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Original Research Article

COMPARATIVE EFFICACY OF AMT AND TOPICAL INSULIN FOR HEALING OF PERSISTENT CORNEAL EPITHELIAL DEFECTS: AN INSTITUTIONAL BASED STUDY

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ABSTRACT

Background: Persistent corneal epithelial defects are non-healing epithelial lesions that may lead to stromal thinning, microbial keratitis, corneal scarring, perforation, and permanent visual impairment. Amniotic membrane transplantation (AMT) is commonly used for refractory defects because it provides a biological scaffold and promotes epithelial regeneration. **Aim:** To compare efficacy AMT and topical insulin for healing of persistent corneal epithelial defects. **Materials and Methods:** This hospital-based prospective comparative interventional study was conducted on a total of 128 patients with persistent corneal epithelial defects and allocated into two equal groups. Group A comprised 64 patients treated with amniotic membrane transplantation, whereas Group B comprised 64 patients treated with topical insulin eye drops at a concentration of 1 IU/mL, administered four times daily. Baseline demographic characteristics, duration and etiology of the defect, epithelial-defect area, best-corrected visual acuity, corneal sensation, stromal changes, healing time, epithelial healing rate, symptomatic improvement, recurrence, treatment failure, and adverse events were assessed. **Results:** Baseline demographic and clinical characteristics were comparable between the groups. Complete epithelial healing by day 7 occurred in 18.75% of the AMT group and 37.50% of the topical insulin group (p=0.018). By day 21, healing was achieved in 70.31% and 89.06% of patients, respectively (p=0.008). Final epithelial closure was significantly higher with topical insulin than with AMT (95.31% versus 81.25%, p=0.028). Mean healing time was significantly shorter in the topical insulin group (11.24 ± 4.18 days) than in the AMT group (16.83 ± 5.62 days; p<0.001). **Conclusion:** Topical insulin was more effective than amniotic membrane transplantation in achieving faster and more complete healing of persistent corneal epithelial defects. It also provided better visual and symptomatic outcomes with fewer procedure-related complications.

INTRODUCTION

The corneal epithelium forms the outermost protective layer of the eye and plays an essential role in maintaining corneal transparency, optical quality and resistance to microbial invasion. Under normal conditions, epithelial injury initiates a coordinated repair response involving migration, proliferation and differentiation of epithelial cells, supported by an intact tear film, basement membrane, limbal stem-cell population and corneal innervation. A persistent corneal epithelial defect occurs when this physiological healing process fails and the epithelial surface remains open despite appropriate conventional treatment for 2 wks. Such defects are clinically important because prolonged loss of epithelial integrity exposes the underlying stroma to inflammation, infection, enzymatic degradation and progressive structural damage. Without timely intervention, the condition can lead to stromal thinning, corneal melting, perforation, scarring and permanent visual impairment.[1] Persistent corneal epithelial defects are not a single disease entity but represent the final manifestation of several ocular and systemic disorders. Common causes include neurotrophic keratopathy, diabetes mellitus, previous microbial or herpetic keratitis, chemical or thermal injury, severe dry-eye disease,

