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A Foldable Nonpenetrating Keratoprosthesis: Medium to Long-Term Clinical Results in Patients with Corneal Blindness due to Noninflammatory Anterior Cornea Disease.

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A foldable nonpenetrating keratoprosthesis: Medium to long-term clinical results in patients with corneal blindness due to noninflammatory anterior Cornea Disease

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Abstract

PURPOSE: To report the medium to long-term safety and performance outcomes of the KeraKlear nonpenetrating artificial cornea (KeraKlear) as the primary procedure in patients with corneal blindness due to noninflammatory anterior cornea disease. **METHODS:** Fifteen patients with corneal blindness (preoperative visual acuity [VA] of ≥20/200) due to a non-inflammatory anterior corneal condition were included in this prospective, single-center study. Preoperative diagnoses included corneal scars, keratoconus, and corneal dystrophies. Diseased corneas were implanted with the KeraKlear (KeraMed Inc., Irvine, California, USA) by a single surgeon (JMV) using a femtosecond laser to create all incisions. Participants were followed up with for as long as 64 months. Uncorrected Snellen VA and postoperative complications were recorded. **RESULTS:** The average age at the time of surgery was 49.6 years old and 67% of patients were female. The patients experienced an average improvement in uncorrected Snellen VA of 7.6 lines (−1.17 logMAR). Average uncorrected vision at the last visit was 20/100 (0.73 logMAR), and median uncorrected vision at the last visit was 20/70 (0.54 logMAR). One patient experienced extrusion of the KeraKlear due to infection. There were no cases of glaucoma, retroprosthetic membrane, or endophthalmitis, the three most common complications of penetrating keratoprostheses (KPro). **CONCLUSIONS:** Medium and long-term outcomes of the KeraKlear indicate that this device is a viable alternative to corneal transplantation as a primary procedure in patients with non-inflammatory causes of corneal blindness, especially when corneal tissue is not available.The KeraKlear does not penetrate into the anterior chamber, and therefore, is less susceptible to the most common complications of penetrating KPro including endophthalmitis, glaucoma, and retroprosthetic membrane.The KeraKlear also has a comparable or improved adverse event rate compared to penetrating keratoplasty.

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Full Text

Introduction

Although cornea transplantation can greatly improve the vision of cornea-blind patients,[1] severe constraints on the number of donor corneas, facilities for tissue storage, surgical operating rooms and trained surgeons limits the percentage of cornea blind patients receiving cornea transplants to <2% annually worldwide.[2],[3],[4] Synthetic alternatives in the form of keratoprostheses have been developed, of these, two have received United States Food and Drug Administration clearance: the Boston keratoprosthesis (KPro) and the AlphaCor. However, the complexity of the required surgical technique, the severe potential complications, and the requirement for donor corneal tissue in the case of the Boston KPro have limited the adoption of these devices to only patients that are likely to fail with corneal transplantation.[5]

The KeraKlear non-penetrating artificial cornea (KeraKlear) offers a potential solution to the aforementioned problems and has been investigated and reported previously in patients who were poor candidates for corneal transplantation. In these prior studies, 15 patients were considered for implantation with the KeraKlear KPro if they had a high risk of failure with standard penetrating keratoplasty (PK).[6],[7] These included patients who had multiple failed PKs with corneal edema, extensive corneal vascularization or scarring, extensive limbal stem cell deficiency or showed conditions with a poor prognosis following PK such as severe chemical injury.[6],[7] In this high-risk population with numerous comorbidities, Alio et al. concluded that the KeraKlear “is a non-invasive, viable alternative to corneal transplantation with potential advantages such as decreased risk of endophthalmitis, expulsive hemorrhage, and worsening glaucoma.” No eyes were lost in these studies and modest improvements in visual acuity (VA) were documented.[6],[7]

In this study, we describe the first long-term study of the KeraKlear nonpenetrating artificial cornea as the primary procedure in the treatment of corneal blindness due to non-inflammatory anterior corneal conditions in 15 eyes. This population included patients that would be considered at the standard risk for PK. The majority of cases of corneal blindness in the world are due to noninflammatory anterior corneal disease.[8]

