Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 2005-2011 | ISSN:2251-6727

Novel Surgical Approach for the Treatment of Neurotrophic Keratopathy—Case Series of Four Cases

Dr. Vineet Pradhan[1] Dr. Sophiya Chaudhary[2], Dr. Chetanya Prakash Gupta[3], Dr. Manish Jain[4]

1. Assistant Professor, Department of Ophthalmology, Mahatma Gandhi Medical College and Hospital, Jaipur-302022, India
2. Junior Resident, Department of Ophthalmology, Mahatma Gandhi Medical College and Hospital, Jaipur-302022, India
3. Professor and Head of Department, Department of Ophthalmology, Mahatma Gandhi Medical College and Hospital, Jaipur-302022, India
4. Professor and Unit Head, Department of Plastics Surgery, Mahatma Gandhi Medical College and Hospital, Jaipur-302022, India

Corresponding author

Dr. Vineet Pradhan, Assistant Professor, Department of Ophthalmology, Mahatma Gandhi Medical College and Hospital, Jaipur, 302022, India

(Received: 07 January 2024 Revised: 12 February 2024 Accepted: 06 March 2024)

KEYWORDS

Surgical Approach, Neurotrophic Keratopathy

ABSTRACT:

Insensate cornea is a difficult and challenging problem to manage throughout the world. Sensations are required to initiate blink reflex, maintain integrity of corneal epithelium and limbal stem cell function. Corneal sensations are provided by ophthalmic division of trigeminal nerve.

INTRODUCTION

Insensate cornea is a difficult and challenging problem to manage throughout the world. Sensations are required to initiate blink reflex, maintain integrity of corneal epithelium and limbal stem cell function. Corneal sensations are provided by ophthalmic division of trigeminal nerve.

Reduced corneal sensation results in reduced reflex tearing, increase risk of corneal surface injuries and poor healing[2]. All these factors lead to epithelial defects that ulcerate and perforate if not treated appropriately. Lack of corneal sensation leads to a clinical condition known as neurotrophic keratopathy. The most common causes are herpes simplex and herpes zoster viral infections, followed by trigeminal neuralgia surgery and acoustic neuroma. Another common etiology of neurotrophic keratopathy is diabetes mellitus. Diabetes either may be the primary cause of neurotrophic keratopathy or secondarily may predispose patients to this condition.

Patients who had facial palsy along with insensate cornea are at even greater risk for corneal disease.

Facial nerve palsy results in lid laxity and the inability to completely close the eyelids leading to chronic exposure, dry eye, loss of corneal clarity and keratitis.

Traditional available treatment options are limited and most of them target to protect the cornea and prevent progression of disease, instead of addressing the corneal denervation leading to recalcitrant progression and vision loss.

Few newer medical modality such as use of Cenegermin eye drops and recombinant humanized nerve growth factor (rhNGR) are being investigated.

Re-innervation of the cornea can be achieved by transfer of a healthy donor nerve into the cornea[4,5,6]

This is called Corneal re-innervation / neurotization. It restores the corneal sensation and corneal healing thus preventing vision loss.

This is a novel surgical procedure in management of Neurotropic Keratopathy (NK).

Here, we present a case series of four cases managed by the surgery of Corneal Neurotization for successful management of Neurotropic Kearatopathy.

METHODS AND MATERIALS

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 2005-2011 | ISSN:2251-6727

The cases presented in the Department of Ophthalmology, Mahatma Gandhi Hospital, Jaipur from March 2022 to October 2023. Each patient was examined in OPD for Snellen's VA and refraction, slit lamp exam, IOP measuring by NCT, EOM examination, Dilated Fundus examination, OCT in each visit. The patients were followed up in 6 weeks duration. The average period of follow up was 6 months.

CASE I

A 22-year-old male presented with RE lagopthalmos associated with irritation and burning in right eye that was unresponsive to medical management.

On presentation, his best corrected visual acuity in right eye was 6/12. LE BCVA 6/6. On Slit lamp examination, he had macular type corneal opacity in inferior quadrant (Figure 1A). He had absent corneal sensation and blink in all four quadrants tested with a wisp of cotton. Corneal sodium fluorescein staining was suggestive of epithelial breakdown with epithelial deficits (Figure 1B). There was lagophthalmos in RE with exposure.

