

# TRANSPLANTATION IN OPHTHALMOLOGY— SINGLE-CENTER PERSPECTIVES

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## ABSTRACT

**INTRODUCTION:** Corneal and amniotic membrane transplantations are the most frequently performed transplantations in the world. Amniotic membrane transplantation demonstrates very high efficiency in the management of the ocular surface damaged by disease or trauma.

**AIM:** The goal of the current study is to prospectively follow and analyze the tendency in ocular transplantation in a single center in Bulgaria.

**MATERIALS AND METHODS:** A group of 206 patients were recruited in total for a period of three years. Of them 28 had corneal transplantation and 158 had amniotic membrane transplantation. Corneal transplant patients were pre-registered on the waiting list and operated as emergency cases due to the short period of time in which the corneal material preserves best quality. Patients for amniotic membrane were planned in general, but 1/3 were operated as a matter of emergency (102 planned and 56 urgent). The procedures were performed following the standard protocols.

**RESULTS:** The results outline the role of amniotic membrane as a follow-up treatment in 1/3 of the cases. After emergency transplantation of amniotic membrane, 12 cases underwent re-operation—corneal transplantation, and 11 received a planned second amniotic membrane transplant. These findings also highlight the main advantage of amniotic membrane—absence of graft rejection and possibility for unlimited re-grafting. Another highlight is the larger number of corneal dystrophies, which underscores the benefits of amniotic membrane transplantation not only for comfort but also for visual improvement.

**CONCLUSION:** In conclusion, amniotic membrane transplantation in Bulgaria follows the international standards, however, corneal transplantation requires revision including the legal regulations, eye bank protocols, and end-user approaches. In the future, tissue engineering will contribute to the provision of more tissue and facilitation of complicated restauration surgeries of the damaged ocular surface.

**Keywords:** *amniotic membrane transplantation, corneal transplantation, graft rejection, eye bank*

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## INTRODUCTION

Corneal and amniotic membrane (AM) transplantations are the most frequently performed transplantations in the world (1,2). The latest tendency is to move from penetration to lamellar corneal transplantation. Unfortunately, this trend has not reduced the rate of graft rejections in total (3,4). Being a relatively new technique in the ophthalmic practice, am-

niotic membrane transplantation demonstrates very high efficiency in the management of the ocular surface damaged by disease or trauma (1,5). Due to recent advances in tissue engineering, now there are two distinct trends: to use amniotic membrane as a transplant or as a biological product—a carrier for ex vivo differentiated cells (6). Nevertheless, application of amniotic membrane as a transplant is the preferred technique in many corneal diseases and especially after trauma or burns.

### AIM

The aim of this article is to prospectively follow and analyze the trends in ocular transplantation in a single center in Bulgaria. The specifics depend on the local law and regulations and definitely differ from other European countries. Such analysis is useful not only for the information, but also for describing the trend and recommending measures for improvement.

### MATERIALS AND METHODS

Transplantations were performed by a single surgeon at the Specialized Eye Hospital, Varna and the patients were prospectively recruited in two cohorts. A total of 206 patients were recruited for a period of three years. Of them 28 had corneal transplantation and 158 had amniotic membrane transplantation. Corneal transplant patients were pre-registered on the waiting list and operated as emergency cases due to the short period of time in which the corneal material preserves best quality. Patients for amniotic membrane are planned in general, but 1/3 were operated as a matter of emergency (102 planned and 56 urgent).

The procedures were performed following the standard protocols described below:

#### *Surgical application of amniotic membrane as a cover*

The patient is prepared under local anesthesia—3 drops of topical anesthetic (Alcaine collyr 0.5%, 15 mL, Alcon Inc.) every 2 minutes. After cleaning the operative field and placing a sterile drape, the eyelids are opened with a blade eyelid speculum and the operative microscope is positioned and adjusted. The anterior surface of the eye is cleaned of residual debris and polished with a “hockey tool” or a polishing sponge. The amniotic membrane is re-

moved in sterile conditions from the container and washed with sterile saline (warmed to room temperature). Under a microscope, the membrane is detached from the carrier and placed with the stromal part to the anterior ocular surface. After positioning and adaptation, 8.0 vicryl is placed as a continuous circular suture with 8 fixation points. The knot remains at 6 o'clock. The membrane is washed until it adheres completely to the anterior surface of the eye and a therapeutic contact lens (silicone-hydrogel) with a moderate modulus is placed in order to ensure optimal protection. Antibiotic drops and a bandage are applied for at least 60 minutes.

