Seoul-Type Keratoprosthesis

Preliminary Results of the First 7 Human Cases

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Objective: To evaluate the clinical efficacy of a newly designed Seoul-type keratoprosthesis (S-KPro).

Methods: The S-KPro, which consists of a polymethyl methacrylate optic, a skirt (polyurethane or polypropylene), and polypropylene haptics, was developed and implanted into 2 unsighted and 5 sighted eyes of 7 patients. One patient had a chemical burn, another had an ocular pemphigoid, and the remainder were diagnosed as having Stevens-Johnson syndrome. The preoperative visual acuities ranged from light perception to hand motions. The average follow-up time was 25.6 months.

Main Outcome Measures: We evaluated anatomical stability, visual acuity, retinal status, and the visual field.

Results: At the last follow-up visit, the S-KPro was well placed in 6 patients. The best-corrected visual acuities of the sighted patients ranged from 20/100 to 20/60 in the affected eye. One patient each experienced retinal detachment or endophthalmitis. Partial extrusion was found in the patient with glaucoma. A retroprosthetic membrane was detected in 1 patient and was treated with an Nd:YAG laser. No glaucomatous visual field defects were found in any of the sighted patients.

Conclusions: Anatomical success was achieved in 6 of 7 eyes. In 3 of the 5 sighted eyes, the S-KPro could rehabilitate corneal blindness not correctable with keratoplasty.

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The treatment of corneal blindness is a major area in the field of ophthalmology. Because corneal blindness cannot be treated with keratoplasty or limbal cell transplantation, a keratoprosthesis (KPro) is required. Although researchers have designed prostheses and made improvements for a more acceptable artificial cornea, many ideas regarding prosthetic design, surgical technique, and treatment of complications remain to be proved.

The type of KPro commonly used consists of an optical stem with an anchoring skirt. Tissue breakdown around the prosthesis and extrusion of the KPro is the major cause of its failure. Therefore, a newly designed Seoul-type keratoprosthesis (S-KPro) was introduced. The prosthesis consists of an optic made of polymethyl methacrylate, a skirt of polyurethane or polypropylene, and haptics of monofilament polypropylene (Prolene; Ethicon Ltd, Edinburgh, Scotland). The main characteristic of the S-KPro is the double-fixed design, which includes anchoring sutures between the cornea and skirt and ab internal scleral fixation of the haptics, synergistically improving the mechanical biostability. The clinical effects of the double fixation on the S-KPro’s biostability were investigated in 7 human subjects.

Results

The S-KPro was anatomically well attached in 6 of the 7 eyes. The outcomes are shown in the Table. The clinical course of each patient was as follows.

Case 1

This 59-year-old patient had had SJS for 14 years. Initially, an S-KPro made with an expanded polytetrafluoroethylene (e-PTFE) skirt (Gore-Tex; W. L. Gore and Associates Inc, Flagstaff, Ariz) was implanted. The best-corrected visual acuity had been 20/100 for 18 months, as previously reported. Although the S-KPro had been well placed, the skirt was gradually being exposed. Therefore, the S-KPro was exchanged with another one, made with a polyurethane skirt, 19 months postoperatively. Even though a retinal detachment occurred 3 days after the operation, the reimplemented S-KPro has been well placed up to now (Figure 2A). Partial degeneration and occluded pores were ob-
PATIENTS, MATERIALS, AND METHODS

DEMOGRAPHICS OF THE PATIENTS

We confirm that the research followed the tenets of the Declaration of Helsinki. Seven patients who provided written informed consent, including 2 unsighted ones, were enrolled in this study (Table). They consisted of 2 women and 5 men, and the mean age was 42.6 years. Five of them were diagnosed as having Stevens-Johnson syndrome (SJS), 1 had a chemical burn, and 1 had an ocular cicatricial pemphigoid (OCP). The preoperative visual acuities ranged from light perception to hand motions. In all study patients, repeated penetrating keratoplasty with amniotic membrane implantation was unsuccessful. The prognosis of all patients was very poor, not only for penetrating keratoplasty but also for keratoprosthesis implantation. One of the unsighted patients had amblyopia, and the other had uncontrolled glaucoma. These 2 patients were engaged to evaluate the anatomical stability of the implanted S-KPro. The mean follow-up time was 23.6 months.

