Management Approaches in Corneal Keratoconus

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Corneal Keratoconus Abstract:is a disease characterised by gradual thinning of central and peripheral stroma resulting in protrusion and reduced visual activity. The aetiology of keratoconus is an underlying genetic predisposition coupled with environmental factors, including eve rubbing and atopy. Spectacles, contact lens and Intrastromal Corneal Ring Segments (ICRS) remain fundamental to optic management of keratoconus. These contact lens and ICRS do not treat underlying disease process. Keratoplasty - Penetrating Keratoplasty (PK), deep anterior lamellar keratoplasty (DALK) treatment of choice for advance form of keratoconus. Therefore, current approach is corneal collagen cross-linking (CXL). CXL aims at stiffing the cornea using a combination of UV-A light and chromophore (Vit-B12, riboflavin) and proposed in various indications, from progressive ecstatic disease to corneal infection.

Keywords:- Best Corrected Visual Acuity (BCVA), Spectacles and Contact Lens (SCL), Intrastromal Corneal Ring Segment (ICRS), Conservative, Intermediate and Advanced Treatment, Keratoplasty -PK, DALK, Corneal Collagen Cross Linking (CXL).

I. INTRODUCTION

Keratoconus is a Greek word [kerato-core; konoscone] meaning cone-shaped protrusion of the cornea [1]. Keratoconus is a non-inflammatory, progressive thinning of the cornea that is usually bilateral and involves the central two-thirds of the cornea [1]. It causes due to eye allergies, excessive eye rubbing [2], connective tissue disorders like Marfan syndrome and Ehlers-Danlos syndrome [3]. It affects both men and women, usually at a young age, with prevalence of **5%** of the population in middle east [4]. Signs and symptoms include blurred vision, disorted vision, astigmatism, double vision, inability to see in dim light, near-sightedness, sensitivity to light, or vision loss [5]. Diagnosis can be made by slit-lamp examination and observation of central or inferior corneal thinning and Computerized video keratography is useful in detecting early stage of keratoconus ₁₆₁. The management of corneal keratoconus involve different methods. The early stage of keratoconus is treated spectacles and contact lens, and disease progression is treated with following surgical methods ICRS, PK, DALK, CXL _[7].

II. CURRENT MANAGEMENT FOR KERATOCONUS

Spectacles and Contact Lens (BCVA)

For best vision. Spectacles are used in early ketaronic cases. It is difficult to achieve patient satisfaction spectacle vision because of various disease factors, such as high irregular astigmatism and significant anisometropia [8]. Contact lens offer satisfactory vision by addressing refractive errors and anterior corneal irregularities in keratoconus patients. The type and use of contact lenses depends on stage of keratoconus, where as soft contact lens used in early stage of disease [8,9]. As the disease progress, Rigid-Gas-Permeable (RGP) lenses [8,9] or scleral lenses [8,10], may be used. RGP lenses usually rest on the apex of the cone. In early or mild keratoconus traditional RGP lenses are used to fit, but it is difficult to get an ideal fit and patient have to accept compromised fit, and it not cause ocular damage [9]. The next type of lens is Scleral lens used for advanced cases and provide good visual performance and comfort 181. These scleral lenses are placed on sclera not on cornea to improve vision in patient with high astigmatism conditions like keratoconus [10].

Intrastromal Corneal Ring Segment (ICRS)

ICRS are medical device made of synthetic material designed to alter morphology and refractive power of cornea [8]. It is safe and reversible technique and originally accepted that ICRS have a key role in treating keratoconus [8,11]. The main aim of ICRS to induce geometric change in central corneal curvature, then reduce refractive error and improve visual acuity [11].

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- Conservative, Intermediate and Advanced Management Options Include: [12]
- *C-1:* use spectacles, contact lenses & treatment for atopy & eye rubbing.
- C-2: Include possibility of CXL (especially in younger subjects).
- I-1: Progress to CXL.
- I-2: CXL + ICRS.
- I-3: CXL +/- ICRS +/- Laser keratorefractive surgery (PRK).



