Limbal versus conjuctival autograft transplantation for management of recurrent pterygium

Thesis

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Abstract:

Pterygium represents a local limbal deficiency. Thus, inclusion of limbal epithelium in the conjunctival graft for pteryguim surgery would achieve better anatomic and functional reconstruction after pterygium removal and, by restoring barrier function of the limbus, could reduce recurrence**.** The aim of work is to compare the safety and efficacy of limbal versus conjuctival autograft transplantation for treating recurrent pterygia.

Keywords: Pterygium, free conjuctival autograft transplantation, limbal conjuctival autograft transplantation, recurrence of Pterygium.

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ABBREVIATIONS

- 5-Fluro uracil. 5FU
- Adenosine triphosphate. ATP
- ATP binding cassette. ABC
- ATP-binding cassette subfamily G, member 2. ABCG2
- Bone marrow. BM
- Breast cancer resistance protein 1. BCRP1
- Cadaveric- conjunctival limbal allograft. C-CLAL
- Cadaveric-keratolimbal allograft. C-KLAL
- Conjunctival autograft. CAG
- Conjunctival limbal autograft. CLAG
- Creatinine kinase 3. CK3
- Cyclosporine A. CsA
- Dulbecco phosphate buffered saline – Calcium magnesium free. DPBS-CMF
- Edetate disodium. EDTA
- Epithelial growth factor. EGF
- Ex vivo expanded limbal autograft. EVELAU
- Free conjunctival autograft transplantation. F-CAT
- Gray. Gy
- Growth medium. GM
- Haematopoietic stem cells. HSCs
- Homologus penetrating central limbokeratoplasty. HPCLK
- Human amniotic membrane. HAM
- Human leukocyte antigen. HLA
- Keratin 3-12-19. K3-K12-K19

• Keratoepithelioplasty.	KEP
• Keratolimbal allograft .	KLAL
• Limbal conjunctival autograft transplantation.	L-CAT
• Limbal stem cell deficiency.	LSCD
• Limbal stem cells.	LSCs
• Living –relative conjunctival limbal allograft.	Lr-CLAL
• Living-related ex vivo expanded limbal allograft.	Lr-EVELAL
• Mitomycin C.	MMC
• Nerve growth factor receptor.	NGF
• Ocular cicatricial pemphigoid.	OCP
• Ocular surface diseases.	OSD
• Penetrating keratoplasty.	PK
• Periodic acid shift.	PAS
• Post –mitotic cells.	PMCs
• Proliferating cell nuclear antigen.	PCNA
• Ruthenium-106.	106Ru
• Scanning electron microscopy.	SEM
• Sequential sectorial conjunctival epitheliectomy.	SSCE
• Stem cells.	SC
• Steven Johnson's syndrome.	SJS
• Strontium-90.	90Sr
• Terminally differentiated cells.	TDCs
• Transient amplifying cells.	TACs
• Tumour growth factor –B.	TGF-B
• Ultraviolet light.	UV-A, UV-B
• Uranium-235.	235U
• Visual acuity.	VA

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Introduction & Aim of the work

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A pterygium is a wing-shaped growth of fibrovascular conjunctiva onto the cornea. Its incidence varies across geographical locations. Several hypotheses have been ascribed to its aetiology. Currently, it is believed that the pterygium is a growth disorder characterised by conjunctivalisation of the cornea due to localised ultraviolet induced damage to the limbal stem cells. Aggressive pterygial fibroblasts are also responsible for corneal invasiveness **(Hirst; 2000).**

The indications for surgery include reduced vision due to encroachment on the visual axis and irregular astigmatism, chronic irritation and recurrent inflammation, restriction of ocular motility, and cosmesis. Numerous surgical techniques including bare sclera excision with or without the use of adjuncts like beta irradiation, thiotepa eye drops, intra- or postoperative mitomycin C (MMC) or antineoplastic agents, amniotic membrane transplantation, conjunctival autograft (CAG) with or without limbal stem cells have been described **(Gris et al.; 2000).**

Despite these innovative procedures, recurrence continues to be a complication. Reported rates of recurrence range from 2% for excision with CAG to 89% for bare sclera excision. Differences in study methodology, patient characteristics, nature of pterygium, geographic area, definition of recurrence, duration of follow-up, and loss to follow-up are some of the factors responsible for widely varying rates of recurrence. Since pterygium has a moderate to high

prevalence 30 degrees above and below the equator, pterygium surgery is fairly common in our country, which is located within the tropics **(Li et al.; 2001).**

Pterygium represents a local limbal deficiency. Thus, inclusion of limbal epithelium in the conjunctival graft for pteryguim surgery would achieve better anatomic and functional reconstruction after pterygium removal and, by restoring barrier function of the limbus, could reduce recurrence **(Hirst.; 2003).**

The aim of work is to compare the safety and efficacy of limbal versus conjuctival autograft transplantation for treating recurrent pterygia.