Methods

Study design

This prospective, single-center study was approved by the ethics committee at the Centro Oftalmologico de Valencia (CEOVAL) and was comprised of 15 patients that were treated with the KeraKlear artificial cornea between August 2010 and July 2014. Cornea blind patients of the Cornea Service at CEOVAL in Valencia, Venezuela, were voluntarily enrolled into the

study after explanation of the surgery and its risks, benefits, and alternatives. Informed consent forms which adhered to the declaration of Helsinki were signed by all patients. Patients were considered for KeraKlear implantation if they exhibited corneal blindness (VA of 20/200 or worse) due to noninflammatory anterior corneal disease. These patients would have been considered for keratoplasty, but could not have keratoplasty either because tissue was unavailable or they could not afford the cost of tissue. The exclusion criteria included full thickness opacity and inflammatory corneal disease such as Stevens–Johnson syndrome, ocular cicatricial pemphigoid, and atopic keratoconjunctivitis. Inflammatory conditions were excluded because of the risk of corneal melting. Preoperative examinations included Snellen VA, intraocular pressure, slit-lamp biomicroscopy, dilated fundoscopy, OCT pachymetry mapping, and evaluation of preexisting ocular conditions. Follow-up assessment occurred at 1 day, 5–9 days, 2 months, 6 months, and 12 months postsurgery, and every 3–6 months thereafter. At all visits, VA, intraocular pressure, and corneal integrity were assessed.

Surgical technique

The details of the device and surgical technique employing a femtosecond laser have been described previously.[9] Briefly, the KeraKlear is a corneal implant made of a clear, biocompatible polymer. The implant has a 7-mm overall diameter and has a 4-mm diameter central optic, and a perforated peripheral skirt which allows fixation within a lamellar corneal pocket [Figure 1]. The KeraKlear is sold commercially outside of the United States in six different models which are called KeraKlear XT. The number after XT indicates the amount of corneal tissue replaced in microns which also corresponds to the depth of the lamellar pocket in microns. The six models are XT200, XT300, XT400, XT500, XT600, and XT700. The manufacturer recommends that the surgeon choose a pocket depth that would leave approximately 100 μ of the corneal tissue posterior to the pocket.{Figure 1}

For example, if the thinnest point on the cornea is 510 μ, a KeraKlear XT400 would be chosen and the femtosecond laser would be set to create an 8 mm diameter corneal pocket at 400 μ depth. This would leave 110 μ of posterior corneal tissue behind the implant. The femtosecond laser would also be used to create a circular trephination incision of 3.5 mm diameter to a depth 20 μ deeper than the lamellar pocket. This would allow the removal of a disk of diseased tissue of 3.5 mm diameter with a thickness of 400 μ. Because the corneal trephination incision tends to expand slightly after the disc of tissue is removed, the 4 mm optic of the KeraKlear will fit precisely within the trephination incision without a gap. [Figure 2] and [Figure 3] show study corneas before and after KeraKlear artificial cornea implantation. In this study, the Ziemer Z6 femtosecond laser (Port, Switzerland) was used. The femtosecond laser was located in a clean procedure room used for LASIK surgery. Implantation of the KeraKlear was also performed in the same clean procedure room.{Figure 2}{Figure 3}

Prior to the creation of the incisions, 1 drop of ofloxacin 0.3% antibiotic and 1 drop of 0.5% proparacaine anesthetic eye drops were instilled into the operative eye. After creation of the lamellar and trephination incisions, 0.12 mm toothed forceps were used to remove the anterior disk of diseased tissue. A blunt spatula was then used to sweep the corneal pocket to ensure that the full 8 mm diameter of the lamellar incision had been created. Using smooth insertion forceps, the KeraKlear was then inserted into the corneal pocket and the skirt of the device was unfurled 360°. In the case of the keratoconus patients, four 10-0 nylon interrupted sutures were passed from the anterior cornea through the peripheral holes of the KeraKlear into the posterior stroma in a nonpenetrating fashion. This was done as a precaution, because it is commonly known that many keratoconic patients rub their eyes vigorously. Finally, a high oxygen-permeability, extended-wear contact lens was placed over the cornea. One drop of ofloxacin 0.3% antibiotic and one drop of 1% prednisolone were administered at the conclusion of each case.

