Intraocular pressure behaviour following penetrating keratoplasty and cataract surgery

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Introduction
Postkeratoplasty glaucoma (PKG) is one of the challenging issues that may compromise the graft.
Objective
The aim of this work was to study the incidence of glaucoma following penetrating keratoplasty (PKP) in pseudophakic or aphakic eyes and in cataractous eyes following combined PKP and cataract surgery and to highlight the risk factors involved in this complication.
Design
This is a prospective interventional nonrandomized study.
Settings
This study was conducted in the outpatient ophthalmology clinic of Kasr El-Aini Cairo University Hospitals between January 2011 and January 2013.
Patients and methods
Fifty-eight pseudophakic or aphakic eyes requiring PKP (group I) and 34 cataractous eyes that required combined PKP and cataract surgery (group II) were enrolled. The primary outcome measure was the change in intraocular pressure (IOP) using a tonopen. The Secondary outcome measures were the results of graft survival and the best corrected visual acuity.
Results
The procedure adopted, whether PKP or combined PKP and cataract, significantly influenced the occurrence of PKG ($P=0.003$, using the χ^2-test). In addition, the aetiology for PKP was a statistically significant factor ($P<0.001$). As regards postoperative graft survival, PKG was found to be a statistically significant risk factor ($P<0.001$, using the χ^2-test).
Conclusion and relevance
The incidence of glaucoma following PKP in pseudophakic eyes was 72.4%, whereas its incidence following combined PKP and cataract surgery was 41.2%, which was a significant difference. Eyes with buphthalmos had the highest incidence of PKG (100%), whereas eyes that had experienced preoperative trauma had the least incidence (25%), which was significant. PKG was found to be a significant risk factor for graft survival ($P<0.001$), with 35.7% of the eyes that developed postoperative glaucoma experiencing graft failure.

Keywords:
graft survival, penetrating keratoplasty, postkeratoplasty glaucoma, pseudophakia

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Introduction

Postkeratoplasty glaucoma (PKG) is one of the challenging issues that may have a negative impact on the survival of the graft. The incidence of PKG has been reported to range between 9 and 35%. Its diagnosis and management are much more difficult than that of primary glaucomas [1].

Diagnostic difficulty arises because of errors in tonometry recordings of a thick or astigmatic corneal graft. In addition, it is often not possible to adequately assess the optic nerve and visual field before surgery or during the immediate postoperative period because of preoperative media opacification and postoperative corneal distortion with high astigmatism, respectively [2].

The pathophysiology of PKG is multifactorial and may be related to distortion of the angle with collapse of the trabecular meshwork, suturing technique, postoperative inflammation, the use of corticosteroids, PAS formation and pre-existing glaucoma. Elevated IOP following penetrating keratoplasty (PK) in an aphakic patient might be the result of angle distortion secondary to a compressed tissue in the angle. Oedema and inflammation after surgery lead to further compromise in the trabecular meshwork function, and the situation is further aggravated by angle distortion. Factors that contribute to angle distortion include tight suturing, long bites (more compressed tissue), larger trephine sizes, smaller recipient corneal diameter and increased peripheral corneal

thickness [3]. In addition, Zimmerman *et al.* [4] proposed that mechanical collapse of the trabecular meshwork in aphakic grafts, due to loss of both anterior and posterior support, is the main problem leading to glaucoma.

The aim of this work was to study the incidence of glaucoma following PKP in pseudophakic or aphakic eyes and in those that had been treated with combined PKP and cataract surgery and to highlight the risk factors involved in this complication. Further, the effect of postoperative glaucoma on the final visual outcome is also evaluated.

Patients and methods

Approval for the study was obtained from the hospital's ethical committee (according to the WMA Declaration of Helsinki). All patients received a thorough explanation of the study design and aims and were requested to provide their written informed consent.

This is a prospective interventional nonrandomized study carried out between January 2011 and January 2013. Patients were selected from the outpatient ophthalmology clinic of Kasr El-Aini Cairo University Hospitals. Fifty-eight pseudophakic or aphakic eyes with a corneal pathology requiring PKP were enrolled in this study. In addition, 34 eyes with cataract and a corneal pathology that required combined PKP and cataract surgery were also included.