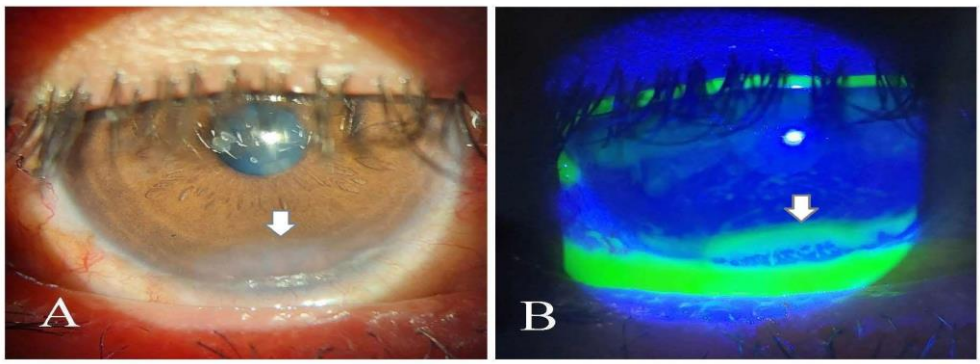
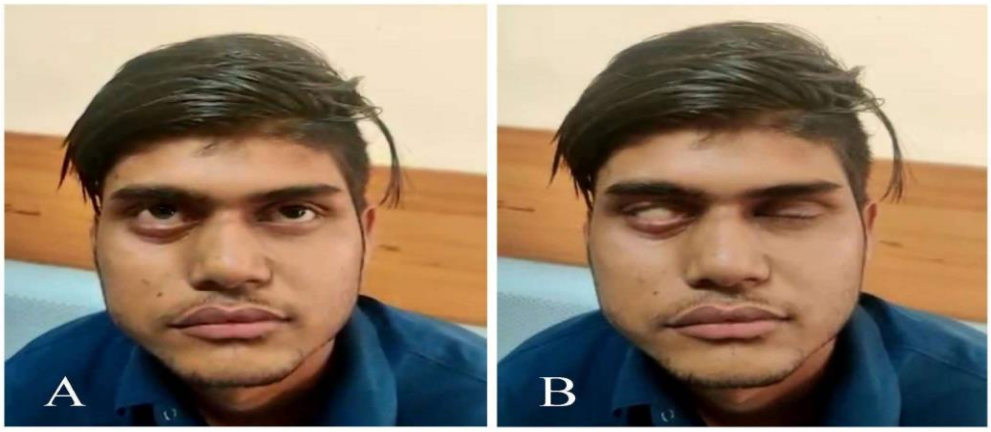


Figure 2 (A, B) – Incomplete right eye closure.



Case II

A 40 years old male came with complaints of recurrent watering, redness and pain in LE for 6 months months, with non-healing defects. He gave a history of LE infection, treated two years back. Old records showed diagnosis of HSV keratitis managed elsewhere with complete resolution. Patient has no associated systemic illness.

He was examined at MGH in Ophthalmology OPD during May, 2022.

On ocular examination RE BCVA 6/9 LE BCVA 6/24, Non contact tonometry was RE 15mmhg and LE 16mmhg.

On Slit lamp examination, RE- WNL, LE- mild conjunctival congestion with corneal haze superiorly 0.5mm X 1mm and healed pannus in superior limbus.

Corneal sensation (tested by cotton wisp) RE- WNL, LE absent in all four quadrants and in center. Sodium fluorescein staining was Positive in area of epithelial

