Cornea 22(5): 420–423, 2003.

Penetrating Keratoplasty in Young Children with Congenital Hereditary Endothelial Dystrophy

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Purpose. To report the visual results and success rate of penetrating keratoplasty (PKP) in a series of young children with congenital hereditary endothelial dystrophy (CHED). **Methods.** This is a retrospective study on twenty-four eyes of 15 patients (seven male and eight female) operated on for CHED. Children less than 12 years of age at the time of surgery who were followed for at least 6 months were recalled. Characteristics of the patients, indications for PKP, final visual outcome, and graft clarity were evaluated. The following tests were employed: McNemmar test for evaluating visual results, Kaplan-Meyer analysis for determination of graft survival, and Mann-Whitney *U* test for evaluating the relationship between visual outcome and age at PKP. **Results.** Patients' age at diagnosis and at initial PKP was 6.5 ± 3.6 and 8.1 ± 2.5 years, respectively. Follow-up period was 35.5 ± 36.2 months. Visual acuity could be evaluated by Snellen chart in 19 eyes. Preoperative visual acuity was less than 20/80 in all of these. Postoperatively, visual acuity was less than 20/80 in nine eyes (47.4%) ($P < 0.002$). Visual acuity improved in 18 (94.7%) of 19 eyes. There was no relationship between age at initial PKP and final visual outcome ($P = 0.35$). At the last examination (24 grafts), 19 were clear (79.1%), two were hazy (8.3%), and three were opaque (12.5%). Allograft rejection was seen in 10 eyes (43.4%), seven of which were endothelial. Excluding one case of trauma, all graft failures resulted from endothelial rejection. The probability of primary graft survival was 88% at 3 years and 74% at 5 years. **Conclusion.** Regarding the difficulties in pediatric keratoplasty and the absence of a relationship between postoperative visual outcome and age at keratoplasty, a conservative approach and careful risk-benefit ratio evaluation are recommended in patients with CHED.

Key Words: congenital hereditary endothelial dystrophy (CHED), penetrating keratoplasty (PKP), visual outcome.

Congenital hereditary endothelial dystrophy (CHED) presents as bilateral diffuse corneal haziness and edema. It is inherited as an autosomal dominant or recessive trait. The latter appears to be more prevalent and is more commonly associated with nystagmus.[1–3] Pathogenesis of the condition is endothelial cell degeneration during intrauterine or infantile periods.[4] The most important differential diagnosis is congenital glaucoma, but birth trauma, mucopolysaccharidosis, and intrauterine infections must also be considered. Visual acuity may be affected to varying degrees and is surprisingly better than the clinical appearance of the eyes;[5,6] however, CHED can lead to amblyopia in children.

There are few published articles reporting PKP for CHED in the literature. There is a high prevalence of CHED in our geographic area,[2,3] and with our increased experience at our tertiary referral center, we present our second report on a younger group of patients.[2]

MATERIAL AND METHODS

All patients aged 12 years or less who had undergone PKP for CHED from 1987 to 1997 with a minimum follow-up of 6 months were recalled, and a complete examination was performed. Preoperative visual acuity was measured by Snellen chart; in those less than 4 years it was estimated by fixation pattern. Clinical diagnosis was based on the presence of bilateral diffuse corneal edema, normal IOP, and normal corneal diameter. Penetrating keratoplasty was planned if the patient presented with or developed signs of compromised binocular cooperation (such as nystagmus or heterotropia) or manifested severe corneal haziness. Surgery was delayed in patients with moderate corneal haziness and orthotropia.

All patients were operated under deep general anesthesia and received 1–2 g/kg mannitol 20% intravenously about 10 min before trephination to prevent iris and lens prolapse during surgery. In all cases a Flieringa ring was fixed to the episclera. Trephine size was 6.5 mm in one case, 7 mm in 12, and 7.5 mm in the remaining 11 cases. Donor-recipient disparity was 0.5 mm in all cases. Donor corneas were punched through the endothelial side, and 10-0 nylon suture material was used for all eyes. In 19 cases suturing was interrupted, in two continuous, and in three others a combined technique was used. At the end of the procedure 20 mg methylprednisolone was injected in the subtenon space. Twenty milligrams gentamicin and 4 mg betamethasone were also injected subconjunctivally. In all cases pathologic reports confirmed the diagnosis.

