International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Topical Insulin Eye Drops for Persistent Epithelial Defect in a Phthisical Eye: A Case Report

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Abstract: ***Persistent epithelial defects in phthisical eyes remain difficult to manage because of chronic inflammation, ocular hypotony, poor epithelial regeneration, and disruption of the normal ocular surface environment. This report describes the clinical course of a 60 year- old woman with a non healing corneal epithelial defect in a phthisical eye following previous endophthalmitis. The patient presented with redness, watering, and foreign body sensation, while slit lamp examination revealed a central epithelial defect over a fibrotic cornea. Conventional treatment with lubricants, topical antibiotics, cycloplegics, and ointment failed to produce healing after two weeks. Topical insulin eye drops at a concentration of 1 IU/ml were then introduced four times daily along with supportive therapy. Gradual improvement was observed within the first week, with marked reduction in defect size by the second week and complete epithelialization by the third week. No local or systemic adverse reactions were encountered during treatment. The therapeutic response may be linked to the ability of insulin to stimulate epithelial cell proliferation, migration, cellular metabolism, and basement membrane adhesion through activation of growth-related signaling pathways. Although advanced structural damage in phthisical eyes limits full visual recovery, topical insulin appears to support restoration of ocular surface integrity in resistant epithelial defects. The case highlights the value of topical insulin as a low cost and biologically relevant adjunct within a broader multimodal treatment strategy for complex ocular surface disease.***

Keywords: persistent epithelial defect, topical insulin eye drops, phthisical eye, corneal wound healing, ocular surface disease

1. Introduction

The corneal epithelium plays a crucial role in maintaining ocular surface integrity and protecting the eye from pathogenic organisms. In a healthy cornea, epithelial cells are continuously regenerated from limbal stem cells with a turnover rate of approximately 7–10 days.[1] Consequently, most acute epithelial defects heal within 1–2 weeks. Persistent epithelial defects (PED), however, are defined as corneal epithelial defects that fail to heal after two weeks of conventional treatment and can lead to serious complications including stromal ulceration and infection.

Persistent epithelial defects in phthisical or prephthisical eye pose major challenge. The factors involved in the pathogenesis of Phthisis bulbi include ocular hypotony, breakdown of the blood–ocular barrier, and chronic intraocular inflammation.[2] Hypotony leads to altered tissue oxygenation, nutrition, and metabolism, thereby impairing normal cellular function and repair mechanisms.[3] Concurrently, disruption of the blood–ocular barrier and persistent inflammation create a hostile microenvironment with increased inflammatory mediators that inhibit epithelial cell proliferation and migration.

Recently, Insulin-like growth factors (IGFs) have been implicated in corneal wound healing through their role in regulating epithelial cell proliferation, differentiation, and migration.[2,3] Insulin, a peptide hormone structurally related to IGFs, has been identified in human tear film and has been shown to enhance corneal epithelial cell proliferation and accelerate epithelial wound healing.[4–6] Experimental studies have demonstrated that topical insulin can reduce epithelial defect size and promote corneal healing.[6]

In this report, we describe the successful use of topical insulin eye drops for the treatment of a persistent epithelial defect in a phthisical eye.

2. Case Report

A 60-year-old woman presented with complaints of persistent redness, watering, and foreign body sensation in the left eye for three weeks. She had a past history of endophthalmitis in the same eye three years earlier, following which she developed severe visual impairment and progressive shrinkage of the globe suggestive of a phthisical eye.

On examination, the best corrected visual acuity in the right eye was 6/9, while the left eye had perception of light present with inaccurate projection of rays in all qradrants. Slit-lamp examination of the left eye revealed diffusely thickened fibrotic cornea with a epithelial defect measuring approximately 4 × 3 mm involving the central cornea with irregular epithelial margins.

The anterior chamber appeared shallow but quiet. Intraocular pressure was digitally soft, and the globe showed clinical features suggestive of a phthisical eye. Posterior segment evaluation was not possible due to hazy cornea.

Fluorescein staining confirmed the presence of a epithelial defect with well-defined staining margins.

The patient was initially managed with preservative-free lubricating eye drops, topical antibiotic prophylaxis, cycloplegic drops, and lubricating ointment at night. Despite two weeks of intensive therapy, the epithelial defect persisted with no improvement.

Considering the non-healing nature of the defect, topical insulin eye drops were initiated. The drops were prepared by diluting regular human insulin (100 IU/ml) with preservative-free artificial tears to obtain a final concentration of 1 IU/ml. The patient was advised to instill topical insulin eye drops four times daily along with continued lubrication.

On follow-up evaluation, gradual reduction in the size of the epithelial defect was observed. At one week, the defect had

reduced to approximately 2 × 2 mm. By two weeks, only minimal punctate fluorescein staining was present. Complete epithelialization was achieved by the third week of treatment.

No local or systemic adverse effects related to insulin therapy were noted during the treatment period, and the ocular surface remained stable on subsequent follow-up visits.

