Comparing the Efficacy of Corneal Collagen Cross-linking and Lamellar Keratoplasty in the Treatment of Keratitis: A Complex Treatment Approach

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Abstract

Introduction: 90% of corneal ulcers and other eye injuries resulting in blindness occur in developing nations, and the increase in corneal disorders and eye injuries is correlated with various diagnostic technologies, environmental deterioration, more difficult eye procedures, and an increase in eye infections. This study aimed to evaluate the safety and effectiveness of comprehensive keratitis treatment with both lamellar keratoplasty and corneal collagen cross-linking (CXL). **Materials and Methods:** The study included 28 patients diagnosed with keratitis who were divided into two groups: the main group (n = 14) and the control group (n = 14). Each patient underwent a comprehensive ophthalmological examination, which included assessments of visual acuity with and without correction, intraocular pressure evaluation, microscopic inspection of the front of the eye, and a thorough examination of the rear of the eye. **Results:** During the 30–180 days of follow-up, the control group experienced a high rate of post-operative astigmatism in seven (50%) patients, while the main group had a lower rate of three (21.4%) patients. Both groups showed a similar trend in the growth of visual acuity from the 90 to 1095 days of follow-up, with a mean visual acuity of 0.4–0.5 with maximum correction. **Conclusion:** The application of ultraviolet light during CXL improves the robustness of both the graft and the recipient's corneal tissue in the suture area. In addition, it directly kills bacteria and viruses, inhibits pathogenic flora, and reduces the risk of recurrent infection.

Key words: Corneal ulcers, intraocular pressure, lamellar keratoplasty, riboflavin, ultraviolet light

INTRODUCTION

The World Health Organization has identified a prevalence of corneal sickness and consequent blindness between 12 and 21% ranking corneal blindnessrelated vision impairment as the second or third most common visual organ ailment.^[1,2]

90% of corneal ulcers and other eye injuries resulting in blindness occur in developing nations, and the increase in corneal disorders and eye injuries is correlated with various diagnostic technologies, environmental deterioration, more difficult eye procedures, and an increase in eye infections.^[3-5] Corneal transplantation is the sole procedure employed to save the eyeball, with lamellar keratoplasty (LK) potentially used to maintain proper eyesight and regenerate corneal cells.

LK is the main treatment for shallow keratitis and is considered to be a safer, more economical, and less complicated surgery than end-to-end transplantation.^[6] However, LK is linked to purulent melting, graft rejection, and the development

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Received: 04-02-2024 **Revised:** 19-03-2024 **Accepted:** 28-03-2024 of graft disease, despite its seeming dependability and security.^[7] Corneal collagen cross-linking (CXL) has emerged as a feasible approach in corneal surgery with promising recent outcomes. This study aimed to evaluate the safety and effectiveness of comprehensive keratitis treatment with both LK and CXL.

MATERIALS AND METHODS

The present study involved 28 patients with keratitis, who were evenly distributed between the main and control groups, with 14 individuals in each group, and a total of 28 eyes were evaluated. Both groups showed a high prevalence of male sex, with 12 males (85.7%) and 2 females (14.3%) in the control group, while the main group comprised 10 males (71.4%) and 4 females (28.6%). The study's follow-up period lasted from 3 to 8 years, with an average age of 32 years among the participants.

Each patient received a standard ophthalmological examination, which included ophthalmoscopy, refraction, tonometry, biomicroscopy, and visometry without correction, and all 28 eyes showed ulcerations in the central or paracentral zone of the cornea, with the depth of the ulcerations being no greater than one-third of the cornea's thickness. In preparation for keratoplasty, the area of concern should be pinpointed to facilitate graft implantation without significantly affecting the optical axis of the eye. The mean visual acuity of the 14 eyes in the control group was 0.09 ± 0.07 , while the mean visual acuity of the 14 eyes in the main group was -0.08 ± 0.09 before surgery. Both the control and experimental groups underwent corneal transplantation.

Statistical analysis was conducted using STATISTICA (V8.0; Statsoft, Tulsa, Oklahoma, USA), and the results are presented as n (%) and mean±standard deviation. The parameters were compared using Student's *t*-test, and a P < 0.05 was considered statistically significant. The Bioethics Committee of the National Surgical Center granted approval for this study under Protocol No. 3 on October 07, 2013.

