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Factors Related to the Donor on the Graft Adherence in Descemet's Membrane Endothelial Keratoplasty: Descriptive Study

Desme Membran Endotelyal Keratoplasti Başarısını Etkileyen Donöre Ait Faktörler: Tanımlayıcı Araştırma

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ABSTRACT Objective: To analyze the effect of the characteristics of the donor and the preparation of donor graft in the success of Descemet's membrane endothelial keratoplasty (DMEK). **Material and Methods:** The patient and donor charts and the surgical videos of the cases that underwent DMEK between June 2017 and June 2020 were analyzed. Age, gender, diagnosis, Descemet's membrane (DM) attachment at the postoperative first week and the last visit from the patients' charts and age, gender, systemic diseases, and drugs from the donors' charts. The cases were divided into 2 groups; the cases with DM detachment (Group 1) and attached DM (Group 2) at the postoperative first week. **Results:** Fifty-three DMEK surgeries from 53 recipients with 53 DM grafts from 41 donors were analyzed. On the first postoperative week, DM was detached in 8 (15.1%, Group 1) cases and attached in 45 (84.9%, Group 2) cases. There were no statistically significant differences in the characteristics of the recipient or donor between groups. However, the amlodipine and doxazosin use of donors were found to be significantly higher in Group 1 (p=0.041, p=0.011; respectively). **Conclusion:** DM grafts may be used, regardless of the characteristics of the donor, in DMEK to compensate for the shortage of donors.

Keywords: Descemet's membrane endothelial keratoplasty; donor; graft adherence; systemic diseases

ÖZET Amaç: Desme membran endotelyal keratoplasti (DMEK) başarısında donöre ait ve donör hazırlama sırasındaki özelliklerin etkisini değerlendirmektir. **Gereç ve Yöntemler:** Haziran 2017-Haziran 2020 tarihleri arasında DMEK uygulanan olgulara ait hasta kartları ve cerrahi videolar incelendi. Hasta kartlarından yaş, cinsiyet ve tanı kaydedildi. Ayrıca ameliyat sonrası 1. haftada ve son muayenede Desme membranının (DM) durumu (yatışık veya dekole) değerlendirildi. Donör yaşı, cinsiyeti, sistemik hastalıkları ve kullandığı sistemik ilaç bilgileri donörün hastane dosyasından elde edildi. Olgular, ameliyat sonrası 1. haftada, DM dekolmanı olan (1. Grup) ve DM yatışık olan (2. Grup) olarak 2 gruba ayrıldı. **Bulgular:** Kırk bir donöre ait 53 DM greft ile DMEK uygulanan 53 olgunun 53 gözü çalışmaya dâhil edildi. Ameliyat sonrası 1. haftada DM 8 (%15,1, 1. Grup) olguda dekole, 45 (%84,9, 2. Grup) olguda ise yatışık olarak izlendi. Gruplar arasında alıcı ve donör özellikleri açısından istatistiksel olarak anlamlı fark saptanmadı. Ancak donörlerde amlodipin ve doksazosin kullanımı 1. Grupta anlamlı olarak fazla bulundu (p=0,041, p=0,011; sırasıyla). **Sonuç:** Donör eksikliği göz önünde bulundurulduğunda, DM greftleri, donör özelliklerine bakılmaksızın DMEK'de kullanılabilir.

Anahtar Kelimeler: Desme membran endotelyal keratoplasti; donör; greft yatışıklığı; sistemik hastalıklar

Descemet's membrane endothelial keratoplasty (DMEK) has become the procedure of choice in most endothelial pathologies.[1] It provides fast visual recovery with fewer complication than penetrating keratoplasty by being a closed system surgery and having less effect on ocular surface. The most common indications of DMEK are Fuchs' endothelial dystrophy (FED) and pseudophakic bullous keratopathy (PBK).[2] While the preferred technique in the treatment of FED and PBK increasingly become DMEK over penetrating keratoplasty, the number of patients waiting for DMEK outweighs the number of donors.[3] On the other hand, some conflicting results in some studies have shown that the characteristics of the donor, such as systemic diseases like diabetes, may affect the preparation, and the outcome of the surgery, which suggests that some donors may not be suitable for DMEK.[4-6]

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In this study, we aim to analyze the effect of the characteristics of the donor and the preparation process of the donor graft on the success of DMEK.

