



MICROINVASIVE DESCOMETOPLASTY: ANALYSIS OF PRELIMINARY RESULTS OF INITIAL 20 CASES

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Abstract

Results of microinvasive descemetoplasty (microDMEK) are presented in 20 patients (21 eyes). The follow-up period was from 3 to 12 months. The surgery technique was performed. During the surgery marginal ruptures of Descemet's membrane, its partial injection into posterior chamber, its prolapse from anterior chamber and incarceration of Descemet's membrane in tunnel incision were observed. Central diastasis of Descemet's membrane occurred in 14%, its peripheral diastasis – in 24%. The transparency of the cornea was achieved in all cases. BCVA was 0.2 and higher during 14 postoperative days in 90% patients. In 15% patients BCVA was 0.9-1.0 in the first two postoperative days. In 1 month after microDMEK BCVA was more than 0.5 in 76% of patients. In 1 month maximal astigmatism of 4.5-5-5^D was in 14%, 3.0-3.75^D in 9%, less than 1.5^D in 90% of cases.

Descemet's membrane grafting allows to use efficiently donor's tissue. Descemet's membrane transplantation excels endokeratoplasty in functional results, rates of rehabilitation, microinvasiveness and cost price. By authors opinion it is impossible to deny further research of this method because of its high availability.

Keywords: endokeratoplasty (DSEK), microinvasive descemetoplasty (microDMEK) descemetoplasty, transplantation of Descemet's membrane (DMEK).

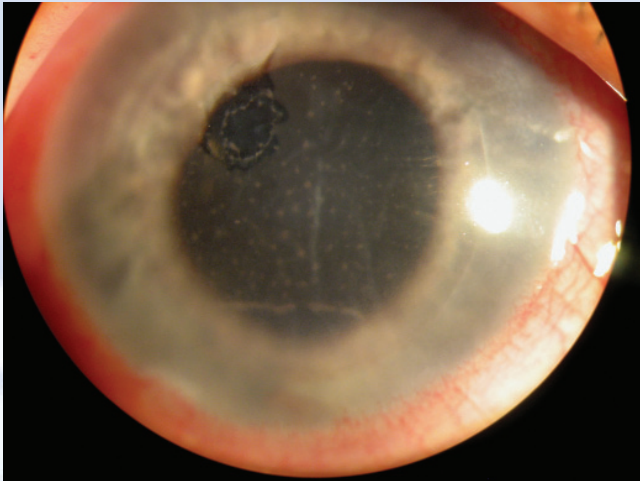
INTRODUCTION

In 2009 endokeratoplasty (DSEK) became a "gold standard" for treatment of endothelial-epithelial dystrophy of cornea [Nuijts R., 2009]. The progress of method development in historical context, main modifications of this method, advantages, shortcomings and complications of both automated and non-automated DSEK are comprehensively presented in scientific publications. For the first time in Russia this methodic procedure was implemented by authors and since 2006 above 100 surgery interventions for DSEK were performed. Maximal follow-up period makes 3 years. We are entirely satisfied with this procedure and its functional results as reflected by our publications (Danilova D., 2008; Oganesyan O., Danilova D., 2008; Oganesyan O., 2009; Oganesyan O. et al., 2009).

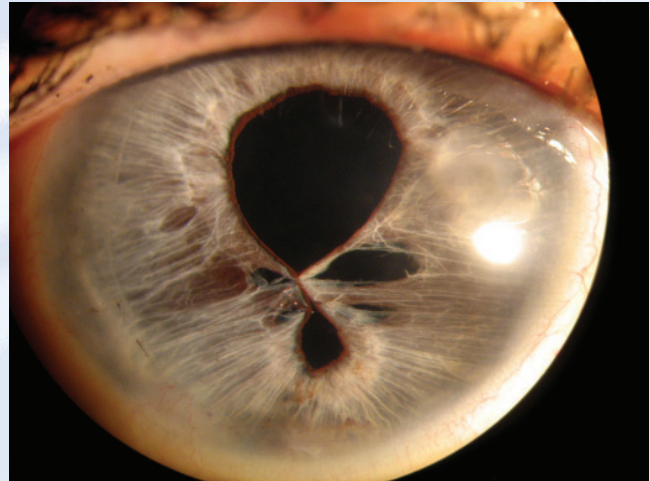
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Despite this latter, from the point of view of theory, transplantology of isolated Descemet's membrane that was for the first time performed in Russia at the Helmholtz Moscow Research Institute of Eye Diseases in 2008 [Oganesyan O. et al., 2008] is a promising one as more pathogenetical, less invasive, with maximum short period of rehabilitation and attainment of visual acuity in case of surgery for endothelial-epithelial dystrophy. Our own procedure was elaborated as a less traumatic methodic for transplantation of Descemet's membrane: microinvasive descemetoplasty (microDMEK) [Vorobjova M. et al., 2009] that differs from the original one in both method of Descemet's membrane transplant formation, method of implantation and its stretching in anterior chamber (Patent Application dated April 2, 2009, incoming No. 016554; registration No. 2009112165). The aim of this communication is to analyze the short-term results of microDMEK in the first 20 patients operated in 2008.