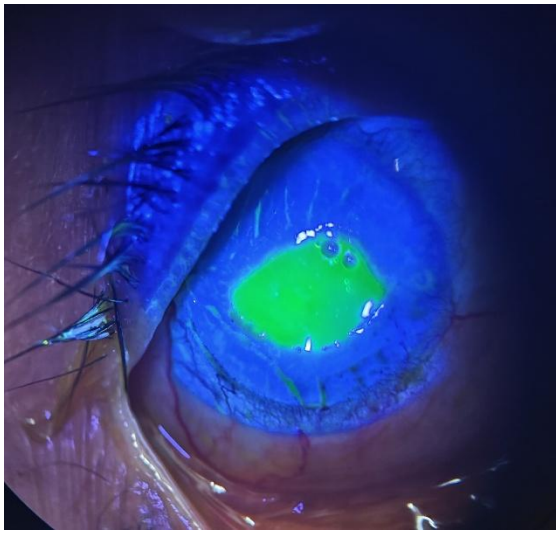

Figure 1: Pthysical eye showing epithelial defect

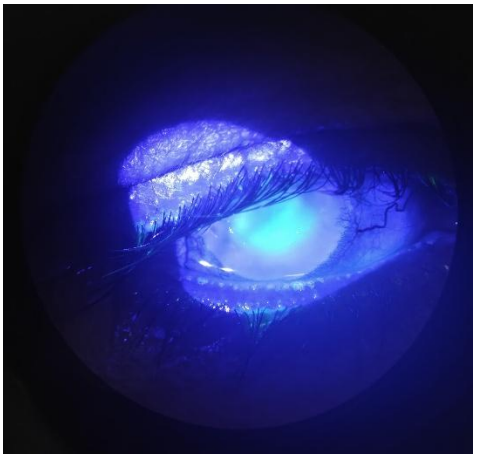

Figure 2: Persistant Epithelial defect in pthysical eye

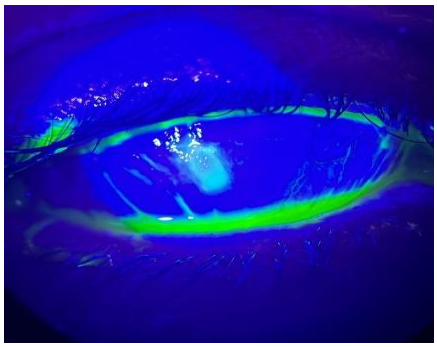

Figure 2: Day 7 of treatment of insulin eye drop

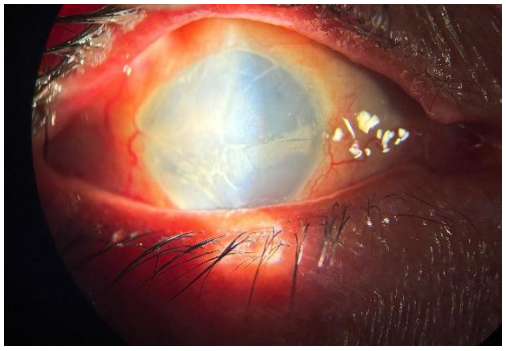

Figure 3: healed epithelial defect

3. Discussion

Persistent epithelial defects (PED) in a Phthisical eye represent an advanced stage of ocular surface compromise characterized by chronic inflammation, reduced corneal sensation, tear film instability, and progressive limbal stem cell dysfunction. In addition, vascular insufficiency and structural disorganization further impair epithelial migration, adhesion, and proliferation, making conventional therapy often inadequate.

Topical insulin has emerged as a potential adjunct in such refractory cases due to its targeted cellular effects. Corneal epithelial and limbal progenitor cells express insulin and insulin-like growth factor-1 (IGF-1) receptors, which mediate epithelial healing responses.[7] Binding of insulin activates intracellular signaling pathways, particularly phosphatidylinositol 3-kinase (PI3K)–Akt and mitogen-activated protein kinase (MAPK/ERK), resulting in enhanced epithelial cell proliferation, migration, and survival.[7,8] Insulin also upregulates Wnt/β-catenin signaling, promoting transcription of cell-cycle regulators such as c-Myc and cyclin D1, thereby facilitating cell cycle progression and regeneration.[8] Furthermore, it improves cellular metabolism via increased glucose uptake, enhances epithelial adhesion to the basement membrane, and reduces apoptosis at the wound edge.[8,4]

Clinical studies have demonstrated that low-dose topical insulin (1 IU/mL) accelerates epithelial healing in persistent epithelial defects associated with neurotrophic keratopathy, diabetic keratopathy, and post-surgical states, with a favorable safety profile.[4,10] However, in pre-phthisical eyes, the therapeutic response may be limited due to severe stromal thinning, ischemia, and advanced limbal stem cell deficiency. Hence, insulin should be considered an adjunct rather than a definitive therapy in such cases. Its use in combination with intensive lubrication, bandage contact lens, tarsorrhaphy, or autologous serum may enhance epithelial stability and delay progression toward complete phthisis.

In conclusion, topical insulin provides a biologically plausible and cost-effective adjunct in the management of PED in pre-phthisical eyes. While it does not reverse the underlying degenerative process, it can facilitate epithelialization and improve ocular surface integrity when incorporated into a multimodal therapeutic approach.

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