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Saudi Journal of Ophthalmology

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ORIGINAL ARTICLE

Mushroom keratoplasty in pediatric patients [☆]

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Received 2 April 2011; revised 19 April 2011; accepted 20 April 2011

KEYWORDS

Mushroom keratoplasty;
 Pediatric keratoplasty;
 Shaped keratoplasty

Abstract Objective: To report the outcome of mushroom keratoplasty for the treatment of full thickness corneal disease in pediatric patients with healthy endothelium.

Methods: A retrospective analysis of pediatric patients who underwent mushroom keratoplasty. The medical records of pediatric patients suffering from full thickness corneal stromal disease with normal endothelium who underwent mushroom keratoplasty at our Institution were included. A two-piece donor graft consisting of a large anterior stromal lamella (9.0 mm in diameter and $\pm 250 \mu\text{m}$ in thickness) and a small posterior lamella (5–6.5 mm in diameter) including deep stroma and endothelium, prepared with the aid of a microkeratome had been transplanted in all cases. Ophthalmic examination including slit lamp examination, best corrected visual acuity, and corneal topography was performed preoperatively and at each postoperative visit on all patients. The endothelial cells were assessed by specular microscopy in these patients.

Results: Six eyes of six patients (five males and one female) were included. The mean age was 9.3 years (range 5–15 years). Average follow-up was 17.8 months (range 9–48 months).

There were no early or late complications recorded. All corneas were clear at the last follow up visit.

[☆] Presented in part at the annual meeting of the American Society of Cataract and Refractive Surgery, San Diego, March, 2011.

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Peer review under responsibility of King Saud University.

doi:10.1016/j.sjopt.2011.04.009



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Preoperative best corrected visual acuity (BCVA) was worse than 20/70 in all six eyes. Postoperatively, four eyes achieved BCVA of 20/40 or better.

Endothelial cell loss (n eyes = 3 averaged 24% (range 19–31%). The mean endothelial cell loss was 24% (range 19–31%) among these patients.

Conclusions: Microkeratome assisted mushroom keratoplasty is a viable surgical option for pediatric eyes with full thickness corneal stromal disease and healthy endothelium. Mushroom keratoplasty combines the refractive advantage of a large penetrating keratoplasty with the survival advantage of a small penetrating keratoplasty. Furthermore, mushroom keratoplasty exhibits the mechanical advantage of a shaped keratoplasty.

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1. Introduction

Acquired full-thickness corneal opacities in the pediatric population most commonly occur as sequelae of trauma or microbial keratitis (Huang et al., 2009). Corneal endothelium is frequently uninvolved, despite the full thickness stromal disease. Deep anterior lamellar keratoplasty, by manual (Melles et al., 1999) or big-bubble (Anwar and Teichmann, 2002) techniques, has been attempted for these eyes, however, focal adhesions or gross breaches of the descemet membrane (DM) render this procedure ineffective for many in this patient group. Newer techniques utilizing femtosecond laser are inappropriate for these eyes, due to the inability of the laser to function in the setting of significant corneal opacity. For these reasons, penetrating keratoplasty (PK) has, to date, been the treatment of choice for these patients.

Long term survival of PK in the pediatric population is limited (Maguire et al., 1994). Contributing factors include the hyperactive immune response leading to increased suture related and rejection related complications and failure, as well as the fact that these corneas are often vascularized (Epstein et al., 1987; Ficker et al., 1988; Thomposon et al., 2003). In addition, activities of children can be unpredictable, and traumatic wound dehiscence is not uncommon following PK in this age group.

We know from the Collaborative Corneal Treatment Study (CCTS) Maguire et al., 1994 and the more recent Corneal Donor Study (CDS) Sugar et al., 2009, that neovascularized corneas exhibit increased risk of rejection. In the past, small diameter grafts have been attempted to treat full thickness corneal disease in high risk cases such as those with corneal neovascularization (Williams et al., 1992, 2008). Small diameter grafts exhibit increased survival, however, astigmatism is high, limiting visual rehabilitation (Williams et al., 1992, 2008), and their use has, therefore, been discontinued. Large diameter grafts have also been attempted, and do exhibit improved postoperative astigmatism, although the chance of failure increases as the size of the graft increases (Mader and Stulting, 1991; Cowden et al., 1989).

