

Outcomes of Fungal Corneal Ulcer with Impending Perforation after Temporary Suture Tarsorrhaphy

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ABSTRACT

Introduction: This study aims to evaluate outcomes and complications of temporary suture tarsorrhaphy (TST) in cases of impending corneal ulcer perforation.

Materials and methods: Case records of patients who underwent temporary suture tarsorrhaphy at Mechi Eye Hospital during a period of 18 months were retrospectively evaluated. All the smear positive fungal keratitis with more than 5mm infiltration involving central and/or paracentral cornea with impending corneal perforation were included. Demographic and clinical profile including – visual acuity, indication for temporary suture tarsorrhaphy, duration of signs and symptoms were noted. The outcomes were evaluated after 1 month and 3 months post tarsorrhaphy, in relation with time to epithelial healing, anatomical success rate, best corrected visual acuity, complications associated with non-healing corneal ulcer, number of temporary suture tarsorrhaphy needed and complications of TST.

Results: The study included 119 cases of smear positive fungal keratitis with mean age of 51.34 ± 15.56 years. In this study, 56.30% of the patients developed epithelial healing at 2 – 4 weeks with mean duration of 23.24 ± 12.09 days of temporary suture tarsorrhaphy. Out of 119 patients, the corneal ulcer healed in 84 patients (70.6%), whereas 35 (29.4%) did not heal. Among those with non-healing ulcers, 15 patients (12.6%) had to undergo evisceration. The anatomical success rate was 87.39% which was statistically significant ($P = 0.001$). Regarding visual outcome, in 62 patients (52.10%) BCVA improved by 2 or more lines, which was statistically significant ($P < 0.05$) resulting in a functional success of 26.89%.

Conclusion: This study concludes that temporary suture tarsorrhaphy could be a useful option for management of corneal ulcers with impending perforation in eye centers with limited resources settings and high disease burden with good anatomical and functional outcome.

Key words: Corneal ulcer, Fungal keratitis, Impending perforation, Temporary suture tarsorrhaphy.

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INTRODUCTION

Corneal infection is a major public health problem worldwide and the most common cause of monocular corneal blindness (Koh, Sun and Hsiao, 2020; Upadhyay *et al.*, 2001; Puri and Shrestha, 2017). The incidence of ulcerative keratitis varies from 20.2 in 100000 per year in developed countries (Koh, Sun and Hsiao, 2020) to 799 in 100000 per year in developing countries (Upadhyay *et al.*, 2001).

Over the past few decades, earlier diagnosis, a better understanding of the pathogenesis and the availability of potent antimicrobial drugs have improved the chances for medical control of infectious keratitis (Chen *et al.*, 2004). However, virulent and resistant forms of infectious bacteria, fungi and Acanthamoeba can still cause keratitis to worsen, even with maximum medical therapy (Amatya *et al.*, 2012). All this medically uncontrolled microbial keratitis may eventually lead to corneal perforation, infectious scleritis, and secondary endophthalmitis (Kenyon and Roberts, 1984). Descemetocoele and perforation are considered ophthalmic emergencies that require immediate intervention with management options that includes tissue adhesives, bandage contact lenses (Garg *et al.*, 2003), patch grafts (Solomon *et al.*, 2002), conjunctival flaps (Nizeyimana *et al.*, 2017), temporary suture tarsorrhaphy (TST) (Rajak S, Rajak J, 2015) and penetrating or lamellar keratoplasty (Anshu *et al.*, 2009).

Tarsorrhaphy is the closure of the eyelids, either temporarily or permanently. Lids can be closed

temporarily with tape, adhesive glue, levator paralysis by botulinum toxin injection or sutures, with or without a bolster (Cosar *et al.*, 2001). A tarsorrhaphy decreases the evaporation rate of tears by decreasing the palpebral fissure width. In addition, immobilization of the lid over the epithelial defect by the tarsorrhaphy decreases the traumatic effect of the moving lids on the healing epithelium (Cosar *et al.*, 2001). Tarsorrhaphy also gives mechanical support to the cornea which tends to perforate due to thinning. A half-open eye allows more oxygen to get to the corneal epithelium than a totally closed or patched eye. Allowance for the administration of eye drops, retention of partial eyesight, and examination of the cornea by having the patient adduct the eye are other advantages of tarsorrhaphy (Cosar *et al.*, 2001).