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exposure keratopathy, limbal stem-cell dysfunction and complications following ocular surgery. Defective corneal innervation is particularly relevant because sensory nerves provide trophic signals that support epithelial metabolism, adhesion and regeneration. Damage to the trigeminal pathway may reduce corneal sensitivity and blink reflexes, disturb tear secretion and impair epithelial repair. Neurotrophic defects may therefore progress with relatively few symptoms despite considerable corneal damage, emphasizing the importance of careful slit-lamp examination, fluorescein staining and assessment of corneal sensation.[2] Initial management is directed toward identifying and treating the underlying cause while creating a favorable environment for epithelial healing. Conventional measures include withdrawal of potentially epitheliotoxic medications, frequent preservative-free lubrication, prophylactic antimicrobial therapy when appropriate, punctal occlusion, therapeutic contact lenses and correction of eyelid or exposure abnormalities. Autologous serum, platelet-derived preparations, scleral lenses, tarsorrhaphy and regenerative biological treatments may be considered when defects remain unresponsive. Nevertheless, management can be difficult because the condition frequently occurs in eyes with multiple contributing abnormalities. Treatment must protect the cornea while promoting epithelial migration and preventing infection, inflammation and stromal degradation. Persistent defects that do not respond to standard medical therapy consequently require more advanced biological or surgical intervention.[3] Amniotic membrane transplantation is an established treatment for refractory ocular-surface defects. The human amniotic membrane consists of an epithelial layer, a thick basement membrane and an avascular stromal matrix containing biologically active components. When applied to the corneal surface, it provides a supportive substrate for epithelial migration, reduces friction from the eyelids and protects exposed nerve endings. Its anti-inflammatory, antifibrotic and antiangiogenic properties may also limit tissue damage and reduce scar formation. Amniotic membrane may be applied as a graft, patch or multilayer construct and can be secured using sutures, fibrin adhesive or a sutureless delivery system. However, AMT requires donor-tissue processing, appropriate storage, procedural facilities and trained personnel. Membrane displacement, premature dissolution, retained sutures, irritation and the possible need for repeat application are additional practical concerns.[4] Topical insulin has emerged as a less invasive and potentially economical treatment for persistent corneal epithelial defects. Insulin is a peptide hormone with metabolic and growth-promoting effects that extend beyond systemic glucose regulation. Insulin receptors are expressed in corneal epithelial tissues, and their activation is believed to stimulate cellular migration, proliferation, protein synthesis and restoration of epithelial integrity. Insulin signalling may also support epithelial–nerve interactions, making topical therapy particularly relevant to neurotrophic and diabetic corneal disease. Topically compounded insulin can be administered directly to the affected ocular surface, thereby providing local exposure while limiting systemic absorption. Its accessibility and ease of application make it an attractive option for patients who have failed routine supportive treatment but do not require immediate tectonic surgery.[5] The clinical preparation of insulin eye drops requires careful attention to concentration, vehicle, sterility, storage conditions and replacement intervals. Regular human insulin is commonly diluted in a sterile preservative-free vehicle and administered several times daily. Because insulin is a protein, inappropriate formulation or storage may result in reduced potency, aggregation or contamination. Normal saline and compatible ophthalmic vehicles have therefore been investigated to identify preparations that retain biological activity while remaining well tolerated by corneal tissues. Standardized compounding protocols are important before topical insulin can be incorporated consistently into routine ophthalmic practice. Patients must also receive clear instructions regarding refrigeration, hand hygiene, instillation technique and avoidance of contact between the bottle tip and ocular surface.[6]

MATERIALS AND METHODS

This hospital-based prospective comparative interventional study was conducted on a total of 128 patients with persistent corneal epithelial defects. Patients were allocated into two treatment groups, with 64 patients receiving amniotic membrane transplantation and 64 patients receiving topical insulin therapy. The efficacy and safety of both treatment modalities were compared using predefined clinical parameters. Patients attending the ophthalmology outpatient department or admitted to the ophthalmology ward with a persistent corneal epithelial defect were screened for eligibility. A persistent corneal epithelial defect was defined as a corneal epithelial defect that failed to heal despite appropriate conventional medical treatment for 2 weeks. Only one eye per patient was included in the study. In patients with bilateral involvement, the eye with the larger or more clinically significant epithelial defect was selected.

Inclusion Criteria

Patients aged 18 years or older with a clinically diagnosed persistent corneal epithelial defect were included. Patients with epithelial defects resulting from neurotrophic keratopathy, previous infective keratitis after adequate control of infection, chemical or thermal injury, neutrophic ulcer, postoperative epithelial breakdown, exposure keratopathy, diabetic keratopathy, limbal stem-cell dysfunction, or other non-healing corneal surface

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disorders were considered eligible. Patients willing to comply with treatment, follow-up examinations, and photographic documentation were included after providing written informed consent.

Exclusion Criteria

Patients with corneal perforation, descemetocele requiring emergency surgical intervention, uncontrolled glaucoma, severe dry eye requiring additional surgical management, extensive corneal stromal melting, intraocular inflammation, active ocular surface malignancy, or known hypersensitivity to insulin or any component of the eye-drop preparation were excluded. Pregnant or lactating women, patients with severe systemic illness that could interfere with follow-up, and those who had previously received amniotic membrane transplantation or topical insulin for the same epithelial defect were also excluded.

Baseline Evaluation

A detailed history was obtained regarding age, sex, occupation, duration of symptoms, presenting complaints, history of ocular trauma or surgery, previous corneal infection, use of topical medications, contact-lens use, diabetes mellitus, systemic neurological disease, autoimmune disease, and other relevant systemic conditions. Previous treatment received for the epithelial defect, including lubricants, antibiotics, therapeutic contact lenses, autologous serum, tarsorrhaphy, or other ocular-surface procedures, was recorded.

Ophthalmic Examination

All patients underwent a comprehensive ophthalmic examination. Best-corrected visual acuity was measured using a Snellen chart and converted to logarithm of the minimum angle of resolution values for statistical analysis. Slit-lamp biomicroscopy was performed to evaluate the location, shape, depth, and margins of the epithelial defect; corneal stromal infiltration, thinning, edema, vascularization, scarring, anterior-chamber reaction, and associated ocular-surface abnormalities were documented. Intraocular pressure was measured wherever clinically feasible.

