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Endophthalmitis After Penetrating Keratoplasty

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Purpose: To determine the incidence of endophthalmitis after penetrating keratoplasty (PK) and patient and donor risk factors.

Design: Retrospective cohort study using national transplant registry data.

Participants: All corneal transplant recipients (n = 11 320) registered on the United Kingdom Transplant Registry undergoing their first PK between April 1999 and December 2006.

Methods: Patients who developed endophthalmitis were identified on the transplant registry. In addition, cases where the fellow cornea from the same donor had been transplanted were included. Clinical information regarding donor and recipient characteristics, surgical details, and postoperative outcomes were collected and analyzed. In cases where endophthalmitis was reported, the diagnosis was verified by a follow-up supplementary questionnaire to the surgeon. Logistic regression was used to investigate differences in the factors associated with the development of endophthalmitis.

Main Outcome Measures: Incidence of endophthalmitis and graft survival.

Results: The overall incidence of endophthalmitis occurring after primary PK in the UK was 0.67%. The incidence of endophthalmitis occurring within 6 weeks of surgery was 0.16%. Graft survival after endophthalmitis was 27% (95% confidence interval, 16–38) at 5 years, with a mean best-corrected visual acuity of 1.13 (logarithm of the minimum angle of resolution) for surviving grafts. Factors associated with endophthalmitis were donor cause of death (infection), high-risk cases, and indication for corneal transplantation.

Conclusion: Endophthalmitis remains a serious issue, with those affected having reduced graft survival and poor visual outcomes. Management of the identified recipient and donor risk factors are important to reduce endophthalmitis risk. In particular, the increased incidence of endophthalmitis when the donor dies of infection requires further explanation and review of current donor eye retrieval and eye bank practices. The delayed presentation of endophthalmitis cases also raises questions regarding possible sequestration of microbes within the corneal tissue and the effect of antimicrobials in storage media. *Ophthalmology 2014;■:1–6 © 2014 by the American Academy of Ophthalmology.*

Endophthalmitis after penetrating keratoplasty (PK) is a serious adverse reaction and, although rare, usually has a poor outcome, with many cases ending up with a visual acuity of counting fingers or worse.[1] The reported incidence of endophthalmitis after PK varies from 0.08% to 0.77%.[1–6] A systematic review by Taban et al[6] found that the rate of acute endophthalmitis (defined as onset within 6 weeks) had, however, changed during the last few decades from 0.142% during the 1970s, 0.376% in the 1980s, 0.453% in the 1990s, to 0.2% in the 2000s.

All data on corneal transplant recipients performed under the National Health Service (NHS) are collected in the UK by NHS Blood and Transplant. This information is collected at the time of surgery (transplant record) and prospectively for ≤5 years postoperatively and recorded on the UK Transplant Registry (UKTR). Additionally, severe adverse reactions such as endophthalmitis must be reported to the UK regulatory authority, the Human Tissue Authority, in compliance with the European Union Tissues and Cells Directive.[7] Provision of follow-up data is a requirement of all surgeons undertaking corneal transplantation in the UK. Therefore, the study of endophthalmitis cases using the UKTR remains a relatively robust means of determining the incidence of endophthalmitis after PK as well as determining associated potential risk factors and prognostic factors. The identification of such factors may enable measures to be put in place to reduce the development of endophthalmitis after corneal transplantation.

Methods

Patients

All patients registered on the UKTR who had undergone a first PK between April 1999 and December 2006 were included. The described research methods and analysis plan adhered to the tenets of the Declaration of Helsinki, and institutional review board

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Table 1. Incidence of Endophthalmitis after First Penetrating Keratoplasty

Year of Transplant	Patients Receiving First PK, n	Incidence of Endophthalmitis (Cases Within 6 Weeks in Parentheses)	
		n	(%)
1999/2000	1440	9 (3)	0.63 (0.21)
2000/2001	1464	8 (2)	0.54 (0.13)
2001/2002	1316	9 (1)	0.68 (0.07)
2002/2003	1479	13 (2)	0.88 (0.14)
2003/2004	1562	9 (2)	0.58 (0.13)
2004/2005	1603	13 (4)	0.81 (0.25)
2005/2006*	2456	15 (4)	0.61 (0.16)
Total	11 320	76 (18)	0.67 (0.16)