Fig 1 Referred from Reference [12]

Keratoplasty –Penetrating Keratoplasty (PK) Deep Anterior Lamellar Keratoplasty (DALK)

Keratoplasty is considered as corneal transplantation. Whereas PK is a full thickness transplant, and done for all effected corneal layers [13]. It is well-established technique and succeed in high rate in keratoconus [14]. DALK is most common indication in keratoconus which useful in preserving own endothelial [15]. DALK procedure successfully performed by considering factors like age, ophthalmic co-morbidities, retina and intraocular pressure [16]. Advanced of DALK over classic pk consist of extracurricular surgery without replacing corneal endothelial, lower rates of graft rejection, no risk for endothelium [17], avoid an open- sky procedure, & shorter period of postoperative instillation of steroid agents, leads to lower incidence of post operative cataract & glaucoma [12]. DALK has fewer intraoperative and postoperative complications including hemorrhage, Anterior synechia, and glaucoma when compared to PK [18]. Limitations of this method include the demanding surgical skills required for performance of DALK technique & fact cannot applied easily in corneas with scars, neovascularization, or previous hydrops [12].

Surgerical Approach in Keratoconus:

• Corneal Collagen Cross-Linkage:

CXL is an invasive technique which strengthen the corneal tissue by using riboflavin and UV-A light [19]. In late 2011, orphan drug status was awarded by the FDA to Avedro's for its formulation of **riboflavin ophthalmic** solution to be used in conjunction with company's particular UV-A irradiation system. CXL using riboflavin

and UV received FDA approval on April 18, 2016 [20]. Main components of CXL, Riboflavin is used as the photosensitizer and UVA to increase the formation of intraand interfibrillar covalent bonds by photosensitized oxidation [21]. It is systemically safe and can be adequately absorbed by corneal stroma topically. It has an absorption peak at 370 nm [20]. Oxygen indicates presence of oxygen is an essential for effective CXL [20].

• Surgical Technique:

CXL entails removing the corneal epithelial, using either an epithelial brush, diluted alcohol or manual scraping. "Some clinicians tend to prefer an excimer laser scrape of the epithelium. After epithelium is removed, the corneal is soaked with riboflavin drops placed over a 30 min period. Then; the CXL device is placed over the patient eye, which is usually held open with a lid speculum. Patients was anaesthetized with topical anaesthesia, usually one drop of Proparacaine or Alacine replenish every 10-15 min, depending on patient's tolerance. The device has a timer with an LCD screen to help to evaluate the progress of the procedure. Following the procedures, some clinicians patch the eye, and some use a bandage contact lens. Antibiotic medications and corticosteroids are typically used for one to four weeks, eyes are typically protected from UV light for 2 months. The device should not be placed too close to the cornea, if higher amount of energy delivered it cause scar to cornea [22].

• CXL Indications:

To improve patient vision in keratoconus disease and in Pellucid marginal degeneration & Terrien's marginal degeneration [20]. International Journal of Innovative Science and Research Technology

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• Types of CXL:

There are two main types include:

✓ Epi-on CXL-

The epithelium is left on during the procedure. The epithelium will be losen by physician with sponge or eye drops before putting B2 drops in eye [23].

✓ Epi-of CXL-

The 8.0-9.0mm central epithelium is removed for procedure then eye drops are placed in eyes [24].

> CXL Protocol:

These guidelines followed from institutions human research ethics committee $_{1251}$.

• Conventional (Dresden) Protocol:

It is a traditional method which Involves debridement of central 8-9 mm zone of corneal epithelium after application of topical anaesthesia in sterile setting, then instil solution of 0.1% of riboflavin in 20% dextrose every 2 min for 30 min and UV-A light (370nm) used [26].

• Accelerated (Anthen's) Protocol:

Also known as high-fluence protocol. It entails epithelium of 50mu with excimer laser, partial topography-guided stromal ablation to max a depth of 80mu, by high fluency CXL using UV-A 10mW/cm^2 for $10 \min_{1271}$.