Picture 1. Endokeratoplastate disease, paralytic mydriasis, pseudophakia.



Picture 1a. 3 months post explantation of the endokeratoplastate, microDMEK and pupilloplasty. Visus=1.0.

MATERIAL AND METHODS

The study involved the first 20 patients (21 eyes) who underwent microDMEK in 2008. There were 11 males and 9 females. The average age made 64.5 years (21-83).

The true primary dystrophy of cornea (clinical dystrophy on phakic eyes without surgery interventions in the anamnesis) was observed in 6 (30%) patients. True secondary dystrophy (dystrophy developed after the surgical intervention without the signs of primary dystrophy on the another eye) was recorded in 11 (55%) patients. In 1 (5%) patient primary-secondary dystrophy (clinical dystrophy developed in an eye with sub-clinical primary dystrophy after the surgery intervention) was observed. In 2 (10%) patients microDMEK was performed in eyes with endokeratoplastate disease: 1 case a year post DSEK and 1 case a week after DSEK. Best corrected visual acuity (BCVA) before surgery made 0.1-0.2 in 6 (33%) patients, while in 14 (67%) patients it was below 0.1. Concomitant pathology was recorded: operated compensated open-angle glaucoma in 3 patients; high degree myopia in 1 patient, post-contusion paralytic mydriasis in 1 patient. At the time of surgery in 19 patients (20 eyes) pseudophakia was observed; 1 patient had native transparent lens.

All patients underwent microDMEK according to our methodic procedure (Patent Application dated April 2, 2009; incoming No. 016554; registration No. 2009112165). In 1 case microDMEK was combined with pupilloplasty on the back-

ground of paralytic mydriasis (Pictures 1-1a).

Patients underwent ophthalmological examination including: visometry, refractometry, biomicroscopy, confocal microscopy or non-contact endothelial microscopy, determination of cornea thickness, ultra sound and electrophysiological investigations, photovideoregistration. Refractometry and endothelial microscopy failed in some patients because of epithelial oedema of cornea. In pre-operative period all patients were exposed to laser iridotomy in the meridian of 6 hours in order to avoid iris blocking in post-surgery period. The period of observation made 3-12 months.

Surgery Technique

All operations were performed under instillation anesthesia. Tunnel incision of 1.8-2.0 mm was inflicted in the meridian of 12 hours. Two paracenteses of 0.8 mm width were performed in the meridians of 3 and 9 hours. Descemetorhexis of 8-9 mm was done: in 2 cases endokeratoplastate was removed. As donor material the native eye-bulb of a donor was used being enucleated no later than 24 hours *post mortem* and preserved in a humid chamber according to Filatov at the temperature of 4°C no longer than 48 hours. After incision of a penetrating corneoscleral disk, Descemet's membrane was separated from the stromal side using the ocular spatula. Trepan blue (0.1%) was introduced underneath the Descemet's membrane. Then from the side of endothelium a penetrating full-layer disk

of 8.25-9.00 mm diameter was incised from donor cornea. The penetrating disk was immersed in BSS solution; due to this latter Descemet's membrane was separated as a "roll" from the underlying stroma. Using a special injector Descemet's membrane transplant was introduced in the anterior chamber through the tunnel incision of 1.8-2.0 mm for 12 hours. Descemet's membrane "roll" was unbent *ab externo* and fixed to the recipient's stroma within the descemetorexis by a bubble of air. No suturing was applied. The solution of corticosteroid and antibiotic was injected subconjunctivally. The soft therapeutic contact lens was applied.

