Intraocular pressure control after clear corneal phacoemulsification in eyes with previous trabeculectomy: a controlled study

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ABSTRACT.

Purpose: To compare intraocular pressure (IOP) control in eyes with or without clear corneal phacoemulsification following trabeculectomy.

Methods: The study group included 30 eyes that underwent uneventful clear corneal phacoemulsification and foldable intraocular lens implantation following trabeculectomy without antimetabolites. Thirty eyes that had undergone filtering surgery without cataract extraction were selected as controls. Case and control groups were matched with respect to age, gender, IOP, number of glaucoma medications, glaucoma type (primary open-angle glaucoma/pseudoexfoliative glaucoma), trabeculectomy time and follow-up. Comparisons between the study and control groups (intergroup) and within the same group at different time-points (intragroup) were performed for IOP, glaucoma medications and bleb morphology. Success rates were investigated by Kaplan-Meier survival analysis and the factors influencing final success by logistic regression.

Results: Intraocular pressure (p = 0.04) and glaucoma medications (p = 0.001) increased during an average follow-up of 26.1 ± 9.9 months in both groups. Intragroup differences became statistically significant after the 6-month visit, but intergroup differences remained insignificant. Bleb height decreased significantly following phacoemulsification in the study group (p = 0.017). Success rates decreased with time in both groups, with no intergroup difference (p = 0.46). The final success rate was negatively correlated with IOP and number of glaucoma medications used at the study entry, while there was a positive correlation between the baseline and final success rates.

Conclusion: Trabeculectomy success decreased in a time-dependent manner in eyes with and without subsequent phacoemulsification. Uncomplicated clear corneal phacoemulsification was not found to have any additional unfavorable influence on IOP control in eyes with filtering blebs.

Key words: trabeculectomy success - phacoemulsification - bleb morphology


Introduction

It has been definitively shown that filtering surgery accelerates cataract development and that cataract extraction becomes necessary in the majority of eyes that undergo trabeculectomy (Advanced Glaucoma Intervention Study (AGIS) Investigators 2001). The majority of studies in the literature have reported that cataract extraction using the extracapsular technique leads to a somewhat reduced bleb function (Manoj et al. 2000; Casson et al. 2002a, 2002b; Jampel et al. 2002).

On the other hand, conflicting results have been reported on phacoemulsification in eyes that have undergone previous filtering surgery. Some researchers have shown that uneventful phacoemulsification does not have deleterious influence on a well functioning bleb, while others have demonstrated that intraocular pressure (IOP) and/or number of glaucoma medications tends to increase after uneventful phacoemulsification (Crichton & Kirker 2001; Derbolav et al. 2002; Rebolleda & Munoz-Negrete 2002; Shingleton et al. 2003). As this represents an important issue in the clinical management of glaucoma patients, strictly controlled studies are needed in order to evaluate the influence of uncomplicated phacoemulsification and in-the-bag intraocular lens (IOL).
implantation in eyes with functioning filtering blebs.

The purpose of this controlled study was to investigate the influence of uneventful clear corneal phacoemulsification and in-the-bag IOL implantation on IOP control in eyes with trabeculectomy blebs. The control group comprised eyes that had undergone previous trabeculectomy but not phacoemulsification. These were matched with the study eyes with regard to age, gender, IOP, glaucoma medications, type of glaucoma (primary open-angle glaucoma/pseudoexfoliative glaucoma), trabeculectomy time and follow-up.

Material

The study protocol had a cohort design. The patients were selected from a pool of 338 patients who underwent trabeculectomy at Beyoglu Eye Education and Research Hospital between 1997 and 2000. The study group was selected from eyes that underwent phacoemulsification following trabeculectomy and the control group from eyes followed without cataract extraction (Fig. 1). The study followed the tenets of the Declaration of Helsinki and was accepted by the hospital's ethical committee.

The study group was selected from 51 patients who underwent phacoemulsification following trabeculectomy. There were two eligibility criteria for the selection process:

1. primary open-angle glaucoma (POAG) and pseudoexfoliative glaucoma (XFG), and
2. IOP < 18 mmHg with or without the use of any glaucoma medications at the time of study entry.

Exclusion criteria were as follows:

1. primary angle closure glaucoma;
2. secondary glaucomas;
3. concomitant eye diseases other than cataract and glaucoma;
4. antimitabolite use either during or after filtering surgery, and
5. posterior capsule rupture and/or vitreous loss during phacoemulsification.