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 2005-2011 | ISSN:2251-6727

defect in superior quadrant. TBUT, RE was 11 seconds and LE was 7 seconds with fluorescein.
Fundus BE Media- clear, Disc- CDR- 0.3:1, vessels- normal in contour and caliber.
The patient was diagnosed to have LE Neurotropic Keratopathy with non-healing epithelial defect.
CASE III
A 55 years old Indian Muslim female with history of type II Diabetes Mellitus since 20 years under medication with control gave ocular history of BE Panretinal photocoagulation done in past. Attended Ophthalmology OPD during Oct, 2022 with complaints of recurrent redness watering and pain off and on for last 6 months RE taken treatment at multiple places.
On ocular examination RE BCVA 6/36 LE BCVA CF 1m
with IOP of RE 18mm Hg and LE 17mm Hg.
SLIT LAMP EXAMINATION RE Conjunctival congestion, central corneal epithelial defect 3-5 clock hours, LE psedophakia, rest WNL.
Corneal sensation (tested by cotton wisp) RE Absent in all quadrants, LE sensation present.
Sodium fluorescein staining positive in the RE from 3-5 clock hours and showed epithelial defects.
Fundus showed RE Media- Slight haze, Disc- CDR- 0.4 Dry macula with multiple laser scars seen LE-Media- clear, post pole optic pallor with dry macula and peripheral laser marks.
A diagnosis of RE Neurotrophic Keratopathy with epithelial defects in a case of lasered PDR patient
Case IV
A 39 years female, operated for trigeminal neuralgia at MGH in Dec, 22, came with the complaints of recurrent pain, redness, watering in LE two months after the surgery.
On ocular examination RE BCVA 6/9 LE BCVA 6/18 with
IOP RE 14mm Hg 15mm of Hg
SLIT LAMP EXAMINATION RE Conjunctiva, cornea, Iris and AC normal LE Conjunctiva, Iris and AC normal, corneal haze present throughout cornea
Corneal sensation (tested by cotton wisp) RE Present LE absent
Sodium fluorescein staining- RE Negative, LE Diffusely Positive in the whole cornea and conjunctiva
Fundus RE Media- clear, Disc- CDR- 0.3:1, vessels - normal in caliber and contour
LE Media- clear, Disc- CDR-0.3:1, vessels - normal in caliber and contour
Treatment- All patients underwent the surgical procedure of Corneal Neurotization by a team of plastic surgeon and eye surgeon. There were no intra op and post op complications. At average of 3 months follow up there was partial resolution of Corneal stromal opacification and great improvement in corneal sensation by testing with a wisp of cotton in all four quadrants at the end of 6 months follow up.
Corneal Neurotization
Right sub brow skin incision was made and dissection was carried down to the periosteum of orbital rim. Supraorbital nerve is identified at supraorbital notch and its deep branch was dissected. 8 cm sural graft was harvested from right leg (Figure-3)

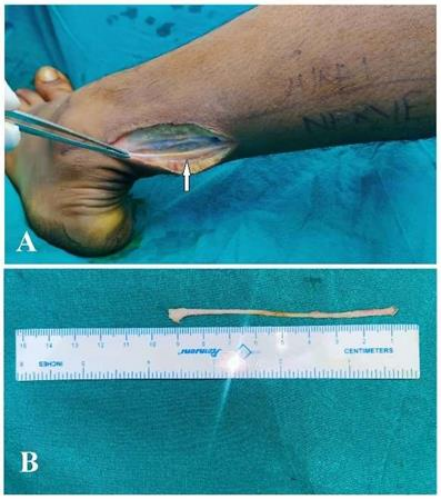


Figure 3 (A, B) Harvested Sural Nerve Graft.

A tunnel was made from the sub brow incision to the superior medial fornix and the sural nerve graft was passed through the tunnel into upper fornix (Figure 4A). Perilimbal conjunctival and Tenon's layer incisions were made at 12, 3, and 9 o' clock, 5 mm away from the limbus to accommodate the nerve fascicles.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 2005-2011 | ISSN:2251-6727