Fungal keratitis responds poorly to antifungal agents, thus surgical intervention in the form of therapeutic penetrating keratoplasty (TPK) is required more frequently (Xie, Dong and Shi, 2001). However, the shortage of corneal donors and trained corneal specialist, low socio economic status of the patients (Upadhyay *et al.*, 2001) and countries with high burden of disease such as in Nepal (Upadhyay *et al.*, 2001) has rendered TPK as a costly and inconvenient modality, especially in high disease burden eye hospitals with limited capacities and resources where there is no Eye Bank. On the other hand, temporary suture tarsorrhaphy (TST) is an easier, cost-effective technique which often helps to buy time for TPK.



This study evaluates the outcomes of TST in impending corneal ulcer perforation in a high volume resource limited center at eastern region of Nepal. The specific objectives of the study are to evaluate the demographic profile, epithelial healing in relation with time, anatomical success rate and complications of TST.

MATERIALS AND METHODS

In this retrospective study, all cases of fungal keratitis that had undergone TST after evaluation by the multiple eye specialist of Mechi Eye Hospital (MEH), Jhapa, between 1st Jan 2018 to 30th June 2019 were included. Ethical approval was obtained from the MEH Institutional Review Board and the study adhered to the tenets of declaration of Helsinki.

Patients with a minimum follow up of 3-month post tarsorrhaphy were included in the study. Information reviewed included patient age and sex, visual acuity (VA) at presentation, size and location of the ulcer, indication for TST, duration of signs and symptoms before TST, time to epithelial healing after TST, complications associated with non-healing corneal ulcer, complications of TST, number of TST needed and the duration of follow up.

The inclusion criteria were smear positive fungal keratitis with ulcer size of more than 5mm horizontally and vertically involving central and/or paracentral cornea. Corneal infiltration with impending corneal perforation were taken. The exclusion criteria were cases of mixed microbial keratitis, perforated corneal

ulcer, endophthalmitis and scleritis during presentation.

All cases had a microbiologic evaluation consisting of microscopic examination of the smears using potassium hydroxide and Gram stain. Smear positive fungal cases were managed with topical natamycin (5%) 2 hourly, fluconazole (0.30%) 2 hourly, atropine (1%) TDS, single course of oral ketoconazole (200mg) BD along with oral acetazolamide 250mg TDS and NSAIDS. Patients with impending perforation were advised for TPK and advised for referral when the donor cornea was not available. The patients who refused for referral citing various reasons were planned for TST.

Appropriate counseling was done and informed consent was taken prior to the surgery. TST was performed by injecting local anesthesia (2% xylocaine) in the upper and lower lids. A Silk 4-0 suture was passed perpendicularly through the meibomian gland orifice of the lower lid and with a good tarsal purchase of 5 to 10mm horizontally taken out from another meibomian gland orifice. Same procedure was repeated in the upper lid and the suture was tied together externally with lashes and knots lying outside. The patients were then discharged from the hospital with topical natamycin (5%) 2 hourly, fluconazole (0.30%) 2 hourly, atropine (1%) TDS, single course of oral ketoconazole (200mg) BD along with oral acetazolamide 250mg TDS and NSAIDS and were asked to follow up after 2 weeks. Those cases that presented with loose



or broken sutures on follow up were planned for repeat TST. TST was also continued on the patients who developed corneal perforation on subsequent visits.

Success was defined as the resolution of the infiltrate and maintenance of the structural integrity of the globe. Resolution of the infiltrate was evident by progressive reduction in symptoms, conjunctival congestion, anterior chamber reaction and healing by scarring and epithelization. The patients were called for follow-up after 2 weeks and evaluation for the corneal ulcer was done. As soon as the resolution of the infiltrate and maintenance of the structural integrity of the globe was achieved, the TST was removed and defined as anatomical success. Functional success was defined as VA more than 6/60 after achieving anatomical success. The cases showing worsening of the clinical condition (as assessed by an increase in the size of the infiltrate or corneal sloughing), persistent perforation even after long duration of treatment and development of endophthalmitis or panophthalmitis were considered treatment failures. In cases of perforated corneal ulcer with endophthalmitis not responding to 2 doses of intravitreal injection consisting of ceftazidime (2.25mg /0.1ml), vancomycin (1mg /0.1ml) and voriconazole (100 µg /0.1 ml) were eviscerated.