The postoperative regimen included topical sulfacetamide 10% four times daily and betamethasone phosphate 0.1% six times daily. A systemic steroid (prednisolone, 1 mg/kg) was adminis-

Submitted September 24, 2002. Revision received March 27, 2003. Accepted March 29, 2003.

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tered in some patients for a few days. Sulfacetamide was discontinued after 5 to 7 days, and betamethasone was tapered gradually and discontinued in 2 to 3 months. Refraction was done as soon as possible, and amblyopia therapy was commenced. Sutures were removed 3 to 24 months (mean 7.8 ± 4.4 months) after surgery.

Patients were examined weekly during the first month, then every 2 weeks for 3 months, monthly up to the first year, and then every 3 months. In each examination, best corrected visual acuity (BCVA), graft clarity, presence of allograft reaction, and response to amblyopia therapy were evaluated. One case (no. 8) was excluded from the survival analysis because of trauma that caused wound dehiscence, iris prolapse, cataract formation, and graft failure.

Graft clarity was classified into three groups. "Clear grafts" were compact corneas with no edema, through which anterior segment examination and refraction were easily possible. If graft edema was present through which iris details were visible, but refraction was not possible, it was classified as hazy; opaque grafts were those corneas through which no anterior segment details could be seen. Both opaque and hazy corneas were considered as failed grafts. A graft rejection episode was defined by intraocular inflammation with keratic precipitates or a rejection line on the endothelium with or without a varying amount of loss of graft clarity. Graft survival was considered the duration from initial PKP up to the first follow-up in which the graft lost clarity; otherwise, the interval between the first and second keratoplasties (regrafting) was termed "survival interval." Only primary grafts were considered in the analysis.

The McNemmar test was used to evaluate the visual results, Kaplan-Meyer method was employed for analysis of survival data, and the Mann-Whitney *U* test was implemented for the relationship of age at surgery to final visual outcome.

RESULTS

Twenty-four eyes of 15 patients (seven male and eight female) underwent penetrating keratoplasty (Table 1). Nine cases had bilateral and six cases had unilateral corneal grafting. Patients' age was 6.5 ± 3.6 years (4 months to 12 years) at the time of diagnosis and 8.1 ± 2.5 years (3.5 to 12 years) at the time of surgery. Follow-up period was 35.5 ± 36.2 months (6 to 120 months). Snellen visual acuity could be obtained in 19 eyes. Preoperative visual acuity was 20/200 in seven eyes (29.1%) and less than 20/200 in 12 eyes (50%). In five cases visual acuity was measured as CSM (central steady maintained). One patient presented with nystagmus, two with strabismus, and four with nystagmus and strabismus. Overall there were seven cases (29.1%) with associated disorders, of which strabismus was the most prevalent.

Of 15 operated children, 12 (80%) were the result of consanguineous marriage; their parents were first cousins in all cases except one, who were second cousins. None of the parents were affected. Of 11 affected families, eight had more than one affected offspring, some of whom were not included in this study. Eight cases had an affected sibling, and two others were cousins.

Pre- and postoperative visual acuity and the condition of the graft on the last examination are shown in Fig. 1. In all patients whose vision could be measured by Snellen chart, preoperative visual acuity was less than 20/80. Postoperatively, visual acuity less than 20/80 was present in nine eyes (47.4%). This change was statistically significant ($P = 0.002$) (Table 2). No significant relationship could be demonstrated between postoperative visual acuity and age (above or below 6 years) at which PKP was performed ($P = 0.35$).

On the last examination, 19 (79.1%) grafts were clear, two (8.3%) were hazy, and three (12.5%) were opaque. Graft rejection was the cause of all graft failures (excluding case 8). In 10 eyes (43.4%) there was at least one episode of graft rejection, of which seven (70%) were endothelial and three (30%) were epithelial. Overall, endothelial rejection occurred in 30.4% of cases and led to graft failure in four. The probability of a clear graft by the Kaplan-Meyer method was estimated to be 88% for the first year with a 95% confidence interval of 75–100%. It was the same for the second and third years (Fig. 2). The probability of graft survival after 5 years was 74% (95% CI 50–100%).

