОФИИ РОГОВИЦЫ МЕТОДОМ ИЗОЛИРОВАННОГО ДЕСЦЕМЕТОРЕКСИСА И УСКОРЕННОГО КОЛЛАГЕНОВОГО КРОССЛИНКИНГА

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✧ В статье анализируется эффективность авторского метода лечения эндотелиальной дистрофии роговицы, включающего в себя десцеметорексис и ускоренный коллагеновый кросслинкинг. При первичной эндотелиальной дистрофии улучшение состояния роговицы и восстановление её прозрачности наблюдалось в 66,6 % случаев (за счёт миграции клеток эндотелия с периферии в центральную зону). При вторичной эндотелиальной дистрофии описанный в статье метод лечения является неэффективным, причём причины этих неудач не совсем ясны и требуют дальнейших исследований.

✧ ***Ключевые слова:*** роговица; эндотелиальная дистрофия; десцеметорексис; ускоренный коллагеновый кросслинкинг.

INTRODUCTION

According to E.S. Libman and E.V. Shakhova (2005), more than 500,000 people in Russia are blind or visually impaired [3]; of them, 90,000 have corneal disorders, and approximately 50,000 require keratoplasty [2, 4]. As of 2004, over 100,000

corneal transplant surgeries were performed annually worldwide, with only 2% of them performed in Russia [3]. There are two main reasons for low rates of corneal transplantation in Russia: problems related to the establishment of organ and tissue banks, and the absence of formal permission for dealing with donor corneas in many healthcare institutions of the Russian Federation. Endothelial corneal dystrophy (ECD) is one of the most common indications for corneal transplantation [14]; therefore, the development of new non-transplant methods to treat ECD remains highly relevant.

Several studies assessing the efficacy of isolated descemetorhexis (DR) in ECD have been recently published [7, 8, 11–13]. However, indications for this method in ECD patients remain controversial. Many authors consider DR insufficiently effective because of the long time required for restoration of corneal transparency (6–12 months) and the relatively low postoperative visual acuity [6, 9, 15].

According to the literature, collagen cross-linking (CCL) has a well-known antihydration effect. Wollensak et al. recommended using CCL for treatment of the dysfunction of the endothelial layer of the cornea [17]. Modification of ultraviolet radiation parameters during CCL may reduce the time required for the procedure. This can be achieved by increasing the power-flux density without changing the total dose, which will reduce the total exposure time [10]. The most common emitters, from various manufacturers, have the following regimens: 9 mW/cm^2 × 10 min exposure, 6 mW/cm^2 × 15 min, 10 mW/cm^2 × 9 min, 18 mW/cm^2 × 5 min, and 30 mW/cm^2 × 3 min [16].

Based on the results of relevant studies [1] and our own clinical experience, we developed a new method of ECD therapy, which is a combination of DR and accelerated CCL (aCCL). The invention has been patented (Patent No. 2647480 from 15.03.2018).

MATERIALS AND METHODS

The study included 17 patients (18 eyes) aged between 61 and 86 years (mean age, 69.5 ± 7.2 years); 3 of them were men and 14 were women. All patients were examined and treated at the Ophthalmology Department of the I.P. Pavlov First Saint Petersburg State Medical University. The follow-up time ranged from 3 to 12 months. Study participants were diagnosed with stage IIa, IIb, or IIIa ECD according to the new classification based on confocal microscopy results only [4]. Thirteen patients had primary Fuchs ECD, and six patients had secondary ECD developed after phacoemulsification. Ophthalmologic examination included visual acuity testing, biomicroscopy of the anterior segment of the eye, and slit-lamp indirect ophthalmoscopy (Nidek, Japan) with photo- and video-recording of pathological changes in the cornea. All patients also underwent confocal microscopy of the cornea with a Confoscan-4 confocal microscope (Nidek, Japan), ocular ultrasound examination (ultrasonic A- and B-scanning, ocular biometry, ultrasonic pachymetry, and optical pachymetry with a Tomey optical biometer), and tonometry with an I-care tonometer or pneumotonometry. Endothelial cell density in the central corneal area could not be evaluated in the majority of cases. However, we performed preoperative assessment of endothelial cell density at corneal periphery (at 6 o'clock).