#### *Penetrating corneal graft*

The patient is prepared for surgery with general anesthesia. The position of the head is agreed on with the anesthesiologist. It is very important that the iris plane be parallel to the floor. After cleaning and draping the operating field, the microscope is positioned. Baron's vacuum trephine is used, with the donor trephine 0.25 mm larger than the recipient size. This is due to the direction of trepanation and the tendency for collagen contraction, which leads to “contraction” of the donor button and “expansion” of the recipient bed.

The donor cornea is prepared first. Thus, in case of complications (improper trephination, endothelial damage), the surgery is postponed. The following steps are followed:

#### *Step 1. Trephination of the donor cornea:*

- ◆ The cornea is removed from the solution and drained.
- ◆ It is positioned on the platform, where 5 marking points are placed, the protective ring is placed and vacuum is created to hold the cornea.
- ◆ The position of the cornea is examined carefully and, if needed, repositioning is done.
- ◆ The guillotine is placed and the trephination is performed with a sharp pressing.
- ◆ The guillotine platform is carefully lifted, the corneoscleral ring is removed, and the donor button remains attached by the vacuum.
- ◆ Vacuum is released and the donor button is carefully moved to a sterile transport platform.

- ◆ The transport platform is moved to the surgical table and a protective viscous substance is placed on the endothelial side.

### **Step 2. Trepanation of the recipient cornea:**

- ◆ Before the beginning of the trephination, a side incision is made (outside the area of the sutures and a cohesive viscous substance is introduced into the anterior chamber).
- ◆ First, the trephine is inspected and the 12 points of the vacuum platform are marked.
- ◆ The center of the trepanation should be determined in order to achieve an optimal optical result.
- ◆ Placing the platform and activating the vacuum (the knife must be at zero position to have control over the thickness of penetration—a quarter turn corresponds to advancement of 50 microns).
- ◆ Trepanation with slow rotation of the trephine is performed in a clockwise direction.
- ◆ At the appearance of a sign of penetration, immediate release of the vacuum is done.
- ◆ The trepanation is finished with a knife or corneal scissors.

### **Step 3. Adaptation of the donor cornea to the recipient bed (except for the cases of combined surgery, which is not the subject of this statement):**

- ◆ The graft is transferred with a special spatula and placed in the recipient bed.
- ◆ Four cardinal stitches are placed in order to achieve optimal adaptation.
- ◆ The remaining 16 stitches are placed sequentially.
- ◆ The anterior chamber is washed.
- ◆ Intracameral and subconjunctival antibiotics are applied.

In case of intraoperative deviations and complications, specific measures were taken, and patient was excluded from the group. In most cases a non-transparent bandage was used for at least 12 hours.

## **RESULTS**

Demographic characteristics and structure of the indications are presented in Table 1. After emergency transplantation of amniotic membrane, 12 cases underwent re-operation—corneal transplantation, and 11 received a planned second amniotic membrane transplant. The results outline the role of amniotic membrane as a follow-up treatment in 1/3

*Table 1. Patients receiving transplantation of amniotic membrane (AM) or cornea for period of three years (May 2016–May 2019)—demographic and clinical characteristics.*

Characteristics	AM Transplantation	Corneal Transplantation
Total number	158	28
Number treated as emergency	56	4
Sex	Male 77 Female 81	Male 12 Female 16
Age	47 ± 17	52 ± 12
Citizens of Varna region	56	11
Citizens of North-East Bulgaria	66	8
Working status	Working 78 Retired (age) 28 Retired (disability) 33 Unemployed 19	Working 9 Retired (age) 6 Retired (disability) 8 Unemployed 5
Diagnosis	Corneal dystrophy 55 Keratopathy 18 Trauma 27 Inflammation 48 Pending perforation 10	Corneal dystrophy 11 Keratopathy 9 Trauma 1 Inflammation 1 Pending perforation 6
Chronology of the treatment	Primary 101 Follow-up 57	Primary 25 Follow-up 3

of cases. These findings also highlight the main advantage of amniotic membrane—absence of graft rejection and possibility for unlimited re-grafting. Another highlight is the larger number of corneal dystrophies, which underscores the benefit amniotic membrane transplantation not only for comfort but also for visual improvement. Number one indication in case of dystrophy is recurrent erosion syndrome. Another benefit of amniotic membrane is availability, which explains why some of the perforations are first treated with AM transplantation. In the eyes followed in these studies the outcome measures were not only mechanical stabilization but also anti-inflammatory and anti-proliferative properties (Fig. 1).