Fig 2 Mechanism of Action of Riboflavin_[28]

➤ Complications of CXL:

Pain, epithelial defects, dry eyes, infectious and noninfectious keratitis, corneal odema and endothelial damage are the complications of CXL that mostly occurred during various clinical trials [29].

- ➤ Contraindications of CXL: [30]
- Corneal thickness of less than 400mu.
- Viral reactivation.
- Several corneal scarring or opacification
- Autoimmune disorders.

> CXL Combined with Laser:

The combination of CXL and laser refractive surgery in keratoconus patient is emerging and exciting therapeutic modality. Incidence of BCVA is 7 of 26 eyes I.e., 27% [31].

III. CONCLUSION

Keratoconus is a degenerative eye disease (corneal dystrophy) which causes cornea to bulge and changes cornea optics and produce blurred & disorted vision. The new management approach is CXL which decreases the rate of corneal transplantation. CXL is an accepted procedure for

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progressive keratoconus disease which Improve eye vision. Over 90% of people have good outcomes with arrested progression of keratoconus at one year after procedure. The aim of this article to improve vision by treating with different management approaches in patients suffering with vision- threatening corneal keratoconus disease.

REFERENCES

- [1]. Ladan Espandar, Jay Meyer "keratoconus- overview and update". Middle East African journal of ophthalmology 17 (1), 15, 2010. doi: 10.4103/0974-9233.61212 PMCID: PMC2880369 PMID: 20543932 View at: Publisher Site | Google Scholar. http://google.com/scholar?hl=en&as_sdt=2C5&q=co rneal+keratoconus+management+&oq=#d=gs_qabs& t=1690126377592&u=%23p%3Dnq1zHpsrT1cJ
- [2]. Sugar, Joel MD; Macsai, Marian S. MD "What Causes Keratoconus"? Cornea 31(6):p 716-719, June 2012. | DOI: 10.1097ICO.0b013e31823f8c72
- [3]. Jay H. Krachmer M.D., Robert S. Feder M.D¹, Michael W. Belin M.D² "Keratoconus and related noninflammatory corneal thinning disorders" https://doi.org/10.1016/0039-6257(84)90094-8
- [4]. José A. P. Gomes, Pablo F. Rodrigues, and Luiz L. Lamazales "Keratoconus epidemiology: A review" Saudi J Ophthalmol. 2022 Jan-Mar; 36(1): 3–6. Published online 2022 Jul 11. doi: 10.4103/ sjopt. sjopt_204_21 PMCID: PMC9375461 PMID: 35971497
- [5]. Yaron S. Rabinowitz MD " Keratoconus" Survey of Ophthalmology Volume 42, Issue 4 https://doi.org/10.1016/S0039-6257(97)00119-7
- [6]. Article "Keratoconus "initiated by: Penny A. Asbell M.D. M.B.A., Theodora Petratos, M.D. Brad H. Feldman, M.D., Alex Kozak, Dr. Shivanand Sheth, Vatinee Y. Bunya, MD, MSCE, Linda Rose, MD, PhD, Gustavo Ortiz-Morales, MD, Sezen Karakus, MD, Penny A. Asbell M.D. M.B.A. Assigned editor: Sezen Karakus, MD Review: Assigned status Up to Date by Sezen Karakus, MD on March 13, 2023.
- [7]. Vishal Jhanji1,2, Namrata Sharma3, Rasik B Vajpayee2 "Management of keratoconus: current scenario" Archive Volume 95, Issue 8 http://dx.doi.org/10.1136/bjo.2010.185868
- [8]. Konstantinos D. Andreanos, Kate Hashemi, Myrsini Petrelli, Konstantinos Droutsas, Ilias Georgalas & George D. Kymionis "Keratoconus Treatment Algorithm" Published: 28 July 2017 Ophthalmology and Therapy volume 6, pages245–262 (2017)
- [9]. Varsha M Rathi,1,2 Preeji S Mandathara,2 and Srikanth Dumpati2 " Contact lens in keratoconus" Indian J Ophthalmol. 2013 Aug; 61(8): 410–415. doi: 10.4103/0301-4738.116066 PMCID: PMC3775075 PMID: 23925325

