Regression of Corneal Vascularization by Laser Treatment

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Correspondence to: Muhammad Nasir Bhatti D-232, block-4 Near Sultani Darbar F.B Area Karachi. **Purpose:** To see the regression of corneal vascularization after ablation with frequency doubled Nd: YAG (532 nm) laser photocoagulation.

Material and Methods: The study was conducted in the Department of Ophthalmology, Isra Postgraduate Institute of Ophthalmology, Al-Ibrahim Eye Hospital, Karachi; from June 2006 to May 2007. In this study evaluation of 50 eyes of 50 patients fulfilling the inclusion criteria. Prelaser assessment-comprised of detailed history, general and ocular examination including anterior segment examination with corneal vascularization measurements. After informed consent, all patients underwent frequency doubled Nd: YAG laser photocoagulation for corneal vascularization. Patients were followed after one week and monthly for three months. Patency of vessels and complications were noted. Final result at the end of three months was recorded (as per proforma).

Result: Total 194 vessels were seen in 50 eyes of 50 patients. Out of 194 vessels, 80 (41.2%) vessels were completely occluded and 114 (58.8%) vessels were recanalized (p-Value < 0.05). Hence, there was 41.2% reduction in corneal vascularization.

Received for publication May' 2009 **Conclusion:** Frequency doubled Nd: YAG (532 nm) laser is an effective tool for the reduction of vascularization in quiescent eyes with vascularised corneal opacities.

ornea provides the outermost layer of eyeball along with sclera¹. It is transparent and avascular, being devoid of both blood and lymphatic vessels². Preservation of transparency is mandatory for corneal functioning3. Corneal vascularization may interfere with corneal transparency, resulting in reduction in visual acuity. It also increases the risk of graft rejection⁴. Due to its grave effects on cornea, various methods have been investigated for controlling or limiting the corneal vascularization. These include medical treatments; such as, topical steroids5, nonsteroidal anti-inflammatory drugs6 and cyclosporin A7. Radiation, diathermy8 and conjuncttival resection are some of invasive treatments that have also been investigated. Laser photocoagulation of corneal vascularization in humans was first reported in early 1970s9. Since then laser photocoagulation of the corneal vessels has been found to be an effective

alternate to above methods with lack of serious complications. This study was undertaken to see the regression of corneal vascularization after ablation with frequency doubled Nd: YAG (532 nm) laser photocoagulation and formulating recommendations for its application in clinical practice as well as future research.

MATERIAL AND METHODS

This study was conducted at Isra Postgraduate Institute of Ophthalmology, Al-Ibrahim Eye Hospital, Malir, Karachi, from June 2006 to May 2007. There were 50 consecutive patients of age 10 to 70 years with quiescent corneal vascularization having feeder vessels of 2 mm or more in length from limbus. Patients with active inflammation of the ocular surface, and history of herpes simplex keratitis of less than three months duration in same eye were excluded. We also excluded the patients with history of diabetes mellitus, hypertension and any other comorbid conditions. Detailed medical and ocular history was taken. History regarding previous treatment of corneal vascularization with laser, systemic steroids, and immunosuppression was also noted. Slit lamp biomicroscopy was done. Number of feeder corneal vessels was recorded by counting the number of red lines of 2 mm or more in length from limbus. Informed consent regarding the procedure and its complications was taken. All data were recorded in a predesigned proforma. Proparacine 1% eve drop was used to induce topical anesthesia. Frequency doubled Nd: YAG laser (532 nm) was used at laser settings of 50 micron spot size, 0.1 second exposure time and power varying between 250 and 550 mW. After positioning of the patient in the slit lamp and the laser beam focused on the feeder vessel, laser shots were applied until blanching of the vessel occured. Each feeder vessel was treated individually. The patients were prescribed topical lubricants four times daily as a placebo for one week following laser treatment. Patients were followed after one week and monthly for three months. At each follow up, complete ocular examination was performed with special emphasis on the number of occluded and recanalized vessels. Patency of the vessels was assessed by observing the flow of blood through corneal vessels. No intervention was done and no additional treatment was given. Data analysis was done by SPSS 10.0 version. Frequencies and percentages were calculated for all qualitative variables, i.e. gender, age groups, causes of corneal vascularization, complications of laser photocoagulation and number of feeder vessels. Mean±SD was computed for age. Sign test was applied to the feeder blood vessels before and after frequency Nd: YAG laser at 5% level of significance.