Measurement of the Corneal Epithelial Defect

The epithelial defect was stained with fluorescein and examined under cobalt-blue illumination. The maximum horizontal and vertical dimensions of the defect were measured in millimetres using the slit-lamp beam scale. The area of the epithelial defect was calculated in square millimetres using standardized digital slit-lamp photographs and image-analysis software. The same measurement technique was used at baseline and during each follow-up visit. Wherever possible, measurements were performed by an examiner who was not involved in treatment allocation.

Pre-Treatment Management

Any active infection was treated and clinically controlled before enrolment. Potentially epitheliotoxic topical medications were discontinued whenever medically appropriate. All patients received preservative-free lubricating eye drops and supportive ocular-surface care. Systemic diseases, including diabetes mellitus, were evaluated and managed in coordination with the appropriate department. Additional interventions likely to affect epithelial healing were avoided unless clinically required as rescue treatment.

Amniotic Membrane Transplantation Group

Patients allocated to Group A underwent amniotic membrane transplantation under aseptic conditions. Preserved amniotic membrane obtained from an authorized tissue bank was used. After topical or local anaesthesia, loose and devitalized epithelium surrounding the defect was gently debrided. The amniotic membrane was placed over the cornea with the basement-membrane side facing upward and secured to the ocular surface using interrupted or continuous sutures, fibrin glue, or an appropriate fixation technique according to the size and location of the defect. A therapeutic bandage contact lens was applied when indicated. Postoperatively, patients received topical broad-spectrum antibiotic eye drops, preservative-free lubricants, and other medications according to the clinical condition of the eye.

Topical Insulin Group

Patients allocated to Group B were treated with topical insulin eye drops. Human regular insulin was diluted under sterile conditions with a suitable preservative-free ophthalmic vehicle to prepare a concentration of 1 IU/mL. The prepared solution was stored under refrigeration and replaced at regular intervals to maintain sterility and stability. Patients were instructed to instil one drop into the affected eye four times daily, along with preservative-free lubricating eye drops. A topical broad-spectrum antibiotic was prescribed when clinically indicated. Patients and attendants were instructed regarding hand hygiene, correct instillation technique, storage of the solution, and avoidance of contact between the dropper tip and the ocular surface.

Follow-Up Assessment

Patients were evaluated at baseline and subsequently at regular follow-up visits until complete epithelial healing or the requirement for rescue treatment. At each visit, best-corrected visual acuity, symptoms, size and area of the epithelial defect, fluorescein staining pattern, corneal clarity, stromal edema, infiltration, thinning, vascularization, anterior-chamber reaction, and treatment-related complications were recorded. Standardized slit-lamp photographs were obtained to document the healing response.

Statistical Analysis

Data was entered into Microsoft Excel and analysed using IBM SPSS Statistics, version 27.0. Continuous variables were presented as mean with standard deviation or median with interquartile range according to the distribution of the data. Categorical variables were expressed as frequencies and percentages. Normality of continuous data was assessed using the Shapiro–Wilk test and graphical

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methods. The independent-samples t-test was used to compare normally distributed continuous variables between the two groups, while the Mann–Whitney U test was used for non-normally distributed variables.

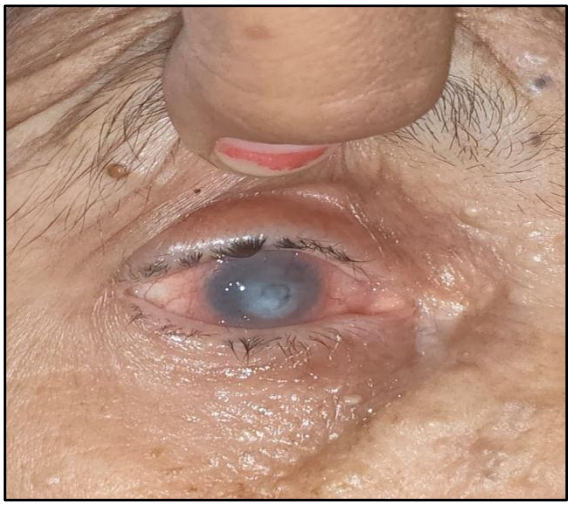

Fig 1: Non healing epithelial defect approx.2 mm x 2mm in the right eye of a 60 yr old patient (post microbial keratitis)