S-KPRO DESIGN AND SURGICAL TECHNIQUE

The design and characteristics of the S-KPro were introduced previously (Figure 1).10 The optic was made of surface-modified polymethyl methacrylate. Polyethylene glycol was used for surface modification to reduce cell adhesion.11 Three of the S-KPros had a polyurethane skirt (thickness, 0.3 mm; porosity, 60%-80%; pore diameter, 40 µm), and the others had a nonwoven polypropylene skirt (Q 2030 NW; Seon-Kyoung Co, Seoul, Korea; fiber diameter, 15-20 µm; basis weight, 30.0 g/m²; thickness, 0.23 mm; pore diameter, 30-60 µm). The S-KPros were implanted in the more visually impaired eyes. The surgical technique for S-KPro implantation was followed as previously mentioned.10

Postoperatively, ointments of topical dexamethasone with polymyxin B sulfate and neomycin sulfate, and oxytetracycline hydrochloride with polymyxin B sulfate, were administered twice a day for 1 month. Ofloxacin and prednisolone acetate were subsequently applied 4 times a day until 2 months postoperatively. Dextran 70 and hydroxypropyl methylcellulose were instilled frequently, and hyaluronate sodium was applied 4 times a day and timolol maleate twice a day up to the present. Whenever the repair surgery was repeated during follow-up, ofloxacin and prednisolone acetate were reapplied for 2 months.

EVALUATION OF KERATOPROSTHETIC EYES

Best-corrected visual acuity, the anterior segment, retinal status, and anatomical stability were examined. The visual field was evaluated in 4 eyes using Goldmann perimetry.

HISTOLOGICAL EXAMINATION

Unfortunately, 1 patient experienced endophthalmitis and underwent evisceration after 7 months of follow-up. This specimen was stained with hematoxylin-eosin to evaluate fibrovascular invasion.

The skirt of the first implanted polyurethane S-KPro partially degenerated. A part of the degenerated skirt was obtained, treated with the same fixation and dehydration method as stated previously,10 and examined using transmission electron microscopy (H-7100; Hitachi, Tokyo, Japan).

served in the polyurethane skirt after 27 months of follow-up (Figure 2B).

CASE 2

This 31-year-old patient experienced a chemical burn in both eyes. An S-KPro made with a polyurethane skirt was implanted. The patient's visual acuity improved to 20/50 with a myopic correction of 7.5 diopters (D).12 Although the S-KPro had been well placed, tissue breakdown around the prosthesis occurred. Repeated buccal mucosa transplantation followed but failed. Retransplantation was frequently postponed for 5 or 6 months because of the patient's personal work commitments, but the S-KPro was well maintained (even with a totally exposed skirt), and the visual acuity was 20/100 (Figure 3). After scleral grafting was conducted, the S-KPro was well maintained in the keratoprosthesis eye up to the last follow-up visit, 36 months after the operation. No retroprosthetic membrane or retinal abnormality was observed.

CASE 3

A 61-year-old man had SJS, and an S-KPro with a polyurethane skirt was implanted. The patient's best-corrected visual acuity was 20/200 with a myopic correction of −5.0 D. The skirt of the S-KPro gradually became exposed. Buccal mucosae were grafted repeatedly, and the S-KPro was well positioned for 23 months. However, the superior part of the S-KPro was partially extruded 24 months after the operation. The allosclera and buccal mucosa were grafted, which restabilized the S-KPro. Although a diffuse retroprosthetic membrane formed repeatedly after 29 months, it was treated 4 times with Nd:YAG laser membranotomy. The patient's visual acuity then returned to 20/200. The S-KPro was well attached at the last follow-up visit (Figure 4). No glaucomatous visual field defect was found (Figure 5).