*Fig. 1. Clinical photography of a patient with crystalline corneal dystrophy of Schneider (a) and the result after superficial keratectomy and AM transplantation (b).*

## DISCUSSION

Corneal transplantation is relatively rare in comparison to amniotic membrane transplantation, which was confirmed by the current single-center study (7). Corneal transplantation restores visual function, especially when the ocular surface is significantly affected, but depends very much on the retrospective consequences and restauration of the normal anatomical relationships between lids, cornea, and conjunctiva (8,9). Apart from the National Transplantation Registry, currently there is a limited information about indications and outcomes of cor-

neal transplantation in Bulgaria. Mostly the outcome measures are based on the graft rejection, which is an important issue but has limited value for evaluation of quality of vision and life of the entire population with ocular transplantation (10–12).

Another important issue that must be discussed is the availability of corneal material. In general, in Bulgaria the eye banks work with limited efficiency and disrupted collaboration. One donor is a source of material for only 2 transplantations. This has a regulatory background as well, as the reimbursement of the transplanting institutions is based not on the surgical protocols but on eye bank invoices. Moreover, importing tissue from a bank outside

the national borders is difficult, very complicated, and rarely practiced. This is an international problem, as discussed by Martin DE et al. (13). However, the good European eye banking practice requires tissue processing, proper register for tissue exchange, and efficient electronic system, which allows allocation and follow-up on all donors and recipients (14). Internationally the eye banks are working on proper manufacturing of the material. Three transplants are usually prepared from one donor: Descemet membrane endothelial keratoplasty (DMEK) transplant pre-loaded, diffuse lamellar keratitis (DLK) button and limbal stem cell transplant for at least one recipi-



ent. In case of the planned penetrating keratoplasty, the limbal stem cells are the second product out of one cornea. Considering the insufficiency of corneal tissue, this is a more efficient and rational way of eye banking.

Nevertheless, corneal tissue is more difficult to acquire, process, store, and distribute. This is the main explanation why amniotic membrane is now more often performed. Human AM has anti-adhesive properties, promotes epithelialization, decreases inflammation, neovascularization, and fibrosis, but still cannot replace corneal transplantation. The outcome from the current study highlights three main applications of AM:

- ◆ emergency solution in case of perforation or impeding perforation;
- ◆ preparation for corneal transplantation or enhancement of the ocular surface after penetration graft;
- ◆ restauration of the ocular surface and conjunctiva.

The current study highlights the latter as the most common indication, but the first one as the most crucial for successful visual outcome. In a study in Mexico that lasted eight years, Chávez-García et al., including a detailed protocol of the donor selection, tissue harvesting, preparation, storage and distribution of amniotic membrane, described the indications of AM transplantation of a total of 1686 amniotic membrane fragments used during that period (15). The five most common indications for amniotic membrane transplantation were pterygium, corneal ulcers, conjunctival surface repair, neoplasms, and persistent epithelial defects. They compared the indications of amniotic membrane use in two different types of institutions: general hospitals and ophthalmologic reference hospitals. It is surprising to find interesting differences between the indications and use rates between these institutions. There was up to a fivefold increase in the use of amniotic membrane for correction of persistent epithelial defects in reference hospitals, which could be explained with the more complex and severe ophthalmological pathologies admitted in reference hospitals (15). In both institutions the most often indication for AM transplantation was pterygium.

Amniotic membrane has different advantages and disadvantages. The way that amniotic membrane is utilized in Bulgaria is as a transplant, which is quite restrictive not only for outpatients but also for some surgical departments. In order to perform transplantation, the center must be accredited following special rules and procedures. This limits the possibility for utilization of this efficient and very effective method of biological treatment. In many countries in Europe there is a regulation for biological products which can be used in outpatient practices. For example, there are a number of products attached or supported by contact lenses, which does not require suturing. The aforementioned approach is not only non-invasive but also cost-efficient and easily repeatable on demand.

## CONCLUSION

In conclusion, amniotic membrane transplantation in Bulgaria is according to the international standards, however, corneal transplantation requires revision including the legal regulations, eye bank protocols and end user approaches. In the future, tissue engineering will contribute to the provision of more tissue and facilitation of complicated restauration surgeries of the damaged ocular surface.

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