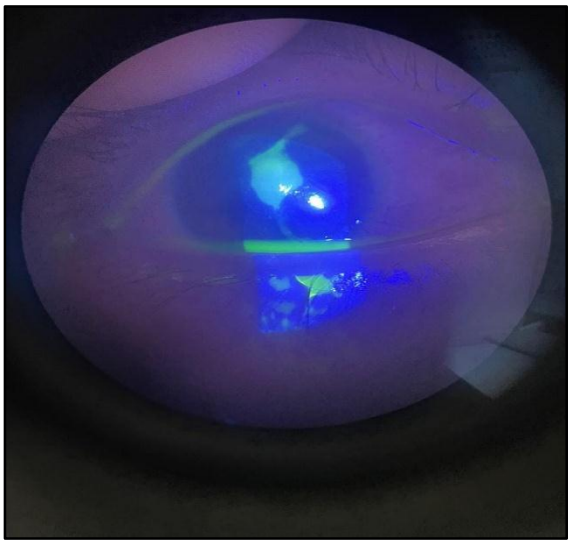

Fig 2: Slit lamp photograph of right eye showing non healing persistent epithelial defect in cobalt blue filter staining with fluorescein dye

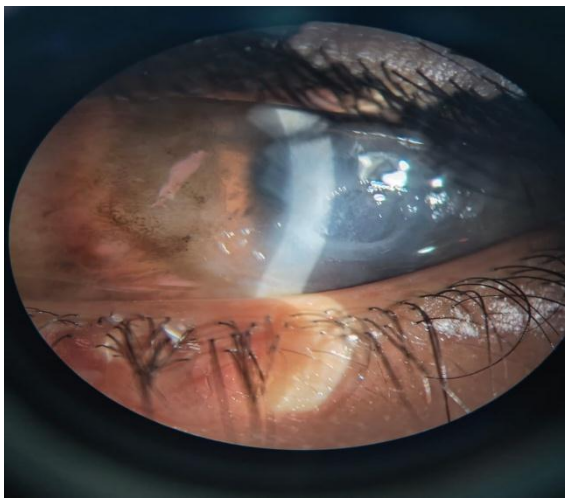

Fig 3: Slit lamp photograph in oblique illumination showing punched out non healing persistent epithelial defect with underlying stromal edema (neurotrophic ulcer)

RESULTS

Table 1: Baseline Demographic Characteristics of the Study Participants

Table 1 presents the baseline demographic profile of the 128 patients enrolled in the study, with 64 patients each in the AMT and topical insulin groups. The mean age of patients in the AMT group was 53.41 ± 13.26 years, while that in the topical insulin group was 51.78 ± 12.84 years. The difference between the groups was not statistically significant (p=0.481), indicating comparable age distribution. Overall, the mean age of the study population was 52.59 ± 13.03 years, suggesting that persistent corneal epithelial defects predominantly affected middle-aged and elderly individuals. The majority of patients belonged to the 41–60 years age group, accounting for 48.44% in the AMT group and 50.00% in the topical insulin group. Patients aged more than 60 years constituted 32.81% and 28.13% of the respective groups, while younger patients aged 40 years or less represented a smaller proportion. No statistically significant differences were observed in the age-group distribution between the treatment groups (all p>0.05), indicating successful baseline matching.

Table 2: Baseline Clinical Characteristics and Causes of Persistent Corneal Epithelial Defects

Table 2 summarizes the baseline clinical features and underlying etiologies of persistent corneal epithelial defects among the study participants. The mean duration of epithelial defects prior to treatment initiation was 25.38 ± 8.74 days in the AMT group and 24.06 ± 8.21 days in the topical insulin group. The difference was not statistically significant (p=0.380), indicating a similar chronicity of disease in both groups at baseline.

The average baseline epithelial-defect area was 15.46 ± 5.28 mm^2 in the AMT group and 14.91 ± 5.06 mm^2 in the topical insulin group (p=0.549). Likewise, baseline visual acuity, measured as

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logMAR BCVA, was comparable between the groups (1.12 ± 0.41 versus 1.08 ± 0.39; p=0.573).

Table 3: Comparison of Corneal Epithelial Healing Between the Two Treatment Groups

Table 3 compares the primary healing outcomes between patients treated with AMT and those receiving topical insulin therapy. A significantly higher proportion of patients in the topical insulin group achieved complete epithelial healing during the early stages of follow-up. By day 7, complete epithelialization had occurred in 37.50% of patients receiving topical insulin compared with only 18.75% of patients treated with AMT (p=0.018). The superiority of topical insulin remained evident during subsequent follow-up visits. By day 14, complete healing was achieved in 71.88% of patients in the topical insulin group compared with 46.88% in the AMT group (p=0.004). Similarly, by day 21, healing rates reached 89.06% and 70.31%, respectively (p=0.008). At the final assessment, complete epithelial closure was observed in 95.31% of patients treated with topical insulin compared with 81.25% of those receiving AMT (p=0.028). Conversely, treatment failure occurred in only 4.69% of patients in the topical insulin group, compared with 18.75% in the AMT group. The requirement for rescue treatment was also significantly lower among patients treated with topical insulin (4.69% versus 18.75%, p=0.028).