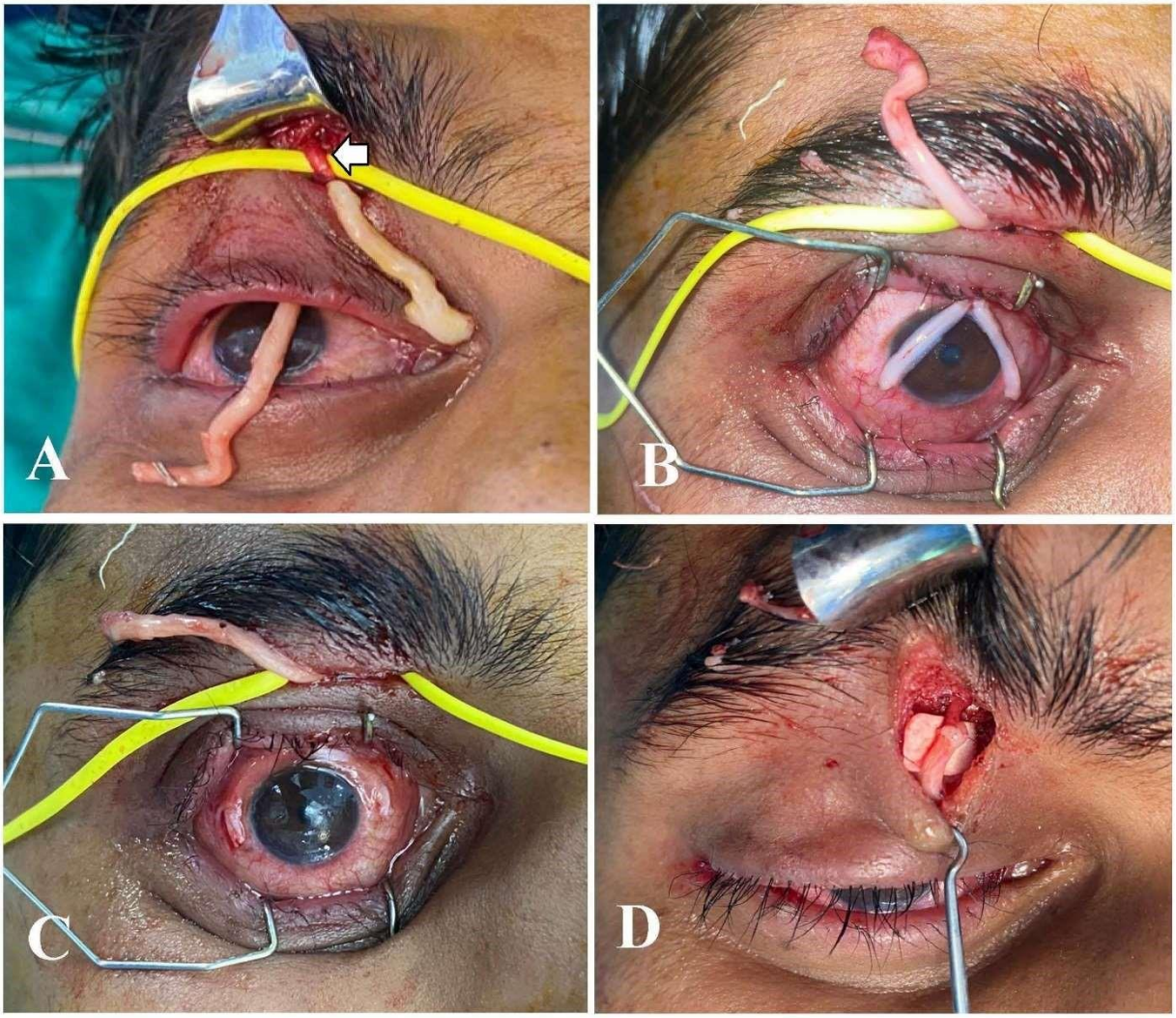


Figure 4 (A) Arrow indicate deep branch of supraorbital nerve. (B) Two separated fascicles of sural nerve at 12'O clock position (C) Sural nerve fascicles suture to sclera at 3'O and 9'O clock position. (D) Sural nerve graft coaptated with supraorbital nerve in end-end fashion.

Blunt dissection was done to create a sub-tenon space from 9'o clock to 3'o clock and from 12'o clock position to upper fornix. Sural nerve graft was brought out at 12'o clock peri-limbal incision. The sural nerve is separated into 2 fascicles (Figure 4B). Both fascicles were passed around the limbus in the Sub Tenon's space and sutured to the sclera at the limbus with 10-0 nylon sutures at 9'o and 3'o clock position (Figure 4C). The conjunctiva was closed to cover the nerve-corneal union. The deep branch of the supraorbital nerve was coaptated with sural nerve graft with 9-0 nylon in end-to-end fashion (Figure 4D).

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 2005-2011 | ISSN:2251-6727

Figure 4 (A) Arrow indicate deep branch of supraorbital nerve. (B) Two separated fascicles of sural nerve at 12'O clock position (C) Sural nerve fascicles suture to sclera at 3'O and 9'O clock position. (D) Sural nerve graft coaptated with supraorbital nerve in end-end fashion.