Post-surgery follow-up

Immediately after surgery patient's movement was not restricted. Biomicroscopy was done in 30-45 minutes. No actions were taken in the absence of coloboma blocking by air. In case of coloboma blocking by air partial emission from the anterior chamber was done. The air was replaced by the solution of BSS and the patient was prescribed bed rest cure on his back during 2 hours. Conservative treatment involved five-fold instillations of antibiotics, corticosteroids and artificial tear during the first week. Then multiplication factor was decreased every 7 days. In case of eye irritation parabulbar injection of 0.5-1.0 mL diprospane was done during 1-2 weeks post surgery. Patients' activity and life-style were unrestricted. Upon uncomplicated course patients' average hospital stay (in bed) made 3 days. In a postsurgery period medical examination and investigation (apart from ultrasound and EPI) were regularly repeated; periodicity made 1 week, 1 month, 3 months, 6 months and 12 months.

RESULTS

The analysis of surgery outcomes was done according to below stated:

- Intraoperative complications;
- Complications of early post surgery period (1 week);
- Complications of late and delayed period;
- Biological outcomes;
- BCVA dynamics;
- Refractometry dynamics;

- Endothelial cells' density dynamics.

Intraoperative complications:

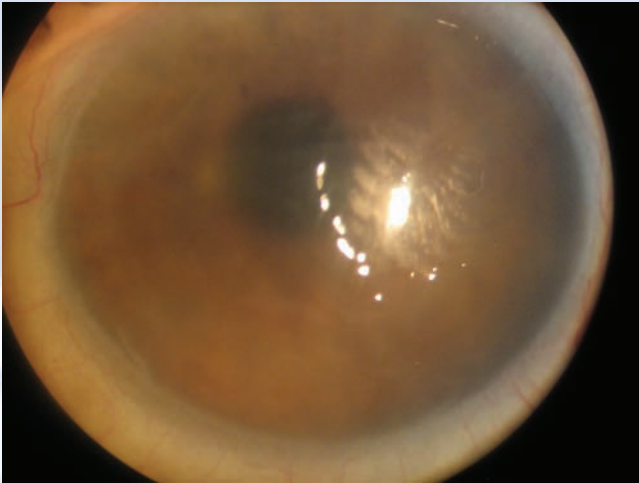
Amongst the specific intraoperative complications that are characteristic for the procedure of Descemet's membrane transplantation (and not only microDMEK) the following was observed:

- marginal rupture of Descemet's membrane,
- partial injection of Descemet's membrane into posterior chamber,
- prolapse of Descemet's membrane from anterior chamber;
- incarceration of Descemet's membrane in tunnel incision

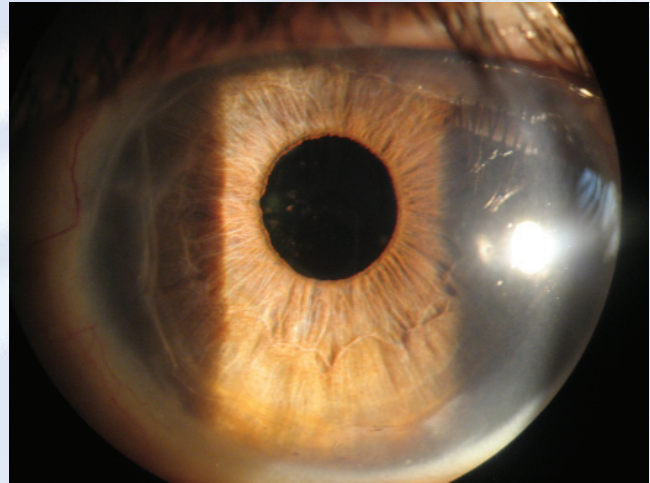
Marginal ruptures of Descemet's membrane were recorded in 4 (19%) cases: in 3 (14%) cases they were observed on the stage of donor Descemet's membrane separation from the underlying stroma and in 1 (4.7%) case the rupture was diagnosed already after the implantation of Descemet's membrane into the anterior chamber of a recipient. In 2 cases of Descemet's membrane peripheral rupture our tactics embraced eccentric incision of a penetrating disk of donor cornea so that the incised disk did not incorporate the ruptured part of Descemet's membrane. In 1 case because of a prolonged linear rupture of Descemet's membrane we had to replace donor material by a new one. If Descemet's membrane rupture was revealed intraocular the surgery intervention proceeded.

Partial injection of Descemet's membrane into posterior chamber occurred in 1 (4.7%) case: the patient had atrophic iris and phenomena of iridodonesis. Further tactics of surgical intervention included withdrawal of a part of Descemet's membrane from the posterior chamber by irrigation. Further on, as became obvious in a post surgery period, this complication had no effect to surgery outcomes.

