RAISED INTRAOCULAR PRESSURE AFTER PENETRATING KERATOPLASTY- HOW UGLY IS THE PROBLEM?
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ABSTRACT

BACKGROUND
Penetrating Keratoplasty (PK) has been one of the most effective and successful organ transplants for over a decade with Post-PK glaucoma, a significant clinical problem because of its frequency of occurrence, difficulty in diagnosis and monitoring and complexity of management leading to irreversible visual loss and graft failure.

MATERIALS AND METHODS
A prospective study conducted over 2 years. 67 cases of penetrating keratoplasty were followed postoperatively for raised intraocular pressure.

RESULTS
We found the incidence of postoperative glaucoma to be 25.4%. Occurrence varied with indication for PK. Statistical significance was obtained when PK was combined with other surgical procedures (p=0.003). There was no difference in interval estimate of postoperative outcome, but 82% of eyes with postoperative elevated Intraocular Pressure (IOP) were found to have graft failure with p value 0.001.

CONCLUSION
The incidence of glaucoma after penetrating keratoplasty is high especially if additional procedures taken at same sitting and results in significant graft failure rates.

KEYWORDS
Penetrating Keratoplasty, Raised IOP, Infectious Keratitis, Corneal Ulcer, Bullous Keratopathy, Post-Penetrating Keratoplasty, Glaucoma.


BACKGROUND
Penetrating Keratoplasty (PK) has been one of the most effective and successful organ transplants for over a decade. Post-PK glaucoma is a significant clinical problem because of its frequency of occurrence, difficulty in diagnosis and monitoring and complexity of management leading to irreversible visual loss and graft failure. Post-PK Glaucoma (PKG) is defined as an elevated IOP greater than 21 mmHg with or without associated visual field loss or optic nerve head changes. The multifactorial aetiology of post-PK glaucoma was classified by Dada et al (2008). The incidence of PKG varies from 9-31% in the early postoperative period and from 18-35% in late postoperative period. The management of Post-Penetrating Keratoplasty Glaucoma (PKPG) remains controversial mainly because of the high risk of graft failure associated with the treatment. If raised intraocular pressure after PK is treated with trabeculectomy or drainage devices, it can trigger graft rejection. The use of cyclodestructive procedures can additionally result in phthisis bulbi. Hence, glaucoma after PK demands utmost surveillance and management. This study was conducted to calculate the incidence of PKPG, identify the risk factors and evaluate the treatment options for raised intraocular pressure after keratoplasty in a tertiary care hospital setting catering to a mix of rural urban population.

MATERIALS AND METHODS
A prospective study was conducted in the Department of Ophthalmology after evaluation by Research Committee and obtaining institutional approval. Patients were enrolled in the study following thorough explanation of purpose of study and obtaining a consent.
Keratoplasty was planned in cases of corneal pathology of varied aetiology like infectious keratitis (non-healing corneal ulcers, corneal abscesses, perforated corneal ulcers and descemetomectomy), corneal scars (adherent leucomas, macular leucomatous opacities, scars due to trauma or keratitis of varied aetiology), bullous keratopathy, regrafts and staphyloma.

All participants underwent a detailed preoperative assessment with special reference to nature of visual loss, associated pain, watering, redness of eye, history of ocular trauma and previous ocular surgery. A detailed local and systemic examination was carried out making a note of visual acuity, position of head, position of eyeball, ocular movements, condition of eyelids and condition of lacrimal sac bilaterally. Bulbar and palpebral conjunctiva examined for congestion, chemosis and signs of trachoma. Note was made of condition of cornea in terms of size, shape, curvature, surface, transparency, ulceration, vascularisation-depth and extent from limbus, sensation (brisk/dull/markedly reduced/absent). Anterior chamber depth and contents were checked. Iris- Pattern, atrophy, synchiae, incarceration and extent were noted. The size, shape, position and reaction to light of pupil documented. Lens evaluated for position, opacity and pigment deposition.

Ocular pressure was recorded in each case. All patients also went through some special examinations. Fluorescein staining of cornea, Schirmer’s test, syringing with antibiotic drops, tonometry with Schiotz tonometer and fundus examination. A slit lamp examination was done in each case with reference to extent, depth of corneal opacity, extent of vascularisation and synchia. Ultrasound B scan was done. Donor eyes balls were obtained from the cadaver as early as possible after death. All donor eyes were thoroughly examined and particulars of each donor eye was noted pertaining to age of donor, cause of death, time of death, time of enucleation, enucleation - transplantation interval. Enucleation was carried out following standard aseptic and handling techniques. Eyeballs were stored in a sterile jar filled with saturated moist atmosphere (cotton soaked in normal saline) at 4°C. Corneoscleral button were stored in MK medium at 4°C for a maximum of 4 hrs. before grafting. Donor eyes from cases of poisoning, septicemia, drowning, infection, malignancy and markedly debilitated conditions were rejected.