Table 4: Changes in Epithelial-Defect Area, Visual Acuity and Clinical Symptoms

Table 4 evaluates changes in objective clinical parameters and patient-reported symptoms during follow-up. At baseline, the mean epithelial-defect area was comparable between the groups (p=0.549). However, significant differences emerged during follow-up. By day 7, the mean defect area had decreased to 6.38 ± 4.17 mm² in the topical insulin group compared with 9.21 ± 4.86 mm² in the AMT group (p<0.001). Similar significant differences were observed at days 14 and 21, demonstrating more rapid reduction in epithelial-defect size among patients treated with topical insulin.

Table 5: Recurrence, Treatment Failure and Adverse Events

Table 5 summarizes treatment failures, recurrences and adverse events observed during the study period. Recurrence of epithelial defects following initial healing was observed in 13.46% of healed patients in the AMT group and 3.28% in the topical insulin group. Although the recurrence rate was lower in the topical insulin group, the difference did not reach statistical significance (p=0.082). Persistence or enlargement of the epithelial defect occurred significantly more frequently among AMT-treated patients (12.50%) than among patients receiving topical insulin (3.13%; p=0.048). Serious complications were uncommon in both treatment groups. Progressive stromal thinning occurred in 4.69% of AMT patients and 1.56% of topical insulin patients, while microbial keratitis developed in only a few cases. Procedure-related complications were observed exclusively in the AMT group.

Table 1: Baseline demographic characteristics of the study participants

Characteristic	AMT group (n=64)	Topical insulin group (n=64)	Total (n=128)	p-value
Age, years, mean ± SD	53.41 ± 13.26	51.78 ± 12.84	52.59 ± 13.03	0.481
Age ≤40 years	12 (18.75%)	14 (21.88%)	26 (20.31%)	0.661
Age 41–60 years	31 (48.44%)	32 (50.00%)	63 (49.22%)	0.860
Age >60 years	21 (32.81%)	18 (28.13%)	39 (30.47%)	0.564
Male	38 (59.38%)	36 (56.25%)	74 (57.81%)	0.858
Female	26 (40.63%)	28 (43.75%)	54 (42.19%)	
Rural residence	35 (54.69%)	33 (51.56%)	68 (53.13%)	0.723
Urban residence	29 (45.31%)	31 (48.44%)	60 (46.88%)	
Diabetes mellitus present	25 (39.06%)	29 (45.31%)	54 (42.19%)	0.591
Hypertension present	22 (34.38%)	19 (29.69%)	41 (32.03%)	0.570
Right eye involved	34 (53.13%)	31 (48.44%)	65 (50.78%)	0.724
Left eye involved	30 (46.88%)	33 (51.56%)	63 (49.22%)	

Table 2: Baseline clinical characteristics and causes of persistent corneal epithelial defects

Clinical characteristic	AMT group (n=64)	Topical insulin group (n=64)	Total (n=128)	p-value
Duration of epithelial defect before treatment, days, mean ± SD	25.38 ± 8.74	24.06 ± 8.21	24.72 ± 8.47	0.380
Baseline defect area, mm², mean ± SD	15.46 ± 5.28	14.91 ± 5.06	15.19 ± 5.16	0.549
Baseline BCVA, logMAR, mean ± SD	1.12 ± 0.41	1.08 ± 0.39	1.10 ± 0.40	0.573
Reduced corneal sensation	37 (57.81%)	40 (62.50%)	77 (60.16%)	0.589
Stromal edema	34 (53.13%)	31 (48.44%)	65 (50.78%)	0.724
Corneal vascularization	19 (29.69%)	17 (26.56%)	36 (28.13%)	0.694
Mild stromal thinning	13 (20.31%)	11 (17.19%)	24 (18.75%)	0.651
Neurotrophic keratopathy	18 (28.13%)	20 (31.25%)	38 (29.69%)	0.987*
Healed infective keratitis	14 (21.88%)	12 (18.75%)	26 (20.31%)	0.589
Postoperative epithelial defect	10 (15.63%)	9 (14.06%)	19 (14.84%)	0.523
Chemical or thermal injury	9 (14.06%)	8 (12.50%)	17 (13.28%)	0.678
Diabetic keratopathy	7 (10.94%)	9 (14.06%)	16 (12.50%)	0.798
Other ocular-surface disorders	6 (9.38%)	6 (9.38%)	12 (9.38%)	0.661

BCVA=best-corrected visual acuity; logMAR=logarithm of the minimum angle of resolution.

