Intraocular Pressure Lowering Effect of Deep Sclerectomy with Mitomycin C and Loose Scleral Flap Suture in Open Angle Glaucoma

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Abstract

Purpose: There are controversial reports regarding the long-term intraocular pressure (IOP) lowering effect of non-penetrating glaucoma surgery (NPGS). The reported complete success rates from studies in different populations around the world are 13% to 77%. This prospective study was aimed to evaluate the IOP lowering effect of deep sclerectomy with Mitomycin C (DSMMC) in a group of Iranian patients with open angle glaucoma.

Methods: Ninety eyes of 87 patients with medically uncontrolled primary open angle glaucoma (POAG) were consecutively enrolled in this prospective study and were surgically treated by DSMMC. All patients had complete eye examination before and at regular intervals after the operation. Surgical success was considered for IOP of ≤21 mmHg.

Results: The mean age was 64±12 years; the mean follow-up was 33±22 months. The mean preoperative IOP of 42±13 mmHg was significantly decreased to the mean final IOP of 22±11 mmHg (P<0.001). The IOP lowering effect of surgery reduced by time (P<0.001). Cystic bleb was developed in 13.3% of eyes. The probability for an IOP ≤21 mmHg was 35% without the use of antiglaucoma drops and 71% with or without the use of antiglaucoma drops.

Conclusion: DSMMC could effectively reduce IOP in eyes with POAG and was accompanied by few operative complications. Most of the patients needed to continue using antiglaucoma drops after the operation. This procedure is not fair whenever low target IOPs are required.

Keywords: Non-Penetrating Glaucoma Surgery, Deep Sclerectomy, Mitomycin C, Open Angle Glaucoma.

Introduction
Trabeculectomy as the most frequently performed surgery for uncontrolled glaucoma is known to be associated with complications like shallow anterior chamber, hypotony, choroidal detachment and progression of cataract. Non-penetrating glaucoma surgery (NPGS) has rapidly evolved in recent years and was found to be associated with little surgical complications. The reported success rates from studies around the world are much different with the complete success rates of 13% to 77% and the qualified success rates of 38% to 95%. Many factors could have affected this wide range of results. One important factor is the variety of surgical techniques being employed by different authors. Another factor is the use of postoperative augmenting procedures like Yag laser goniopuncture, needling and injection of antimetabolites. The effect of race and ethnicity on the response to glaucoma surgery is another factor for consideration. High success rates were reported from older studies but relatively lower success rates were found in more recent studies of NPGS. Hence, more such studies deserve to be performed around the world to define the intraocular pressure (IOP) lowering efficacy of these procedures. Since there was no previous report of non-penetrating surgery from Iran, and to avoid operative complications of trabeculectomy, this prospective study was performed to evaluate the safety and IOP lowering efficacy of deep sclerectomy with the use of Mitomycin C (DSMMC) and loose scleral flap suture in a group of Iranian patients with open angle glaucoma.

Methods
Ninety-six eyes of 93 patients with medically uncontrolled primary open angle glaucoma (POAG) were consecutively enrolled in this prospective study and were treated by DSMMC. This study was performed in Isfahan University of Medical Sciences and Aban eye clinic, Isfahan, Iran from 1998 to 2007. The included eyes had gonioscopically open angle and did not have previous glaucoma surgery or any laser intervention for the treatment of glaucoma. The patients were referred to the university hospital out patient department or the private clinic of the authors. The included cases had uncontrolled IOP of >21 mmHg in spite of maximum tolerable medical treatment or progressive glaucomatous field loss and optic disc cupping. Eyes with chronic angle closure glaucoma, uveitis, corneal opacity, and previous surgery were not included. Eyes with a follow-up period of less than 12 months were excluded. Patient agreement was obtained by signing a written consent after being informed about the risks and benefits of this procedure. The study was approved by the Ethics Committee of the Isfahan medical school. The patients had complete eye examination before the operation which included Goldmann applanation tonometry with slit-lamp, gonioscopy, fundoscopy, and automated visual field examination. Eye examination was repeated in each follow-up visit which was performed at the 1st day, 1 week, 1 month, and every three months then after in the postoperative period. Visual field was checked every 6 months postoperatively. All eyes were operated by the first author. Intra and postoperative complications, the number of drops, the condition of the filtering bleb (being defined by slit-lamp examination as failed or formed) were checked at each postoperative visit. Post DSMMC IOP rise was treated by antiglaucoma drops accordingly but no subsequent augmenting procedure like Yag laser goniopuncture, needling, and or injection of antimetabolites were employed for IOP control. The statistical analysis of the collected data was performed by student T-test, ANCOVA, Pearson Correlation, Kaplan-Meier, and log-rank tests. P-value of <0.05 was considered to be statistically significant. Complete success time was defined as the time duration between the first postoperative day and the earliest time that IOP raised above 21 mmHg, qualified success time duration was defined as the time duration between the first postoperative day and the latest time that the IOP could be kept ≤21 mmHg by the help of antiglaucoma drops.