After routine preoperative preparation of the eye for intraocular surgery, local antibiotic drops were instilled at frequent intervals. Patients were given oral aceclozamide 500 mg 2 hrs. prior to surgery. Surgery was performed under local anaesthesia. Keratoplasty done was either alone or combined with other procedures like len extraction with anterior vitrectomy, triple procedure, cataract surgery done secondarily or regrafting. The effect of all these additional interventions on postoperative rise in IOP was also analysed.

Donor button was prepared from corneoscleral button from the endothelial side. Care taken to avoid anterior chamber collapse and corneoscleral button with endothelial side up, placed on viscoelastic filled Teflon block 0.5 mm oversized handheld manual trephination done in all cases.

Pupil of recipient was constricted before procedure so that iris - lens diaphragm remains away from damage. A partial depth trephination with a trephine was followed by completion with #11 blade and corneoscleral scissors. Methyl cellulose 2% was injected in anterior chamber to prevent damage to intraocular contents. In some cases, synechiotomy and removal of exudative membrane instillation of antibiotic in anterior chamber was done after excision of recipient corneal button. Few cases require trimming of edges of recipient cornea. Peripheral buttonhole iridectomies were done. The recipient bed was coated with methyl cellulose and the donor button was transferred to the recipient bed taking care not to traumatisate the corneal endothelium or epithelium.

In all cases, four primary sutures with 8-0 silk were applied at 12, 6, 9 and 3 o’clock positions followed by secondary suturing. Secondary suturing of the graft was done by either continuous or interrupted 10-0 monofilament nylon sutures. Care was taken to tightly secure graft to host and knots buried to avoid postoperative discomfort. Topical antibiotic was instilled followed by pad and bandaging in the end.

First postoperative dressing was done after 24 hours followed by daily dressing using antibiotic and steroid eye drops. During each dressing, following points were noted:- Clarity of graft, graft edges, condition of sutures (loosening, breakage, suture infiltration or absence), epithelial defect, vascularisation, anterior chamber depth, synchia, iris prolapse, state of pupil, condition of IOL (intraocular lens), intraocular tension (dual/Schiotz tonometer) and visual acuity. The IOP was recorded after 2 weeks in all the cases except in some cases where there was indication of raised IOP, it was read even earlier. Topical steroids were given thrice daily for initial 4 weeks and then tapered over 6 months. Topical 0.05% cyclosporine was given as prophylaxis to eliminate any chance of graft rejection for a month. Topical 0.5% Tropicacyl given twice daily to prevent any synchiae formation for initial 4 weeks. Systemic steroids 1 mg/kg was started from first postoperative day and gradually tapered off. Patients followed up weekly for initial one month after discharge, then every two weeks for next two months and finally once a month for a year.

All data was entered on excel sheet by Microsoft. P values calculated using Fisher’s exact test an interval estimate of difference of proportions calculated for outcome.

RESULTS
Study was conducted over a period of 2 yrs. A total of 67 cases of Penetrating Keratoplasty (PK) were recruited and followed up. Out of the 67 cases, 53 cases (79.1%) were males and 14 (20.9%) were females. We had maximum cases 34 (50.7%) in the age group 41-60 years followed by 12 cases (17.9%) in 21-40 years age group, 11 cases (16.4%) in 61-80 years and 7 (13.2%) cases below 20 years of age. Three cases 3 (4.5%) were above 81 yrs. of age.

Out of the total 67 cases of our study, the main indication for PK was infectious keratitis in 35 cases (52.23%), corneal scars in 22 cases (32.83%), regrafts in 5 cases (7.46%),
bullous keratopathy in 4 cases (5.97%) and staphyloma in only one case (0.01%). The primary outcome measure in this study was raised IOP (intraocular pressure) after PK.

The overall incidence of raised IOP after PK calculated in this study was 25.4%. Table 1 shows the distribution of raised IOP with age group stratification and indication for PK.