TABLE 1. *Patients' pre- and postoperative data (n = 24)*

No.	Eye	Age at diagnosis (yrs)	Age at surgery (yrs)	Preoperative VA	Postoperative VA	Rejection	Total follow-up (mos)	Final clarity
1	L	8	12	5/100	20/200	+	9	Opaque
2	R	8	10	20/200	20/80	–	6	Clear
	L		9	20/120	20/80	–	16.4	Clear
3	R	0.6	7	20/200	20/120	–	6.7	Clear
	L		5	20/200	20/120	+	25.7	Clear
4	R	6.5	7	C+S+M+	20/120	+	120	Clear
	L		8	C+S+M+	20/80	–	118.6	Clear
5	R	11	11	2/100	20/60	–	27	Clear
	L		12	2/100	20/80	+	14.6	Clear
6	R	9	11	3/100	20/60	–	52.1	Clear
7	R	6	6.5	3/100	20/40	–	68.4	Clear
	L		7.5	2/100	20/80	+	53	Hazy
8	R	7	7	3/100	20/160	–	6	Hazy
9	R	5	5	2/100	20/120	–	24.6	Clear
	L		6	3/100	20/60	–	17.2	Clear
10	R	12	12	20/160	20/120	–	6.4	Clear
11	R	7	7	8/100	20/120	–	34.2	Clear
	L		8	3/100	20/120	–	20.6	Clear
12	R	5	5	C+S+M+	20/60	+	92.2	Clear
	L		10	20/200	2/100	+	12	Opaque
13	L	0.3	3.5	C+S+M+	C+S+M+	–	6	Clear
14	R	1.5	7	C+S+M+	20/50	+	19	Clear
	L		8	20/200	20/50	+	6	Clear
15	R	11	11	1/100	20/50	+	89.6	Opaque

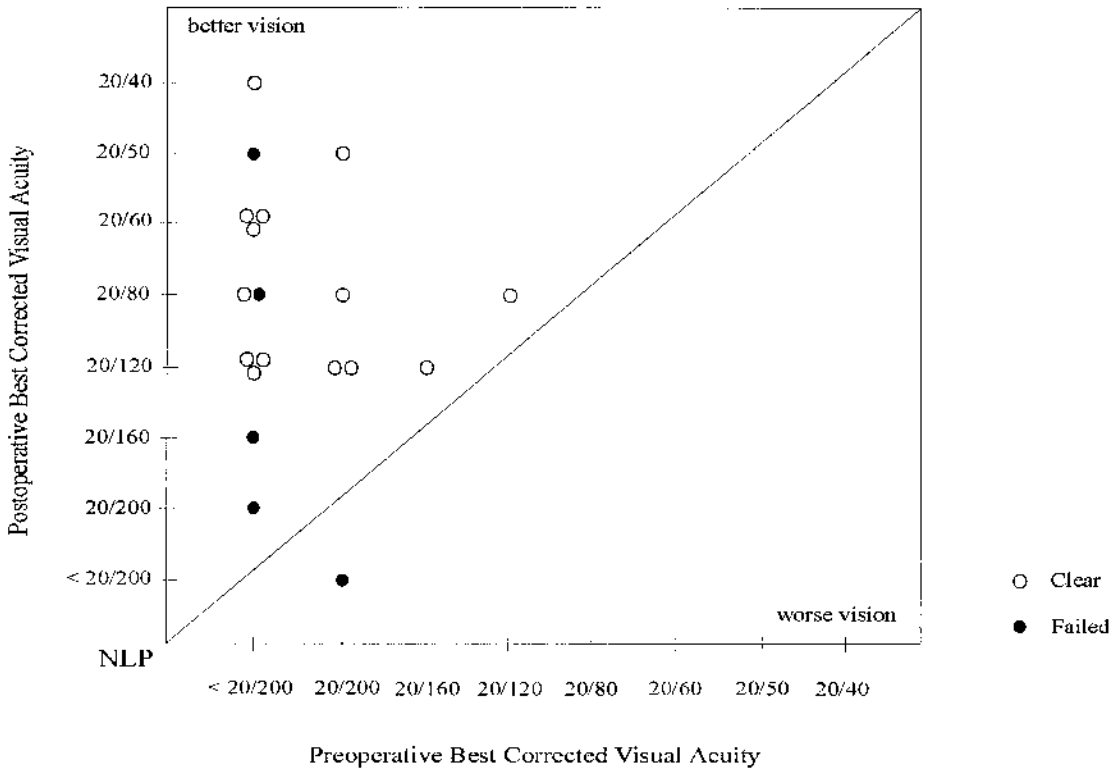

FIGURE 1. Preoperative and postoperative visual acuity during the follow-up period. The condition of the graft on the last examination is also shown.