In 1 (4.7%) case the prolapse of Descemet's membrane from anterior chamber was observed and in 1 case its incarceration in tunnel incision was recorded. In case of Descemet's membrane prolapse from anterior chamber the same transplant was re-introduced into anterior chamber; successful spreading and non-complicated post-surgery period followed. Descemet's membrane incarcerated in tunnel incision was *ab externo*



Picture 2. Secondary endothelial-epithelial dystrophy, pseudophakia.



Picture 2a. 6 months post microDMEK. Pseudophakia. Marginal non-progressing diastasis of Descemet's membrane. Visus = 1.0.

implanted into anterior chamber. No complications proceeded in the post-surgery period.

Complications of early post surgery period (1 week)

A typical complication of Descemet's membrane transplantation procedure is its diastasis, and in case of progression entire dislocation might occur. In our study central diastasis of Descemet's membrane with manifestation of corneal oedema occurred in 3 (14%) cases. In 1 (4.7%) case of these 3 untimely injection of air brought forth total dislocation of Descemet's membrane. This latter was the reason for us to perform spreading and fixation again. In all 3 cases during the post-surgery period air was injected into the anterior chamber 3 times achieving the stable fixation of Descemet's membrane to the stroma of recipient, but accompanied by iatrogenic insufficiency of an endothelial layer. This condition made us perform the repeated microDMEK using new transplantation material in a period of 6-20 days after the first transplantation of Descemet's membrane.

Marginal, non-progressing diastasis of Descemet's membrane without oedema of cornea was observed in 5 (24%) cases (Pictures 2 and 2a). In 3 cases single injection of air was done to achieve adherence of marginal diastasis. In 2 other cases of diastasis no air was injected due to high visual acuity; no effects to the functional and biological outcomes of surgery followed.

Complications of late and delayed period

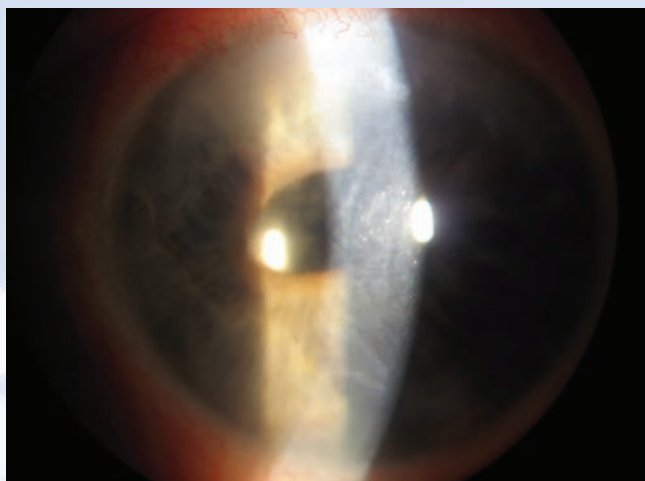
In 2 weeks after the successful surgery and non-complicated early post-surgery period we revealed 1 (4.7%) case of marginal diastasis of Descemet's membrane without oedema of cornea in an eye with visual acuity 1.0 without correction (Pictures 3, 3a, 3b). Due to high visual acuity, adhesion of Descemet's membrane in optical centre and absence of corneal oedema, no surgical manipulations were applied by us. During the entire period of observation (7 months) no negative dynamics was recorded.

Biological outcomes

After the performed surgical intervention for transplantation of Descemet's membrane with the use of the methodic procedure developed by us, recovery of cornea transparency and a decrease of corneal syndrome were achieved in all patients. It should be mentioned that in 3 cases recovery of cornea transparency was possible after the repeated microDMEK.

BCVA dynamics

Visometry was possible only after resorption of air above the pupil of an eye. In a period from 1 day to 2 weeks after the successful surgery in more than 90% patients visual acuity was 0.2 and above. In 3 (15%) cases BCVA during 1-2 post-surgery days made 0.9-1.0 (Picture 4). In a month following surgery, 16 (76%) cases of



Picture 5. Prior to microDMEK. Endothelial-epithelial dystrophy, pseudophakia.



Picture 5a. 10 months post microDMEK. Visus=0.7.

Endothelial cells' density dynamics

In preoperational period determination of endothelial cells' density was not possible due to oedema of cornea in majority of patients. The dynamics of the average loss of endothelial cells after surgery was as follows:

- in 1-month period it made 372 cells/mm² (12.6%);
- in 3 months it achieved 565.7 cells/mm² (23.8%);
- in 6 months it amounted 643.3 cells/mm² (28.7%).