MATERIAL AND METHODS

SUBJECTS

Fifty-three patients who underwent DMEK surgeries were enrolled in this retrospective study. The study was approved by Adana City Training and Research Hospital Local Ethics Committee (date: December 30, 2020, no: 73, 1207) and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects. Age, gender, preoperative diagnosis, Descemet's membrane (DM) attachment at the postoperative first week and the last visit were recorded from the patients' charts. DM membrane attachment was evaluated by using slit-lamp biomicroscopy, and anterior segment optical coherence tomography in suspected cases. Only, the patients with FED and PBK were included in the study. The cases were divided into 2 groups regarding DM attachment at the first postoperative week; the cases with DM detachment (Group 1) and totally attached DM (Group 2).

The characteristics of donors, from whom the DM grafts were prepared, were analyzed from the donors' charts. The DM grafts were grouped as tight roll (≤2 mm) and loose roll (>2 mm) from the surgical videos. Age, gender, systemic diseases, and drugs of donors were recorded and compared between groups.

The donors were harvested by an experienced technician of the eye bank and preserved in Eusol-C (Corneal Chamber, Alchimia, Ponte San Nicolo, Italy) at +4°C until the procedure for at most 7 days. The donors with a history of any ocular surgery and the grafts with Descemet folds and/or endothelial precipitates were excluded.

The first 200 cases of the surgeon, the surgeries that include another procedure, such as synechiotomy, vitrectomy, transscleral intraocular lens implantation, and the patients with a history of vitrectomy and trabeculectomy were excluded from the study.

GRAFT PREPARATION

Submerged corneas using backgrounds away technique was used to prepare all the grafts.[7] Donor cornea was placed endothelial side up on a vacuum punch (Katena Products, Inc. New Jersey, USA) with a diameter predetermined according to the diameter of the recipient's cornea from limbus to limbus. After staining the edges of DM with trypan blue 0.06% solution, approximately 180 degrees was scraped from trabecular meshwork to central cornea by a crescent knife under the fluid. The scraped edge of DM was grasped with a tying forceps and stripped towards central cornea, then restained. Superficial partial-thickness trephination was performed from the endothelial side and DM was stripped with a tying forceps until 360 degrees of DM was free from the stroma. Donor graft was restained with trypan blue for better visualization and aspirated into a glass injector system (DMEK Surgical Disposable Set, INNOVA Medical Ophthalmics, Toronto, Canada) in the fluid to deliver the anterior chamber (AC) of the recipient eye.

SURGICAL PROCEDURE

All the procedures were performed under subtenon anesthesia by a single surgeon with previously described techniques.[8,9] The corneal epithelium was removed to improve the visualization of the AC. Clear corneal incisions from temporal and nasal quadrants were made with a 23 gauge knife. The AC was then filled with air. Recipient DM, 0.5 mm larger than the DM graft, was scored then stripped 360 degrees by a reverse sinskey hook and removed outside the AC. Corneal incision at the superior quadrant was performed with a 2.8 mm knife. The rolled DM graft in the glass injector system was inserted into the AC. The tapping technique together with intracameral short bursts of fluid was used to unfold and position the graft with the endothelium at the outer side. The AC was then filled with air. Therapeutic contact lens was placed on the corneal surface at the end of the procedure. The patient was kept in supine position for 2 hours in the recovery room. The patients were checked for pupillary block, and if pupillary block occurred, some air was removed from the side port with a 30G needle at the slit lamp biomicroscopy.

The patient was then discharged home and instructed to remain supine for 48 hours. All patients were started on standard postoperative topical corticosteroids 5 times a day and tapered monthly; and antibiotics 5 times a day for 1 week. The patients were examined on the postoperative first day, first week, first month, and then monthly for 6 months.

STATISTICAL ANALYSIS

Data analysis was performed using the Statistical Package for Social Sciences for Windows software (SPSS version 16.0, SPSS Inc., Chicago, USA). The normality distribution of the variables was tested using Kolmogorov Smirnov test. The descriptive statistics of the normally distributed continuous variables were presented as mean±standard deviation. Student's t-test was used to compare the normally distributed variables between the groups. Categorical variables were presented as frequency (%) and compared between the groups with chi-square test. Differences with p value of <0.05 were considered statistically significant.

