COMPARATIVE EVALUATION OF CONVENTIONAL MEDICAL TREATMENT ALONE VERSUS CONVENTIONAL MEDICAL TREATMENT WITH AMNIOTIC MEMBRANE TRANSPLANTATION IN INFECTIVE CORNEAL ULCER

Muhammad Naeem[1], Mushtaq Ahmad[2], Hina Mehwish Khan[3], Mohammad Naeem Khan[4]

[1-4] Department of Ophthalmology, Hayatabad Medical Complex, Peshawar - Pakistan.
Address for correspondence:
Dr. Muhammad Naeem Khan
Department of Ophthalmology, Hayatabad Medical Complex, Peshawar - Pakistan.
E-mail: drnaeemps@yahoo.com
Date Received:
May 08, 2013
Date Revised:
March 30, 2014
Date Accepted:
March 31, 2014

ABSTRACT

Objective: To compare the effect of amniotic membrane transplantation along with conventional therapy and the conventional therapy alone for the treatment of infective corneal ulcer.

Methodology: This study was conducted at Ophthalmology Department, Hayatabad Medical Complex Peshawar. The duration of study was 6 months, i.e., from April 2010 to October 2010, in which a total of 68 patients were included using WHO software for sample size determination. They were divided into two equal groups of 34 each. Non probability purposive sampling technique was used.

Results: In this study, mean age was 50±0.24 years. Forty six (67.6%) patients were male while 32.4% (n=22) patients were female. Conventional Medical Treatment alone was effective in 87% (n=30) cases while Conventional Medical Treatment with Amniotic Membrane was effective in 96% (n=33) cases with a p-value of 0.03.

Conclusion: This study showed encouraging results of amniotic membrane transplantation along with conventional treatment in corneal ulcer in improving both symptoms and signs.

Key Words: Corneal ulcer, Conventional medical treatment, Amniotic membrane transplantation (AMT).

This article may be cited as: **Naeem M, Ahmad M, Khan HM, Khan MN. Comparative evaluation of conventional medical treatment alone versus conventional medical treatment with amniotic membrane transplantation in infective corneal ulcer. J Postgrad Med Inst 2014; 28(2):206-10.**

INTRODUCTION

Corneal ulcer continues to be sight threatening disease and may lead to permanent corneal opacity or persistent epithelial defect. In spite of intensive antibiotic treatment, corneal damage can occur as a result of keratolytic and inflammatory process caused by infection or scarring and of neovascularisation relating to the healing process[1]. The ophthalmic literature describes a multitude of surgical procedures for corneal reconstruction. Recently, preserved human amniotic membrane has emerged as a useful tool in the reconstruction of the ocular surface disorders[2].

Amniotic membrane transplantation (AMT) in ocular surgery has become wide spread and the number of clinical situation in which it has been applied has rapidly expanded[3, 4]. Much has been published on its use in persistent epithelial defect and corneal perforation[5], limbal stem cell deficiency, conjunctival reconstruction following excision of neoplasia[6], and for reformation of fornices as well as in acute ocular burns[7]. There are only few randomized control clinical trials evaluating the effectiveness of amniotic membrane for ptergium surgery, acute ocular burns and neurotrophic ulcers[8,9]. Certain characteristics like anti-inflammatory, antiangiogenic, antiinfective, antifibroblastic activities make the amniotic membrane ideal for application in ocular surface disorders[2]. When amniotic membrane acts as a graft with epithelium growing on it, amniotic tissues persist and integrate with the superficial corneal stroma[10]. Sudesh et al reported significant relative improvement in symptoms like pain in two groups, improvement was 24% in patients without AMT and it was 48% in patients with AMT. Similarly improvement in signs like corneal ulcer size was in 10% patients without AMT and it was 35.2% in patients with AMT[11].

All the characteristics of amniotic membrane e.g. anti-inflammatory, anti-angiogenic, anti-infective and anti-fibroblastic are useful in corneal ulcer healing. When amniotic membrane is used in the management of corneal epithelial defects in the presence of intact limbus, complete re-epithelialization is readily achieved[12]. Limited data is available regarding AMT along with conventional medical treatment of corneal ulcer in our region. Therefore, this study was designed to compare the efficacy of AMT in addition to conventional therapy and conventional therapy alone in patients with infective corneal ulcer presenting to Ophthalmology Department Hayatabad Medical Complex Peshawar.