All data were entered in Microsoft Excel 2013 and analyzed using the Statistical Package for Social Sciences (SPSS) Version 20 software (IBM Corporation). For descriptive analysis mean, standard deviation, proportion,

percentage and various diagrams were calculated / presented. For inferential statistics, parametric and non-parametric tests were carried out to find significant differences among the patients at 95.0% confidence where p value < 0.05 .

RESULTS

During the 18 months' study period, 450 cases were planned for TST out of which 119 patients (26.44%) fulfilling the inclusion and exclusion criteria were included for the study. There were not any cases of both eye involvement.

Mean age of the patients in this study was 51.34 ± 15.56 years (range 20—92 years) with a male-to-female ratio of 2.22:1. Only 3 patients (2.52%) had a VA of more than 6/60, 41 patients (34.45%) had VA between 6/60 to counting finger - close to face (CF-CF) and 75 (63.03%) had hand movement (HM) to perception of light (PL) at first visit. The patients presented to the cornea service 3 to 45 days (mean 19.34 ± 10.62 days) after the onset of symptoms, with only 7.57% of the patients presenting within 1 week. During presentation, 37 (31.09%) patients were on topical antibiotics, 14 (11.76%) patients were on topical antibiotics and antifungal agents and seven patients (5.88%) were on topical antibiotics and steroids. 61 (51.26%) patients were using unknown medicines.

Out of 119 patients, 84 patients (70.60%) developed healing ulcer and 35 (29.40%) developed non-healing ulcer within 2 weeks.

Among 35 non healing cases, 1 patient presented with corneal perforation with endophthalmitis and had to undergo evisceration whereas 34 patients resulted in corneal perforation only and TST with intensive medical therapy was continued as before. After 4 weeks, among these perforated cases 20 (16.80%) developed healing ulcer and only 14 (11.76%) had to undergo evisceration. Altogether 15 patients (12.61%) had to undergo evisceration whereas 87.39% of the patients healed by corneal scarring. Indications for evisceration were total corneal sloughing in 9 (7.56%) patients, corneal perforation with endophthalmitis in 1 (0.84%) patient and choroidal detachment (CD) along with perforation and endophthalmitis in 5 (4.20%) patients. With this data, anatomical success rate was 87.39% which was statistically significant (Pearson chi-square: P=0.001).

In all cases with healed ulcer, 56.30% developed epithelial healing at 2-4 weeks with mean duration of 23.24 ± 12.09 days of TST.

In our study, there were 8 (6.72%) patients with diabetes mellitus (DM) and 2 (1.68%) cases of hypertension (HTN). Among 8 diabetic patients, 6 patients were freshly diagnosed with high blood glucose and 2 patients were diagnosed previously with good glycemic control. Out of 8 patients with co-existing DM, 6 cases (75%) that were freshly diagnosed developed perforation. Among 6 cases of perforation 5 (62.50%) had to undergo evisceration whereas remaining 3 (37.50%) patients had the ulcer resolved resulting in a corneal scar. The two corneal ulcer patients with systemic HTN resolved completely.

VA as shown in figure 1 suggests that most of the patients improved VA by 2 to 3 lines according to Snellen's chart at 3 months. Thus, functional success according to VA more than 6/60 was seen in 32 patients (26.89%). Out of 119 patients who came for follow-up at 3 months, 62 patients (52.10%) had BCVA improved by 2 or more lines, which was statistically significant (P<0.05).