The patients were divided into two groups according to the type of dystrophy (Table 1).

Group 1 included patients with primary Fuchs ECD (clinical examples showing the cornea are shown in Figures 1 and 2), whereas group 2 comprised patients with secondary ECD (clinical examples are shown in Figures 3 and 4).

All patients underwent two-stage treatment that included isolated DR with 5.0 mm diameter followed by aCCL (9 mW/cm^2 × 10 min exposure). The mean time between DR and aCCL was 21.5 ± 2.9 days.

Three patients in group 1 additionally underwent phacoemulsification with intraocular lens implantation, which was performed simultaneously with isolated DR (Figures 5 *a* and 5 *b*).

Table 1

Characteristics of patients groups

Таблица 1

Характеристики групп пациентов

Parameter	Group 1 (11 patients, 12 eyes)	Group 2 (6 patients, 6 eyes)
Mean age, yr	68.5 ± 7.3 (61–86)	71.5 ± 7.5 (61–79)
Central corneal thickness before treatment, μm	729 ± 80.6	684 ± 92.6
Peripheral ECD before treatment, cells/mm^2	1697 ± 316.6 (1192–2444)	1572 ± 57 (1489–1635)
BCVA before treatment	0.14 ± 0.05	0.03 ± 0.01
Note: ECD, endothelial cell density; BCVA, best corrected visual acuity		

Procedure of isolated DR

After preparing the surgical field, epibulbar anesthesia, and installing the blepharostat, we marked a 5-mm area of DR on the epithelial side of the cornea using a special marker. Using a 2.2-mm spear-shaped knife, we created a corneal tunnel incision at the 11 o'clock position. Descemet's membrane was stained with trypan blue solution. Then the dye was washed out, and the anterior chamber was filled with a dispersive viscoelastic. DR was performed using reverse forceps (Katena, USA) according to the preoperative marking. The viscoelastic was washed out of the anterior chamber, and the corneal tunnel was hydrated. At the end of the procedure, a steroidal anti-inflammatory drug was injected under the conjunctiva. During the postoperative period, patients received antibiotic eye drops (1 drop 3 times a day for 7 days), dexamethasone (1 drop 3 times a day for 3 weeks, with a gradual decrease in dosage), nonsteroidal anti-inflammatory drugs (1 drop TID for 3 weeks), a hyperosmolar agent, and artificial tears.

RESULTS AND DISCUSSION

Patients were examined before treatment, 2 to 3 weeks after DR, and then 3, 6, and 12 months after aCCL.

We observed restoration of corneal transparency and improvement of visual functions in seven patients (eight eyes) with primary Fuchs ECD. The time to restoration varied: restoration occurred after 1.5 months in five patients, 2 months in two patients, and 3 months in one patient. The remaining four patients had no positive dynamics after 8 months.

The dynamics of morphological/functional characteristics of the cornea and visual acuity in the postoperative period are shown in Tables 2 and 3.

The postoperative period was characterized by progressive edema in the central cornea (in the area of DR) and emergence of folds in the deep layers of the stroma. Stromal edema increased until aCCL. After aCCL, we observed gradual reduction of central corneal thickness, restoration of corneal transparency, and improvement of visual functions (Figure 6).