We describe mushroom keratoplasty for the treatment of full-thickness corneal opacity in the setting of healthy endothelium in the pediatric population. This procedure involves transplantation of a relatively small central area of the endothelium and deep stroma, combined with transplantation of a large anterior stromal lamellar. The resulting “mushroom” shaped two-piece graft combines the refractive advantages of a large anterior lamellar keratoplasty, with the survival advantage of a small PK (Busin and Arffa, 2005; Saelens et al., 2008). A minimal amount of healthy host endothelium is removed, however, the optical advantages of a PK are present.

Importantly, this type of keratoplasty provides a stronger wound profile, not only preventing wound dehiscence in the setting of minor trauma, but also allowing sutures to be removed at an earlier date, reducing the chance of suture related complications.

We present the results of an evaluation of mushroom keratoplasty performed in pediatric patients presenting to our institution with full thickness corneal stromal opacities in the setting of otherwise healthy endothelium.

2. Methods and materials

We reviewed the medical records of all patients of age 0–15 years inclusive that underwent mushroom keratoplasty by the same surgeon (M.B.) at our institution from January 2006 to November 2010 inclusive.

Informed consent had been gained from all legally responsible parents or guardians for the surgery performed. Analysis of the data obtained was performed by means of a standard spreadsheet program.

A complete ophthalmological examination had been performed preoperatively. This included slit-lamp biomicroscopy, best corrected visual acuity (BCVA), applanation tonometry, ocular motility, and funduscopy or B-scan of the posterior segment. Visual acuity was measured by Snellen chart in all patients. Corneal vascularization was evaluated by slit-lamp examination and rated according to the extension (number of clock hours involved) and depth (superficial or deep stroma). In addition, at all postoperative examination times (12, 24, and 36 months) corneal topography analysis (EyeSys 2000; EyeSys Technologies, Inc., Houston, Texas) and endothelial cell count (cornea module of HRT-II Heidelberg Technology, Heidelberg, Germany) were performed. Postoperative endothelial cell density (ECD) was evaluated centrally, i.e., in the area of the posterior donor button; the values recorded were compared with those obtained preoperatively from the eye bank, thus considering the cell loss as a percentage of the preoperative *in vitro* value, as described in a previous paper from our group (Busin et al., 2008). Follow-up examinations occurred at regular intervals, including but not limited to day one, day two, week two, month one, month three, month six, and then annually thereafter.

3. Surgical technique

Patients all received general anesthesia, with the addition of peribulbar injection of a 50% mixture of lidocaine 2%, and bupivacaine 0.5%.

Surgery was performed with the surgeon sitting at the 12 o'clock position. The main surgical steps are illustrated in Fig. 1. Mushroom keratoplasty was performed using our standard technique, as has been previously described (Busin and Arffa, 2005). In brief, the host cornea was trephined to approximately 200 μm in depth and 8.5 mm diameter using a suction trephine (Hessburg Barron Trephine, Altomed, Tyne and Wear, UK) centered in relation to the limbus. The anterior lamellar was then removed by manual dissection, with a circular blade (MicroFeather circular blade, Feather Safety Razor Co., Osaka, Japan).

The donor cornea was mounted on the artificial anterior chamber of the automated lamellar therapeutic keratoplasty system (ALTK; Moria SA, Antony, France); a 200- μm head was used to split the donor cornea into anterior and posterior lamellae. The anterior and posterior lamellae of the donor tissue were then punched from the endothelial side to 8.5 and 6.0 mm, respectively (Barron Donor Corneal Punch, Altomed, Tyne and Wear, UK). Next, a full-thickness trephination of the remaining host cornea was performed, with a 6.0 mm suction trephine centered over the pupil. The host corneal button was then completely removed using a corneal scissors. The 6.0 mm donor button, consisting of endothelium, DM, and posterior stroma was then placed, over a small amount of viscoelastic, on the recipient bed. No sutures were used to attach this posterior lamellar. The anterior donor lamellar, consisting of epithelium and anterior stroma was then placed in position, overlying the posterior donor button or "stem". The anterior lamellar was sutured to the host cornea with a double continuous 10-0 nylon suture. Finally, the anterior chamber was filled with balanced salt solution, injected with a 30-gauge needle through a peripheral corneal tunnel.