METHODOLOGY

This study was conducted at Ophthalmology Department Hayatabad Medical Complex Peshawar. Duration of study was 6 months (from 26th April 2010 to 26th October 2010) in which a total of 68 patients were included and were divided into two equal groups (Group A: Conventional Medical Treatment alone and Group B: Conventional Medical Treatment with Amniotic Membrane Transplantation). Non probability purposive sampling technique was used in this comparative study.

All patients age 15 years and above with infective corneal ulcer of 3 mm or more were included in the study. Patients with typical viral ulcer (because non availability of diagnostic methods for viruses), perforated corneal ulcer (due to their different management plan) and ulcers with endophthalmitis (as management of such cases can affect the conventional medical treatment) were excluded from the study.

The study was approved by the ethical committee of Hayatabad Medical Complex Peshawar. Patients who fulfilled the inclusion criteria were enrolled in the study after taking informed written consent. Detailed history of ocular pain, watering and discharge was taken followed by ocular examination in all the patients. Ocular examination included visual acuity testing on Snellen's chart and thorough slit lamp examination of conjunctiva, cornea, anterior chamber, iris, pupil, and lens. Ulcers were diagnose by slit lamp examination after staining with flouresin and confirmed by scrapings. Patients were divided into two equal groups randomly by lottery method. One group received medical treatment with AMT and another group received Medical treatment alone. Ulcer size score was noted at 3rd and 42nd post-operative days. Data was analyzed by SPSS 10.0. Mean and standard deviation was calculated for quantitative variables like age. Frequency and percentage was calculated for qualitative variables like gender and size of ulcers. Student Chi square test was used to compare the reduction of ulcer size between age and gender. P value of ≤ 0.05 was considered significant.

RESULTS

Among 68 patients, 6(9%) were of less than 20 years, 10(15%) were in age range 21-30 years, 14(20%) were in age range 31-40 years, 18(26%) were in age range 41-50 years, and 20(30%) were in age range 51-60 years, respectively. The mean age of the sample was 50 ± 0.24 years. Forty six (67.6%) patients were males while 22 (32.4%) patients were females.

Pre-operative and post-operative observations of corneal ulcer size between two groups i.e., Conventional Medical Treatment alone (Group A) and Conventional Medical Treatment with Amniotic Membrane Transplantation (Group B) respectively, is shown in Table 1.

The treatment of corneal ulcer with Conventional Medical Treatment alone was effective in 30 (87%) cases (Table 2). In these 30 patients, two were of less than 20 years age, 4 were in the age range 21-30 years, 6 were in the age range 31-40 years, 9 were in the age range 41-50 years and 9 were in the age range 51-60 years. There were 18 males and 12 females.

Treatment with Conventional Medical Treatment with Amniotic Membrane Transplantation was effective in 33 (96%) cases (Table 2). Out of these 33 patients, two were of less than 20 years age, 4 were in the age range 21-30 years, 6 were in the age range 31-40 years, 10 were in the age range 41-50 years and 11 were in the age range 51-60 years. There were 20 males and 13 females.

DISCUSSION

Corneal ulcer is more common in males as is evident by various studies. Basak et al[13] in their study reported 70.6% males and 29.4% females. In another study by Srinivasan et al[14], 61.3% were males and 38.7% were females. In our study also there were 68% males and only 32% females. Males get corneal infection more commonly because they usually work in the fields where chances of corneal trauma are more. Predisposing risk factors for microbial keratitis vary tremendously with geographical location. Non-surgical trauma to the eye accounted for 48.6–65.4% of all corneal ulcers in the developing countries like Nepal[15] and India[14]. In the United States it is contact lens wearing that is a major risk factor for microbial keratitis. In our study, history of injury to the cornea was present in 52% patients. The most common mode of injury (30%) was organic matter. Basak et al[13] found history of injury to cornea in 82.9% of patients, with vegetative matter being the most common mode of injury, present in 59.6% of patients. In another study by Srinivasan et al[14] injury to the cornea was

Table 1: Observations of corneal ulcer size (n=68)

	Pre-operative corneal ulcer size (mm)*			Post-operative corneal ulcer size (mm)									
				Day 01**			Day 03***			Day 42****			
	3-5	6-8	>8	3-5	6-8	>8	3-5	6-8	>8	<3	3-5	6-8	>8
Group A (n=34)	21(61.8%)	12(35.3%)	1(2.9%)	21(61.8%)	12(35.3%)	1(2.9%)	23(67.7%)	10(29.4%)	1(2.9%)	30(88.2%)	4(11.8%)	0	0
Group B (n=34)	19(55.9%)	12(35.3%)	3(8.8%)	19(55.9%)	12(35.3%)	3(8.8%)	24(70.6%)	9(26.5%)	1(2.9%)	33(97.1%)	1(2.9%)	0	0
Total	40	24	4	40	24	4	27	19	2	63	5	0	0