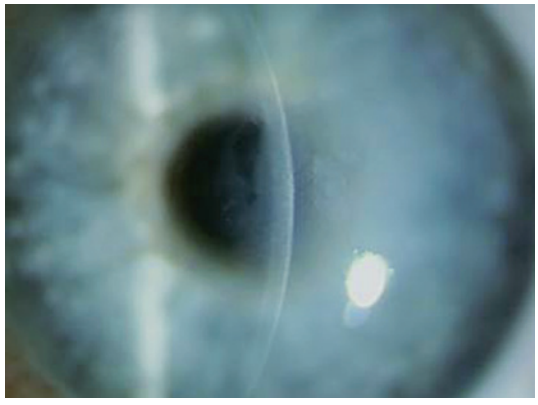


Fig. 1. Patient G., 69 years, with Fuchs endothelial corneal dystrophy before treatment

Рис. 1. Больная Г., 69 лет, с эндотелиальной дистрофией роговицы Фукса до лечения

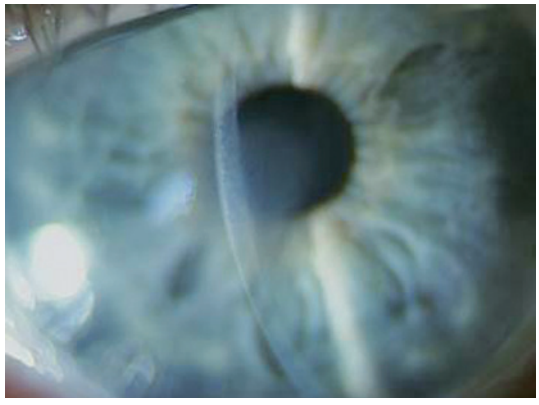


Fig. 2. Patient R., 63 years, with Fuchs endothelial corneal dystrophy before treatment

Рис. 2. Больная Р., 63 года, с эндотелиальной дистрофией роговицы Фукса до лечения

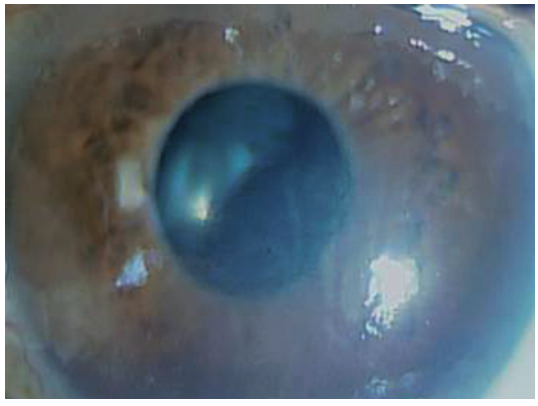


Fig. 3. Patient D., 64 years, with the secondary ED before treatment

Рис. 3. Больной Д., 64 года, со вторичной эндотелиальной дистрофией роговицы до лечения

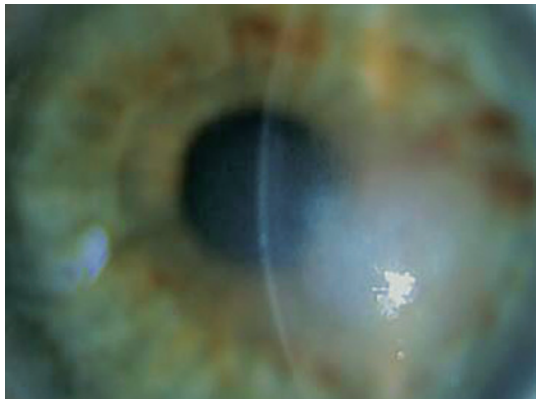
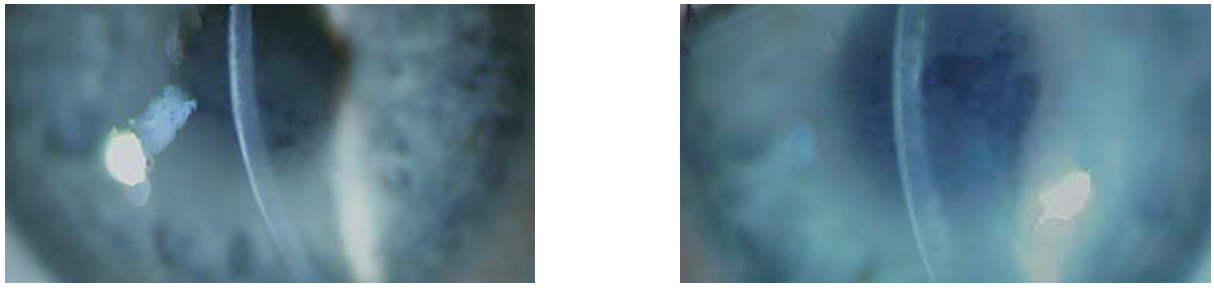