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Table 3: Comparison of corneal epithelial healing between the two treatment groups

Healing outcome	AMT group (n=64)	Topical insulin group (n=64)	p-value
Complete epithelial healing by day 7	12 (18.75%)	24 (37.50%)	0.018
Complete epithelial healing by day 14	30 (46.88%)	46 (71.88%)	0.004
Complete epithelial healing by day 21	45 (70.31%)	57 (89.06%)	0.008
Complete epithelial healing at final assessment	52 (81.25%)	61 (95.31%)	0.028
Failure to achieve complete healing	12 (18.75%)	3 (4.69%)	0.028
Time to complete epithelial healing, days, mean±SD†	16.83 ± 5.62	11.24 ± 4.18	<0.001
Median healing time, days (IQR)†	16.00 (12.00–21.00)	10.00 (8.00–14.00)	<0.001
Mean epithelial healing rate, mm²/day	0.91 ± 0.37	1.34 ± 0.48	<0.001
Final reduction in epithelial-defect area	88.42 ± 19.36%	97.16 ± 9.84%	0.002
Requirement for rescue treatment	12 (18.75%)	3 (4.69%)	0.028

†Calculated among patients who achieved complete epithelial healing.
IQR=interquartile range.

Table 4: Changes in epithelial-defect area, visual acuity and clinical symptoms

Outcome	AMT group (n=64)	Topical insulin group (n=64)	Between-group p-value
Baseline defect area, mm²	15.46 ± 5.28	14.91 ± 5.06	0.549
Defect area at day 7, mm²	9.21 ± 4.86	6.38 ± 4.17	<0.001
Defect area at day 14, mm²	4.83 ± 4.02	2.16 ± 3.05	<0.001
Defect area at day 21, mm²	2.11 ± 3.31	0.68 ± 2.17	0.005
Final defect area, mm²	1.79 ± 3.08	0.42 ± 1.84	0.003
Baseline BCVA, logMAR	1.12 ± 0.41	1.08 ± 0.39	0.573
Final BCVA, logMAR	0.78 ± 0.37	0.62 ± 0.34	0.012
Mean improvement in BCVA, logMAR	0.34 ± 0.22	0.46 ± 0.25	0.005
Improvement of ≥2 Snellen lines	35 (54.69%)	47 (73.44%)	0.027
Complete relief of ocular pain	44 (68.75%)	55 (85.94%)	0.021
Resolution of photophobia	42 (65.63%)	53 (82.81%)	0.027
Resolution of foreign-body sensation	46 (71.88%)	56 (87.50%)	0.028
Improvement in corneal clarity	38 (59.38%)	49 (76.56%)	0.038

Table 5: Recurrence, treatment failure and adverse events

Outcome/adverse event	AMT group (n=64)	Topical insulin group (n=64)	p-value
Recurrence after initial epithelial healing†	7/52 (13.46%)	2/61 (3.28%)	0.082
Persistence or enlargement of defect	8 (12.50%)	2 (3.13%)	0.048
Progressive stromal thinning	3 (4.69%)	1 (1.56%)	0.619*
Microbial keratitis	2 (3.13%)	1 (1.56%)	1.000*
Corneal perforation	1 (1.56%)	0 (0.00%)	1.000*
Membrane displacement or premature dissolution	5 (7.81%)	Not applicable	—
Suture-related irritation	6 (9.38%)	Not applicable	—
Transient ocular irritation after treatment	3 (4.69%)	5 (7.81%)	0.717*
Allergic or toxic ocular-surface reaction	1 (1.56%)	2 (3.13%)	1.000*
Documented systemic hypoglycaemia	Not applicable	0 (0.00%)	—
At least one treatment-related adverse event	12 (18.75%)	5 (7.81%)	0.118
Discontinuation due to adverse events	2 (3.13%)	1 (1.56%)	1.000*

DISCUSSION

The present study included 128 patients with comparable baseline demographic characteristics in the AMT and topical insulin groups. The overall mean age was 52.59 ± 13.03 years, and 57.81% of the participants were male. Diabetes mellitus was present in 39.06% of the AMT group and 45.31% of the topical insulin group, with no significant difference between the groups (p=0.591). Similarly, baseline epithelial-defect area, duration of the defect and visual acuity were comparable, reducing the likelihood that these factors influenced the observed treatment difference. Abdi et al. (2024) prospectively treated 23 refractory persistent epithelial defects with topical insulin 1 IU/mL four times daily and found clinically meaningful improvement in 16 patients (69.60%). Improvement occurred in 68.00% of nondiabetic and 71.00% of diabetic patients, suggesting that the epithelial response to topical insulin was not restricted to patients with diabetes. This supports the present finding that topical insulin remained effective despite diabetes being present in 45.31% of treated patients.[7] Neurotrophic keratopathy was the most frequent cause of persistent epithelial defects in the present study, accounting for 28.13% of AMT cases and 31.25% of topical insulin cases. Reduced corneal sensation was correspondingly common, affecting 57.81% and 62.50% of patients, respectively. These findings are clinically relevant because deficient corneal innervation reduces trophic support to epithelial cells and delays healing. Soares et al. (2022) evaluated topical insulin in 21 eyes with refractory stage 2 or stage 3 neurotrophic keratopathy and reported complete re-epithelialization in 90.00% of eyes within 7–45 days.[8] In the present study, topical insulin produced a significantly faster healing response than AMT. Complete epithelialization by day 7 was achieved in 37.50% of the topical insulin group compared with 18.75% of the AMT group (p=0.018), while the corresponding rates by day 14 were 71.88% and