RESULTS

After surgery, all patients in both groups experienced symptoms, such as photophobia, inflammation of both eyelids, minor swelling of the eyelids, and excessive tearing. On the 1st day post-surgery, all patients were prescribed a combination of artificial tears and broad-spectrum antibiotics, including both ointment and eye drops. In addition, patients with corneal epithelial defects were treated with local repair stimulants.

In the main group, two (14.3%) patients had epithelial deficiencies, while in the control group, 4 (28.6%) patients had these issues. Of the 14 control group participants,

1 (7.1%) had recurrent infections and 2 (14.3%) encountered suture-related problems.

During the 30-180 days of follow-up, the control group experienced a high rate of post-operative astigmatism in seven (50%) patients, while the main group had a lower rate in 3 (21.4%) patients. Both groups showed a similar trend in the growth of visual acuity from the 90 to 1095 days of follow-up, with a mean visual acuity of 0.4-0.5 with maximum correction. The control group had a larger astigmatism of 0.48 \pm 0.09 diopters compared to the main group, which had an astigmatism of 0.32 ± 0.11 diopters. Both groups experienced interface space artifacts in 14.3% (2 eyes) of the cases. LK has done as per was performed according to the accepted protocol, in which the graft diameter was determined either by measuring the recipient's corneal bed diameter or by adding 0.5 mm. The average graft diameter was 6.5 mm. Figure 1 illustrates the number of patients according to graft diameter used in the transplant illustrated in Figure 1.

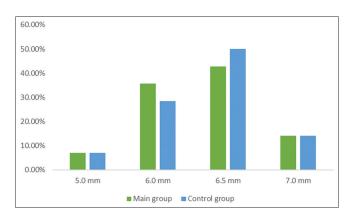
We injected riboflavin using an insulin syringe and placed it at the surgical site, securing it with a continuous nylon suture (10.0) before initiating CXL surgery in the primary group [Figures 2-4].

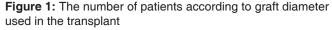
The following illustrations demonstrate the key steps of this procedure:

DISCUSSION

From 2002 to 2004, the World Health Organization carried out many non-randomized preventative trials in India, Myanmar, and Bhutan.^[8] Applying antibiotic ointment right after a corneal abrasion was shown to decrease the occurrence of ulcers when analyzed alongside previous data.^[9,10]

A study on transplanting corneal indications in developing nations revealed that corneal scarring and keratitis were the main causes of transplantation. Corneal scars represented 28.1% of the indications, whereas keratitis accounted for





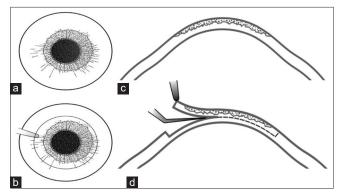


Figure 2: A case of keratitis before the operation (a and b) and after removal of the affected layers (c and d)

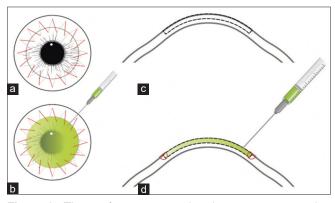


Figure 3: The graft was secured with a continuous nylon suture (10.0) (a and b), and riboflavin solution was injected using an insulin syringe (c and d, b)

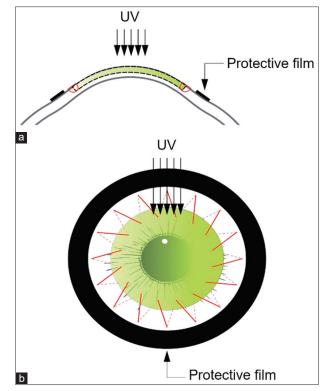


Figure 4: The protective layers (a and b) protect the surrounding tissues from ultraviolet radiation emanating from the operation field

50.5%. Active infectious keratitis constituted around 12.2% of all transplants.^[11] These results suggest that suppurative keratitis and its consequences are major contributors to eyerelated health issues, particularly in countries with limited resources.

CXL is recommended to reduce the risk of emergency keratoplasty and reinfection.^[12] In addition, lamellar grafting should be performed to minimize the possibility of rejection. It is important to note that initiation of proper antimicrobial therapy is crucial for preventing potential complications. Studies have shown that if the diagnosis is postponed, in half of the cases, the eyes can heal with satisfactory visual results.^[13]

Topical antibacterial drugs are beneficial for most people but may not be sufficient for advanced cases. In such cases, riboflavin and ultraviolet light have been utilized as adjuvant treatments for refractory keratitis and have demonstrated potential efficacy.^[14-16]

The suggested complex therapy for infectious keratitis which combines LK and CXL corneal collagen has several benefits, including fewer complications, shorter duration of treatment, and favorable functional outcomes. This approach is a more efficient alternative to the traditional LK.