Fig. 4. Patient K., 68 years, with the secondary ED before treatment

Рис. 4. Больная К., 68 лет, со вторичной эндотелиальной дистрофией роговицы до лечения



a *b*

Fig. 5. Cornea with Fuchs endothelial corneal dystrophy before treatment (*a*); 2 days after the isolated DR and ACXL and phacoemulsification with intraocular lens implantation (*b*)

Рис. 5. Роговица с эндотелиальной дистрофией роговицы Фукса до лечения (*a*); через 2 дня после изолированного десцеметорексиса с факоэмульсификацией и имплантацией ИОЛ (*b*)

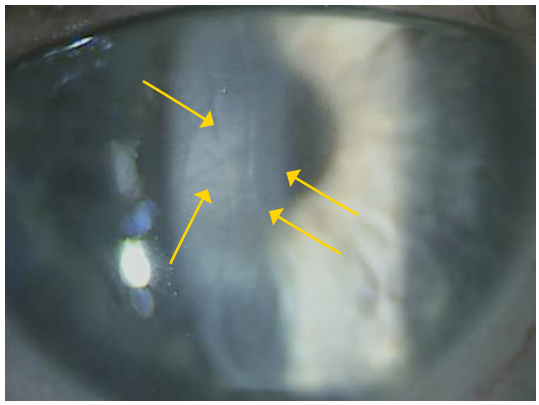


Fig. 6. Cornea after the isolated DR and ACXL (arrows indicate the folds of the deep layers of the stroma)

Рис. 6. Роговица после изолированного десцеметорексиса и ускоренного коллагенового кросслинкинга (стрелками указаны складки глубоких слоёв стромы)

Corneal transparency was not restored in two patients with primary ECD, although they had single endothelial cells in the area of DR. These patients underwent penetrating keratoplasty 8 months later.

Thus, 8 of 12 patients (66.6%) with primary Fuchs ECD had a pronounced positive effect with restoration of corneal transparency (Fig. 7), complete resorption of corneal edema, appearance of endothelial cells in the DR area (Fig. 8), and significant improvement of visual acuity. The high success rate of combination therapy (DR + aCCL) in patients with primary ECD can probably be explained by the fact that a pool of healthy endothelial cells is preserved at the corneal periphery. The high density of these morphologically normal cells ensures their migration into the DR area.

All patients in group 2 (six eyes) had no positive dynamics 8 months postoperatively, although the

Table 2

Dynamics of Central cornea thickness in patients of the first group

Таблица 2

Динамика центральной толщины роговицы у пациентов первой группы

Parameter	Before DR	Before aCCL	2 wk postop	3 mo postop	6 mo postop	12 mo postop
CCT, μm	719.5 ± 75.9	757.9 ± 89.9	647.1 ± 91.8	608 ± 39.3	592 ± 41.6	562
No. of eyes	8	8	8	8	4	1
CCT, central corneal thickness; DR, descemetorhexis; aCCL, accelerated collagen cross-linking						

Table 3

Dynamics of the best corrected visual acuity in patients of the first group

Таблица 3

Динамика корригированной остроты зрения у пациентов первой группы

Parameter	Before DR	Before aCCL	2 wk postop	3 mo postop	6 mo postop	12 mo postop
BCVA	0.13 ± 0.05	0.13 ± 0.07	0.39 ± 0.18	0.48 ± 0.09	0.63 ± 0.31	1.0
No. of eyes	8	8	8	8	4	1
BCVA, best corrected visual acuity; DR, descemetorhexis; aCCL, accelerated collagen cross-linking						

