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Chapter 5

Trabeculotomy Augmented by Postoperative Topical Medications vs. Trabeculectomy Augmented by Mitomycin C

Hiroshi Kobayashi

Abstract

Purpose: To study the safety and hypotensive effect of trabeculotomy augmented by postoperative topical medical treatment in patients with open-angle glaucoma and to compare with trabeculectomy augmented by mitomycin C.

Methods: In an non-randomized consecutive case series, we studied 82 patients with open-angle glaucoma who underwent trabeculotomy augmented by postoperative medical therapy or trabeculectomy augmented with Mitomycin C. Forty-two patients underwent trabeculotomy followed by latanoprost 0.004%, timololmaleate XE 0.5% and brinzolamide 1% and 40 patients underwent trabeculectomy augmented with Mitomycin C. Patients were followed-up for 12 months and a success rate based on intraocular pressure was compared.

Results: Mean baseline intraocular pressure was 27.9 ± 5.4 mmHg in the trabeculotomy group and 28.3 ± 4.2 mmHg in the trabeculectomy group (P = 0.7). Mean postoperative intraocular pressure was 15.1 ± 2.1 mmHg at 3 months, 14.7 ± 2.1 mmHg at 6 months, and 14.9 ± 2.0 mmHg at 12 months in the trabeculotomy group and 12.2 ± 1.9 mmHg at 3 months, 12.8 ± 3.0 mmHg at 6 months, and 13.9 ± 4.2 mmHg at 12 months in the trabeculectomy group. Mean intraocular pressure in the trabeculotomy group was significantly higher than that in the trabeculectomy group at 3 and 6 months (P < 0.0001 at 3 months; P = 0.0005 at 6 months) and there was no significant difference between the two groups at 12 months (P = 0.1). At 12 months, 42 patients (100%) in the trabeculotomy group and 37 patients (92.5%) in the trabeculectomy group achieved an intraocular pressure of less than or equal to 20 mmHg and a minimum of 30 percent reduction (P = 0.1). In the trabeculectomy group, 15 patients...
(37.5 %) received laser suture lysis, 6 patients (15.0 %) underwent needling procedure, and 3 patients (7.5 %) underwent additional surgery, although no patient in the trabeculotomy group received postoperative intervention except for topical medical treatment. In the trabeculotomy group, patients with higher preoperative intraocular pressure showed a significantly higher intraocular pressure at 12 months postoperatively (P < 0.0001), although there was no significant correlation between them in the trabeculectomy group.

Conclusions: There was no significant difference in hypotensive efficacy between patients undergoing trabeculotomy augmented by postoperative topical medications and those undergoing trabeculectomy augmented by Mitomycin Cat 12 months. In those receiving trabeculotomy, patients with higher preoperative intraocular pressure showed a significantly higher intraocular pressure at 12 months even though less than 20 mmHg.

Keywords: trabeculotomy, trabeculectomy, postoperative medication

1. Introduction

Trabeculectomy has been a standard procedure for medically uncontrollable glaucoma [1]. Serious postoperative complications are not infrequently associated with trabeculectomy [2-5]. These include flat anterior chamber, hypotony and choroidal detachment caused by overfiltration, late-onset bleb-related complications, including endophthalmitis, and cataract progression. Shigeeda et al. demonstrated that 44.5% of patients who had undergone trabeculectomy augmented with mitomycin C showed a success defined as an intraocular pressure of less than 16 mm Hg after 8 years [6]. However, Tanihara et al. demonstrated that medical treatment following trabeculotomy provided an additional intraocular pressure reduction and that this surgery produced long-term stability of intraocular pressure control [7]. Trabeculotomy infrequently causes serious complications and seldom requires additional postoperative interventions [8, 9]. The aim of this study is to study the safety and hypotensive effect of trabeculotomy augmented by postoperative medical treatment in patients with open-angle glaucoma and to compare with trabeculectomy augmented by mitomycin C.

2. Patients and methods

In a non-randomized consecutive case series, we studied 82 patients with open-angle glaucoma who underwent trabeculotomy augmented by postoperative medical therapy or trabeculectomy augmented with mitomycin C. A diagnosis of glaucoma was on the gonioscopic finding along with appearance of the optic nerve head cupping and visual alteration according to the guideline of Japan Glaucoma Society [10]. Excluded were patients with angle-closure glauco-
ma or posttraumatic, uveitic, neovascular, or dysgenetic glaucoma, as well as patients undergoing previous ocular surgery. Before March, 2010, all patients underwent trabeculectomy augmented with mitomycin C, and after April, 2010, all patients underwent trabeculectomy followed by latanoprost 0.004% (Xalatan™, Pfizer, New York, NY, USA), timolol maleate XE 0.5% (Timoptol XE 0.5%™, Santen, Osaka, Japan), and brinzolamide 1% (Azopt™, Alcon, Fort Worth, TX, USA). Patients were followed up for 12 months and the success rate based on intraocular pressure was compared. The study protocol and consent forms were approved by the Human Subjects Committee. When both eyes were eligible, the right eye became the study eye.

