

Original Article

Treatment of Recurrent Corneal Epithelial Defect by Autologous Serum Eye Drop

Hossein Mohammad Rabei¹, Ghazal Norouzi¹, Kouroshe Sheibani^{2*}

¹ Imam Hossein Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

² Basir Eye Safety Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Background: The aim of the present study was to evaluate the efficacy of autologous serum eye drop in treatment of recurrent corneal epithelial defect.

Materials and Methods: Fourteen patients with recurrent corneal epithelial defect were studied. Autologous serum was prepared from the patients and diluted in 20% normal saline. The patients were instructed to use the autologous serum every six hours. Patients were followed for a mean period of 18 months.

Results: Four males (28.6%) and 10 females (71.4%) entered the study. Four patients stopped the treatment after three months with complete satisfaction from treatment. Patients reported a reduction in frequency and severity of attacks 4.6±2 weeks after the start of treatment. The mean number of attacks before the procedure was 7.6±0.9 per year which was reduced to 2.2±0.9 per year after treatment ($p<0.001$). The main side effects in patients were eye pruritus and redness which were well tolerated by patients.

Conclusion: Autologous serum application seems to be a safe and effective method to treat recurrent corneal epithelial defect.

Keywords: Autologous serum, cornea, epithelium, recurrent

*Corresponding Author: Kouroshe Sheibani. Basir Eye Safety Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: sh_kouroshe@hotmail.com

Please cite this article as: Rabei HM, Norouzi Gh, Sheibani K. Treatment of Recurrent Corneal Epithelial Defect by Autologous Serum Eye Drop. *Novel Biomed.* 2015;3(1):30-2.

Introduction

Recurrent corneal epithelial defect is a relatively common disease often starting with an epithelial scratch or in a person with primary epithelial basement membrane dystrophy, and causes recurrent epithelial defects¹. It causes pain, foreign body sensation and redness of the eyes¹. The interval between the episodes of recurrent corneal epithelial defect might be a few days or a few years². These attacks in most people are mild and occur with long intervals, so the patient does not see an ophthalmologist and the epithelial defect heals itself but some patients experience more frequent or more

severe episodes which cause them to seek treatment. The usual treatments in acute phase are antibiotic drops, contact lens and hypertonic (%5) saline eye drop which might be used for months². These treatments usually affect but a few patients still show recurrence despite above mentioned treatments. Autologous serum drops have been used to treat refractory corneal epithelial defect in various diseases³⁻⁸. Autologous serum contains vitamins A, epithelial growth factor, fibronectin and transforming growth factor- β , which are all important factors in the proliferation and migration of corneal epithelial cells^{3,4}. The present study was designed to investigate

the use of autologous serum in treatment of recurrent corneal epithelial defect in this group of patients.

Methods

In this prospective study 14 patients with recurrent corneal epithelial defect which was not responding to conventional treatments underwent treatment using autologous serum. Informed consent was provided by patient and the study was approved by ethic committee of Shahid Beheshti University of Medical Sciences. All patients had baseline corneal epithelial defects at the start of study and had at least three recurrence episodes in 6 months prior to entering the study. None of the patients had clear signs of corneal epithelial basement membrane dystrophy or other corneal dystrophies. We excluded patients with dry eye and any evidence of Meibomian gland dysfunction.

From each patient 10cc of whole blood was taken and was kept at room temperature until clot formation was complete. Then it was centrifuged for ten minutes. Serum was taken and after filtering was diluted to %20 using normal saline. The resulting solution was poured in 5cc bottles and was stored at -20 degrees centigrade. Freezed bottles were given to patients and patients were instructed to move one bottle to 4 degrees centigrade part of their refrigerator and wait for it to thaw before usage. Patients were instructed to use the drops every six hours for at least three months after all their symptoms were subsided. Patients also received Chloramphenicol eye drops every 6 hours and NaCl 5% eye ointment every night. Autologous serum was prescribed one drop every 6 hours. Patients were examined daily until the epithelial defect improved. After the epithelial defect healed the Chloramphenicol eye drop was stopped but NaCl 5% eye ointment and autologous serum drop were continued for at least 3 months after healing. Patients were followed for an average of 18 months (12 to 24 months) after the start of treatment.

Results

Fourteen patients with a mean age of 35 ± 10.3 years (median: 32 years, range 58-25 years) were enrolled in this study. Four patients (28.6%) were male and 10

patients (71.4%) were female.

A history of corneal abrasion by an object or nail scratch was present in 11 patients (78.6%).

Patients were treated for on average of 4 months with autologous serum. Patients were followed for an average of 18.7 ± 4.7 months. Four patients discontinued the treatment after 3 months with near complete subside of their symptoms.

In average after 2 ± 4.6 weeks of treatment, patients reported a reduction of the severity and frequency of attacks. Complications during treatment were red and itchy eyes, in three patients (21.4%) and one patient (7.1%), respectively. Another three patients (21.4%) showed both symptoms. Severity of complications in patients with intolerance to treatment was not enough to create a group as intolerance to treatment.