(Eyes with minor complications such as transient corneal oedema and inflammatory reaction following phacoemulsification and those with transient anterior chamber shallowing, choroidal detachment/hyponit and hyphema after trabeculectomy were included.)

A total of 33 eyes met the above criteria and were included in the study arm. Those with follow-up of < 6 months (three eyes) were dropped from the study. Finally, 30 eyes of 30 patients were included in the study group. Study eyes were prospectively followed (prospective cohort).

Recruitment of the control group

The control group was selected from a pool of 287 patients who underwent trabeculectomy using the same surgical technique (without antimitabolites) during the same time period at the same hospital as the study group, but did not have cataract surgery (Fig. 1). The selection process was performed by retrospective chart review (retrospective cohort) and we identified a control eye for each study eye. Therefore, a total of 33 eyes were selected and 33 study-control pairs were produced. The case and control groups did not statistically differ in terms of glaucoma type (POAG/XFG), gender, mean age, IOP or number of glaucoma medications.

The study-control pairs were matched on a one-to-one basis according to the trabeculectomy time. The matching was carried out in the following manner: the time interval between

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**Fig. 1. Flowchart of recruited patients and those lost to follow-up.**
the trabeculectomy and phacoemulsification operations was calculated for each eye in the study group; these eyes were then individually matched with control eyes for which follow-up data for equivalent periods of time were available.

As three eyes were dropped from the study group during first 6 months, we also excluded their control partners, so that the control group finally included 30 eyes.

Methods
Preoperative examination of the study eyes included detailed slit-lamp examination for the detection of XFG and type of cataract (cortical, nuclear, posterior subcapsular and combinations).

Itraocular pressure was measured with Goldmann application tonometry in the morning (between 09.00 and 11.00 hours). The average of the latest three IOP measurements taken before surgery was recorded as the ‘preoperative IOP’. The number of glaucoma medications was recorded. For the evaluation of bleb morphology, we used a classification system employed in our clinic: ‘diffusely elevated’ (microcystic and well functioning); ‘moderately elevated’ (moderately functioning), and ‘flat’ (barely visible and non-functional).

Preoperative data for the control eyes, on the other hand, were collected from the medical records.

Trabeculectomy technique
Trabeculectomy surgery was performed under limbus-based conjunctival flaps at the superior quadrant and rectangular scleral flaps of at least half thickness. No antimetabolites were used.

Phacoemulsification technique
Phacoemulsification surgery was performed through a sutureless temporal clear corneal tunnel incision. The Alcon Legacy phacoemulsification machine was used in all cases (Alcon, Fortworth, TX, USA). The ‘stop-and-chop’ technique was preferred for nucleus emulsification. A three-piece hydrophobic acrylic foldable IOL (Alcon AcrySof) was implanted into the capsular bag in all eyes. A capsular tension ring (CTR) was implanted in eyes with XFG and zonular weakness.

Control visits were scheduled at 3, 6 and 12 months and each year following phacoemulsification in the study group. Additional visits were scheduled in order to determine the surgical success after a new glaucoma medication was added or discarded. In the control group, follow-up data were collected from the records during the corresponding time intervals. Follow-up times were matched in each case, and control pair. The study was terminated for a particular case-control pair if the follow-up of the case was terminated or data for the control were unavailable.

Four parameters were selected as outcome measures and evaluated at each of the control visits: IOP, number of glaucoma medications, surgical success rate and bleb morphology. During control visits, IOP was measured by Goldmann application tonometry in the morning (between 09.00 and 11.00 hours). The number of glaucoma medications was recorded.

In our standard trabeculectomy follow-up protocol, we would first attempt digital massage if IOP was > 17 mmHg. If that failed, the decision to start a medication would then be made. No postoperative antimetabolite injection or bleb needling were performed in any of the study or control eyes.

The surgical success of the trabeculectomy was expressed in the following manner: IOP < 17 mmHg without using any glaucoma medications was considered a ‘complete success’; IOP < 17 mmHg with medications was considered a ‘relative success’, and IOP > 17 mmHg despite using glaucoma medications was considered as a ‘failure’.

The classifications for bleb morphology used for the control group were the same as for the study group: ‘diffusely elevated’ (microcystic and well functioning); ‘moderately elevated’ (moderately functioning), and ‘flat’ (barely visible and non-functional).

Statistics
For statistical analysis, SPSS for Windows Version 11.0 was used. Changes in IOP, glaucoma medications and surgical success were analysed by using repeated measures ANOVA. Intragroup (data within the same group at different control visits) and intergroup (case and control group data) comparisons were performed.