RESULTS

Out of 50 corneal vascularization patients, 33 (66%) were males and 17 (34%) were females (M: F = 1.94: 1). Age range of patients was 10–70 years, mean \pm SD 38.58 \pm 17.5 years. Most of the patients 16 (32%) belonged to the age group 25–39 years, 11 (22%) patients belonged to the age group 10–24 years, 10 (20%) were between 40–54 years and 13 (26%) were between 55–70 years.

Out of 50 patients, 25 (50%) patients were presented with infective keratitis, 16 (32%) were presented with trauma and in 3 (6%) patients aphakic

bullous keratopathy was the cause of corneal vascularization. Other causes accounted for 18% cases including aphakic bullous keratopathy, dry eye, keratoconus and vernal keratoconjunctivitis (Table 1).

Table 1: Distribution according to the causes of
corneal vascularization n=50

Causes	No. of Patients n (%)
Infective Keratitis	25 (50)
Trauma	16 (32)
Aphakic Bullous Keratopathy	3 (6)
Dry Eye	2 (4)
Keratoconus	2 (4)
Vernal Keratoconjunctivitis	2 (4)

Corneal vessels were treated in all 50 patients and total 194 vessels were seen in all patients. Out of 194 vessels, 80 (41.2%) vessels were occluded and 114 (58.8%) vessels were recanalized (p-Value < 0.05). Hence, there was 41.2% reduction in corneal vascularization (Fig. 1).

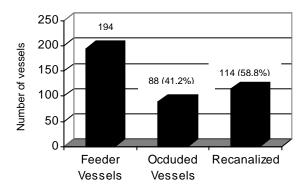


Fig. 1: Sequential changes in lasered vessels n = 50

Post laser results at the end of three months (p-Value < 0.05)

Out of 50 cases, laser photocoagulation was performed in right affected eye in 30 (60%) patients and in left affected eye in 20 (40%) patients.

Out of 50 patients, post laser complications were seen in 20 (40%) patients; corneal haemorrhage occurred in 12 (24%) patients and iris damage in 8 (16%) patients (Fig. 2).

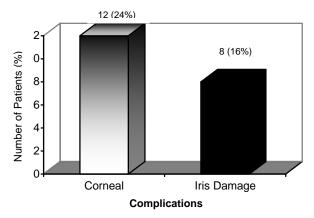


Fig. 2: Complication of laser photocoagulation n=50

DISCUSSION

Corneal neovascularization is a sight-threatening condition that is associated with corneal graft rejection ¹⁰, infections¹¹⁻¹³ contact lens wear¹⁴, metabolic disorders and nutritional deficiency states. Persistent corneal vascularization is undesirable for various reasons. It is a major risk factor for corneal graft survival¹⁵. Apart from graft rejection, vascularization can cause edema, scarring, and lipid keratopathy leading to decrease in visual acuity. The advantages and disadvantages of corneal vascularization have long been recognized. The need to treat corneal opacification, recurrent immune-mediated inflamma-tion and reduced vision has always been felt, and various methods to occlude corneal vessels have been developed and used over years.

In our study, 50 patients were included. The gender distribution (66 % males against 34% females) shows a male preponderance. Most of our patients 16 (32%) belonged to age group of 25-39 years.