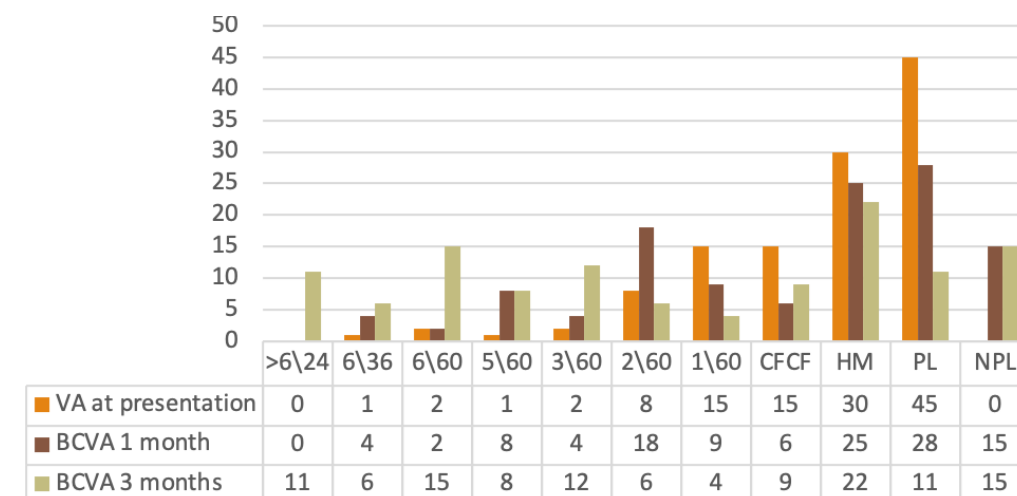


Figure 1: Visual outcomes at 1 month and 3 months.



Among 119 cases of TST, 9 (7.50%) patients had to undergo repeated TST on 1st postoperative day due to premature tarsorrhaphy failure, which occurred due to an improper technique probably due to poor tarsal purchase during suturing. Only 1 (0.80%) patient developed eyelid margin distortion after 1 month. In all of the cases TST had to be repeated every 15 days due to loose or broken sutures. On average, the mean duration of TST was applied for 23.24 ± 12.09 days.

DISCUSSION

Due to the limited efficacy of topical and systemic antifungal agents, medical management is most often inadequate especially in patients with a chronic course of disease or those receiving multiple medications. The occurrence of corneal perforation can be related to a chronic course, delayed management, inappropriate diagnosis and management, and thus surgical intervention is required more frequently (Xie, Dong and Shi, 2001). In our study, we only selected fungal corneal ulcer because fungal ulcers are more prevalent in our region (Puri and Shrestha, 2017; Amatya *et al.*, 2012; Ou and Acharya, 2007). This high prevalence may be due to the agriculture-based lifestyle of the population of this region, which predisposes them to ocular trauma (Upadhyay *et al.*, 2001). The tropical climate of plains may also have contributed to this high prevalence. Another reason could be related to the use of topical corticosteroids, often prescribed by local level health practitioners for red eye (16.6%) before visiting to the hospital (Puri and Shrestha, 2017).

Mean age of the patients in our study was 51.34 ± 15.56 years with the majority of the patients (63.87%) in their fourth to sixth decades of life. This age group is socioeconomically active and morbidity would affect entire families. Sitoula *et al.*, 2015 reported that the mean age of the patients with corneal ulcer to be 44 ± 16 years in their study which was conducted at eastern region of Nepal. Similarly, (Puri and Shrestha, 2017) stated that the majority of their patients (71.20%) belonged to the age group of 26 to 55 years. Numerous studies have reported gender difference in the prevalence of corneal ulcer as males are mostly involved in outdoor activities than females and seek medical services more than females do (Puri and Shrestha, 2017; Amatya *et al.*, 2012). Our finding also suggests a similar trend (M:F = 2.22:1).

In our study, only 3 patients (2.52%) had a VA better than 6/60, 41 patients (34.45%) had VA between 6/60 to CF-CF and 75 (63.03%) had HM to PL at first visit. This is because we selected only cases with central and para-central infiltration. Majority of our cases presented after 2 weeks (mean 19.34 ± 10.62 days) of ocular symptoms. Many patients seek medical care at an advanced stage of the disease when treatment at local clinics has failed. This may be the reason that they usually present late in our hospital.

Only 15 (12.61%) of 119 eyes showed progressive worsening of the infiltrate and failure to preserve the structural integrity of the globe when managed with this modality