The intergroup differences in bleb morphology were evaluated using the chi-square test, while intragroup changes within the same groups were investigated using the Friedman test.

Rates of complete and relative success were evaluated with Kaplan-Meier survival analysis and compared in the case and control groups with log-rank test.

Univariate and multivariate logistic regression analyses were carried out in order to establish the true independent risk factors for final success. Patient age, glaucoma type (POAG or XFG), phacoemulsification surgery, IOP, glaucoma medications and surgical success at the time of study entry (not before filtering surgery) were investigated as potential risk factors.

P-values < 0.05 were considered as statistically significant. The study power for the detection of an intergroup difference > 2 mmHg by assuming ‘α as 0.05’ was calculated to be 92.5% at the 3- and 6-month visits, and 81.5% at the 1-year and 83% at the 2-year visits, respectively.

Results
Patient characteristics are shown in Table 1. The study design ensured that the study and control groups did not statistically differ in terms of age, gender, IOP, number of glaucoma medications and glaucoma type (POAG versus XFG).

In the study group, the mean time between trabeculectomy and phacoemulsification was 18.5 ± 18.4 months (range 1-63 months). According to the study protocol, there was an approximately equivalent time interval (18.2 ± 12.1 months) between the trabeculectomy and study entry in the control group.

The mean follow-up was 25.9 ± 9.9 months (range 6-48 months) in the study and 26.3 ± 10.2 months (range 6-52 months) in the control group. One-year follow-up data were available for 86.7% and 2-year data for 80% of eyes.

Changes in IOP
When compared with the baseline IOP, a steady but slow increase was observed in both the case and control groups throughout the follow-up (Table 2). That increase became statistically significant at the 6-month visit...
Table 1. Baseline patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Study group (n = 30)</th>
<th>Control group (n = 30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>71.8 ± 5.1</td>
<td>69.6 ± 6.3</td>
<td>0.14</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>8/21</td>
<td>11/19</td>
<td>0.04</td>
</tr>
<tr>
<td>Presence of XFG</td>
<td>16/30</td>
<td>15/30</td>
<td>0.88</td>
</tr>
<tr>
<td>IOP (mmHg)</td>
<td>10.8 ± 4.1</td>
<td>10.7 ± 3.8</td>
<td>0.92</td>
</tr>
<tr>
<td>Glaucoma meds (no)</td>
<td>0.2 ± 0.5</td>
<td>0.3 ± 0.7</td>
<td>0.40</td>
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</tbody>
</table>

(p = 0.04) and remained so throughout the rest of follow-up (p = 0.001).

Intergroup differences were not statistically significant, however, in that the mean IOP in the study and control groups did not differ from one another during follow-up visits (p = 0.39).

Table 2. Change in intraocular pressure.

<table>
<thead>
<tr>
<th></th>
<th>Study group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10.8 ± 4.1</td>
<td>10.7 ± 3.8</td>
<td>0.92</td>
</tr>
<tr>
<td>Month 3</td>
<td>11.0 ± 3.6</td>
<td>11.7 ± 4.0</td>
<td>0.53</td>
</tr>
<tr>
<td>Month 6</td>
<td>11.7 ± 4.1</td>
<td>12.2 ± 3.9</td>
<td>0.58</td>
</tr>
<tr>
<td>Year 1 (n = 52)</td>
<td>12.4 ± 5.1</td>
<td>12.6 ± 3.9</td>
<td>0.90</td>
</tr>
<tr>
<td>Year 2 (n = 48)</td>
<td>14.0 ± 4.2</td>
<td>13.2 ± 3.3</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Changes in bleb morphology

A sudden decrease in bleb height was observed in the study group immediately after phacoemulsification surgery and there was a statistically significant intergroup difference during the first 6 months of follow-up (p = 0.017) (Table 4). However, intergroup differences were not statistically significant at the year 1 and 2 visits (p = 0.33 and p = 0.65, respectively).

Changes in surgical success

The surgical success rates are shown in Table 5. They decreased in both groups in a time-dependent manner (p = 0.001) but there was no intergroup difference (p = 0.45). There was a moderate correlation between baseline bleb morphology and final success rate. For the initial diffusely elevated, moderately elevated and flat blebs, the final success rates were 47.8%, 22.2% and 20%, respectively.

Kaplan-Meier survival analysis

The case and control groups did not differ statistically from one another in terms of complete success rates (p = 0.017). Neither phacoemulsification surgery (p = 0.79) nor patient age had any influence on final success (p = 0.58). Eyes with XFG had better success rates at the 6-month visit but the significance was lost after 1 year. The length of time between trabeculectomy and phacoemulsification did not have any correlation with final success rates in the study group (p = 0.91).