CASE 4

This 57-year-old patient had SJS and underwent S-KPro implantation. Its skirt was made of polypropylene. The patient's visual acuity was 20/200 with a hyperopic correction of 2.5 D. However, the skirt gradually became exposed after 6 months, and buccal mucosae were grafted 5 times. No glaucomatous defect was found during 2 years of follow-up. The S-KPro is well placed, and the retina has remained flat. No retroprosthetic membrane has been observed.

CASE 5

A 55-year-old woman had had an OCP for 20 years. She underwent implantation with an S-KPro that had a poly-
propylene skirt. Her best-corrected visual acuity was 20/60 with a myopic correction of 4 D. The retina was flat, and the visual field was nearly normal. Even with an episode of endophthalmitis at 2 months postoperatively, the visual acuity and electroretinal response were recovered with the application of topical antibiotics. The S-KPro was well attached until 7 months after the operation. Unfortunately, increasing pain with a sudden decrease in visual acuity recurred and resulted in evisceration, even though fortified antibiotics were aggressively administered. The vitreous culture was positive for *Enterococcus* fascia. A histologic examination revealed that no matrix had accumulated in the skirt, with little fibroblast invasion (*Figure 6A*).

**CASE 6**

A 31-year-old woman had developed SJS when she was 6 years old. She had an S-KPro with a polypropylene skirt.
implanted. Even though her visual acuity did not improve because of an amblyopia, the S-KPro has remained well attached, with skirt exposure, for 21 months. No other complication has since been detected.

**CASE 7**

This 33-year-old patient had had SJS for 20 years. A high intraocular pressure was incidentally detected. A polypropylene S-KPro was implanted and remained in place for 11 months. The patient’s visual acuity did not improve because of a total cupping of the disc. A partial dislocation of the S-KPro was detected 11 months after the procedure. An additional repair procedure was recommended, but the patient refused because the eye was unsighted.

The purpose of this study was to examine the biocompatibility of the double-fixed design of the S-KPro. The main problem with keratoprosthetic surgery is the extrusion of an implant. Tissue breakdown, the main cause of extrusion, seems to be inevitable surrounding the skirt of the keratoprosthesis. To enhance fibrovascular tissue invasion, a porous polymer with a pore diameter of 30 µm or larger was used for the skirt. Nevertheless, the cornea melted and exposed the skirt, thereby requiring an additional tissue graft. Buccal mucosal or scleral grafts were conducted repeatedly. The double-fixed design provided sufficient time to allow proper management of the exposed skirt, with improved stability. Even though the corneal fixation loosened, the S-KPro was well placed in most of the eyes. This suggests that the haptics anchored to the sclera may play an important role in extrusion.

In case 1, to cover the wound exposure between the cornea and skirt, the e-PTFE S-KPro was exchanged with one with a more porous skirt; this resulted in retinal detachment. Therefore, tissue grafts with the buccal mucosa and sclera were performed on the other eyes with skirt exposure instead of exchanging the S-KPro. The sclera was used to remove the dead space between the skirt and surrounding tissue. These procedures were relatively safe compared with the exchange and helped to stabilize the S-KPro. In conclusion, reinforcement with tissue grafting was regarded as a better choice than S-KPro exchange as a way to manage skirt exposure.