In our study, there was 41.2% reduction in corneal vascularization. It is comparable to Sharma and Samal¹⁶ who reported a reduction of 54.15% in corneal vascularization at three months follow-up. Their study included 30 eyes (30 cases). The reason for higher success rate in their study is that Sharma A and Samal A used topical betamethasone 0.1% drops twice daily for one week after laser therapy. This had an additional vasoablative effect¹⁷. Sheppard JD Jr and Epstein RJ¹⁸ reported 7 patients for corneal neovascularization treated with argon laser (514 nm)

using dihematoporphyrin ether (DHE). They reported 52.5% reduction in corneal neovascularization at 6 months follow-up. In comparison to our study Sheppard used DHE as photosensitizer in addition to laser therapy. DHE helps in better visualization and photocoagulation of corneal neovascularization. Nirankari VS¹⁹ has reported a reduction of 45.3% in corneal vascularization at 4 months follow-up. His study included 13 eyes (13 cases).

Regarding complications, the most obvious complication of laser therapy is iris damage. In our study 8 (16%) patients had iris damage. Iris damage in our study is comparable to Epstein RJ and Hendricks RL²⁰ who reported iris damage in 18% cases. Marsh RJ²¹ reported iris damage as minor complication. In our study iris damage was associated with slight peaking of pupil in the direction of damaged iris patch. Iris excavation and peaking of pupil were almost imperceptible after six to eight weeks. Corneal hemorrhage was seen in 12 (24%) of our patients. Sharma¹⁶ reported corneal haemorrhage in his 26% patients. Marsh RJ²¹ also documented corneal haemorrhage. Corneal haemorrhage was resolved in 2 weeks in all our patients. This resolution of haemorrhage occurred without any consequence and no treatment was required. Corneal thinning, descemetocele, corneal perforation and crystalline deposits on iris are other complications documented in literature²². In our patients no such complications were observed following laser treatment.

An important and encouraging finding which we observed during our study was improvement in visual acuity. Although, visual acuity notation was not included in our study, but it was performed as a part of routine follow-up. Two of our patients with best corrected visual acuity of less than 4/60 improved to the best corrected visual acuity of 6/24 at the end of three months. In these cases, secondary lipid keratopathy was the cause of decreased vision. After ablation of corneal vessels, lipid exudation partially resolved resulting in increase in corneal transparency and visual acuity improvement subsequently. There are few reports of visual acuity improvement documented in literature²³.

Three of our lasered patients underwent penetrating keratoplasty. All of them had clear grafts and no recurrence of corneal vascularization was observed till now. One complication which occurred in all three patients was the epithelial defect. It is usually present in most cases of penetrating keratoplasty that have been done at our hospital and it takes about a week to heal. But in our patients, it took 2-3 weeks to heal. This may be related to extensive laser which probably damaged limbal stem cells at the site of corneal blood vessel ablation.

In the light of current research, following recommendations about laser photocoagulation of corneal blood vessels will help in future research as well as in clinical practice. Laser treatment of corneal vascularization is not indicated in presence of active or recurrent inflammation. Therefore, the corneal lesion which is stimulating the vascularization, should be suppressed first with appropriate treatment. Anterior segment angiography should be done before or at the time of laser as it will increase the efficiency of laser photocoagulation by delineating the efferent vessels (arteries). The power of laser should be adequate enough to blanch the respective corneal vessel as the use of excess laser power causes increased post laser inflammation providing stimulus for revascularization.

CONCLUSION

Laser photocoagulation is an effective treatment for corneal vascularization. It is a safe outpatient procedure and well tolerated by the patient. Lack of serious complications makes it an effective alternate to other methods for reducing corneal vascularization in quiescent eyes with vascularised corneal opacities.