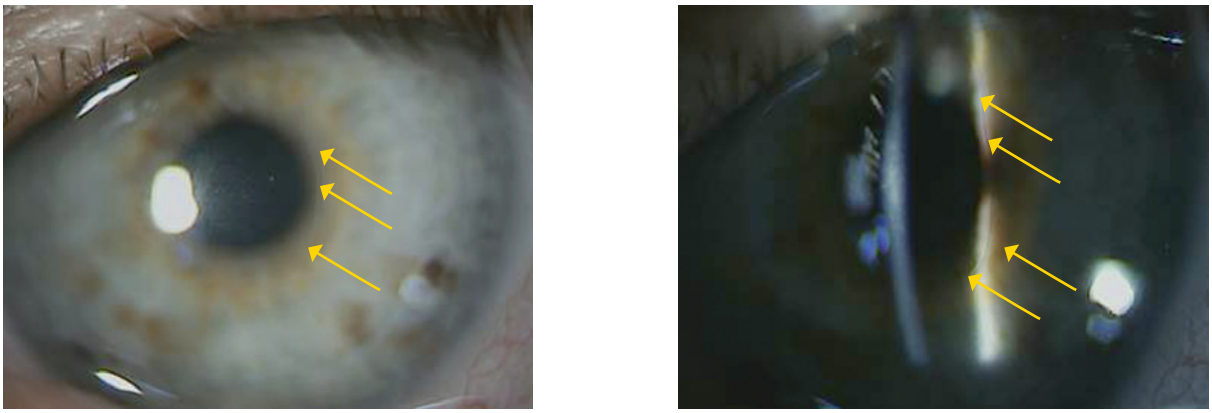
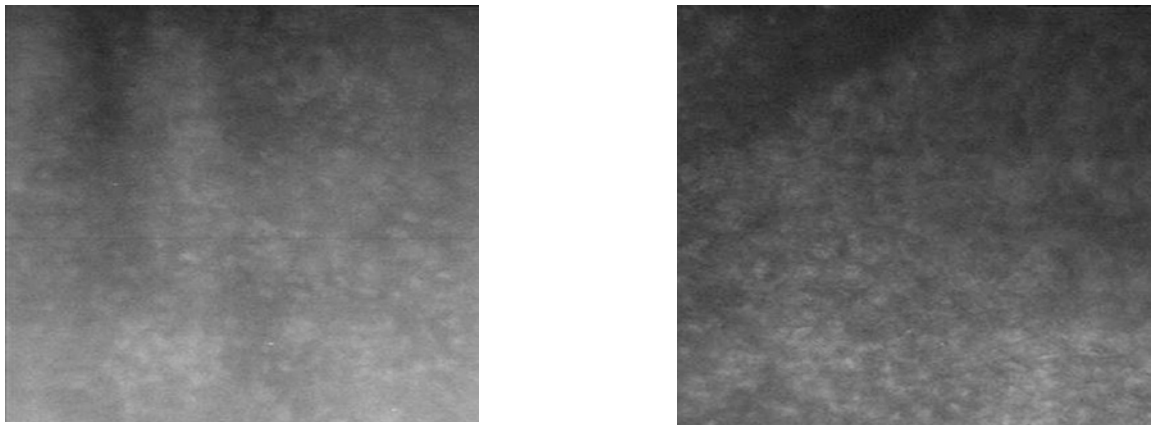


Fig. 7. The restoration of corneal transparency 1,5 months after the isolated DR and ACXL (arrows indicate the border of the descemetorhexis)

Рис. 7. Восстановление прозрачности роговицы через 1,5 месяца после изолированного десцеметорексиса и ускоренного коллагенового кросслинкинга (стрелками указан край десцеметорексиса)



a *b*

Fig. 8. Confocal microscopy of endothelial cells (1503 cells/mm^2) 3 months after the isolated DR and ACXL (*a*); confocal microscopy of endothelial cells (1693 cells/mm^2) 3.5 months after the isolated DR and ACXL (*b*)