In case 1, an S-KPro made with an e-PTFE skirt with an average pore diameter of 20 µm was initially implanted. The pore size of the skirt material was too small to accept fibrovascular ingrowth, which was considered to be the cause of the skirt exposure. The e-PTFE S-KPro was replaced with one made with a polyurethane skirt (pore size ≥ 30 µm) because e-PTFE with a pore diameter of 20 µm or more is not commercially available and the pore size of polyurethane is easily fabricated. However, after long-term follow-up in humans, polyurethane with a large pore size was found to dissolve easily (cases 1 and 3). Additionally, with in vivo experiments, nonwoven polypropylene was found...
to have an excellent property that encourages fibroblast ingrowth compared with polyurethane (Mee Kum Kim, MD, unpublished data, 2001). Given this data, we finally exchanged polyurethane with polypropylene as the skirt material for the other patients. Researchers have paid much attention to porous polymers such as Proplast12,13 (a combination of polytetrafluoroethylene and vitreous carbon), e-PTFE,14 polyurethane,15 and hydrogels16,17 to enhance fibrovascular invasion. However, the effect of such porous materials on fibrovascular invasion is somewhat controversial. Whereas sufficient fibroblast ingrowth and matrix accumulation without any skirt exposure were found in both polyurethane and polypropylene in an animal study (Mee Kum Kim, MD, unpublished data, 2001), skirt exposure was observed in all human eyes in our study irrespective of the skirt material. This difference might result either from the insufficient protection from tears, mechanical stress by fibrotic eyelids with trichiasis, or abnormally malfunctioning fibroblasts in the diseased human eye. In particular, surgically induced inflammation in SJS may be the leading cause of tissue necrosis. Management of these factors should be considered important, as well as the choice of porous polymer.

Although a retroprosthetic membrane developed repeatedly in case 3, it was handled 4 times with Nd:YAG laser membranotomy. Repeated laser membranotomy was known to be efficient for treating the retroprosthetic membrane18,19 and was performed up to 7 times.20 Therefore, Nd:YAG laser treatment seems to be relatively safe and effective in treating eyes that have undergone S-KPro implantation.

Endophthalmitis, known to occur frequently in patients with keratoprosthetics,21 developed in case 5. Most cases of endophthalmitis are due to gram-positive cocci.22 This patient also had an Enterococcus infection, which is reported to be a common cause of endophthalmitis23 and keratitis.24 The patient was diagnosed as having OCP, and preoperative diagnosis of this condition or SJS is a major risk factor for endophthalmitis in keratoprosthetic eyes. Although skirt exposure was found in all eyes implanted with S-KPros, most patients did not experience endophthalmitis. Therefore, altered ocular immunity, as suggested by Nouri et al,22 may be related to endophthalmitis.

The microscopic findings were also remarkable. An abnormally thickened, squamous, metaplastic epithelial layer occupied more than half of the corneal thickness and accounted for the isolation of the skirt from the stroma, which interfered with the fibroblast invasion (Figure 6B). As usual, an intrastromal pocket was made halfway into the cornea for S-KPro implantation; however, the pocket should have been situated deeper than halfway for patients with a metaplastic cornea.

Another characteristic of the S-KPro is polyethylene glycol-grafting polymerization of the optics to reduce cell adhesion, in expectation of a decrease in retroprosthetic membrane formation. A retroprosthetic membrane was not found in most patients with the exception of case 3. Therefore, this modification might contribute to a decrease in the formation of the membrane. However, its effect on the reduction of retroprosthetic membrane formation is somewhat unclear because many factors are involved, such as inflammation, wound exposure, and bleeding during surgery. Future studies should examine the effect of polyethylene glycol-grafting polymerization on decrease in retroprosthetic membrane formation.

One of the disadvantages of the S-KPro is that the intraocular pressure cannot be measured. Therefore, β-blockers were routinely applied, and the visual field was periodically examined. No glaucomatous visual field defects were found in any of the sighted patients during follow-up. The threat of uncontrolled glaucoma often requires simultaneous or subsequent implantation of a drainage shunt.23 However, an additional drainage implant could not be used with the S-KPro implant, so more
work is recommended to enable the installation of a drainage device with the S-KPro.

The outcome of the keratoprosthetic surgery was related to the preoperative diagnosis.\textsuperscript{20} Patients who underwent S-KPro implantation had either SJS, OCP, or a chemical burn with a severely damaged ocular surface. Accordingly, the outcome tended to be less favorable compared with the results reported by other groups. However, it is important to evaluate the feasibility of the S-KPro and to learn adequate treatment for its complications.

In conclusion, the double-fixed design improves the mechanical stability of the S-KPro when used with additional grafting. The S-KPro enables 3 of 5 sighted patients to perform daily activities and continue their normal routine. The long-term outcome is pending.

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