- [10]. Varsha M Rathi,1 Preeji S Mandathara,2 Mukesh Taneja,1 Srikanth Dumpati,1 and Virender S Sangwan1 "Scleral lens for keratoconus: technology update" Clin Ophthalmol. 2015; 9: 2013–2018. Published online 2015 Oct 28. doi: 10.2147/OPTH.S52483 PMCID: PMC4630203 PMID: 26604671
- [11]. Jorge L. Alio,1,2 Alfredo Vega-Estrada,1,2 Santiago Esperanza,1,2 Rafael I. Barraquer,3 Miguel A. Teus,4 and Joaquim Murta5 "Intrastromal Corneal Ring Segments: How Successful is the Surgical Treatment of Keratoconus?" Middle East Afr J Ophthalmol. 2014 Jan-Mar; 21(1): 3–9. doi: 10.4103/0974-9233.124076 PMCID: PMC3959038 PMID: 24669139
- [12]. McGhee, Charles N. J. PhD, DSc, FRCOphth; Kim, Bia Z. MBChB; Wilson, Peter J. PhD, FRCOphth "Contemporary Treatment Paradigms in Keratoconus" Cornea 34():p S16-S23, October2015. | DOI: 10.1097/ICO.0000000000000504 https://journals.lww.com/corneajrnl/
- [13]. Alexandra Mădălina Gănescu. Med Pharm Rep. 2022 Oct "Current approaches in the management of patients with keratoconus" https://pubmed.ncbi. nlm.nih.gov/36506602/
- [14]. Francisco Arnalich-Montiel, Jorge L. Alió del Barrio, and Jorge L. Alió " Corneal surgery in keratoconus: which type, which technique, which outcomes?" Eye Vis (Lond). 2016; 3: 2. Published online 2016 Jan 18. doi: 10.1186/s40662-016-0033-y PMCID: PMC4716637 PMID: 26783544
- [15]. Farid Karimian and Sepehr Feizi " Deep Anterior Lamellar Keratoplasty: Indications, Surgical Techniques and Complications " Middle East Afr J Ophthalmol. 2010 Jan-Mar; 17(1): 28–37. doi: 10.4103/0974-9233.61214 PMCID: PMC2880371 PMID: 20543934
- [16]. Mayank A. Nanavaty, * Kanwaldeep Singh Vijjan, and Camille Yvon "Deep anterior lamellar keratoplasty: A surgeon's guide" J Curr Ophthalmol. 2018 Dec; 30(4): 297–310. Published online 2018 Jul 10. doi: 10.1016/j.joco.2018.06.004 PMCID: PMC6276733 PMID: 30555961
- [17]. Lisa C, Machado Soares R, Fernández-Vega-Cueto L , Alfonso-Bartolozzi B, Alfonso JF "Modified Deep Anterior Lamellar Keratoplasty Technique to Rescue Failed Penetrating Keratoplasty" Published 15 November 2022 Volume 2022:16 Pages 3741—3749 DOI https://doi.org/10.2147/OPTH.S382916
- [18]. Ladan Espandar1and Alan N. Carlson1 "Lamellar Keratoplasty: A Literature Review" Volume 2013 | Article ID 894319 | https://doi.org/10.1155/ 2013/894319
- [19]. Vishal Vohra; Sahib Tuteja; Bharat Gurnani; Harshika Chawla " Collagen Cross Linking for Keratoconus" Last Update: March 16, 2023.