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46.88% (p=0.004). Mean healing time was 11.24 ± 4.18 days with topical insulin and 16.83 ± 5.62 days with AMT (p<0.001). Dhillon et al. (2020), in a prospective study of 60 patients with persistent epithelial defects, reported a mean healing time of 18.33 ± 13.46 days in the 30 patients treated with AMT. Ten of the total 60 eyes, equivalent to 16.70%, remained unhealed after four weeks.[9] At final assessment, complete epithelial closure was achieved in 81.25% of patients treated with AMT and 95.31% of those treated with topical insulin (p=0.028). Lee et al. (1997) treated 11 eyes with persistent corneal epithelial defects using preserved human amniotic membrane and reported successful healing in 10 eyes, corresponding to a success rate of 90.91%. Mean healing time in their series was 3.9 ± 2.3 weeks, and no recurrence occurred during a mean follow-up of 9.0 ± 5.9 months among successfully treated cases. Their AMT success rate was higher than the 81.25% recorded in the present study, although their average healing time of approximately 27 days was longer than the 16.83 days observed here. Differences in defect etiology, baseline defect severity, surgical technique and criteria for complete healing may explain these variations. Nevertheless, both studies confirm that AMT is an effective treatment, while the present direct comparison indicates that topical insulin may provide a higher final closure rate.[10] The mean epithelial healing rate in the present investigation was significantly greater with topical insulin than with AMT, at 1.34 ± 0.48 mm²/day versus 0.91 ± 0.37 mm²/day (p<0.001). The final percentage reduction in defect area was also greater with topical insulin, at 97.16 ± 9.84% compared with 88.42 ± 19.36% after AMT (p=0.002). Prabhasawat et al. (2001) evaluated single- and multilayer AMT in 28 eyes with refractory epithelial defects, stromal thinning or perforation and reported successful epithelial healing in 23 eyes, giving an overall success rate of 82.10%. Success rates were 80.00% in defects without stromal thinning, 84.60% in defects with stromal thinning and 80.00% in eyes with perforation. Their overall result closely corresponds to the 81.25% complete-healing rate in the present AMT group. The substantially higher 95.31% closure rate and greater reduction in defect area with topical insulin in the present study suggest that insulin may be particularly useful before resorting to a surgical membrane procedure in suitable nonperforated defects.[11] Both anatomical and functional outcomes favored topical insulin in the present study. The final residual defect area was 0.42 ± 1.84 mm² with topical insulin and 1.79 ± 3.08 mm² with AMT (p=0.003). Final BCVA was 0.62 ± 0.34 logMAR in the topical insulin group compared with 0.78 ± 0.37 logMAR in the AMT group (p=0.012), and improvement of at least two Snellen lines occurred in 73.44% and 54.69% of patients, respectively (p=0.027). Maqsood et al. (2021) studied 93 persistent epithelial defects treated with a human amniotic membrane-derived dry matrix and reported complete healing in 58.00%, partial healing in 28.00% and no improvement in approximately 13.98%. The mean treatment duration was 22.4 ± 12.3 days. Visual acuity improved in 27.00% and remained stable in 59.00%; mean BCVA changed only modestly from 1.74 ± 0.73 to 1.64 ± 0.79 logMAR. Compared with these findings, the present AMT group had a higher complete-healing rate of 81.25%, while the topical insulin group demonstrated both a higher healing rate and a greater frequency of clinically meaningful visual improvement.[12] Recurrence after initial healing occurred in 13.46% of AMT-treated eyes and 3.28% of topical-insulin-treated eyes in the present study, although this difference was not statistically significant (p=0.082). Persistence or enlargement of the defect was significantly more common after AMT than topical insulin, at 12.50% versus 3.13% (p=0.048). AMT-specific complications included membrane displacement or premature dissolution in 7.81% and suture-related irritation in 9.38%, whereas no systemic hypoglycaemia occurred with topical insulin. Seitz et al. (2009) reported a 70.00% primary surgical success rate for AMT in persistent epithelial defects following penetrating keratoplasty. Among successfully treated eyes, 44.00% subsequently developed recurrence during a mean follow-up of 16 ± 13 months; recurrence varied according to the AMT technique and was lowest with the sandwich technique. The lower AMT recurrence rate of 13.46% in the present study may reflect differences in etiology, because Seitz et al. included only post-keratoplasty eyes, which often have severe neurotrophic and ocular-surface dysfunction.[13]