All patients received topical tobramycin and dexamethasone (TobraDex, Alcon, Fort Worth Texas), two hourly by day, tapered to once daily over a 6 month period. Patients with corneal neovascularization, and, therefore, who were at increased risk of immunologic rejection, also received systemic steroids (Prednisolone 1 mg/kg tapered over 3 months). Sys-

temic acyclovir (400 mg twice daily) was given for 1 year to the patient with a history of herpetic keratitis.

In all cases, both sutures were removed within 9 months from surgery. Patients 8 years old or younger had all sutures removed by 6 months.

4. Results

Six eyes of six patients were included in this series. The average age at surgery in the study was 9.3 years (range 5–15 years). Five were males and one was female. Four eyes were phakic and two aphakic prior to the transplant surgery.

Three corneal scars resulted from previous penetrating eye injury, and two of these patients were aphakic, and one had traumatic cataract at the time of transplantation. One eye had a history of herpetic keratitis, and one of bacterial keratitis. The remaining patient had keratoconus with almost full thickness corneal opacity. These three patients were phakic at the time of transplantation, and remained so. Deep corneal vascularization with at least 3 o'clock hours of involvement was present in the two post infective cases.

Two patients had concurrent insertion of secondary posterior chamber intraocular lens (IOL), and one patient underwent combined phacoemulsification and insertion of IOL. All procedures were uneventful. There were no episodes of graft rejection. No cases have developed cataract to date, and there have been no additional early or late complications thus far. All grafts remained clear at the final examination. Figure 2. shows an example of the postoperative appearance. Visual results are summarized in Table 1.

At last follow-up (mean 17.8 months after surgery, range 9–48 months), best spectacle corrected visual acuity (BSCVA) was equal to or better than 20/40 in four of the six eyes. The mean refractive cylinder was 4.50 Diopters (D) or less in five of six cases, averaging 2.6 D. The endothelial cell loss, calculated from the difference between eye bank data and endothelial cell density at last follow up, averaged 24% (range 19–31%), considering the three patients for which data was available.

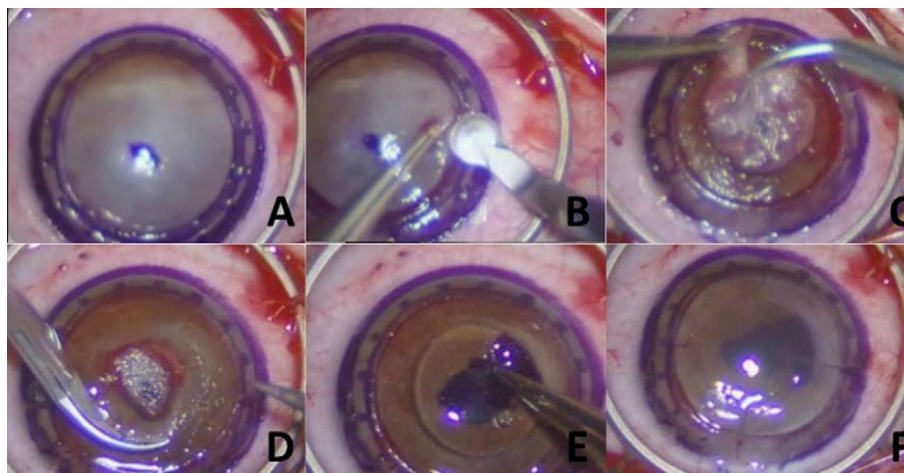


Figure 1 Surgical steps of mushroom keratoplasty. (A) Appearance post trephination, 9.0 mm diameter and approximately 250 μm depth. (B) Manual lamellar dissection. (C) Debulking completed with corneal scissors. (D) After 6.5 mm central full thickness host trephination, posterior button is removed with scissors. (E) Donor posterior lamellar (6.5 mm) placed. (F) Anterior 9 mm donor lamellar placed and sutured in place.