ISSN No:-2456-2165

- [20]. Brad H. Feldman, M.D., Erica Bernfeld M.D., Vandana Reddy, MD, Alain Saad, MD, Amanda Mohanan Earatt MBBS MS(Ophth) MRCS(Glasgow) MRCSEd FICO, Brian Shafer, MD " Corneal Collagen Cross-Linking" https://eyewiki.aao.org/ Corneal_Collagen_Cross-Linking
- [21]. Mirko R. Jankov II, Vesna Jovanovic, Ljubisa Nikolic,1 Jonathan C. Lake,2 Georgos Kymionis,3 and Efekan Coskunseven4 " Corneal Collagen Cross-Linking" Middle East Afr J Ophthalmol. 2010 Jan-Mar; 17(1): 21–27. doi: 10.4103/0974-9233.61213 PMCID: PMC2880370 PMID: 20543933
- [22]. Michelle Stephenson, Contributing Editor " At Last, Cross-Linking Comes to U.S. Surgeons" Review of Ophthalmology | July 2016.
- [23]. Yu Liu, Dan Shen, Hao-yu Wang, Deng-feng Liang & Qing-yan Zeng "Independent-effect comparison of five crosslinking procedures for Progressive Keratoconus based on Keratometry and the ABCD Grading System using Generalized Estimating Equations (GEE)" Published10 January 2023 DOI https://doi.org/10.1186/s12886-022-02744-w
- [24]. Kenneth A. Beckman MD 1 2, Preeya K. Gupta MD 3, Marjan Farid MD 5, John P. Berdahl MD 6, Elizabeth Yeu MD 7 8, Brandon Ayres MD 9, Clara C. Chan MD, FRCSC 16 17, José A.P. Gomes MD, PhD 18 19, Edward J. Holland MD 10 11, Terry Kim MD 3 4, Christopher E. Starr MD 12 13, Francis S. Mah MD 14 15, the ASCRS Cornea Clinical Committee " Corneal crosslinking: Current protocols and clinical approach" Journal of Cataract & Refractive Surgery Volume 45, Issue 11, November 2019, Pages 1670-1679.
- [25]. Nacim Bouheraoua, Lea Jouve, Vincent Borderie, and Laurent Laroche "Three Different Protocols of Corneal Collagen Crosslinking in Keratoconus: Conventional, Accelerated and Iontophoresis" J Vis Exp. 2015; (105): 53119. Published online 2015 Nov 12. doi: 10.3791/53119 PMCID: PMC4692706 PMID: 26650390
- [26]. Angela Y. Zhu, Albert S. Jun, and Uri S. Soiberman " Combined Protocols for Corneal Collagen Cross-Linking with Photorefractive Surgery for Refractive Management of Keratoconus: Update on Techniques and Review of Literature" Ophthalmol Ther. 2019 Oct; 8(Suppl 1): 15–31. Published online 2019 Oct 11. doi: 10.1007 s40123-019-00210-3 PMCID: PMC6789054 PMID: 31605317
- [27]. Madeline W. Yung, MD " Corneal Cross-Linking Protocols Made Easy: Tips for Ophthalmology Residents" PUBLISHED IN CORNEA on MAY 1, 2020
- [28]. Duoduo Wu, Dawn Ka-Ann Lim, Blanche Xiao Hong Lim, Nathan Wong, Farhad Hafezi, Ray Manotosh, Chris Hong Long Lim " Corneal Cross-Linking: The Evolution of Treatment for Corneal Diseases" Volume 12 - 2021 | https://doi.org/10.3389/fphar.2021.6866630

- [29]. Agarwal, Richa; Jain, Parul, Arora, Ritu " Complications of corneal collagen cross-linking" Indian Journal of Ophthalmology 70(5):p 1466-1474, May 2022. | DOI: 10.4103/ijo.IJO_1595_21
- [30]. Adel Alhayek and Pei-Rong Lu "Corneal collagen crosslinking in keratoconus and other eye disease" Int J Ophthalmol. 2015; 8(2): 407–418. Published online 2015 Apr 18. doi: 10.3980/j.issn.2222-3959.2015.02.35 PMCID: PMC4413599 PMID: 25938065
- [31]. Chan, Colin MBBS (Hons) FRANZCO " Corneal Cross-Linking for Keratoconus: Current Knowledge and Practice and Future Trends" Asia-Pacific Journal of Ophthalmology 9(6):p 557-564, November-December 2020. | DOI: 10.1097/APO.00000000000335