3. Surgical procedure

**Trabeculectomy:** All surgeries were performed by a single surgeon. A modified Cairns-type technique was performed [1]. After making a fornix-based conjunctival flap and dissecting a limbus-based 4 x 4-mm scleral flap, mitomycin C 0.04%-soaked sponges were placed underneath the conjunctival flap for 3 minutes. Afterward, 250 ml of balanced salt solution (Balanced Salt Solution Plus™; Alcon, Fort Worth, TX, USA) was used to wash the surgical area. Paracentesis was carried out followed by a peripheral iridectomy. A scleral flap was sutured with 10/0 nylon, and a conjunctival flap was also sutured with 10/0 nylon with wing stretch technique.

If the bleb was flat or the intraocular pressure was not low enough, laser suture lysis was carried out. If the bleb became flat or localized, needling with angled V-lance was carried out.

**Trabeculotomy:** After making a fornix-based conjunctival flap, a 4 x 4-mm 4/5 thickness limbus-based scleral flap was created. The outer wall of the Schlemm’s canal was incised and removed. The Nagata’s semicircular trabeculotome probe was inserted into the Schlemm’s canal, and an ocular viscoelastic device (Healon 1%™, Abbott Medical Optics, Santana, CA, USA) was filled in the anterior chamber to reduce postoperative hyphema. The trabeculotome was in-rotated to disrupt the inner wall of the canal, and the viscoelastic material was manually replaced with balanced salt solution. The scleral flap was then sutured watertight with seven 10/0 nylon sutures.

4. Evaluation of outcomes

All patients underwent a detailed ophthalmic examination, including Humphrey visual field analysis and gonioscopy. Patient progress was reviewed at 1 and 3 days; 1 and 2 weeks; and 1, 2, 3, 4, 5, 6, 9, and 12 months after surgery, and intraocular pressure was studied. Intraocular pressure was measured with a Goldman applanation tonometer. Three measurements were recorded in each eye, the mean of which was used in the calculations, with an interval of 2 weeks before surgery at the same time (±1:00). Postoperatively, intraocular pressure was measured at the same time (±1:00) as at baseline. The optic nerve was examined with a
Goldman three-mirror lens and measurements were taken of the size of the disk, the vertical and horizontal cup/disk ratios, the presence of rim notching or splinter hemorrhage, and the presence of peripapillary atrophy. Visual field testing with a Humphrey visual field analyzer (Humphrey-Zeiss, Dublin, CA, USA), Program 30-2 SITA STNADARD™ testing was carried out before surgery and at 6 and 12 months after surgery. Best-corrected visual acuity was measured at the 1-, 2-, 3-, 4-, 5-, 6-, 9-, and 12-month visits, and the logarithm of the minimum angle of resolution (logMAR) was calculated and used for all statistical analyses.

The presence of complications was determined intraoperatively and at every postoperative visit. Hypotony was defined as an intraocular pressure of less than 4 mm Hg after surgery. A shallow anterior chamber was defined as reported by Teehasaenee and Ritch [11]. An intraocular pressure spike was defined as an intraocular pressure on the first postoperative day of greater than or equal to 3 mm Hg higher than the preoperative level.

The surgery was considered a success with an intraocular pressure between 6 and 20 mm Hg and an intraocular pressure reduction of greater than or equal to 30% without additional surgery, compared to the preoperative level with medical therapy. A failure was defined when an eye required further glaucoma surgery or lost visual function.

In case of postoperative intraocular pressure measurements of greater than 21 mm Hg in the trabeculectomy group, despite all procedures including laser suture lysis, 5-fluorouracil injection, and needling, intraocular pressure-lowering medication was added. In case of complications requiring surgery or still inadequate intraocular pressure control in both groups, additional procedures could be performed as required.

Study End. All patients were meant to reach a 12-month follow-up, but the following were considered as endpoints: (1) the need for any further surgical procedure (except laser suture lysis, 5-fluorouracil injection, and needling); (2) an intraocular pressure of greater than 21 mm Hg on two consecutive visits; and (3) patient failure to attend scheduled visits, allowing for a margin of tolerance. If the study was ended before month 12, the last values obtained in the trial were considered as the final data.