Discussion

The classic treatment for recurrent corneal epithelial defect is helpful in most patients but a small percentage of patients are still suffering from the disease attacks despite prophylactic treatments.

Uses of autologous serum drops in treatment of persistent defects of the corneal epithelium has been investigated in various studies³⁻⁸, but based on our knowledge use of autologous serum drops to treat recurrent epithelial defect has not been previously studied in Iran. Fourteen patients in our study had corneal epithelial defects but the epithelial defect was not stable. Patients were chosen to be treated with this method because of frequent and severe attacks and no response to treatment using usual methods.

Serum contains a number of biological factors that can affect the healing process. For example, serum contains factors that stimulate epithelial mitosis such as: substance P^{9,10}, extracellular matrix components such as; fibronectin, growth factors for the onset of epithelial cell migration (like; transforming growth factor β , epithelial growth factor) and growth factors stimulating epithelial cells in mitosis (EGF); protease inhibitors and anti-apoptosis factors¹¹. It is not fully known how each of these factors accelerate epithelial repair, but on the whole, these factors facilitate the healing of epithelial defects¹².

Studies have indicated the gelatinase (matrix metalloprotease 2 and 9 enzymes) activity in corneal epithelium of recurrent epithelial defect is higher than

average¹³. Gelatinase has a negative effect on the basal epithelial cell repair by breaking different types of collagen such as; X, VII, V and IV. Metalloproteinase family enzymes influence negatively on adhesion molecules (like fibronectin and Laminin) which create adhesion between cells in the basal layer of epithelium and basement membrane¹³. Totally, these factors weaken the binding of epithelial cells to the basement membrane. In our study, autologous serum usage reduced the incidence of recurrent attacks which was probably because of strengthening of connections between the epithelial cells and basement membrane.

A complication during treatment was eye redness and itching which did not lead to treatment rejection by the patient. According to the results obtained from our study it might be possible to use autologous serum as a replacement therapy in patients with recurrent epithelial defect.

The low number of samples and lack of a control group are some deficiencies of the present study and to reach more reliable results double blind controlled randomized trials are suggested.

Conclusion

Autologous serum application seems to be a safe and effective method to treat recurrent corneal epithelial defect.

References

1. Fraunfelder FW, Cabezas M. Treatment of recurrent corneal erosion by extended-wear bandage contact lens. *Cornea*. 2011;30(2):164-6.
2. Ewald M, Hammersmith KM. Review of diagnosis and management of recurrent erosion syndrome. *Curr Opin Ophthalmol*. 2009;20(4):287-91.
3. Tsubota K, Goto E, Fujita H, Ono M, Inoue H, Saito I et al. Treatment of dry eye by autologous serum application in sjogren,s syndrome. *Br Ophthalmol*. 1999;83:390-5.
4. Matsumoto Y, Dogru M, Goto E, Ohashi Y, Kojima T, Ishida R, Tsubota K. Autologous serum application in the treatment of neurotrophic keratopathy. *Ophthalmology*. 2004;111(6):1115-20.
5. Ogawa Y, Okamoto S, Mori T, Yamada M, Mashima Y, Watanbe R et al. Autologous serum application in the treatment of severe dry eye in patients with chronic graft- versus- host disease. *Bone Marrow Transplant*. 2003;31(7):579-83.
6. Van Setten GB, Viinikka L, Tervo T, Pesonen K, Tarkkanen A, Perheentupa J et al. Epidermal growth factor is a constant component of normal human tear fluid. Graefe,s Arch Clin component Exp Ophthalmol. 1989;227:184- 7.
7. Tsubota K, Goto E, Shimmura S, Shimazaki J. Treatment of persistent corneal epithelial defect by autologous serum application. *Ophthalmology*. 1999;106:1984-9.
8. Poon AC, Geerling G, Dart JK, Fraenkel GE, Daniels JT. Autologous serum eyedrops for dry eyes and epithelial defects: clinical and in vitro toxicity studies. *Br Ophthalmol*. 2001;85:1188-97.
9. Sato Y, Katajira F, Inous S, et al. Efectes of sho-hange-kabukuryo- to and Nichin- to on levels of calcitonin gene- related peptide and levels of calcitonin gene- related peptide and substance P in human plasma. *Biol Bull*. 2004;27:2032- 4.
10. Nagano T, Nakamura M, Nakata K, et al. Effects of substance P and IGF- 1 in corneal epithelial barrier function and wound healing epithelial barrier function and wond healing in a rat model of neurotrophic keratopathy. *Invest Ophthalmol Vis Sic*. 2003;44: 3810-5.
11. Higuchi A, Shimmura S, Takeuchi T, et al. Elucidation of apoptosis induced by serum deprivation in cultured conjunctival epithelial cells. *Br J Ophthalmol*. 2006;90:760-4.
12. Pflugfelder SC. Is autologous serum a tonic for the ailing corneal epithelium? *Am J Ophthalmol*. 2006;142:316-7.
13. Reidy JJ, Paulus MP, Gona S. Recurrent erosions of the cornea: epidemiology and treatment. *Cornea*. 2000;19(6):767-71.