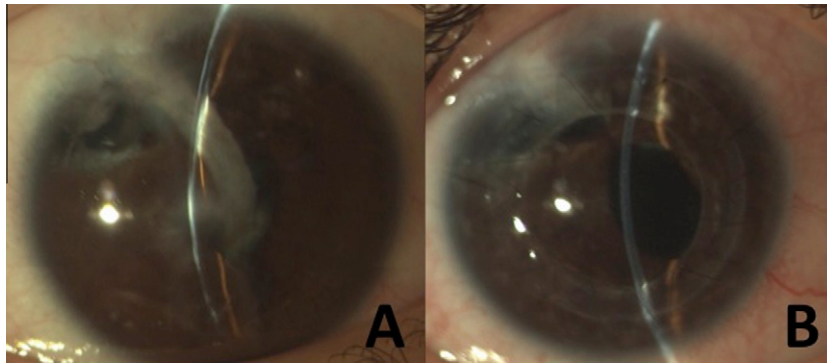


Figure 2 (A) Pre-operative appearance of a patient with healed full-thickness corneal wound following penetrating eye injury. (B) Post-operative appearance of the same patient, 4 months following mushroom keratoplasty.

Table 1 Patient demographic data and visual results.

Patient	Age/sex	Diagnosis	NV	Lens status	Surgery combined with	Pre-op BSCVA and refraction	Post-op BSCVA and refraction	F/U	ECL
MC	5/M	PEI	N	A	Secondary PCIOL	20/200 + 17/+ 3.0 × 30	20/50–2/–4.5 × 50	11	N/A
ML	8/M	PEI	N	P	Phaco/IOL	CF	20/400	9	N/A
AM	13/M	Post MK	Y	P	Nil	CF	20/25–4.0/–4.5 × 180	9	N/A
AP	8/M	Post PEI	N	A	Secondary PCIOL	20/70 + 10	20/22.5–2.5/–2.5 × 40	18	22
VSR	7/F	Post HSK	Y	P	Nil	20/200	20/22.5–2.0/–81.0 × 175	48	31
MS	15/M	KCN	N	P	Nil	20/200	20/22.5 0/–0.5 × 155	12	19

Abbreviations: M = male, F = female, NV = neovascularization, N = no, Y = yes, A = aphakic, P = phakic, PCIOL = posterior chamber intraocular lens, Phaco = phacoemulsification, Pre-op = preoperative, BSCVA = best spectacle corrected visual acuity, F/U = follow-up, ECL = endothelial cell loss, N/A = not available.

5. Discussion

Penetrating keratoplasty in children is a high risk procedure (Maguire et al., 1994; Epstein et al., 1987; Ficker et al., 1988; Thomposon et al., 2003; Al-Ghamdi et al., 2007). Increased surgical difficulties, as well as the unpredictable postoperative course results in an increased rate of graft failure for these patients, and parents are usually counseled regarding at best a moderate prognosis (Al-Ghamdi et al., 2007).

Most cases of PK failure in children with acquired corneal opacities occur relatively early in the post-operative period (Al-Ghamdi et al., 2007; Ehrich et al., 1991; Stulting et al., 1984). Ehrich et al. report most failures in the first 6 months, (Ehrich et al., 1991) whilst Stulting et al. report most failures in this group occurring in the first 12 months (Stulting et al., 1984). Al-Ghamdi et al. reported that 65.2% of graft failures in the pediatric age had occurred by the end of the first year, and 88% by the end of the second year (Al-Ghamdi et al., 2007).

In addition to the young age, corneal neovascularization is a common finding in acquired full-thickness corneal disease. Corneal neovascularization is known to be one of the main risk factors for the development of post-PK endothelial rejection and consequent graft failure (Maguire et al., 1994; Sugar et al., 2009). This is particularly true when deep stromal vascularization exceeds 3 o'clock hours in extension, as it is often the case in eyes with post-infectious scars of various origins (Thomposon et al., 2003; Price et al., 1993; Dandona et al., 1997; Vail et al., 1994). In these eyes, full-thickness grafts of

small diameter have shown higher long-term survival rates than those of conventional size (7.0–8.0 mm), but their use has been discontinued due to the unacceptably high degree of astigmatism (Williams et al., 1992, 2008).