RESULTS

Fifty-three DMEK surgeries from 53 recipients with 53 DM grafts from 41 donors were analyzed. On the first postoperative week, DM detachment was seen in 8 (15.1%, Group 1) cases and DM grafts were totally attached in 45 (84.9%, Group 2) cases. Air reinjection was performed once in 6 (11,3%) patients and twice in 2 (3.8%) patients. DM attachment was achieved in 4 (7.5%) and reDMEK was performed due to failure in 4 (7.5%) patients. The mean age of the recipients was 69.95±7.9 (51-87) years and no statistically significant difference was found when compared between groups (p=0.506). In 1 (12.5%) patient in Group 1 and in 9 (20%) patients in Group 2 had glaucoma and in 1 (2.2%) patient in Group 2 had diabetic macular edema. No statistically significant difference was found between groups in terms of ocular comorbidities (p=0.858). There were also no statistically significant differences between groups in other characteristics of recipients (Table 1).

The age, gender, systemic diseases [hypertension, diabetes mellitus, hyperlipidemia, chronic renal, failure, solid tumors (breast, pancreas, lung cancer)] and most of the systemic drugs (angiotensin receptor blockers, beta blockers, statins, antiaggregans, oral antidiabetics, insulin) of the donor were similar when compared between groups (p=0.591, p=0.705, p=0.574, p=0.653; respectively). However, the use of amlodipine and doxazosin were found to be significantly higher in Group 1 than in Group 2 (p=0.041, p=0.011; respectively). The donor data were summarized in Table 2. Of the DM grafts from each eye of the same 3 donors, while one is attached at the first postoperative week, the other was detached.

No statistically significant difference between groups were found in terms of the type of the DM graft roll (p=0.718).

DISCUSSION

DMEK provides a faster visual recovery in endothelial pathologies with fewer complication rates when

TABLE 1: The characteristics of the recipients.

	Group 1 (n=8)	Group 2 (n=45)	p value
Age (years)	65.87±14.2 (65-81)	68.17±10.7 (51-87)	0.506
Gender (F/M)	5/3	28/17	0.655
Diagnosis			
FED	1 (12.5%)	8 (17.8%)	0.589
PBK	7 (87.5%)	37 (82.2%)	
Ocular disease			
None	7 (87.5%)	35 (77.8%)	0.858
Glaucoma	1 (12.5%)	9 (20%)	
DME	0	1 (2.2%)	

F: Female; M: Male; FED: Fuchs' endothelial dystropy; PBK: Pseudophakic bullous keratopathy; DME: Diabetic macular edema.

TABLE 2: The characteristics of the donors.

	Group 1 (n=8) n (%)	Group 2 (n=45) n (%)	p value
Age (years)	64.25±5.8 (41-84)	64.68±7.7 (54-71)	0.879
Gender (F/M)	4/4	18/27	0.597
Systemic disease			
Diabetes	2 (25)	9 (16.9)	0.748
Hypertension	4 (50)	19 (35.8)	0.683
Hyperlipidemia	3 (37.5)	11 (20.7)	0.440
Chronic renal failure	4 (50)	10 (18.9)	0.101
Breast cancer	2 (25)	3 (5.7)	0.159
Endometrium cancer	0 (0)	3 (5.7)	0.452
Lung cancer	0 (0)	4 (7.5)	0.380
Systemic drugs			
Metformin	2 (25)	8 (15.1)	0.574
Insulin	2 (25)	2 (3.8)	0.053
Sevelamer	1 (12.5)	1 (1.9)	0.181
Karvedilol	2 (25)	9 (16.9)	0.823
Furosemid	3 (37.5)	6 (11.3)	0.117
Ramipril	0 (0)	8 (15.1)	0.178
Valsartan	0 (0)	8 (15.1)	0.178
Amlodipine	4 (50)	6 (11.3)	0.041
Metoprolol	2 (25)	9 (16.9)	0.823
Doxazosine	3 (37.5)	1 (1,9)	0.011
Klopidogrel	1 (12.5)	17 (32.1)	0.131
Asetil salicylic asid statin	2 (25)	16 (30.2)	0.479
Paklitaxel	2 (25)	12 (22.6)	0.837
	2 (25	7 (13.2)	0.700

F: Female; M: Male.

compared to penetrating keratoplasty.[1] Therefore, the increasing popularity of DMEK results in an increasing need for donors. In this study, we evaluate the characteristics of the donor and the recipient in the outcome of DMEK to better identify the indication and the selection of the donor. Only one experienced surgeon performed all the surgeries, and the first 200 cases of the surgeon were excluded from the study to eliminate the surgeon factor in the outcome. The phakic patients, patients with a history of glaucoma surgery or vitrectomy, and the complex surgeries, such as DMEK with pupilloplasty, synechiotomy, and cataract surgery, were also excluded to standardize the protocol and eliminate the procedural factor in the outcome. Moreover, the donors under 50 years of age were also excluded, as it is known that younger donors are more prone to failure in DM graft preparation and higher unfolding time results in early postoperative endothelial loss.[10]