DISCUSSION

According to foreign scientific press, the most frequent indication for transplantation of posterior layers, including transplantation of Descemet's membrane is Fuchs primary dystrophy of cornea [Price F., Price M., 2006; Balachandran C., 2008], whereas our 3-year experience in performing surgery interventions manifests that above 65% cases have indication for surgery interventions due to secondary endothelial-epithelial dystrophy. It might be associated with peculiarities of primary dystrophy prevalence in different populations. One cannot exclude that it is connected with the targeted search and diagnosis of this pathology state abroad.

The unreasonable long conservative therapy of endothelial dystrophy of cornea, which is peculiar for domestic school of ophthalmology, presents an important aspect for surgical treatment of endothelial-epithelial dystrophy of cornea. Therefore, in majority of cases visual acuity of

patients before surgery is below 0.1, while according to scientific publications [Balachandran C., 2008], foreign specialists perform operations at visual acuity of a few tenths. Omitting the assessment of this approach, one might confidently state that *a priori* expected functional results of surgical treatment will be worse because of severe dystrophic changes in the stroma of cornea, as well as due to inability to perform detailed ophthalmologic diagnosis of retinal pathology and *nervus opticus* before surgery.

The problem of high significance is an adequate selection of patients in order to achieve utmost functional results, on the one hand, and not to discredit the method, on the other hand. To our mind, currently due to availability of efficient procedures of posterior keratoplasty, as well as taking into account the temporal effect of conservative treatment and attending costs, it is pivotal to reconsider the duration of medicine-based therapy in favour of earlier surgical treatment.

Our own MicroDMEK procedure differs from the generally accepted one:

- in method of Descemet's membrane formation and separation,
- in incision thickness/size of 1.2-2 mm (according to common technique it is 3.0 mm and above),
- in the applied cartridge (according to common technique the standard cartridge for intraocular lens is used),
- in *ab externo* method of spreading (common technique implies *ad interno* mode).

MicroDMEK is characterized by maximum sparing attention towards the endothelium, namely: in Descemet's membrane separation from the underlying stroma from the stromal side. To our mind, the most valuable point of the newly developed microDMEK procedure is implantation through the injector of small diameter. We consider the generally applied implantation technique through the standard cartridge for intraocular liquid is excessively traumatic for the endothelium, as the Descemet's membrane is in an "open" state, i.e. it passes the cartridge channel by the entire surface of the endothelial layer significantly damaging the endothelium all over the transplant area. In contrast to that, in case of a "rolled" Descemet's membrane transplant in case of microDMEK the surface of endothelial layer contacts with the cartridge walls a few times smaller and, therefore, the endothelial tissues are less traumatized. The small incision inflicted during the microDMEK is more neutral in refractive aspect and more reliable either in the course of surgery, or in post-surgery period in view of ensuring the adequate hermeticity of the incision. Currently, we are engaged in development of a procedure to prove the comparably atraumatic feature of microDMEK *versus* the traditionally applied technique; it will be based on endothelial cells loss.

The analysis of observed intraoperative complications such as Descemet's membrane ruptures, partial implantation into the posterior chamber, prolapse of Descemet's membrane and its incarceration in tunnel incision revealed that the difficulty was associated with acquirement of the technique and appropriate skills; this latter is confirmed by the following: mentioned complications were observed in the first 7 patients. We never encountered abovementioned complications later on. Delicate and deliberate actions at the stage of Descemet's membrane transplant formation, achievement of a moderate hypotonia of the eye bulb, correct position of a cartridge in the anterior chamber, correct position of a Descemet's membrane in a cartridge, *miosis medicamentosa*, - all these manipulations allowed us to minimize the probability of the mentioned complications already at the stage of implantation. In our series of investigation we were in a position to replace donor material in 4.7% cases that, on the average, corresponds

with data of J. Lie: at the stage of Descemet's membrane transplant formation 5.5% transplants became inappropriate-to-use because of Descemet's membrane ruptures [Lie J., 2009].

Diastasis and dislocation of Descemet's membrane are characteristic complications of the early postoperative period when Descemet's membrane transplantation procedure is applied. According to G. Melles the frequency of diastasis and dislocation in his series of studies made 30% in the first 10 patients and 20% in the first 50 patients [Melles G., 2009]. In our series of studies central diastasis occurred in 14% cases, while dislocation made 4.7%. Nowadays, the invert fixation of a transplant and dysfunction of the endothelium are considered the main causes of such outcomes. There are no specific recommendations to avoid mentioned complications. This problem requires further investigation.