5. Statistical analysis

The sample size was chosen to assure a power of at least 90% in detecting at least a 2-mm Hg difference between groups with a standard deviation of 2 mm Hg with a two-sided α error of 5%.

Evaluation of continuous variables was achieved using the Student’s t-test. To evaluate the difference in intraocular pressures between follow-up intervals, the paired t-test was used. All t-tests were two-tailed. Categoric variables were evaluated with the chi-square test, the Fisher exact test, or the Spearman rank correlation as appropriate. A level of P < 0.05 was accepted as statistically significant. Each potential confounding variable was screened for association with the outcome. Only those confounding variables that were statistically associated were eligible to be incorporated into the potential final multivariate model.
For the pairing of groups, age, sex, best-corrected visual acuity, and intraocular pressure at baseline were used for matching. We studied a correlation between the paired observations. If observations were correlated, the F-test was used to study two population variances.

Because a representation of mean intraocular pressure over time could be misleading because of exclusion of cases after failure, the mean intraocular pressure was recalculated by carrying forward the last intraocular pressure reading before repeat surgery. The proportion of surgical failures and adverse events in each treatment group was compared. Success was evaluated on the basis of Kaplan-Meier cumulative probability (log rank test).

6. Results

Table 1 shows the demographics of the patients. Forty-two patients underwent trabeculotomy followed by latanoprost 0.004%, timolol XE 0.5%, and brinzolamide 1%, and 40 patients underwent trabeculectomy augmented with mitomycin C.

<table>
<thead>
<tr>
<th></th>
<th>Trabeculotomy augmented by postoperative medication group</th>
<th>Trabeculectomy group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>42</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.3 ± 9.7 (38 - 78)</td>
<td>67.2 ± 8.2 (41 - 81)</td>
<td>0.1</td>
</tr>
<tr>
<td>Gender</td>
<td>24 men, 18 women</td>
<td>18 men, 22 women</td>
<td>0.3</td>
</tr>
<tr>
<td>Best-corrected visual acuity</td>
<td>0.681 (0.02 – 1.0)</td>
<td>0.752 (0.1 – 1.0)</td>
<td>-</td>
</tr>
<tr>
<td>LogMAR best-corrected visual acuity</td>
<td>0.166±0.338</td>
<td>0.124±0.195</td>
<td>0.3</td>
</tr>
<tr>
<td>HFA30-2 MD (dB)</td>
<td>-15.55 ± 6.32 (-26.33 - -4.91)</td>
<td>-16.20 ± 5.10 (-27.48 - -4.88)</td>
<td>0.7</td>
</tr>
<tr>
<td>Intraocular pressure (mmHg)</td>
<td>27.9 ± 5.4 (23 - 46)</td>
<td>28.3 ± 4.2 (23 - 42)</td>
<td>0.7</td>
</tr>
<tr>
<td>Number of anti-glaucomatous drugs</td>
<td>3.1 ± 0.7 (2 to 4)</td>
<td>3.2 ± 0.7 (2 to 4)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

LogMAR: Log of the minimum angle of resolution
HFA 30-2 MD: Humphrey visual field analyzer Program 30-2 Mean deviation
Parenthesis indicates a range.

Table 1. Demographics of Patients
Mean baseline intraocular pressure was 27.9 ± 5.4 mm Hg in the trabeculotomy group and 28.3 ± 4.2 mm Hg in the trabeculectomy group (P = 0.7). Mean postoperative intraocular pressure was 15.1 ± 2.1 mm Hg at 3 months, 14.7 ± 2.1 mm Hg at 6 months, and 14.9 ± 2.0 mm Hg at 12 months in the trabeculotomy group, and it was 12.2 ± 1.9 mm Hg at 3 months, 12.8 ± 3.0 mm Hg at 6 months, and 13.9 ± 4.2 mm Hg at 12 months in the trabeculectomy group (Figure 1, Table 2). Mean intraocular pressure in the trabeculotomy group was significantly higher than that in the trabeculectomy group at 3 and 6 months (P < 0.0001 at 3 months; P = 0.0005 at 6 months), and there was no significant difference between the groups at 12 months (P = 0.1). At 12 months, 42 patients (100 %) in the trabeculotomy group and 37 patients (92.5 %) in the trabeculectomy group achieved an intraocular pressure of less than or equal to 20 mm Hg and a minimum of 30 percent reduction (P = 0.1) (Figure 2, Table 3).