CONCLUSION

Topical insulin was more effective than amniotic membrane transplantation in promoting healing of persistent corneal epithelial defects. It resulted in faster epithelial closure, a higher healing rate, greater reduction in defect size, and better visual and symptomatic improvement. Topical insulin was also well tolerated and associated with fewer procedure-related complications. It may therefore be considered a safe, simple, and effective treatment option for persistent corneal epithelial defects.

REFERENCES

1. Kwon JE, Kang C, Moghtader A, Shahjahan S, Bibak Bejandi Z, Alzein A, et al. Emerging treatments for persistent corneal epithelial defects. Vision (Basel). 2025;9(2):26. doi: 10.3390/vision9020026.
2. NaPier E, Camacho M, McDevitt TF, Sweeney AR. Neurotrophic keratopathy: current challenges and future prospects. Ann Med. 2022;54(1):666-673. doi: 10.1080/07853890.2022.2044518.
3. Sanders FWB, Huang J, Alió del Barrio JL, Hamada S, McAlinden C. Amniotic membrane transplantation: structural and biological properties, tissue preparation, application and clinical indications. Eye (Lond). 2024;38(4):668-679. doi: 10.1038/s41433-023-02777-5.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

4. Sell S, de la Presa M, Thakur S, Eslani M, Jeffrey J, Sheppard JD, et al. Comparison of persistent epithelial defect treatment with sutureless cryopreserved and dehydrated amniotic membrane. Am J Ophthalmol. 2023;251:32-42. doi: 10.1016/j.ajo.2022.12.007.
5. Diaz-Valle D, Burgos-Blasco B, Gegundez-Fernandez JA, Garcia-Caride S, Puebla-Garcia V, Peña-Urbina P, et al. Topical insulin for refractory persistent corneal epithelial defects. Eur J Ophthalmol. 2021;31(5):2280-2286. doi: 10.1177/1120672120958307.
6. Vicario-de-la-Torre M, Puebla-García V, Ybañez-García L, López-Cano JJ, González-Cela-Casamayor MA, Brugnera M, et al. Topical insulin eye drops: stability and safety of two compounded formulations for treating persistent corneal epithelial defects. Pharmaceutics. 2024;16(5):580. doi: 10.3390/pharmaceutics16050580.
7. Abdi P, Ghaffari R, Azad N, Alshaheeb A, Latifi G, Soltani Shahgoli S, et al. Topical insulin for refractory persistent corneal epithelial defects. Sci Rep. 2024;14(1):12459. doi: 10.1038/s41598-024-63091-y.
8. Soares RJDSM, Arêde C, Sousa Neves F, da Silva Fernandes J, Cunha Ferreira C, Sequeira J. Topical insulin—utility and results in refractory neurotrophic keratopathy in stages 2 and 3. Cornea. 2022;41(8):990-994.
9. Dhillon HK, Bahadur H, Raj A. A comparative study of tarsorrhaphy and amniotic membrane transplantation in the healing of persistent corneal epithelial defects. Indian J Ophthalmol. 2020;68(1):29-33. doi: 10.4103/ijo.IJO_617_19.
10. Lee SH, Tseng SCG. Amniotic membrane transplantation for persistent epithelial defects with ulceration. Am J Ophthalmol. 1997;123(3):303-312. doi: 10.1016/S0002-9394(14)70125-4.
11. Prabhasawat P, Tesavibul N, Komolsuradej W. Single and multilayer amniotic membrane transplantation for persistent corneal epithelial defect with and without stromal thinning and perforation. Br J Ophthalmol. 2001;85(12):1455-1463. doi: 10.1136/bjo.85.12.1455.
12. Maqsood S, Elsawah K, Dhillon N, Soliman S, Laginaf M, Lodhia V, et al. Management of persistent corneal epithelial defects with human amniotic membrane-derived dry matrix. Clin Ophthalmol. 2021;15:2231-38. doi: 10.2147/OPTH.S299141.
13. Seitz B, Das S, Sauer R, Mena D, Hofmann-Rummelt C. Amniotic membrane transplantation for persistent corneal epithelial defects in eyes after penetrating keratoplasty. Eye (Lond). 2009;23(4):840-848. doi: 10.1038/eye.2008.140.

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