Group A: Conventional Medical Treatment alone
Group B: Conventional Medical Treatment with Aminotic Membrane Transplantation
P Value: 0.00*, 0.00**, 0.01***, 0.03****

Table 2: Effectiveness of corneal ulcer between two groups (n=68)

Effectiveness Of Corneal Ulcer	Groups		Total
	Group A	Group B	
Yes	30(88.2%)	33(97.1%)	63
No	4(11.8%)	1(2.9%)	5
Total	34	34	68

Group A: Conventional Medical Treatment alone
Group B: Conventional Medical Treatment with Amniotic Membrane Transplantation
Chi square test was applied in which P value was 0.03

present in 65.4% patients, with injury from paddy 25.4% being the most common followed by vegetative matter 15.1%. In our study, fungal corneal ulcers were the commonest amongst all types of ulcers which is similar to study reported by Basak et al[13] in which 59.3% patients were having fungal infection. In another study by Leck et al[16] fungi were identified as the principal etiological agents causing corneal ulceration in 44% of all cases in Ghana.

In various studies, amniotic membrane has been found to provide symptomatic relief in various forms of ocular surface disorders. Pires et al performed AMT in 50 consecutive eyes with symptomatic bullous keratopathy and found that 43(90%) of eyes became free of pain postoperatively. Epithelial defect healed rapidly in 45 out of 50 (90%) eyes within 3 weeks[17]. Heiligenhaus et al studied retrospective, non-comparative case series of seven patients with acute ulcerative and necrotizing herpetic stromal keratitis[18]. Single or multilayer AMT with epithelial side facing up was performed. The main outcome measures were wound healing of the corneal ulcers and decrease of stromal inflammation[18]. In our study, there was definite improvement in symptoms like ulcer size with amniotic membrane transplantation as compared to patients not undergoing AMT. In our study, signs of infective corneal ulcers improved more in patients with amniotic membrane transplantation as compared to the control group.

In our study 1 (5%) patient without AMT and 6 (30%) patients with AMT were having hypopyon of more than 3 mm. After 1 week, hypopyon of more than 3 mm was still present in 1 (5%) of the patient without AMT while in patients with AMT, only 2 (10%) patients had hypopyon more than 3 mm. After 1 week, the improvement in hypopyon was significantly more in patients with amniotic membrane transplantation. The results of this study indirectly indicate that the actions of anti-bacterial and anti-fungal drugs were not hampered by amniotic membrane. Topical drugs might have reached the cornea through the amniotic membrane itself or entered from the gap between the sutures of amniotic membrane. Kim et al[19] evaluated penetration and drug levels in tears after topical ofloxacin instillation in rabbit eyes with AMT. The mean tear levels of ofloxacin in AMT group were higher than those in non-AMT group. So he concluded that amniotic membrane has some potential to act as an effective drug delivery system. Faster healing of ulcers with amniotic membrane transplantation

might be because of anti-inflammatory, anti-angiogenic, anti-infective and anti-fibroblastic activity of amniotic membrane[15]. The above discussion, compared with the results of our study clearly demonstrates that amniotic membrane transplantation is beneficial in infective corneal ulcers. Combined with conventional treatment, it can be used as a treatment modality in cases of moderate size ulcers, and as a temporary measure for symptomatic relief in severe ulcers.

LIMITATION

Effectiveness of corneal ulcer size was based on relief of symptoms and the answers were taken as Yes and No. However, we understand that this may not be sufficient and should be considered as a limitation of this study.

CONCLUSION

This study showed encouraging results of amniotic membrane transplantation along with conventional treatment in corneal ulcer in improving both symptoms and signs, but small size of sample was the limiting factor in our study. Hence large prospective and controlled trials with more number of patients are required for better assessment of role of amniotic membrane transplantation in addition to conventional medical treatment in patients with corneal ulcer.