Figure 1. Trabeculotomy
## Trabeculotomy Augmented by Postoperative Topical Medications vs. Trabeculectomy Augmented by Mitomycin C

http://dx.doi.org/10.5772/60089

### Figure 2. Trabeculotomy

**Trabeculotomy**

<table>
<thead>
<tr>
<th>Intraocular pressure (mmHg)</th>
<th>Trabeculotomy group</th>
<th>Trabeculectomy group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>27.9 ± 5.4 (23 – 46)</td>
<td>28.3 ± 4.2 (23 – 42)</td>
<td>0.7</td>
</tr>
<tr>
<td>1 month</td>
<td>15.1 ±2.1 (11 – 20)</td>
<td>10.3 ± 2.0 (8 – 17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3 months</td>
<td>15.1 ±2.1 (11 – 20)</td>
<td>12.2 ± 1.9 (8 – 23)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>6 months</td>
<td>14.7 ± 2.1 (12 – 20)</td>
<td>12.8 ± 3.0 (8 - 23)</td>
<td>0.0005</td>
</tr>
<tr>
<td>9 months</td>
<td>14.9 ± 1.9 (12 – 18)</td>
<td>13.4 ± 3.7 (8 - 24)</td>
<td>0.0113</td>
</tr>
<tr>
<td>12 months</td>
<td>14.9 ± 2.0 (12 – 20)</td>
<td>13.9 ± 4.2 (8 – 25)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

### Intraocular pressure (%)

<table>
<thead>
<tr>
<th>Intraocular pressure (%)</th>
<th>Trabeculotomy group</th>
<th>Trabeculectomy group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>-44.3 ± 8.4 (-65.8 - -28.6)</td>
<td>-64.4 ± 8.0 (-90.6 - -44.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3 months</td>
<td>-44.9 ± 8.7 (-65.8 - -28.6)</td>
<td>-57.2 ± 8.5 (-73.8 - -41.7)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
### Table 2. Intraocular pressure change

<table>
<thead>
<tr>
<th>Time</th>
<th>Trabeculotomy augmented by postoperative medication group</th>
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<tr>
<td></td>
<td>Number of anti-glaucomatous medications 3.1 ± 0.7 (2 to 4)</td>
<td>3.2 ± 0.7 (2 to 4)</td>
<td>0.9</td>
</tr>
<tr>
<td>At 12 months</td>
<td>Intraocular pressure 14.9 ± 2.0 (12 – 20)</td>
<td>13.9 ± 4.2 (8 – 25)</td>
<td>0.1</td>
</tr>
<tr>
<td>Success</td>
<td>42 (100.0 %)</td>
<td>37 (92.5 %)</td>
<td>0.1</td>
</tr>
<tr>
<td>Failure</td>
<td>0 (0 %)</td>
<td>3 (7.5 %)</td>
<td></td>
</tr>
<tr>
<td>&lt;16 mmHg</td>
<td>37 (84.0 %)</td>
<td>33 (82.5 %)</td>
<td>0.5</td>
</tr>
<tr>
<td>&lt;12 mmHg</td>
<td>8 (19.0 %)</td>
<td>23 (57.5 %)</td>
<td>0.0211</td>
</tr>
<tr>
<td>Number of anti-glaucomatous medications</td>
<td>3.0 ± 0.0 (3)</td>
<td>0.5 ± 0.9 (0 - 3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Parenthesis indicates a range.

### Table 3. Surgical outcome at 12 months

<table>
<thead>
<tr>
<th>Time</th>
<th>Trabeculotomy augmented by postoperative medication group</th>
<th>Trabeculectomy group</th>
<th>P</th>
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</tr>
<tr>
<td></td>
<td>Number of anti-glaucomatous medications 3.1 ± 0.7 (2 to 4)</td>
<td>3.2 ± 0.7 (2 to 4)</td>
<td>0.9</td>
</tr>
<tr>
<td>At 12 months</td>
<td>Intraocular pressure 14.9 ± 2.0 (12 – 20)</td>
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<td></td>
</tr>
<tr>
<td>&lt;16 mmHg</td>
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</tr>
<tr>
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<td>23 (57.5 %)</td>
<td>0.0211</td>
</tr>
<tr>
<td>Number of anti-glaucomatous medications</td>
<td>3.0 ± 0.0 (3)</td>
<td>0.5 ± 0.9 (0 - 3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Parenthesis indicates a range.