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>Total Number of Eyes</th>
<th>Total Number of Eyes with Raised IOP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Infectious Keratitis</td>
</tr>
<tr>
<td>0-20</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>21-40</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>41-60</td>
<td>34</td>
<td>4</td>
</tr>
<tr>
<td>61-80</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>&gt;80</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>N</td>
<td>67</td>
<td>7</td>
</tr>
</tbody>
</table>

*Table 1. Age and Indication for PK Distribution of Raised IOP*

Evaluation of raised IOP after PK and its relationship with indication for PK was done using Fisher’s exact test and two-tailed p values obtained for each indication. It showed no statistically significant association of raised IOP with the indication for which PK was undertaken (Table 2).

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Total Number Eyes that Underwent PK n (%) (N=67)</th>
<th>Number of Eyes with Raised IOP Post PK n (%), (N=17)</th>
<th>*p value</th>
<th>Average Raised IOP n (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious keratitis</td>
<td>35 (52.23)</td>
<td>7 (41.17)</td>
<td>0.4</td>
<td>28</td>
</tr>
<tr>
<td>Corneal scar</td>
<td>22 (32.83)</td>
<td>6 (35.29)</td>
<td>1</td>
<td>29</td>
</tr>
<tr>
<td>Regraft</td>
<td>5 (7.46)</td>
<td>2 (11.76)</td>
<td>0.59</td>
<td>25</td>
</tr>
<tr>
<td>Bullous keratopathy</td>
<td>4 (5.97)</td>
<td>2 (11.76)</td>
<td>0.26</td>
<td>26.6</td>
</tr>
<tr>
<td>Staphyloma</td>
<td>1 (0.16)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Table 2. Association of Raised IOP Post PK with Indication for PK *p value Significant at <0.5

A statistically significant association was however found between post PK, raised IOP and additional surgical procedures, if undertaken. 26 cases underwent additional surgeries along with PK of which raised IOP was found in 12 cases as compared to 41 cases that underwent PK alone of which 5 had raised IOP in postoperative period. The relative risk ratio was 3.78, CI (confidence interval) 1.5-9.4 and p value 0.003, which was highly significant (Table 3). Of the 26 cases, PK with cataract surgery with anterior vitrectomy was done in 12 cases, triple procedure in 6 cases, PK with cataract was done in 2 cases and re-grafting in 6 cases.

<table>
<thead>
<tr>
<th></th>
<th>Raised IOP n (%)</th>
<th>Normal IOP n (%)</th>
<th>RR and (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PK + additional procedures</td>
<td>12 (46.2%)</td>
<td>5 (13.2%)</td>
<td>3.78 (1.5-9.4)</td>
</tr>
<tr>
<td>PK only</td>
<td>14 (53.8%)</td>
<td>36 (87.8%)</td>
<td></td>
</tr>
</tbody>
</table>

*Table 3. Relative Risk (RR) and Confidence Interval (CI) of Raised IOP when Additional Procedures are Undertaken with PK, p value-0.003

Management of raised IOP was medical, initially in all cases. It was successfully controlled medically in 5 (29.4%) patients and in the remaining 12 (70.6%) surgical management in the form of trabeculectomy was needed. Repeat trabeculectomy had to be done in 1 (5.9%) case with MMC after 1 month of doing the 1st trabeculectomy. In another case, MMC was used primarily during trabeculectomy. Mean IOP 2 weeks after surgical management was 16.6 mmHg (12.2-20.6 mmHg).

Status of eye was tabulated at the end of study in each case. Table 4 shows the outcome distribution with respect to raised or normal IOP post PK.

<table>
<thead>
<tr>
<th></th>
<th>Clear n (%)</th>
<th>Hazy n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raised IOP</td>
<td>2 (12), (N=17)</td>
<td>15 (88), (N=17)</td>
</tr>
<tr>
<td>Normal IOP</td>
<td>28 (56), (N=50)</td>
<td>22 (44), (N=50)</td>
</tr>
<tr>
<td>Proportion N=67</td>
<td>0.44 (95% CI, 0.33-0.56)</td>
<td>0.55 (95% CI, 0.43-0.66)</td>
</tr>
</tbody>
</table>

*Table 4. Graft Outcome at End of Study, p Value by Fisher’s Exact Test = 0.0017

The interval estimate for difference between the proportions of hazy and clear grafts at the end of the study was computed to be, -0.71 to 0.39, which means that overall, there was no significant difference in graft outcomes in the study. On further breaking down, the data to graft outcomes among eyes with raised postoperative IOP and
those with normal IOP, it was observed that a large percentage (88%) of eyes with raised IOP developed hazy corneas. This was statistically very significant at p value of 0.0017.