Review of literature

Aetiology

Coroneo (1990) proposed that the initial biologic event in pterygium was an alteration of limbal cells due to chronic UV light exposure, resulting in concomitant breakdown of the limbal barrier and subsequent conjuctivalization of the cornea. This theory was subsequently confirmed by **Dushku and Reid (1994)** who, using specific monoclonal antibodies, demonstrated the presence of altered limbal basal cells invading normal cornea along the basement membrane in both primary and recurrent pteryguim speciemens.

Fibroblasts From pterygium have been shown to behave as neoplastic cells in vitro and random histological examination has revealed neoplastic features. Polymerase chain reaction studies have revealed viral presence (herpes simplex virus, cytomegalovirus, human papilloma virus in particular, has been correlated with neoplastic lesion of conjuctiva. Thus, it has been suggested that pteryguim possesses similarities to neoplasia and could be considered a benign neoplastic lesion **(Duncan et al.; 1997).**

Among the genes that play a key role in multistage carcinogenesis are the tumor suppressor genes which are often inactivated by mutation or loss of genetic material in one allele. If the remaining normal allele is lost (loss of heterozygosity) a tumor can potentially develop. Additionally, neoplastic cells show instability of the microsatellite DNA reflecting an elevated mutational rate. A previous study on pterygium revealed a significant incidence of loss of heterozygosity for 17 q 11.2-q 21(47%) and a moderate incidence of microsatellite DNA (13%). The fact that loss of heterozygosity at 9 q 31-33 was more frequent in recurrent pteryguim and also correlated with known risk

factors such as young age and high altitude of residence **(Detorakis et al.; 1998).**

Ultraviolet light exposure (both UV-A and, especially, UV-B appears to be the most significant contributory factor in the development of pterygia. This may explain why the incidence is vastly greater in populations near the equator and in persons who spend much time outdoors. Other agents that may contribute to the formation of pterygia Include allergens, noxious chemicals, and irritants (e.g., wind, dirt, dust, air pollution). Heredity may also be a factor **(Beden et al.; 2003).**

Histopathology

Whatever the etiology, pterygia represent a degeneration of the conjunctival stroma with replacement by thickened, tortuous elastotic fibers. Activated fibroblasts in the leading edge of the pterygium invade and fragment Bowman's layer as well as a variable amount of the superficial corneal stroma. Multipotential stem and progenitor cells may be involved in the pathogenesis of pterygium through its differentiation into fibroblasts and vascular endothelial cells. The detection of T lymphocyte infiltration in pterygium epithelium strongly supports the suggestion that cellular immunity plays an important role in pterygium formation. Epidermal growth factors have been localized in pterygium tissue, and are significantly induced by UV-B in pterygium-derived epithelial cells. This may be the means by which UV irradiation causes the pathogenesis of pterygium **(Di Girolamo et al.; 2004).**

Histologically, pterygium development resembles actinic degeneration of the skin. Surface cells in pterygium exhibit squamous metaplasia with increased goblet cell density. These changes are most pronounced directly over

the pterygium surface. Pterygia often persist after surgical removal; these lesions appear as a fibrovascular scar arising from the excision site. These "recurrent pterygia" probably have no relationship to ultraviolet radiation, but rather may be likened to keloid development in the skin **(Ye et al.; 2004)**

Many researchers have suggested that pterygium is a manifestation to localized, interpalpebral limbal stem cell dysfunction or deficiency, perhaps as a consequence of ultraviolet light related stem cell destruction **(Frau et al.; 2004).**

A polymorphism in codon 72 of p53 produces variant p53 proteins and a specific codon 72 genotype has been reported as more often associated with tumour formation than others. It was thus proposed that the p53 codon 72 polymorphism influences the expression and function of p53, and it is logical that this polymorphism may play a role in p53 protein expression in pterygium **(Tsai; 2005).**

Indications for Treatment

There are a number of generally accepted reasons for removing pterygium. Few people would argue that a pterygium that extends close to the visual axis and appears to be active should be removed. This is based on the understanding that whenever a pterygium is removed, there will be some scarring in the cornea as a result. If the scarring extends close to the visual axis, irregular astigmatism and reduced vision may occur **(Anduze and Merritt; 1985).**

There would also be little disagreement that pterygia that restrict eye movement should be removed. Conversely, there may be some argument about the usefulness of removing pterygia that result in significant degrees of