Patients excluded from our study were those with contraindications to PKP, such as advanced ocular surface disorders, uncontrolled glaucoma before PKP, posterior segment pathology that required both posterior and anterior segment intervention or that might affect the final visual outcome, and aphakic eyes with a defective posterior capsule for which intervention required an anterior vitrectomy and scleral fixation of the intraocular lens (IOL).

Preoperative examination

A full ophthalmological history was taken, with particular emphasis on previous ocular surgery or trauma. Details of topical medication given for glaucoma, uveitis, infections or ocular surface disorders were recorded.

Slit lamp examination of the cornea, the anterior chamber (AC), the iris and the IOL was performed. Intraocular pressure (IOP) was measured using a tonopen (Tono-Pen XL; Reichert Technologies, Depew, New York, USA).

Ultrasound biomicroscopy of the AC angle was performed in eyes with a history of pre-PKP glaucoma, open-globe injuries or corneal perforation. Ultrasonography of the posterior segment was resorted to whenever a detailed fundus examination was not feasible because of opacification of the media. Electroretinography was performed and the visual evoked potential was ascertained for these cases requiring ultrasonography.

Operative procedure

PKP was performed using a Barron suction radial trephine (Katena Products Inc.) on the recipient cornea, and a Barron punch trephine (Katena Products Inc., Denville, New Jersey, USA), which was 0.5 mm larger, was used to obtain the donor tissue from the endothelial aspect of the donor button. Eight radial interrupted 10-0 nylon sutures in addition to a 16-bite running 10-0 nylon suture were applied to hold the graft.

Open-sky repositioning or replacement of the existing IOL was performed whenever necessary. Open-sky extracapsular cataract extraction was performed in the combined PKP-cataract procedures. A continuous curvilinear capsulorhexis was performed and the IOL was placed in the bag.

Healon (14 mg/ml, 1.4%, Biocorneal II; Croma-Pharma GmbH, Stockerauerstrasse, Korneuburg, Austria) was the viscoelastic used in all surgeries and it was meticulously removed from the AC at the end of surgery using a double-way cannula. Eyes lacking sufficient posterior capsule to support the IOL and that required scleral fixation sutures were excluded from the study.

Postoperative examination and follow-up

On the first postoperative day, all eyes were subjected to a slit lamp examination to evaluate the graft clarity, depth of the AC, position of the IOL and the IOP (using a tonopen). Glaucoma was defined as persistent increase of IOP (> 21 mmHg) or the requirement for increased treatment in patients with a previously high IOP.

Incidence of any early postoperative complications was recorded. Examinations were repeated daily for a week and then at weekly intervals for 2 months.

Visual acuity was assessed from week 2 and best corrected visual acuity (BCVA) was measured at week 4. The visual fields in eyes with elevated IOP were measured at week 4. Ultrasound biomicroscopy of the angle was performed in eyes with glaucoma not earlier than 2 months postoperatively.

In case of uncontrolled glaucoma, glaucoma filtration surgery was performed not earlier than 3 months following the PKP. Systemic steroids were routinely tapered 2 months postoperatively, whereas topical steroids were continued for at least 6 months, except in steroid responders in whom topical steroids had to be stopped earlier. The shortest follow-up period was 24 months.

Statistical analysis

Data were statistically described in terms of mean ± SD, median and range, or frequencies (number of cases) and percentages when appropriate. The Student's *t*-test was used to compare numerical variables for independent samples between two groups, and the one-way analysis of variance (ANOVA) for more than two groups, when normally distributed, and the Mann–Whitney *U*-test was used for independent samples and the Wilcoxon signed-rank test for dependent samples when not normally distributed. For comparing categorical data, the χ^2-test was performed. The exact test was used when the expected frequency was less than 5. Correlation between various variables was ascertained using the Spearman rank correlation equation for non-normal variables. All *P* values

less than 0.05 were considered statistically significant. All statistical calculations were carried out using the computer program SPSS (statistical package for the social science; SPSS Inc., Chicago, Illinois, USA) version 18 for Microsoft Windows.

Results

Ninety-two eyes were enrolled in the study. Fifty-eight eyes were pseudophakic or aphakic and were categorized as group I; in this group patients' ages ranged from 22 to 76 years, with a mean of 56.76 ± 12.58 years, and the female : male ratio was 10 : 19. Thirty-four eyes underwent combined PKP and cataract surgery and they were categorized as group II. In this group, patients ages ranged from 6 to 70 years, with a mean of 38.76 ± 19.10 years, and the female : male ratio was 11 : 6.