and had to undergo evisceration. With this data, the anatomical success rate was 87.39%. This success rate was comparable with other procedures which are described for the management of impending corneal perforation in literature. In a study conducted by (Garg *et al.*, 2003) they performed application of N-Butyl Cyanoacrylate Tissue Adhesive in Fungal Keratitis in which 24.20% cases were diagnosed as treatment failure. In a study of analysis of conjunctival flap surgery in fungal keratitis, total of 3 study patients experienced postsurgical complications of corneal perforation (1 patient) and purulent exudate spreading (2 patients) out of 16 patients. (Nizeyimana *et al.*, 2017) For impending perforation, TPK or lamellar keratoplasty are considered as a standard treatment (Garg *et al.*, 2005). In a study done by (Xie, Dong and Shi, 2001) 4 cases (3.70%) out of 108 underwent enucleation after TPK. Similarly, 5 (4.62%) out of 108 underwent enucleation after TPK conducted in Taiwan by (Chen *et al.*, 2004). Study conducted in Nepal concluded anatomical success rate of 89.50% after TPK. (Bajracharya and Gurung, 2015) Regarding therapeutic success rate of lamellar keratoplasty, in a comparative study between therapeutic deep anterior lamellar keratoplasty (TDALK) and TPK, a success rate of 84.60% was achieved in the TDALK group and 88% in the TPK group out of 26 and 100 patient respectively. Of the 12 eyes with recurrence of infection in the TPK cohort, 9 (9%) developed endophthalmitis with poor outcomes and underwent evisceration (Anshu *et al.*, 2009).

Comparing the results from our study with these standard treatments, TST offers a simple yet effective treatment modality which can be easily recommended due to the relative ease of procedure, high efficacy, cost effectiveness and the ability to delay an otherwise emergent specialized surgical repair.

In our cases, 56.30% developed epithelial healing at 2-4 weeks with mean duration of 23.24 ± 12.09 days of TST. As we compare our study with amniotic membrane graft (AMG), (Solomon *et al.*, 2002) concludes that ocular surface inflammation was markedly reduced with complete epithelialization in 3 weeks, and stable corneal thickness was demonstrated within the first 2 months postoperative.

In our study, 5 out of 8 (62.50%) patients had to undergo evisceration with history of DM, which is high compared to the study (Hongyok and Leelaprute, 2016) done in Thailand where it was 13%. Patients with diabetic keratopathy have impairments of the epithelial basement membrane, epithelial wound healing, epithelial-stromal interactions, endothelial function and corneal nerve functions (Bikbova *et al.*, 2012). These all lead to delayed wound healing and results in severe complications.

In this study, 62 patients (52.10%) had BCVA improved by 2 or more lines with functional success in 32 patients (26.89%). All the patients who were recruited in this study presented with central or paracentral infiltration and the outcome

(87.39%) was a corneal scar at 3 months. In the majority of the patients enrolled in the present study, the aim of TST was to prevent or stop corneal perforation and/or inflammation and to preserve the eyeball, rather than to improve the patient's vision. On the contrary, the improved or unchanged postoperative VA observed in the present study does indicate that TST along with intensive medical therapy was successful even in improving vision.

By postponing definitive surgical procedures such as TPK or lamellar keratoplasty until the inflammation has subsided, the success rate may be promoted. Higher recurrences of infection in corneal grafts after TPK were associated with fungal keratitis, retro-iris and vitreous exudates, and increasing graft size (Chatterjee and Agrawal, 2020). In this regard, TST may be an effective alternative. Even comparing our result with other similar procedures to maintain structural integrity such as tissue adhesives have limited role in large perforation and may need to be reapplied as a result of dislodgment from the ulcer bed because of mechanical disruption or continuous inflammation and tissue destruction in the surrounding stroma (Garg *et al.*, 2003). In case of conjunctival flap to maintain integrity, the conjunctiva covers the entire cornea, it obstructs any view of the anterior chamber, which increases the difficulty of monitoring disease progression. Furthermore, when

patients with short fornices were subjected to the Gunderson's flaps technique, blepharoptosis as a complication of the technique was observed in some cases (Nizeyimana *et al.*, 2017).

The problem noticed with this modality was premature tarsorrhaphy failure probably due to poor tarsal purchase during suturing. As a result, nine (7.50%) cases required repeated TST on the first postoperative day.

CONCLUSION

This study concluded that TST adjunct to medical therapy can be a promising alternative for the treatment of refractory fungal keratitis with good anatomical and functional success. In relation with time to epithelial healing, most of the cases healed within 1 month, which is comparatively shorter in relation to the chronic course of the disease. With only single case of lid margin distortion as a complication of this procedure, TST in impending corneal ulcer perforation is of paramount importance in those countries in which there is a shortage of corneal donors, low socio economic condition of patients and where corneal ulcer is very prevalent such as in developing countries like Nepal .



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