In some studies, DMEK is shown to be more successful in FED than PBK.[11] In this study, we found similar success rates between FED and PBK. This finding is important, especially in developing countries because, while, in developed countries, FED is the most common indication for DMEK, in our clinic, PBK is much more common than FED. Preexisting glaucoma was found to be related to graft failure in PK and Descemet's stripping automated endothelial keratoplasty.[12,13] However, research for evaluating the relation of preexisting glaucoma and DMEK is limited.[13] In one study by Treder et al., no significant differences in patients with or without preexisting glaucoma in the graft failure rate in DMEK.[14] In this study, the preexisting glaucoma of the recipient was found to be similar between groups. Thus, the glaucoma of the recipient must not discourage the surgeon from performing DMEK.[14] In contrast to this, in our study, only the patients with medically managed glaucoma patients were evaluated that eliminates the effects of previous surgery.

The systemic diseases, especially diabetes, of the donor have been evaluated for the outcomes of DMEK and conflicting results have been shown. In some studies, it was found that diabetes causes failure in graft preparation.[15,16] However, in a study by Price et al., although failure rates in graft preparation were increased in diabetic donors, no significant difference was shown in postoperative graft adherence status.[6] We also found no significant differences in graft adherence status in patients with and without diabetes at the postoperative first week and at the last follow-up visit. It was suggested that the stronger adhesions of DM and posterior stroma causes graft preparation more difficult.[6] In this study, we did not discard any tissue due to failure in preparation. It may be because of the experience of the surgeon. Also, while DM graft was being prepared, if a tear occurred in one quadrant the stripping was continued from the opposite quadrant. Even if all the quadrants were used, trephination was made eccentrically to involve the least disrupted tissue and successful outcomes of surgery were achieved. Thus, we suggest that, regardless of the diabetic status of the patient, all tissues should be used in DMEK. In our study, no differences in any other systemic disease, including hypertension, hyperlipidemia, cancer, and chronic renal failure, were found between groups. As a result, no donor tissue should be discarded according to the systemic status of the donor in concern of the outcome of the surgery.

As far as we know, no research on the effect of the systemic drugs of the donor in outcomes of corneal transplantation. In this study, we found that in the group with DM detachment, only the use of amlodipine and doxazosin were significantly higher than the patients with total DM attachment. Amlodipine is a calcium channel blocker, commonly used in the control of high blood pressure. In a study by Green et al., exposure of the cornea with calcium channel blockers has been shown to result in an increased rate of corneal swelling and possible endothelial dysfunction.[17] It is hard to compare the systemic use with direct exposure to conclude and because of the design of this study, we cannot explain the biochemical basis of its effect. Also, the small number of sample, it also may be a statistical artefact. However a possible explanation in a study by Müskens et al. evaluates the relationship between antihypertensives and glaucoma, is that calcium channel blockers reducing ocular perfusion which may also affect the endothelial function.[18] On the other hand, in their study, Zheng et al. have shown amlodipine is the most significantly associated drug with primary open angle glaucoma.[19] Thus, it may also be suggested that raised intraocular pressure may disrupt the endothelial function and the attachment of the DM graft.

Both eyes used for DMEK of the 3 donors, one was totally attached and the other was detached at the first postoperative week. This may suggest that the outcome of the surgery relates to multiple factors, not only donor status. However, the small number of cases makes it hard to conclude.

The limited number of cases and the retrospective nature are the main limitations of the study. Also, no endothelial cell count was measured because of the lack of the device in our clinic.

CONCLUSION

DM grafts may be used, regardless of the characteristics of the donor, in DMEK to compensate for the shortage of donors for the increased number of patients waiting for DMEK.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Yusuf Koçluk, Burcu Kasım;* ***Design:*** *Burcu Kasım, Burak Özkan;* ***Control/Supervision:*** *Yusuf Koçluk, Burcu Kasım;* ***Data Collection and/or Processing:*** *Burak Özkan, Burcu Kasım;* ***Analysis and/or Interpretation:*** *Burak Özkan, Burcu Kasım;* ***Literature Review:*** *Burcu Kasım;* ***Writing the Article:*** *Burcu Kasım;* ***Critical Review:*** *Yusuf Koçluk;* ***References and Fundings:*** *Burcu Kasım;* ***Materials:*** *Yusuf Koçluk, Burak Özkan;* ***Other:*** *Burcu Kasım.*

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