**DISCUSSION**

The mean age of patients in this study was 47.85 years (range 5-90 years). Majority fell in the age group 41-60 years. Male-to-female ratio was 3.8:1 with 79.1% males and 20.9% females. Ethan M. Kutzcher et al in 2004 in their study reported that the mean patient age was 43 years (range, 4-86 years); 23 (66%) were men and 12 (34%) were women. Mansour Al-Muhaimeed et al (2002) reported the sex ratio 1.7:1 with mean age 40.6 yrs. The distorted male-to-female ratio in this study compared to others was hypothesised to be due to socioeconomic paradigm as the rural population is prone to be selectively attentive to medical rehabilitation of the males.

Irvine and Kaufman et al (1969) first reported the high incidence of increased IOP following PK. They reported a mean maximum pressure of 40 mmHg in aphakic transplants and 50 mmHg in combined transplants and cataract extraction in the immediate postoperative period. There was an early rise on day 2-3, which usually resolved rapidly. It was followed by a late rise in IOP 2-3 weeks postoperatively. Since then, various authors have reported the incidence of glaucoma following PK to be from 9 to 31% in the early postoperative period 3,6,7 and from 18 to 35% in the late postoperative period. One of the primary objectives of this study is to calculate the incidence of raised IOP post PK and we found it to be 25.37% (17 cases out of the 67 cases). In the various studies done by G Chandras Sekhar et al (1993) 10 reported the incidence as 27.4% and Franca et al (2002) 11 reported it as 21.5%. These were similar to that found in our study. But, Andrea Mistlberger et al (1997) 12 and Sihota (1998) 13 had lower incidence rates at 14% and 10.6%, respectively.

When we broke down the cases of postoperative raised IOP according to the indications that led to keratoplasty, we found no significant association between any indication and raised IOP. In this study, however, 50% of cases that had undergone surgery due to bullous keratopathy developed raised IOP later, closely followed by re-graft cases at 40%, but the numbers are too small for statistical significance. Dada et al (2008) reported a wide range of cases at 20-70% of bullous keratopathy and 50% of re-graft cases suffering glaucoma, but Mansour et al (2002) reported a lower frequency at 26.9% in re-graft cases. Kirkness et al (1988) 14 reported a higher incidence of glaucoma in patients undergoing PK following corneal perforation, especially those following suppurative keratitis due to Peripheral Anterior Synechia (PAS) formation and secondary angle closure. The rates of chronic glaucoma after PK differ significantly based on the indication for PK (from a low of 0-12% for keratoconus to a high of 75% after infectious keratitis). We also identified that some other factors may play a causal factor in postoperative raised IOP such as- PAS, steroid induced, vireous, viscoelastic, aphaikia and pseudophakia. These factors merit a separate study to evaluate their role.

We found a significant association when keratoplastic was bundled with other surgical procedures (RR 3.78, CI 1.5-9.4). Andrea Mistlberger et al (1997) 12 from a database of 1122 penetrating keratoplasties performed at Moorfields Eye Hospital in London (1992) a total of 153 eyes (14%) were complicated by glaucoma within a time period of four years after surgery. In this study, it was also reported that the risk greatly increases in cases of combined cataract or lens implantation with anterior vitrectomy or “anterior segment revision.” Anterior chamber dysgenesis syndromes appear to have the highest incidence of this complications.

We also found a significant risk of graft rejection and hazy cornea in cases with high IOP postoperatively, which was similar to that reported by Adams GG et al (1997). 15 In this study, 104 acute corneal rejection episodes in 94 patients were studied retrospectively. 16 Episodes in 15 eyes were associated with raised Intraocular Pressure (IOP) on admission, 3 had previously elevated IOP. At six weeks, six (37.5%) still required hypotensive therapy. Five of the six eyes with graft failure at review had raised IOP either pre-graft at rejection or at follow-up.

There are a few limitations of the study. The sample size take is small and a larger study needs to be done to reinforce some of the significant but statistically small observations in this study. Also, Armaly et al (1963). 16 indicated that approximately one third of normal eyes and more than 90% of patients with primary open-angle glaucoma respond with greater than 6 mm Hg of IOP elevation after receiving a 4-week course of topical dexamethasone 0.1%. 7,17 Following intravitreal injection of triamcinolone, over 50% of non-glaucomatous eyes will have an increase in IOP. This increase in IOP can occur as long as 6 months after the injection. However, in this study, we could not study the effect of steroids on IOP as all cases were matched for postoperative steroid prescription.

**CONCLUSION**

Raised intraocular pressure after penetrating keratoplasty has a high incidence and is affected by a multitude of factors including multiple procedures at the same sitting and the indication for performing penetrating keratoplasty. It significantly affects the outcome of graft resulting in striking high failure rates.

**REFERENCES**