Discussion

The influence of phacoemulsification on IOP control in patients with functioning filtering blebs has been previously investigated. In an uncontrolled study, it was reported that in 49 eyes with well functioning filtering blebs and without glaucoma medications, IOP increased a statistically significant amount following phacoemulsification, but postphaco IOP was still less than that before trabeculectomy (Rebolleda & Munoz-Negrete 2002). In separate uncontrolled studies, statistically significant increases in IOP and number of glaucoma medications were reported following phacoemulsification in previously filtered eyes (Crichton & Kirker 2001; Derbolav et al. 2002; Shingleton et al. 2003).

However, in none of these studies was a well known feature of traditional filtration surgery taken into account: the time-dependent decrease in the surgical success of trabeculectomy function (Chen et al. 1997). Ehrnrooth et al. (2002) studied the longterm results of trabeculectomy in eyes without cataract surgery and reported that the year 1 success rate of 82% decreased to 40% at the end of year 4. We thought that in order to reach valid and appropriate conclusions about the influence of phacoemulsification surgery on functioning filtering blebs, a well matched control group (eyes followed without phacoemulsification following trabeculectomy) should be incorporated in the study design.

In a retrospective, case-control study, any adverse effect of temporal clear corneal phacoemulsification on IOP control could not be demonstrated in eyes with filtering blebs (Park et al. 1997). On the other hand, another group reported that a greater percentage of filtered eyes needed additional glaucoma medications following superior quadrant clear corneal phacoemulsification (Casson et al. 2002a, 2002b). In another controlled study, it was found that phacoemulsification surgery could adversely influence the success of antimetabolite augmented trabeculectomy surgery (Swamynathan et al. 2004).
were individually matched with the study eyes according to the trabeculectomy time (time interval between filtering surgery and study entry) and length of follow-up. Our study’s design was similar to those of Casson et al. (2002a, 2002b) and Caprioli et al. (1997), but the eyes in our study group were prospectively followed (prospective cohort). However, the control eyes were selected and data collected by retrospective chart review (retrospective cohort), our study was non-masked and could include some biases. Another possible source of bias in the current study might be the exclusion of those eyes in which posterior capsular rupture and/or vitreous loss occurred during phacoemulsification. This might lead to an underestimation of the possible unfavourable influence of phacoemulsification on the filtering bleb.

Our results were quite similar to those of Caprioli et al. (1997), but somewhat different from those of Casson et al. (2002a, 2002b). We found that IOP control progressively worsened and the number of glaucoma medications had to be increased both in eyes with and without phacoemulsification following filtering surgery in a time-dependent manner. In our study, all the trabeculectomies were performed without antimetabolites and therefore it would not be appropriate to compare our results with those of Swamy Nathan et al. (2004).

The influence of phacoemulsification on bleb morphology has been the subject of various studies in the literature (Chen et al. 1998). A decrease in bleb height has been described as the usual finding following phacoemulsification and the presence of a functional (diffusely elevated) bleb prior to cataract surgery has been reported not to guarantee longterm IOP control after phacoemulsification (Rebolleda & Munoz Negrete 2002). Most studies have found that bleb appearance changed somewhat and bleb function deteriorated after phaco surgery, but extensive fibrosis and the complete loss of bleb function have been rarely reported. Manoj et al. (2000) were unable to detect complete cicatrization of the filtration blebs in any of their study eyes following phacoemulsification surgery.

In our study, worsening of bleb morphology (decrease in bleb height and size) did indeed occur in both the control and study eyes. The changes observed in the bleb morphology were somewhat different between the two groups, however. In the control group a slow and time-dependent progressive flattening was observed, while a sudden decrease in bleb height occurred immediately following phacoemulsification surgery in most of the study eyes. We propose that reduction of aqueous production and augmentation of uveoscleral outflow due to the inflammation caused by phacoemulsification surgery probably contributed to that rapid reduction of bleb height and/or size in our study eyes. It took 6 months or longer for the inflammation induced by the cataract surgery to subside and bleb morphology of study and control eyes only became similar after the year 1 control visit. We considered that conventional outflow was only minimally influenced by phaco surgery in our cases because only those eyes with open angles were selected for the study.