DISCUSSION

CHED usually presents at birth or shortly thereafter as bilateral diffuse corneal haziness with normal corneal diameter and normal IOP.[1–3,7,8] It is not a rare disease in some countries,[2,3] where it may result from a higher prevalence of consanguineous marriage. There are reported cases of CHED misdiagnosed as congenital glaucoma,[2,3] but an association of congenital glaucoma and CHED has also been reported,[9–12] and it should be differentiated from congenital glaucoma. Absence of corneal vascularization or other anterior segment abnormalities provides a more favorable prognosis for PKP,[6] but visual results may still be unsatisfactory.

Postoperative VA in patients whose vision could be measured by Snellen chart has been reported to be 20/80 or better in 21 to 78%.[1–3,6] In our series, 52.6% of the eyes had visual acuity of 20/80 or better. In none of our cases did visual acuity improve to greater than 20/40. This shows that there is a varying degree of amblyopia in all cases; nevertheless, there was no relation between visual outcome and the age at which PKP was performed.

Pearce et al reported only 25% graft clarity in 16 primary PKPs after 3 months.[8] Kirkness et al reviewed the results of PKP in 31 eyes of 20 patients with an average follow-up of 39 months. PKP was done in patients between 10 and 15 years of age, and graft clarity was reported in 84%.[1] Sajjadi and co-workers reported the results of 37 eyes in 21 patients with an average follow-up of 36 months. The average age at PKP was 9.5 years, and 92% of the grafts were clear.[2] Al-Rajhi and Wagoner reported the largest series to date, with 56 eyes of 40 patients and an average follow-up of 3 years. Mean age at the time of surgery was 11.8 years. In this study, 62.5% of grafts were clear on final examination. Chance of graft survival was 92% at the end of the first year, 72% at 2 years, and 56.5% at 5 years.[3] In this series graft clarity was relatively higher in the late-onset type (92%) compared with the congenital type (56%). These results are comparable to those of Kirkness and

TABLE 2. *Pre- and postoperative visual acuity in patients whose vision could be measured by Snellen chart (n = 19)*

	Postoperative VA ≥20/80 no. (%)	Postoperative VA <20/80 no. (%)	Total
Preoperative VA <20/80	10 (52.6%)	9 (47.4%)	19 (100%)
Preoperative VA ≥20/80	0	0	0
Total	9 (47.4%)	10 (52.6%)	19 (100%)

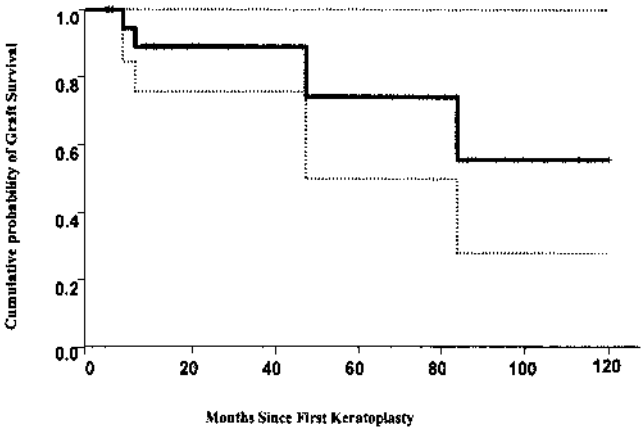

FIGURE 2. Kaplan-Meyer survival curve with 95% confidence interval (dotted lines).

Sajjadi, because in both of these studies keratoplasty was performed rather late. Schaumberg and co-workers reported the results of PKP in 16 eyes of 9 patients. Mean age was 40 months with an average follow-up of 70 months. Eleven (69%) of 16 eyes retained graft clarity on the last examination. The 2-year survival rate for initial grafting was 71% (95%CI 47–95%).[6]

Our findings are compatible with the abovementioned reports. Graft survival for the first 3 years is 88% (95%CI 75–100%), and 74% (95%CI 50–100%) at 5 years. In the current series PKP was performed only if the patient presented with or developed signs of compromised binocular cooperation or severe corneal haziness. With the above criteria we could not find any relation between the age at which PKP was performed and final visual outcome.

Because of the difficulties of pediatric keratoplasty and the absence of a relationship between postoperative visual outcome and age at keratoplasty, a conservative approach and thoughtful risk-benefit ratio evaluation are recommended in patients with CHED.

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