Each group was further divided into subgroup A in which there was no history of glaucoma (IA and IIA) and subgroup B with a positive history of glaucoma controlled medically or by previous glaucoma surgery (IB and IIB). The mean preoperative IOP was 19.86 ± 8.53 mmHg in group I and 17.53 ± 5.70 mmHg in group II, whereas the mean postoperative IOP was 25.28 ± 6.52 mmHg in group I and 21.88 ± 8.25 mmHg in group II. Using the Wilcoxon test the difference between the preoperative and postoperative IOP was found to be statistically significant ($P<0.001$).

The cause of PKP varied among the patients: in eight patients (8.7%) the cause was due to trauma, in 30 (32.6%) it was due to infection, in 48 (52.2%) it was due to pseudophakic bullous keratopathy, and in six patients (6.5%) it was due to the presence of buphthalmos.

Postoperatively, we had 16 eyes (27.6%) with no glaucoma in group I and 20 eyes (58.8%) in group II were cured of glaucoma. In contrast, 42 eyes (72.4%) in group I developed glaucoma, of which 30 (71.4%) were controlled medically and 12 eyes (28.6%) needed glaucoma surgery; 14 eyes (41.2%) from group II also developed glaucoma, of which four (28.6%) were controlled medically and 10 eyes (71.4%) needed surgery.

Thus, the difference in the incidence of postoperative glaucoma between the two groups, determined using the χ^2-test, was statistically significant ($P=0.003$). The difference in the incidence of postoperative glaucoma between subgroups IA, IB, IIA and IIB, ascertained using the Fisher exact test, was also statistically significant ($P<0.001$).

Further, the risk factors for glaucoma, namely, age, sex, aetiology, procedure and preoperative glaucoma, were studied. The effect of each of these factors was studied on the occurrence of postoperative glaucoma and also on its grade (medically vs. surgically controlled). Age was found to be an insignificant risk factor for the incidence of postoperative glaucoma, as determined using the Mann–Whitney *U*-test ($P=0.242$), whereas it was found to be significant for the method of control of glaucoma, as determined using one-way ANOVA ($P=0.002$). Sex was found to be statistically significant, using the χ^2 and Fisher exact tests ($P=0.017$ and 0.004, respectively).

The aetiology for PKP was statistically significant for the development ($P<0.001$, using Fisher's exact test) and grade of postoperative glaucoma ($P<0.001$, using the Fisher exact test) (Table 1).

The procedure adopted, whether PKP or combined PKP and cataract, significantly influenced the occurrence of postoperative glaucoma ($P=0.003$, using the χ^2-test) and its grade ($P<0.001$, using Fisher's exact test). Even after the procedure was adjusted for the preoperative history of glaucoma, we saw significant results with respect to the occurrence of postoperative glaucoma ($P<0.001$, for groups I and II) and its grade ($P<0.001$, for groups I and II), using Fisher's exact test.

The postoperative BCVA was correlated to the occurrence of glaucoma and was found to be statistically significant ($P<0.001$, using the Mann–Whitney *U*-test and $P<0.001$ and $r=0.489$, using Spearman's test, respectively). When correlated to the method of glaucoma control also it was found to be statistically significant ($P<0.001$, using ANOVA and $P<0.001$ and $r=0.521$, using Spearman's test, respectively).

In addition to postoperative glaucoma, graft survival and the factors affecting it were also studied. Postoperative glaucoma and the grade of glaucoma were found to be statistically significant risk factors ($P<0.001$, using the χ^2-test and $P<0.001$, using Fisher's exact test, respectively).

The aetiology for PKP, the adopted PKP procedure, the preoperative history of glaucoma, age and sex were statistically insignificant risk factors for graft survival ($P=0.834$, using Fisher's exact test; $P=0.466$, using the χ^2-test; $P=0.061$, using the χ^2-test; $P=0.195$, using ANOVA; and $P=0.659$, using the χ^2-test, respectively).

Table 1 Correlating the aetiology for penetrating keratoplasty (to postoperative glaucoma whether medically or surgically controlled

	Postoperative glaucoma			
Aetiology	No glaucoma (%)	Medically controlled glaucoma (%)	Surgically controlled glaucoma (%)	*P* value
Trauma	75.0	0.0	25.0	
Infection	60.0	20.0	20.0	<0.001
PBK	25.0	54.2	20.8	
Buphthalmos	0.0	33.3	66.7	

PBK, pseudophakic bullous keratopathy.
$P<0.05$, statistically significant.