Рис. 8. Конфокальная микроскопия эндотелиальных клеток в центральной зоне (1503 кл/мм^2) через 3 месяца после изолированного десцеметорексиса и ускоренного коллагенового кросслинкинга (*a*); конфокальная микроскопия эндотелиальных клеток (1693 кл/мм^2) через 3,5 месяца после десцеметорексиса и ускоренного коллагенового кросслинкинга (*b*)

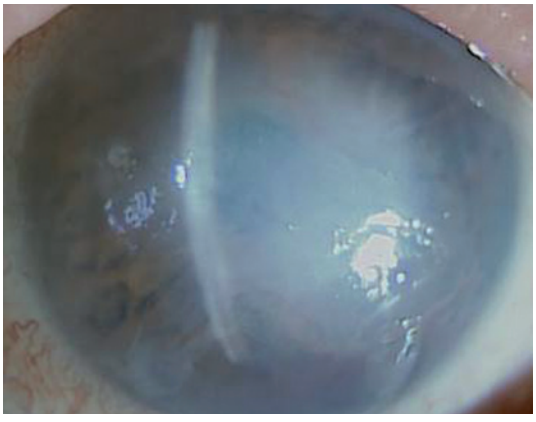


Fig. 9. Patient S., 77 years, with the secondary ED 8 months after the isolated DR and ACXL with negative dynamics

Рис. 9. Больной С., 77 лет, со вторичной эндотелиальной дистрофией роговицы через 8 месяцев после изолированного десцеметорексиса и ускоренного коллагенового кросслинкинга с отрицательной динамикой

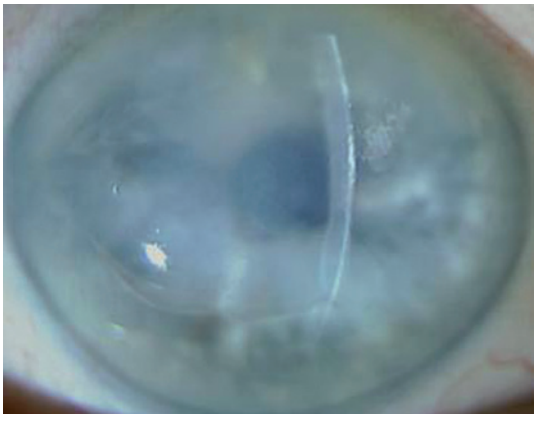


Fig. 10. Patient R., 68 years, with the secondary ED 8 months after the isolated DR and ACXL with negative dynamics

Рис. 10. Больная Р., 68 лет, со вторичной эндотелиальной дистрофией роговицы через 8 месяцев после изолированного десцеметорексиса и ускоренного коллагенового кросслинкинга с отрицательной динамикой

initial condition of their cornea was the same as in group 1 patients (Figures 9 and 10). These patients underwent penetrating keratoplasty.

Despite the fact that the density and morphological characteristics of endothelial cells (assessed by endothelial microscopy at the corneal periphery at 6 o'clock) were comparable in patients in the two groups, we assume that patients with secondary ECD had damaged endothelium in both the central and the peripheral cornea. Further studies are needed to identify the reasons underlying this lack of endothelial cell regeneration in patients with secondary ECD.

CONCLUSIONS

- Isolated DR with subsequent aCCL is an effective non-transplant surgical method for primary ECD.
- Analysis of clinical data demonstrated that corneal stabilization and improvement in visual function occurred no earlier than 3 to 4 months postoperatively.
- Simultaneous phacoemulsification and isolated DR with subsequent aCCL (after 2 to 3 weeks) appear to be a promising treatment strategy for complete rehabilitation of patients with primary ECD and cataract.
- Isolated DR in combination with aCCL is not recommended for patients with secondary ECD.

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