Long term management

Postoperatively, patients continued to wear a high oxygen permeability 30-day extended wear contact lens, which was replaced every 30 days. Twice daily, one drop of ofloxacin 0.3% was administered to the operative eye long term for prevention of infection. In addition, a contact lens re-wetting solution, OptiFree Replenish (Alcon, Fort Worth Texas) was administered 3–4 times a day for prevention of contact lens related complications.

Data collection

Data including patient demographics, diagnosis, and Snellen VA (converted to logMAR) were collected both pre- and post-operatively on all fifteen patients during the study period. For calculation of lines of improvement, change between hand motions to count fingers (CF) vision and CF to 20/400 were considered one line change each. Complications and other adverse events were recorded during follow-up visits.

Results

Fifteen eyes were implanted with the KeraKlear KPro by a single surgeon (JMV). Preoperative diagnoses included corneal scars (due to trauma and or infection), keratoconus, and corneal dystrophies [Table 1]. Average age at time of surgery was 50 years old and 67% of patients were female.{Table 1}

The average follow-up period was 43 months (range = 18–64 months). The median follow up period was 46 months. As a group, the patients experienced an average improvement in uncorrected Snellen VA of 7.6 lines (range 1–11 lines). Mean pre-operative logMAR was 1.66. The average best uncorrected VA during the postoperative follow-up period was 0.49 logMAR (20/60 Snellen), representing a mean change of − 1.17 logMAR. The average uncorrected logMAR at the last visit was 0.75 (20/100 Snellen). The median uncorrected logMar was 0.54 (20/70 Snellen). Ninety-three percent (14 of 15) of patients had an improvement in VA at the last visit compared to the pre-operative period. One of the patients in the study had a macular scar which limited VA to 20/400. One patient, who was noncompliant with regular replacement of the bandage contact lens and stopped using prophylactic antibiotics, developed bacterial keratitis which led to extrusion of the KeraKlear. Three patients who had a preoperative diagnosis of corneal scarring developed progressive corneal scarring deep to the implant which worsened vision after an initial dramatic improvement in VA. The remaining 12 patients had clear posterior corneas at all visits. No patients had worse VA at last follow-up compared to before implantation. No cases of endophthalmitis, retroprosthetic membrane, or glaucoma were observed. Overall, the KeraKlear appeared to be well tolerated within the cornea without any obvious signs of inflammation after implantation. All fifteen KeraKlear implants remained clear during the follow-up period.

KeraKlear outcomes were compared to that of PKP,[10],[11] Boston KPro [12] and AlphaCor Artificial Cornea [Table 2].[13] It is important to clarify that the underlying pathologies of the Boston Kpro and Alphacor were much more severe than those in this study. Therefore, it would be expected that the VA outcomes in these two groups would be worse than that of the KeraKlear. However, it is notable that the KeraKlear was not associated with the significant complications seen with penetrating keratoprosthesis, including retroprosthetic membrane, endophthalmitis and glaucoma. No patients developed any of these three complications during the follow-up period.{Table 2}

Discussion

The KeraKlear offers distinct advantages over penetrating KPros: (1) there is no need for corneal donor tissue; (2) nonpenetrating surgery appears to minimize the risk of endophthalmitis, retroprosthetic membrane, and glaucoma; (3) the ability to perform surgery in a nonsterile, office environment; and (4) preservation of the ability to perform PK or deep anterior lamellar keratoplasty (DALK). Moreover, there is a short learning curve for the procedure; surgeons comfortable with cataract surgery or LASIK have the skill set needed to successfully perform the surgery.

The KeraKlear also offers advantages over PK, including the lack of need for donor tissue and the ability to perform surgery in an office environment. Because of the nonpenetrating nature of the KeraKlear procedure, complications such as endophthalmitis and expulsive hemorrhage should also theoretically be minimized. The average visual improvement provided by the KeraKlear in a Venezuelan population was comparable to PKP in a population of Middle Eastern patients being treated for keratoconus and corneal scarring [Table 2].[10],[11] Importantly, KeraKlear implantation was not associated with the development of glaucoma in this study. We hypothesize that this may be due to the absence of topical corticosteroids in

the postoperative regimen as well as maintenance of normal angle morphology. Larger studies will be needed to confirm whether or not the KeraKlear has any impact on glaucoma.