CONCLUSION

The effects of ultraviolet light on CXL can be attributed to two mechanisms. At the suture location, an immediate and discernible enhancement in the robustness of both the corneal tissue of the recipient and the graft was observed. Second, ultraviolet light has a direct bactericidal and virucidal effect on pathological flora, which ultimately leads to a decrease in the frequency of recurrence of infectious processes.

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AUTHOR CONTRIBUTIONS

Clinical management: NT, YU, LG, AO, KY; Performed work: NT, YU, LG: Designed and generated idea; AO, KY, SD, KK; Prepared manuscript: YU, AO, KY, SD, KK.

REFERENCES

 World Health Organization. Blindness and Vision Impairment. Geneva: World Health Organization, 2023. Available from: https://www.who.int/news-room/factsheets/detail/blindness-and-visual-impairment [Last

Turgunbaev, et al.: Lamellar keratoplasty versus corneal collagen cross-linking in treating keratitis

accessed on 2023 Nov 14].

- 2. Kasparova EA, Fedorov AA, Yang B. Clinical results of modified crosslinking in the treatment of purulent keratitis and corneal ulcers. Vestn Oftalmol 2020;136:64-73.
- Whitcher JP, Srinivasan M, Upadhyay MP. Corneal blindness: A global perspective. Bull World Health Organ 2001;79:214-21.
- Ma J, Zhao L, Yang Y, Yun D, Yu-Wai-Man P, Zhu Y, et al. Associations between regional environment and cornea-related morphology of the eye in young adults: A large-scale multicenter cross-sectional study. Invest Ophthalmol Vis Sci 2021;62:35.
- 5. Tuli S, Gray M. Surgical management of corneal infections. Curr Opin Ophthalmol 2016;27:340-7.
- Fontana L, Parente G, Tassinari G. Clinical outcomes after deep anterior lamellar keratoplasty using the bigbubble technique in patients with keratoconus. Am J Ophthalmol 2007;143:117-24.
- Seyedian MA, Aliakbari S, Miraftab M, Hashemi H, Asgari S, Khabazkhoob M. Corneal collagen crosslinking in the treatment of progressive keratoconus: A randomized controlled contralateral eye study. Middle East Afr J Ophthalmol 2015;22:340-5.
- 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.
- 9. Getshen K, Srinivasan M, Upadhyay MP, Priyadarsini B, Mahalaksmi R, Whitcher JP. Corneal ulceration in South East Asia. I: A model for the prevention of bacterial ulcers

at the village level in rural Bhutan. Br J Ophthalmol 2006;90:276-8.

- Maung N, Thant CC, Srinivasan M, Upadhyay MP, Priyadarsini B, Mahalakshmi R, *et al.* Corneal ulceration in South East Asia. II: A strategy for the prevention of fungal keratitis at the village level in Burma. Br J Ophthalmol 2006;90:968-70.
- Dandona L, Ragu K, Janarthanan M, Naduvilath TJ, ShenoyR, RaoGN. Indications for penetrating keratoplasty in India. Indian J Ophthalmol 1997;45:163-8.
- Agrawal N, Singh SK. Collagen cross-linking in recalcitrant corneal ulcers: A case series. Nepal J Ophthalmol 2016;8:47-53.
- 13. Jones DB. Decision-making in the management of microbial keratitis. Ophthalmology 1981;3:814-20.
- Price MO, Tenkman LR, Schrier A, Fairchild KM, Trokel SL, Price FW Jr. Photoactivated riboflavin treatment of infectious keratitis using collagen crosslinking technology. J Refract Surg 2012;28:706-13.
- Chan E, Snibson GR, Sullivan L. Treatment of infectious keratitis with riboflavin and ultraviolet-A irradiation. J Cataract Refract Surg 2014;40:1919-25.
- 16. Alshehri JM, Caballero-Lima D, Hillarby MC, Shawcross SG, Brahma A, Carley F, *et al.* Evaluation of corneal cross-linking for treatment of fungal keratitis: Using confocal laser scanning microscopy on an *ex vivo* human corneal model. Invest Ophthalmol Vis Sci 2016;57:6367-73.

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