Efficacy of Cultivated Corneal Epithelial Stem Cells for Ocular Surface Reconstruction

Essay

Submitted for Partial Fulfillment
of Master Degree in Ophthalmology

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2016

﴿اللَّهُ نُورُ

السَّمَوَاتِ والأَرْضِ مَثَلُ نُورِهِ كَمِشْكَاةٍ فِيهَا
مِصْبَاحٌ المِصْبَاحُ فِي زُجَاجَةٍ الزُّجَاجَةُ كَأَنَّهَا
كَوْكَبٌ دُرِّيٌّ يُوقَدُ مِن شَجَرَةٍ مُّبَارَكَةٍ زَيْتُونَةٍ لاَّ
شَرْقِيَّةٍ ولا غَرْبِيَّةٍ يَكَادُ زَيْتُهَا يُضِيءُ ولَوْ لَمْ
تَمْسَسْهُ نَارٌ نُّورٌ عَلَى نُورٍ يَهْدِي اللَّهُ لِنُورِهِ مَن
يَشَاءُ ويَضْرِبُ اللَّهُ الأَمْثَالَ لِلنَّاسِ
واللَّهُ بِكُلِّ شَيْءٍ عَلِيمٌ ﴾

سورة النور الآيـــــه رقم ٣٥

Acknowledgement

I would like to express my deep thanks, gratitude and appreciation to ***Professor Dr. Rafeek Mohamed FouadEl Ghazawy,*** *M.D. Professor of Ophthalmology Faculty of Medicine Ain Shams University for his extensive help, kind supervision and the continuous encouragement throughout the course of this work.*

Also, many great thanks and appreciation are also owed to ***Dr. Yousra Ahmed Thabet Farweez,*** *M.D. Lecturer of Ophthalmology Faculty of Medicine Ain Shams University for her great help, sincere cooperation and fruitful support during the conduction of this work.*

Lastly, my great thanks to everyone who participated in one way or another in making this work possible.

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List of Abbreviations

AM	:	Amniotic membrane
AMT	:	Amniotic membrane transplantation
BSA	:	Body surface area
CLET	:	Cultivated Limbal stem cell
COL	:	Collagen
COMET	:	Cultivated Oral mucosal epithelial transplantation
FF	:	Feeder-free
IOP	:	Intraocular pressure
LESCs	:	Limbal epithelial stem cells
LF	:	Limbal fibroblast
LSCD	:	Limbal Stem Cell Deficiency
MAT	:	Matrigel
MEF	:	Mouse embryonic fibroblast
OCP	:	Ocular cicatricial pemphigoid
OSHA	:	Occupational Safety & Health Administration
PK	:	Penetrating keratoplasty
SJS	:	Stevens–Johnson syndrome
VA	:	Visual acuity

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Introduction

Severe ocular surface diseases, such as Stevens–Johnson syndrome (SJS), thermal and chemical injury, and ocular cicatricial pemphigoid, can lead to severe visual loss from corneal limbal stem-cell deficiency (LSCD). **(*Dua, et al., 2000*)& (*Prabhasawat et al,2012*)**.

These conditions can result in an abnormal corneal surface, chronic inflammation, conjunctival epithelial ingrowth (conjunctivalization) invading the cornea, corneal vascularization, poor epithelial integrity manifested as an irregular surface, recurrent epithelial erosion or persistent epithelial ulceration, and destruction of the basement membrane, leading to fibrous ingrowth. (***Tseng, 1989***)

The clinical presentations include photophobia, corneal opacity, corneal ulcer, corneal perforation, and decreased or lost vision, patients with LSCD are poor candidates for conventional penetrating keratoplasty (PK) due to the absence of limbal stem cells in the donor corneal button. **(*Holland EJ,1996*) & (*Tsai RJ and Tseng SC,1994*)**

A variety of surgical approaches, such as amniotic membrane (AM) and limbal transplantation , have been

proposed to reconstruct the damaged needed. However, in vivo limbal transplantation has some limitations and disadvantages, such as donor size inadequacy in the autograft and a high incidence of graft rejection in allograft transplantation. Cultivated corneal limbal epithelial transplantation (CLET) has been described as an interesting treatment modality for these patients. ***(Pellegrini G et al, 1997) &*** (***Shimazaki et al., 2007***)

Corneal limbal epithelium from donor corneas are taken either from Contralateral normal eye (for autografting) or from a cadaveric limbal donor (for allografting). **(*Prabhasawat et al,2012***)