In contrast, PK is known to be associated with the development of glaucoma. One notable study by Kirkness and Ficker presented incidence of postoperative glaucoma as 14%,[14] and ranges from 9% to 31% in the early postoperative period to as high as 18%–35% late postoperatively have also been reported.[15],[16] In a Middle Eastern population being treated for corneal scarring, PKP was associated with glaucoma in 28% of cases.[11] Additional glaucoma surgery is often required following PK, and though drainage devices provide the most successful lowering of intraocular pressures, they have the lowest rates of graft survival.[17]

Endothelial graft rejection is another common complication of PK. The rate of endothelial rejection after PK has been reported to range between 21% and 27% depending on the original diagnosis.[18],[19] As implantation of the KeraKlear does not replace the endothelium, endothelial rejection is not possible.

DALK of course, also has the advantage of preserving the endothelium and does not have the risk of endothelial rejection and theoretically should be less susceptible to expulsive hemorrhage and endophthalmitis. DALK has no significant difference in VA or refractive outcomes compared to PK according to a large meta-analysis.[20] Therefore the VA outcomes of KeraKlear and DALK should also be similar. However, in DALK, the surgical technique is much more challenging because of the need to dissect stroma away from the delicate Descemet's membrane. Perforation of Descemet's membrane occurs in 15%–32% of DALK cases, often resulting in the need to convert to PK.[21],[22] In the case of the KeraKlear, because the incision is made by a femtosecond laser and leaves a residual stromal bed of at least 100 μ, the risk of perforation of the cornea and damage to the endothelium is minimized.

In this study, all incisions were made using a femtosecond laser. In some parts of the world, femtosecond lasers may not be available or the cost of the procedure prohibitive. In these places, the use of a semi-automated corneal pocket maker such as the Dioptex (Linz, Austria) may be more appropriate. The cost of this semi-automated corneal pocket maker is approximately $35,000 USD, which is acceptable in most parts of the world for a reusable device. Success with the use of the Dioptex corneal pocket maker for KeraKlear implantation in patients with failed corneal transplants has been previously reported.[23] In each of these cases improvement in VA was demonstrated. Manual dissection, however, is not a viable option as it is impossible to guarantee the regular creation of a lamellar pocket 100 μ away from the endothelium.

As this study was enacted for purposes of evaluating clinical feasibility in fifteen patients with noninflammatory anterior corneal disease, one limitation involves how the KeraKlear implant would fare in a larger population with additional ocular co-morbidities, such as glaucoma or other noncorneal ophthalmic conditions. Three of the 11 patients who had a history of corneal scarring developed progressive scarring posterior to the implant which resulted in less of an improvement in vision over time. It is unclear if there will be further worsening over time. We also do not know which patients are at risk for this complication. Another limitation of the KeraKlear is that the device is only indicated for use in cases that do not have a dense full thickness corneal opacity. Fortunately, the majority of corneal blindness worldwide is due to corneal scarring and stromal dystrophies which occur in the anterior cornea, allowing for meaningful vision improvement with the KeraKlear.[8] In cases of full-thickness cornea edema, visual improvement is still possible by de-bulking the majority of the edematous tissue.[7],[23]

Conclusion

In summary, this medium to long-term study in patients with noninflammatory anterior corneal disease suggests that the KeraKlear nonpenetrating keratoprosthesis is a viable alternative to corneal transplantation, especially when corneal tissue is not available. Theoretically, the nonpenetrating nature of KeraKlear surgery may minimize some of the more serious complications of penetrating KPros and PK including glaucoma, expulsive hemorrhage, and endophthalmitis. At the time of the writing of this paper, none of these three complications have been reported with the use of KeraKlear. The KeraKlear is well-tolerated and produces similar improvements in visual outcomes when compared to PK and currently-available KPros, while still leaving these more invasive surgeries available. It has been shown that the results of PKP and DALK after extrusion of the KeraKlear can result in a clear graft after an average follow up of 17 months.[24]

The ability to produce similar VA outcomes as PKP and DALK, the absence of catastrophic complications and the ability to perform keratoplasty successfully in cases of failure all support the KeraKlear as a primary procedure, especially in patients with noninflammatory conditions. The KeraKlear has the potential to greatly expand the number of patients who can be treated for corneal blindness worldwide by decreasing the need for corneal transplant tissue, corneal surgeons, and sterile operating rooms.

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Conflicts of interest

There are no conflicts of interest.

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