Table 2 The incidence of postoperative glaucoma in each of the subgroups (IA, IB, IIA and IIB)

Group	Preoperative glaucoma	Postoperative glaucoma (%)			*P* value
		No glaucoma	Medically controlled glaucoma	Surgically controlled glaucoma	
PKP in pseudophakia	No glaucoma (I A)	42.1	36.8	21.1	
	Glaucoma (I B)	0.0	80.0	20.0	<0.001
PKP + cataract	No glaucoma (II A)	83.3	8.3	8.3	
	Glaucoma (II B)	0.0	20.0	80.0	

PKP, penetrating keratoplasty.
$P<0.05$, statistically significant.

Discussion

Post-PK glaucoma is defined as an elevated IOP greater than 21 mmHg, with or without associated visual field loss or optic nerve head changes [2].

The incidence of glaucoma following PKP in pseudophakic eyes in this series was 72.4%, whereas its incidence following combined PKP and cataract surgery was 41.2%. This difference between the two groups was found to be statistically significant ($P=0.029$). The incidence in the literature ranges from 9 to 35% [1].

Several risk factors for post-PKP glaucoma have been implicated in our work. The aetiology for PKP was a statistically significant factor for the development ($P<0.001$) and grade of postoperative glaucoma ($P<0.001$). Eyes with buphthalmos had the highest incidence of postoperative glaucoma (100%), whereas eyes with preoperative pseudophakic bullous keratopathy had an incidence of 75%, eyes with preoperative infection had an incidence of 40% and eyes with preoperative trauma had an incidence of 25%.

Further, adjusting the procedure for the preoperative history of glaucoma significantly influenced the occurrence of postoperative glaucoma ($P<0.001$, for groups I and II) and its grade ($P<0.001$, for groups I and II). The incidence of postoperative glaucoma in each of these subgroups is shown in Table 2.

Age was found to be an insignificant risk factor for the incidence of postoperative glaucoma ($P=0.242$), whereas it was found to be significant for the method of control of glaucoma ($P=0.002$). Sex was found to be a significant risk factor for both ($P=0.017$ and 0.004, respectively), with a higher incidence in male (72%) than in female (47.6%) patients.

Goldberg *et al.* [5] reported that the incidence of PKG is associated with the indications for PK. Patients with pseudophakic bullous keratopathy, corneal perforation and graft rejection were shown to be at high risk for PKG.

Secondary glaucoma following PKP in pseudophakic and aphakic eyes has a negative effect on the final visual outcome. Postoperative BCVA was significantly poorer for patients with glaucoma, and worse in those eyes in which glaucoma was managed by oral rather than topical medication. This particular observation may reflect more advanced glaucoma-induced visual loss [6].

In our work, there was a direct fair correlation between postoperative BCVA and the occurrence of glaucoma ($P<0.001$, $r=0.489$).

The presence of glaucoma at or following PK was seen to have a significant adverse effect on graft outcome in terms of both visual function and graft survival [6].

In our study, postoperative glaucoma was found to be a statistically significant risk factor for graft survival ($P<0.001$), with 35.7% of the eyes that developed postoperative glaucoma experiencing graft failure, and 100% of the eyes that did not develop glaucoma having clear grafts. In contrast, the aetiology for PKP, the adopted surgical procedure, the preoperative history of glaucoma, age and sex were found to be statistically insignificant risk factors ($P=0.834$, 0.466, 0.061, 0.195 and 0.659, respectively).

Reinhard *et al.* [7] estimated the 3-year graft survival rate in patients with a preoperative history of glaucoma to be 71%, in contrast to 89% in those without such a history. A high incidence of graft failure has been reported if a glaucoma operation is performed following the occurrence of PK [8]. Some studies therefore suggest treating glaucoma with mitomycin-C trabeculectomy [9] or with a glaucoma drainage device [10] combined with PK surgery.

Another study by Stewart *et al.* [6] showed that, although overall graft survival was negatively associated with the presence of glaucoma, it was also dependent on the indication for PK and the presence of risk factors. The modality of glaucoma management influences graft survival. Graft survival rates of patients whose glaucoma was managed by medical therapy alone were higher than in those who underwent glaucoma surgery.

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Conflicts of interest

There are no conflicts of interest.

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