Temporalis Transfer

A curvilinear incision was made in temporal hairline as shown in figure 5A. Deep temporalis fascia. A 15mm wide strip of deep temporal fascia along with 20 mm tongue of temporalis muscle is harvested keeping fascia attached at the upper end. Temporalis fascia is then divided into 2 strips.

Another curvilinear incision was made at lateral margin of orbit temporalis muscle along with two fascial slings brought out from the lateral orbital incision via subcutaneous tunnel 9Figure 5B). Third incision was made at medial canthus and medial canthal tendon was dissected. The upper fascial strip was passed through upper eye lid in a plane above the tarsal plate and approx. 5mm above the lid margin and brought out at medial canthal incision. Similarly lower strip was passed from the lower lid. The two strips were sutured with each other and to the medial canthal tendon, creating an overlap of lower lid by upper lip by 2mm (Figure 5C).

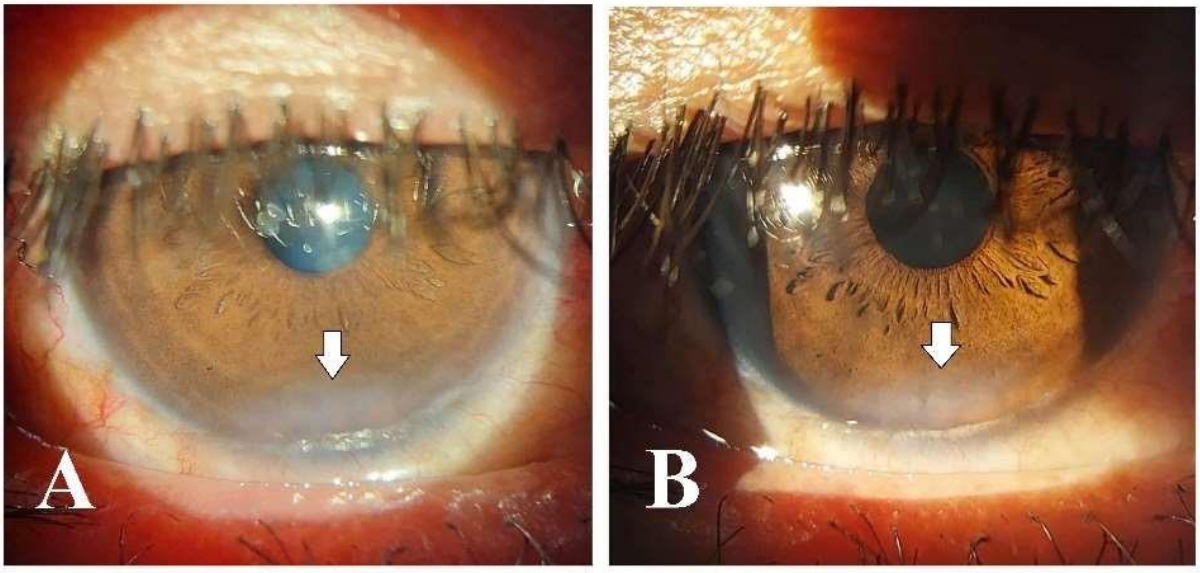


Figure 5 (A) Temporal hairline incision to harvest temporalis muscle with deep temporal fascia. (B) Two temporal fascial slings brought out at lateral orbital margin. (C) Both slips passed through eyelid and sutured to medial canthal tendon.

There were no intra op and post op complications. At 4 months follow up, there was partial resolution of corneal stromal opacification and greatly improved corneal sensation by testing with a wisp of cotton in all 4

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 2005-2011 | ISSN:2251-6727

quadrants (Figure 6). Right eye closure was near complete (Figure 7).

DISCUSSION

Neurotrophic keratopathy is a degenerative disease of the corneal epithelium resulting from impaired corneal innervation. A reduction in corneal sensitivity or complete corneal anesthesia is the hallmark of this disease and is responsible for producing epithelial keratopathy, ulceration and perforation. Although numerous ocular and systemic diseases may result in neurotrophic keratopathy, there is one common insult: a lesion of the trigeminal nerve (cranial nerve V) or its branches.