### 7. Relationship between intraocular pressure before surgery and at 12 months after surgery

Figure 3 shows the relationship between intraocular pressure before surgery and 12 months after surgery. In both groups, there was a significant increase in the intraocular pressure reduction in relation to an increase in preoperative intraocular pressure (mm Hg: P < 0.0001 in both groups; %: P < 0.0001 in the trabeculotomy group, P = 0.1 in the trabeculectomy group). In the trabeculotomy group, patients with higher preoperative intraocular pressure showed a significantly higher intraocular pressure at 12 months postoperatively (P < 0.0001), although
there was no significant correlation between them in the trabeculectomy group ($P = 0.2$) (Figure 3). At 12 months, 8 eyes (19.0 %) in the trabeculotomy group and 23 eyes (57.5 %) in the trabeculectomy group achieved an intraocular pressure of less than or equal to 12 mm Hg, and there was a significant difference between the two groups ($P = 0.0211$) (Table 3).

8. Postoperative intraocular pressure-lowering procedures

In the trabeculectomy group, 15 patients (37.5 %) received laser suture lysis, 6 patients (15.0 %) underwent needling procedure, and 3 patients (7.5 %) underwent additional surgery, although no patients in the trabeculotomy group received any postoperative intervention except for topical medical treatment (Table 4).
9. Incidence of complications and adverse events

Complications are listed in Table 5. In the trabeculectomy group, 5 eyes (12.5%) exhibited hypotony and flat/shallow anterior chamber. In the trabeculotomy group, hyphema was observed in 14 eyes (33.3%) and intraocular pressure spike in 3 eyes (7.1%). All the bleeding disappeared within one week. No progression of cataract was found in the two groups.

10. Discussion

There was no significant difference in hypotensive efficacy between patients undergoing trabeculotomy augmented by postoperative topical medication and those undergoing...
trabeculectomy augmented by mitomycin C at 12 months postoperatively. In the current study, 42 eyes (100%) in the trabeculotomy group and 37 eyes (92.5%) in the trabeculectomy group were considered to be a success defined as an intraocular pressure of less than or equal to 20 mm Hg and a minimum of 30 percent reduction. There was no significant difference in the success rate or intraocular pressure between the trabeculotomy group and the trabeculectomy group at 12 months although the intraocular pressure was higher in the trabeculotomy group at every visit after surgery.

Each surgery had its own advantage. In the trabeculotomy group, all patients showed an intraocular pressure of less than or equal to 20 mm Hg at 12 months. However, patients with higher preoperative pressure showed a relatively higher intraocular pressure at 12 months even though it was less than 20 mm Hg. There was a significant increase in the intraocular pressure at 12 months in relation to the increase in preoperative intraocular pressure. Postoperative intraocular pressure was calculated from the preoperative intraocular pressure by using a correlation equation as follows:

\[ \text{Intraocular pressure at 12 months} = 0.26 \times \text{preoperative intraocular pressure} + 7.71 \quad (r^2=0.440, \ P < 0.0001) \]

Patients receiving trabeculotomy experienced less postoperative surgical interventions than those receiving trabeculectomy. In addition, 3 patients in the trabeculectomy group underwent additional surgery although no patient in the trabeculotomy group did.

In contrast to the trabeculotomy group, there was no significant correlation between preoperative intraocular pressure and postoperative intraocular pressure in patients undergoing trabeculectomy augmented by mitomycin C. This procedure can be employed in all patients to achieve lower postoperative pressure regardless of how high the preoperative intraocular pressure might be. At 12 months, there was a significantly larger percent of eyes of less than or equal to 12 mm Hg in patients undergoing trabeculectomy compared with trabeculotomy despite of postoperative medications. Several investigators have demonstrated that it was pivotal to set a target pressure and achieve it based on patients’ visual function [12-15]. Patients with greater visual function deterioration need lower target pressures to maintain residual visual function. According to the target pressure, indication for each of these methodologies should be carefully considered prior to any surgical interventions.

This study has important limitations. The sample size of this study was small, therefore not powered to detect small differences. The small sample size also precluded assessment of safety. Furthermore, a masked study design could have reduced observer bias. The postoperative follow-up period also was short, and therefore we could not assess long-term efficacy and safety.

Although the sample size in each group was small, the current study demonstrated that (1) there was no significant difference in hypotensive efficacy between patients undergoing trabeculotomy augmented by postoperative topical medications and those undergoing trabeculectomy augmented by mitomycin C at 12 months postoperatively and (2) in those receiving trabeculotomy, patients with higher preoperative pressure showed a significantly higher intraocular pressure at 12 months even though less than 20 mm Hg. Future study of a
large population is needed to verify these observations. However, this information may be clinically valuable when treating patients with open-angle glaucoma.

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References