REFERENCES

1. Nordlund ML, Pepose JS. Corneal response to infection. Krachmer JH Mannis MJ Holland EJ eds. Cornea, Fundamentals, Diagnosis and Management. Mcra hill 2005;95-114.
2. Dua HS, Gomes JAP, King AJ, Maharajan VS. The amniotic membrane in ophthalmology. Surv Ophthalmol 2004;49:51-77
3. Wylegala E, Taranawska D. Amniotic membrane transplantation with cauterization for keratoconus complicated by persistent hydrops in mentally retarded patients. Ophthalmol 2006;113:561-4.
4. Ainsworth G, Rotchford A, Dua HS. A novel use of amniotic membrane in the management of tube exposure following glaucoma tube shunt surgery. Br J Ophthalmol 2006;90:417-9.
5. Hick S, Demers PE, Brunette I. Amniotic membrane transplantation and fibring glue in the management of corneal ulcers and perforations: a review of 33 cases. Cornea 2005;24:369-77.
6. Gunduz K, Ucakhan OO, Kanpolat A. Nonpreserved human amniotic membrane transplantation for conjunctival reconstruction other excision of extensive ocular surface neoplasia. Eye 2005;20:351-7.
7. Tseng SC, Di Pascuale MA, Liu Dt. Intraoperative mitomycin C and amniotic membrane transplantation for fornix reconstruction in sever cicatricial ocular surface diseases. Ophthalmol 2005;112:896-903.
8. Tamhane A, Vajpayee RB, Biswas NR. Evaluation of amniotic membrane transplantation as an adjunct to medical therapy as compared with medical therapy alone in acute ocular burns. Ophthalmol 2005;112:1963-9.
9. Khokar S, Natung T, Sony P. Amniotic membrane transplantation in refractory neurotrophic corneal ulcers: a randomized controlled clinical trial. Cornea 2005;24:654-60.
10. Resch MD, Schlotzer-Schrehardt U, Hofmann-Rummelt C. Adhesion structures of amniotic membranes integrated into human corneas.Invest Ophthalmol Vis Sci 2006;47:1853-61.
11. Arya SK, Aggarwal M, Chander J, Sonika, Sood S. Comparative evaluation of amniotic membrane transplantation with conventional medical treatment verses conventional medical treatment alone in suppurative keratitis. Internet J Ophathalmol Vis Sci 2009;6:6-10.
12. Maharajan VS, Shanmuganathan V, Currie A, Hopkinson A, Powell-Richards A, Dua HS. Amniotic membrane transplantation for ocular surface reconstruction: indications and outcomes. Clin Exp Ophthalmol 2007; 35:140-7.
13. Basak SK, Basak S, Mohanta A, Bhowmick A. Epidemiological and microbiological diagnosis of suppurative keratitis in Gangetic West Bengal, eastern India. Indian J Ophthalmol 2005;53:17-22.
14. Srinivasan M, Gonzales CA, George C, Cevallos V, Mascarenhas JM, Asokan B et al. Epidemiology and aetiological diagnosis of corneal ulceration in Madurai, South India. Br J Ophthalmol 1997;81:965-71.
15. Upadhyay MP, Karmacharya PC, Koirala S, Shah DN, Shakya S, Shrestha JK, et al. The Bhaktapur eye study: ocular trauma and antibiotic prophylaxis for the prevention of corneal ulceration in Nepal. Br J Ophthalmol 2001;85:388-92.
16. Leck AK, Thomas PA, Hagan M, Kaliamurthy J, Ackuaku E, John M. Aetiology of suppurative corneal ulcers in Ghana and South India, and epidemiology of fungal keratitis. Br J Ophthalmol 2002;86:1211-5.
17. Pires RT, Tseng SC, Prabhasawat P, Puangsricharern V, Malskin SL, Kim JC, et al. Amniotic membrane transplantation for symptomatic bullous keratopathy. Arch Ophthalmol 1999;117:1291-7.
18. Heiligenhaus A, Li H, Hernandez Galindo EE, Koch JM, Steuhl KP, Meller D. Management of acute ulcerative

and necrotising Herpes simplex and zoster keratitis with amniotic membrane transplantation. Br J Ophthalmol 2003;87:1215-9.

19. Kim H, Sah W, Kim Y, Kim J, Hahn T. Amniotic membrane, tear film, corneal and aqueous level of ofloxacin in rabbit eyes after amniotic membrane transplantation. Cornea 2001;20:628-4.

CONTRIBUTORS

MN concieved the study and wrote the manuscript. MA, HMK and MNK did data analaysis, drafted and revised the manuscript. All authors contributed significantly to the final manuscript.