PK = penetrating keratoplasty.
*Typical financial year starts in April of 1 year through March of the following year. The financial year in 2005/2006 also included data from April 2005 to December 2006.

approval was obtained. Data were collected by NHS Blood and Transplant from the UK Ocular Tissue Transplant Audit transplant record and follow-up forms at 1, 2, and 5 years after PK. The clinical information collected included preoperative data (such as indication, presence of inflammation and ocular surface disease, glaucoma and degree of corneal vascularization, eye laterality), perioperative events (donor and recipient characteristics and complications), and postoperative outcome (best-corrected visual acuity [BCVA]), unaided visual acuity, complications, medications, refractive data, rejection episodes, graft survival, and reasons for graft failure). Low-risk graft indications were ectasias, dystrophies, and corneal opacification. High-risk graft indications were infection, injury, and ulcerative keratitis. All transplanted corneas were stored by organ culture at 34°C for ≤4 weeks before being issued. The definition of "presumed endophthalmitis" used in this study was based on a clinical diagnosis made by the operating surgeon. The diagnosis was verified by a follow-up supplementary questionnaire to the surgeon. Additional information, such as causative organism, date at which endophthalmitis was diagnosed, and type of treatment given, was also sought by this questionnaire.

All statistical analyses were performed with SAS version 9.1 software (SAS Institute Inc., Cary, NC). Logistic regression was used to investigate multivariate differences in the factors associated with the development of endophthalmitis. Fisher's exact test was used to investigate univariate differences. Only those factors with $P \leq 0.1$ were entered into the forward stepwise regression procedure to determine those factors associated with the development of endophthalmitis. Cox proportional hazards regression was used to determine whether graft survival was lower for endophthalmitis cases in comparison with the fellow donor corneal transplants. Odds ratios (ORs) and relative risks are quoted with 95% confidence intervals (CIs). Two-sample *t* tests were used to investigate differences in logarithm of the minimum angle of resolution (logMAR) BCVA between endophthalmitis cases and fellow donor corneal transplants.

Results

Of 11 320 first PKs undertaken between April 1999 and December 2006, 95 patients were reported to have developed endophthalmitis. Nineteen of these cases were misclassified, having other diagnoses such as suture-related corneal abscess. There were, therefore, 76 cases of clinical endophthalmitis in the 7-year period, giving an annual incidence of 0.67% (standard deviation [SD] 0.12). The annual incidence of endophthalmitis for the period April 1999 to December 2006 is shown in Table 1.

Ten cases of endophthalmitis occurred within the first week after surgery, 8 cases between weeks 1 and 6, 14 between weeks 6 and 12, and 31 occurred after 12 weeks. There were 13 cases where the time of onset was not available. Information regarding culture results from intraocular sampling was obtained in only 24 cases. Microorganisms were isolated in 13 (54%) of these cases, of which 4 were fungal (3 *Candida* and 1 *Fusarium*). The remaining organisms were *Pseudomonas* sp., *Streptococcus* sp., *Staphylococcus* sp., and *Mycobacterium* sp. No information was available on donor rim cultures because these procedures are not routinely performed in the UK. No growth of microorganisms had been observed from sampling of the organ culture storage medium before all corneas were issued for transplantation.

Risk Factors

A list of factors considered in the logistic regression modeling is provided in Table 2. Donor cause of death, indication, reason for graft, surgical procedures and complications, and suturing method were each found to be associated ($P \leq 0.1$) in univariate analyses with the development of endophthalmitis and were included in the logistic regression model. Death to enucleation time, days in organ culture, and recipient risk factors (inflammation, infection, glaucoma, ocular surface disease, or other) were not considered to be associated with an increased risk of endophthalmitis ($P > 0.1$).

The logistic regression model of the factors that were found to be associated with endophthalmitis is shown in Table 3. The odds of developing endophthalmitis were >4 times greater for corneas from donors in whom the cause of death was infection compared with those from donors who died from other causes ($P = 0.001$). There was no evidence to suggest a difference for any of the other donor causes of death. Of the 7 cases of endophthalmitis where the donor had died from an infection, 5 cases died from septicemia and 1 from meningitis. In the 1 other case, the exact type of infection was not recorded. For the 18 cases that developed endophthalmitis within 6 weeks, donor cause of death was not found to be a significant risk factor ($P = 0.2$), although this may be owing to the small sample size.