At the same time, as obvious by our experience, marginal, non-progressing diastasis of Descemet's membrane without the oedema of cornea neither requires reposition nor affects the results and outcomes of surgery; this is confirmed by 2 cases of marginal diastasis when we did not perform its reposition by injection of air: no impact on the surgery results proceeded. One case of delayed diastasis of the periphery when high BCVA and transparency of cornea were preserved might serve as another proof. It is important to consider that repeated injection of air and the attempt to unbent the folds of Descemet's membrane bring forth additional traumatism of endothelium and loss of endothelial cells.

The achievement of 100% biological results after microDMEK during the period of observation is one of the main, optimistic, and promising arguments in favour of microDMEK procedure. The unconditional means for achieving such results is the technical possibility of atraumatic repeated surgery intervention in the earliest time-interval after the primary operation with development of iatrogenic insufficiency of endothelium, with invert fixation of Descemet's membrane after its dislocation. The minimal volume of donor tissue ensures low immunogenicity of a transplant, and hence the utmost prerequisites are created to minimize the probability of immune reaction of rejection.

The achievement of high BCVA in a short period post surgery is another argument in favour of microDMEK [Balachandran C., 2008; Melles G. et al., 2008]. According to C. Balachandran, in his series of studies BCVA of 0.5 and above in a period of 1-3 months post surgery was recorded in 89% patients, while 57% had BCVA 0.8 and above. In our study a period of 3 months after the operation BCVA 0.5 and above was observed in 87% cases, whereas BCVA 1.0 was in 24% cases. Lower number of patients with the best visual acuity confirms our statement that *a priori* the functional results of surgical intervention would be worse as a result of deep dystrophic changes in stroma of cornea, as well as due to impossibility to perform a detailed ophthalmoscopic diagnosis of pathology in retina and visual nerve before surgery because of patients' late referrals to surgical intervention.

Regarding data on refractometry, it is necessary to emphasize that in patients with primary or primary-secondary endothelial-epithelial dystrophy with non-complicated phacoemulsification in anamnesis, patients with intraocular lens implantation the postoperative astigmatism never exceeded 0.75^D. High degrees of astigmatism revealed after microDMEK were observed in patients with extracapsular extraction of cataract in the anamnesis or patients with complicated, sometimes repeated surgery intervention in the anamnesis. We consider that high astigmatism revealed after microDMEK in this category of patients was induced not by the microDMEK, but by the previous surgical interventions. The oedema of cornea observed before microDMEK hindered to record the state; only recovery of transparency of the oedema after microDMEK allowed to reveal astigmatism that was "in place" before microDMEK.

The loss of endothelial cells is an important index in surgery of cornea, it has a significant impact to "survival" of the transplant. In a series of investigation with a period of observation of

1-2 years, the loss of endothelial cells during the first 6 months made 18%-29%, during 1 year it was 24-34%, while in 2 years it achieved 36%. Thus, maximum loss of cells occurs in the first months after operation (about 25%) [Dapena I. et al., 2009]. Our data entirely coincide with data of foreign authors. Maximal loss of cells in our series occurred in the first 3 months after surgery (23.8%) and in 6 months after the operation (28.7%). Overall, this is comparable with the loss of endothelial cells either after endokeratoplasty, or after penetrating keratoplasty.

CONCLUSION

The newly developed microDMEK procedure is efficient, reproducible, atraumatic, and at the utmost microinvasive amongst the existing methods of Descemet's membrane transplantation. Nowadays, the method of Descemet's membrane transplantation is at the stage of improvement and study. In its technical complex features and frequency of complications it yields to the method of endokeratoplasty, but by functional results and the rate of rehabilitation, as well as by the pathogenecity, microinvasiveness and cost value it surpasses endokeratoplasty, as there is no necessity of keratom and femtolaser.

For the first time in ophthalmological practice we have proposed and successfully implemented the reverse approach to transplantation of posterior layers of cornea: Descemet's membrane transplantation in patients earlier exposed to endokeratoplasty [Oganesyan O. et al., 2009]. Descemet's membrane transplantation might significantly improve the life of patients in countries where transplantation of donor cornea is not popular due to religious considerations.

The possibility of efficient use of transplantation material while applying the procedure of Descemet's membrane is pivotal: the intact stroma of a donor is applicable for deep anterior layer-wise keratoplasty.

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