There were some differences between the previous studies and ours. First of all, we set the criteria of TOP < 18 mmHg without any antiglaucoma medication’ for complete success and ‘IOP < 18 mmHg with medications’ for relative success. In many studies, target IOP had been selected as 22 mmHg instead of 18 mmHg (Casson et al. 2002a, 2002b; Derbolav et al. 2002). We set < 18 mmHg as the target pressure because the Advanced Glaucoma Intervention Study (AGIS) Investigators (2000) demonstrated that halting the progression of visual field damage could be achieved only if IOP was kept at < 18 mmHg on all control visits in eyes with advanced glaucoma.

The second important difference was our patient selection criteria. In contrast with previous studies, we also included those eyes considered as relative successes (those already using glaucoma medications at study entry) in

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Table 3. Change in the number of glaucoma medications.

<table>
<thead>
<tr>
<th></th>
<th>Study group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.2 ± 0.5</td>
<td>0.3 ± 0.7</td>
<td>0.40</td>
</tr>
<tr>
<td>Month 3</td>
<td>0.2 ± 0.5</td>
<td>0.5 ± 0.8</td>
<td>0.14</td>
</tr>
<tr>
<td>Month 6</td>
<td>0.4 ± 0.6</td>
<td>0.6 ± 0.8</td>
<td>0.30</td>
</tr>
<tr>
<td>Year 1 (n = 52)</td>
<td>0.7 ± 0.8</td>
<td>0.8 ± 0.9</td>
<td>0.51</td>
</tr>
<tr>
<td>Year 2 (n = 48)</td>
<td>1.0 ± 1.0</td>
<td>12 ± 11</td>
<td>0.57</td>
</tr>
</tbody>
</table>

* Statistically significant.

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Table 4. Change in bleb morphology.

<table>
<thead>
<tr>
<th></th>
<th>Study group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Diffusely elevated: 21</td>
<td>25</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>Moderately elevated: 6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flat: 3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td>Diffusely elevated: 15</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderately elevated: 11</td>
<td>2</td>
<td>0.012*</td>
</tr>
<tr>
<td></td>
<td>Flat: 4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Month 6</td>
<td>Diffusely elevated: 17</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderately elevated: 11</td>
<td>3</td>
<td>0.017*</td>
</tr>
<tr>
<td></td>
<td>Flat: 2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Year 1 (n = 52)</td>
<td>Diffusely elevated: 13</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderately elevated: 11</td>
<td>6</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>Flat: 2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Year 2 (n = 48)</td>
<td>Diffusely elevated: 9</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderately elevated: 11</td>
<td>11</td>
<td>0.65</td>
</tr>
<tr>
<td></td>
<td>Flat: 4</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant.

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addition to those considered as complete successes, because we thought that such a study population would more accurately reflect the common patient population in daily practice. At the study entry, complete success was present in 76.7% and partial success in 23.3% of our study and control groups. Rates of complete success decreased to 56.7%, 53.8% and 41.7% in the study group and 53.3%, 46.2% and 45.8% in the control group at the 6-month, 1-year and 2-year visits, respectively. The study and control groups did not statistically differ from one another in terms of the decreasing success rates.

In our study, we performed logistic regression analysis in order to identify the independent variables that had significant influence on the surgical success. In that analysis, it was found that a low IOP without concomitant use of glaucoma medications at study entry was associated with better survival at the end. As compared with final failures, the mean baseline IOP was 2 mmHg lower in the finally successful eyes (9.7 mmHg versus 11.7 mmHg). This was also the case in the study by Rebolleda & Munoz-Negrete (2002). The multivariate logistic regression model also proved that undergoing uneventful phacoemulsification and in-the-bag IOL implantation would not have any statistically significant influence on IOP control following trabeculectomy.

In our study, the type of glaucoma (POAG or XFG) was not shown to influence the final success. This might be somewhat contrary to the relevant literature. Pseudoexfoliative glaucoma has been described as being generally associated with an increased number of complications and more inflammation due to the disturbance of the blood-aqueous barrier (Ritch et al. 2002). It has also been shown that phacoemulsification may independently reduce IOP more in eyes with XFG than in those with POAG (Shingleton et al. 2003). In our study, IOP control was indeed slightly better in eyes with XFG than in those with POAG in the short term (during the first year), probably due to that influence, but this was not the case in the long term.

In conclusion, our study demonstrated that the success of filtering surgery gradually diminished and IOP control progressively worsened in a time-dependent manner. As our results demonstrated that uneventful clear corneal phacoemulsification did not have any additional deleterious influence on that course, we suggest that cataract surgery may be performed in eyes with functioning filtering blebs whenever necessary.

References

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