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REFERENCE

- 1. **Snell RS.** The Eyeball. In: Clinical anatomy of the eye. 2nd ed. London: Blackwell, 1998: 13-213.
- 2. **Regina M, Zimmerman R, Malik G, et al.** Lymphangiogenesis concurrent with haemangiogenesis in the human cornea. Clin Experiment Ophthalmol. 2007; 35: 541-4.
- Johnson AC, Li X, Pearlman E. MyD88 functions as a negative regulator of TLR3/TRIF-induced corneal inflammation by inhibiting activation of c-Jun N-terminal kinase. J Biol Chem. 2008; 283: 3988-96.
- 4. Williams KA, Lowe M, Bartlett C, et al. All Contributors. Risk factors for human corneal graft failure within the Australian corneal graft registry. Transplantation. 2008; 86: 1720-4.
- Aydin E, Kivilcim M, Peyman GA, et al. Inhibition of experimental angiogenesis of cornea by various doses of doxycycline and combination of triamcinolone acetonide with low-molecular-weight heparin and doxycycline. Cornea. 2008; 27: 446-53.
- Pakneshan P, Birsner AE, Adini I, et al. Differential suppression of vascular permeability and corneal angiogenesis by nonsteroidal anti-inflammatory drugs. Invest Ophthalmol Vis Sci. 2008; 49: 3909-13.
- Sonmez B, Beden U, Erkan D. Regression of severe corneal stromal neovascularization with topical cyclosporine 0.05% after penetrating keratoplasty for fungal corneal ulcer. Int Ophthalmol. 2009; 29: 123-5.
- Pillai CT, Dua HS, Hossain P. Fine needle diathermy occlusion of corneal vessels. Invest Ophthalmol Vis Sci. 2000; 41: 2148-53.
- Cherry PM, Faulkner JD, Shaver RP, et al. Argon laser treatment of corneal neovascularization. Ann Ophthalmol. 1973; 5: 911-20.
- Chong EM, Dana MR. Graft failure IV. Immunologic mechanisms of corneal transplant rejection. Int Ophthalmol. 2008; 28: 209-22.
- 11. Siatiri H, Moghimi S, Malihi M, et al. Use of sealant (HFG) in corneal perforations. Cornea. 2008; 27: 988-91.
- Robert PY, Liekfeld A, Metzner S, et al. Specific antibody production in herpes keratitis: intraocular inflammation and corneal neovascularisation as predicting factors. Graefes Arch Clin Exp Ophthalmol. 2006; 244: 210-5.
- Saita N, Fujiwara N, Yano I, et al. Trehalose 6,6'-dimycolate (cord factor) of Mycobacterium tuberculosis induces corneal angiogenesis in rats. Infect Immun. 2000; 68: 5991-7.
- 14. **Bergenske P, Long B, Dillehay S, et al.** Long-term clinical results: 3 years of up to 30-night continuous wear of lotrafilcon A silicone hydrogel and daily wear of low-Dk/t hydrogel lenses. Eye Contact Lens. 2007; 33: 74-80.
- 15. **Thompson RW Jr, Price MO, Bowers PJ, et al.** Long term graft survival after penetrating keratoplasty. Ophthalmology. 2003; 110: 1396-402.

- Sharma A, Samal A, Narang S, et al. Frequency doubled Nd:YAG (532 nm) laser photocoagulation in corneal vascularisation: efficacy and time sequenced changes. Indian J Ophthalmol. 2001; 49: 235-40.
- Banciu M, Metselaar JM, Schiffelers RM, et al. Antitumor activity of liposomal prednisolone phosphate depends on the presence of functional tumor-associated macrophages in tumor tissue. Neoplasia. 2008; 10: 108-17.
- Sheppard JD Jr, Epstein RJ, Lattanzio FA Jr, et al. Argon laser photodynamic therapy of human corneal neovascularization after intravenous administration of dihematoporphyrin ether. Am J Ophthalmol. 2006; 141: 524-9.
- Nirankari VS. Laser photocoagulation for corneal stromal vascularization. Trans Am Ophthalmol Soc. 1992; 90: 595-669.
- 20. **Epstein RJ, Hendricks RL, Harris DM.** Photodynamic therapy for corneal neovascularization. Cornea. 1991; 10: 424-32.
- Marsh RJ. Argon laser treatment of lipid keratopathy. Br J Ophthalmol. 1988; 72: 900-4.
- 22. Marsh RJ, Marshall J. Treatment of lipid keratopathy with the argon laser. Br J Ophthalmol. 1982; 66: 127-35.
- Baer JC, Foster CS. Corneal laser photocoagulation for treatment of neovascularization. Efficacy of 577 nm yellow dye laser. Ophthalmology. 1992; 99: 173-9.