The increased survival of small PKs may be due to the lower antigenic load or the greater distance from the vascular supply at the limbus, and resultant lower frequency of rejection episodes (Mader and Stulting, 1991). A further explanation could relate to previous evidence showing that endothelial cells migrate across the graft-host junction of a PK, from areas of high endothelial cell density, to areas of lower density (Imaizumi, 1990; Groh et al., 1999; Langenbacher et al., 2002). This may occur from the graft to the host, in eyes with endothelial disease such as Fuchs' endothelial dystrophy, or may occur from the host to the graft in cases with healthy host endothelium, such as those described herein. As we are transplanting only a minimal amount of host endothelium (approximately 25%), it is theoretically possible for the healthy host endothelial cells to repopulate the small diameter posterior button following an irreversible episode of graft rejection in these patients (Imaizumi, 1990; Groh et al., 1999; Langenbacher et al., 2002). Rearrangement of endothelial cells between the donor and recipient may provide explanation for the 100% graft survival in this study.

Deep Anterior Lamellar Keratoplasty (DALK) is frequently not effective for the treatment of full-thickness corneal disease. This is due to the gross disruption of the full corneal thickness following PEI, and the often present adhesions between DM and corneal stroma following microbial keratitis.

Deep corneal scars provide an obstacle for DALK that only few surgeons are able to overcome (Fontana et al., 2007; Sarnicola and Toro, 2010). For these reasons, manual or big-bubble DALK are often complicated by perforation of DM in these cases. Femtosecond laser is also not an option, as the corneal opacity would be expected to hinder the penetration of the LASER.

Ebeling and Carrel developed and performed the first mushroom shaped penetrating keratoplasty in 1921 (Ebeling and Carrel, 1921). This was before the advent of the operating microscope. In the setting of the obvious technical difficulties, the procedure did not gain popularity at that time. Much more recently, shaped keratoplasties have gained increasing popularity, in large part due to the stronger wound profile and improved visual outcome (Francheschetti, 1951; Busin, 2003; Bahar et al., 2008). Mushroom keratoplasty provides a shaped wound edge, much less likely to dehiscence in the event of minor trauma. Wound dehiscence is a lifelong concern following PK in the pediatric population, especially whilst the patients are young and their activities unpredictable.

With the use of the microkeratome, we have revisited the idea of mushroom keratoplasty. This two-piece donor graft provides the advantage of centration of the posterior "stem" of the graft on the pupil, whilst being able to center the anterior "hat" on the limbus. This is important for optimal visual outcome in the setting of the relatively small posterior graft. The posterior lamellar maintains its position without the need for sutures, similar to deep lamellar endothelial keratoplasty (DLEK) (Melles et al., 1998). The interface created by two microkeratome dissected surfaces is negligible, as demonstrated by laser *in situ* keratomileusis (LASIK), and also by other types of anterior and posterior microkeratome-assisted lamellar surgery. Good vision is the rule rather than the exception in patients undergoing these procedures (Busin et al., 2005; Chen et al., 2008; Shortt et al., 2006).

In conclusion, mushroom keratoplasty provides the optical benefits of a PK, with the wound stability and increased survival of a lamellar keratoplasty. The refractive advantage of a large graft is present, in addition to the increased survival of a small graft. Most of the recipient endothelium is preserved, providing the opportunity for reorganization of the host endothelium across the graft host junction in the event of a rejection episode. Visual and refractive results of mushroom keratoplasty in children compare favorably with those of conventional PK, at least in the medium term. Further studies would be required to adequately assess the long-term survival of these grafts.

Financial disclosures

Dr. Busin has received travel reimbursement and royalties from Moria (Antony, France).

Dr. Beltz and Dr. Scorgia have no proprietary or commercial interest in any of the materials discussed in this article.

The study was not funded by any source.

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