In bilateral ocular surface disease stem cells could be taken from hair follicles and other tissues may serve as autologous sources of adult was cultivated for 4 weeks on a denuded amniotic membrane carrier, was transplanted onto the corneal surface up to the limbus. Lamellar keratoplasty, using preserved donor graft without epithelium, was performed simultaneously for five chronic-phase patients showing corneal stromal scarring. (***Shimazaki et al., 2007***)

Compared to conventional keratolimbal allografts, cultivated Corneal limbal epithelium transplantation requires a smaller amount of donor tissue for cultivation, a shorter time to achieve complete corneal epithelialization, and less exposure to donor immunity.(***Shortt et al., 2007***)

The technique of cultivating corneal epithelium on amniotic membrane relieved symptoms, reduced inflammation, improved the condition of the ocular surface, and increased vision. Moreover, cultivated Corneal limbal epithelium transplantation provided a better environment for a subsequent keratoplasty and perhaps a better chance of corneal graft survival. **(*Prabhasawat et al,2012***)

However, the success rate of this procedure depended on the extent of previous ocular damage, especially lid abnormalities and corneal stromal destruction, and on postoperative complications.

This procedure is a straightforward and useful treatment for patients with limbal stem-cell deficiency, especially in cases with adequate tear flow and normal eyelids. **(*Prabhasawat et al,2012***)

However, for those with severe ocular surface destruction or uncorrectable lid deformities, keratoprosthesis might be a better treatment option . **(*Prabhasawat et al,2012*)**

Aim of the work

Review of clinical outcomes of cultivated corneal limbal epithelial transplantation using human amniotic membrane for corneal limbal stem-cell deficiency.

Severe Ocular Surface Disease

Severe ocular surface disease:

Stem cell deficiency can be congenital or acquired. Congenital stem cell deficiency occurs as a result of hereditary aplasia of limbal stem cells as in cases of aniridia. (***Dua, et al., 2000***)

More often though, stem cell deficiency is acquired as a result of extraneous insults that acutely or chronically destroy the limbal stem cells. These include chemical or thermal injuries, ultraviolet and ionizing radiation, Stevens-Johnson syndrome, advanced ocular cicatricial pemphigoid, multiple surgery or cryotherapy, contact lens wear, or extensive/chronic microbial infection such as trachoma. Keratitis associated with multiple endocrine deficiencies, neurotrophic (neural and ischaemic) keratopathy and chronic limbitis also lead eventually to stem cell deficiency but are less common. (***Dua & Azuara-Blanco, 2000***)

Depending on the extent of limbal involvement, stem cell deficiency can be partial or total and the clinical features of stem cell deficiency vary from mild to severe, include the following:

(a) Loss of limbal anatomy with contiguous or patchy fluorescein staining of conjunctiva derived cells at the limbus and extending onto the peripheral cornea.

(b) Irregular, thin epithelium which is seen in mild or early cases where a sheet of conjunctival/ metaplastic epithelium consequently covers the cornea without any notable vascularization.

(c) Stippled fluorescein staining of the area covered by abnormal epithelium. The abnormal fluoresceinstaining "conjunctivalised" epithelium may take on the pattern of columns, whorls.

(d) Unstable tear film with rapid tear film break up time over the area of abnormal epithelium.

(e) Filaments and erosions.

(f) Limbal Stem Cell Deficiency superficial and deep vascularization.

(g) Persistant epithelial defects and chronic non-healing ulceration of the corneal epithelium or cycles of repeated breakdown followed by healing, associated with chronic low grade inflammation leading to ulceration, melting and perforation.

(h) Fibrovascular pannus.

(i) Scarring, keratinisation and calcification which are the end stage of LSCD. (***Dua, et al., 2000***)

Cases of Acquired stem cell deficiency

1)Ocular cicatricial pemphigoid

Ocular cicatricial pemphigoid (OCP) is a chronic cicatrizing conjunctivitis of autoimmune etiology. Although it is a chronic vesiculobullous disease primarily involving the conjunctiva, it frequently affects other mucous membranes, including the mouth, (Fig. 1), oropharynx, genitalia, and anus. The skin is involved as well in approximately 15% of cases. It affects women more than men by a 2:1ratio. Patients are usually older than 60 and rarely younger than 30. (***Sutphin, et al., 2011***)