Patients with neurotrophic keratopathy should undergo a complete medical and surgical history, a review of medications and an ocular examination. Although the clinical diagnosis may be made without difficulty, the management of neurotrophic keratopathy can be quite challenging.

Clinical Causes

Any condition affecting the trigeminal nerve or its branches can cause corneal anesthesia, resulting in neurotrophic keratopathy. The most common causes are herpes simplex and herpes zoster viral infections, followed by trigeminal neuralgia surgery and acoustic neuroma. During surgery, damage may occur to the trigeminal nucleus, root or ganglion, or to the ophthalmic branch of the nerve.

Toxicity from chronic use of topical ocular medications also may cause nerve damage and resultant corneal anesthesia. Topical medications that may result in anesthesia include timolol, betaxolol, sulfacetamide and diclofenac sodium.

Another common etiology of neurotrophic keratopathy is diabetes mellitus. Diabetes either may be the primary cause of neurotrophic keratopathy or secondarily may predispose patients to this condition. Diabetic patients who undergo pan-retinal photocoagulation receive a secondary insult to the ciliary nerves.

Clinical Findings

Neurotrophic keratopathy can be divided into three stages based on the Mackie classification.

Stage 1 is characterized by mild, nonspecific signs and symptoms, including rose bengal staining of the inferior palpebral conjunctiva (the earliest sign).

Stage 2 involves a non-healing corneal epithelial defect.

Stage 3 characterized by stromal melting leading to perforation.

CORNEAL SENSITIVITY TESTING

Corneal sensitivity is a vital piece of information and may be measured qualitatively with a piece of twisted cotton or quantitatively with a Cochet-Bonnet esthesiometer. This device quantifies corneal sensitivity by the length of a nylon filament required to initiate a blink or patient response. The nylon filament may be extended to as long as 6 cm. One study reported that only those patients with values of 2 cm or less developed epithelial sloughing and ulceration.1 It is important to remember that in some cases, such as herpes simplex and herpes zoster keratitis, the anesthesia of the cornea may be sectoral and therefore different quadrants of the cornea should be tested separately.

An article in the Japanese Journal of Ophthalmology reported on patients with persistent epithelial defects due to neurotrophic keratopathy. Patients were treated for 28 days with a substance P-derived peptide (FGLM)-amide and insulin-like growth factor (IGF-1). Complete epithelial resurfacing was achieved in eight of nine patients with no adverse effects.4

Corneas that appear to be very thin despite lubrication and tarsorrhaphy often require cyanoacrylate glue and a bandage contact lens. If perforation has already occurred, glue may be applied if the defect is less than 2 mm; otherwise a lamellar or penetrating keratoplasty is needed.2

Despite early and appropriate therapy, neurotrophic keratopathy may still progress to stage 3 diseases by traditional methods of treatments. Our case series of four cases showed marked improvement by the novel surgical technique.

CONCLUSION

Corneal neurotization is a novel technique to restore the corneal sensation. This method showed excellent results in corneal reinnervation, healing of corneal epithelium, vision improvement and quality of life improvement.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 2005-2011 | ISSN:2251-6727

REFERENCES

1. Garcia-Hirschfeld J, Lopez-Briones LG, Belmonte C. Neurotrophic influences on corneal epithelial cells. Exp Eye Res. 1994;59(5):597-605.
2. Gallar J, PozoMA, Rebollo I, Belmonte C. Effects of capsaicin on corneal wound healing. Invest Ophthalmol Vis Sci. 1990;31(10):1968-1974.
3. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. Clin Ophthalmol. 2014 Mar 19;8:571-9. doi: 10.2147/OPTH.S45921. PMID: 24672223; PMCID: PMC3964170.
4. Elbaz, U. et al., 2014. Restoration of Corneal Sensation With Regional Nerve Transfers and Nerve Grafts: A New Approach to a Difficult Problem. JAMA Ophthalmology, pp.1–7.
5. Terzis JK, Dryer MM, Bodner BI. Corneal neurotization: a novel solution to neurotrophic keratopathy. Plast Reconstr Surg. 2009 Jan;123(1):112-120
6. Bains R.D., Elbaz U., Zuker R. Corneal neurotization from the supratrochlear nerve with sural nerve grafts: a minimally invasive approach. Plast. Reconstr. Surg. 2015;135:397–400.