Surgical technique
After local anesthesia with topical and subconjunctival injection of 2% xylocaine, a 6.0 vicryl limbal stay suture was put. A fornix based conjunctival flap of about 60 degrees was prepared and properly dissected from
sclera. A rectangular 4×7 mm limbal based scleral flap with its longer axis parallel to the limbus was prepared. The sclera flap was extended anteriorly 1.00 mm inside the clear cornea. A cellulose sponge soaked with 0.2 mg/ml MMC solution was applied under the scleral flap and the tenon’s capsule for 4 minutes. MMC was then irrigated by 20 cc of normal saline. A 3.5×6.5 mm deep scleral dissection was carried out in the bed under the scleral flap; the dissection was again extended 1 mm into the clear cornea. The scleral dissection was deep enough to cut through the schlemm’s canal and leave a thin layer of scleral tissue over the choroids. Sectioning of the schlemm’s canal was being confirmed by oozing of the aqueous humor. The wall of the canal was removed along with this deep sclerectomy in the whole length inside the scleral bed leaving the schlemm’s canal as a groove. No further attempt was made to remove the corneal tissue over the trabecular meshwork or to peel the endothelial lining of the schlemm’s canal. The scleral flap was sutured back by one or two loose interrupted 10.0 nylon sutures, which were buried inside sclera. The conjunctiva was sutured by two interrupted 10.0 nylon sutures to the anterior limbal area as though to stretch the conjunctiva to either side to get a water tight closure, conjunctival sutures were buried inside the limbal tissue. Postoperative patching was performed for 24 hours; uncomplicated monocular cases were left unpatched. Postoperative topical drops included sulfacetamide 10% q6h and betametasone 1% q4h which were used for about three weeks. The frequency of drops were monitored according to the extent of conjunctival congestion.

Results

Ninety eyes were remained in this follow-up study (six eyes were excluded due to inadequate follow-up) which included 50 eyes of males and 40 eyes of female. There were 72 phakic eyes and 18 pseudophakic eyes. The phakic eyes included 28 eyes with clear lens and 44 eyes with senile lens opacity. The pseudophakic eyes had uncomplicated 3.2 mm incision phacoemulsification cataract surgery and posterior chamber lens (PCL) implantation for more than 6 months before DSMMC. The mean age was 63.64±12.28 (30-82) years, the mean cup disc ratio was 82.26% ±19.45 (20%-99%), and the mean follow-up was 32.75±21.88 (12-108) months.

The mean preoperative IOP of 41.93±12.83 (20-80) mmHg was significantly decreased to the final mean IOP of 21.83±10.81 (10-70) mmHg (Student T-test, P<0.001). The mean IOP reduction was 20.08±15.76 (-20.00 to 59.00) mmHg, the mean percentage of IOP reduction was 44.46±26% (-40% to 83%). Graph 1 shows the mean and the range of IOP of the study population at different steps of this follow-up study. Comparing the mean postoperative values of IOP indicates that the IOP lowering effect of surgery had significantly reduced during the first two weeks (Student T-test, P<0.001) and again between two weeks and one month after surgery (P<0.001). Graph 2 shows a general view of the sorted preoperative IOP values and the corresponding postoperative IOP values at the first and the last follow-up days.

The overall probability for complete and qualified success (95% confidence interval) were 35% and 71% respectively, these rates were 40% and 77% at one year, 37% and 70% at two years, 35% and 62% at three years. The Kaplan-Meier cumulative probability of complete success is shown in graph 3 and graph 4, the cumulative probability of qualified success is shown in graph 5.

The mean number of drops statistically reduced from 2.13±1.05 (0-3) in the preoperative period to 1.80±1.07 (0-4) in the postoperative period (P<0.021) which does not seem to be clinically significant. The snellen acuity changed from 0.98±0.46 (logMAR) in the preoperative period to 0.91±0.73 (logMAR) in the postoperative period (P=0.064).

Significantly higher success time duration was found in eyes with lower IOP values at the first postoperative day. (Pearson Correlation test, R=0.322, P<0.015). Testing between subjects effects showed a significant relation between the percentage of IOP reduction and the bleb anatomy (failed versus formed) (ANCOVA, P<0.003). Significant effect of bleb anatomy on the success time duration was found in phakic eyes, formed blebs had a significantly higher complete success time duration in comparison with failed blebs (log-rank, P<0.0091) (Table 1).
phakic eyes had a significantly higher percentage of IOP reduction in comparison with pseudophakic eyes (ANCOVA, P<0.017).

Graph 1. Preoperative and postoperative values of intraocular pressure of 90 eyes with POAG being treated by DSMMC
POAG: Primary open angle glaucoma
DSMMC: Deep sclerectomy with Mitomycin C

Graph 2. Correlation between the sorted preoperative and the corresponding first and last postoperative IOP values of 90 eyes with POAG being treated by DSMMC
POAG: Primary open angle glaucoma
DSMMC: Deep sclerectomy with Mitomycin C
Graph 3. Survival function of complete success (Kaplan-Meier)

Graph 4. Survival function of complete success (Kaplan-Meier)
Graph 5. Survival function of qualified success (Kaplan-Meier)

Graph 6. Survival functions of complete success in two subgroups (Kaplan-Meier, log-rank, P<0.0091)
Table 1. Final bleb anatomy and related data values of phakic eyes with POAG being treated by DSMMC

<table>
<thead>
<tr>
<th>Bleb anatomy at the end of follow up</th>
<th>Mean age (years)</th>
<th>Mean preoperative IOP (mmHg)</th>
<th>Mean IOP at the day 1 (mmHg)</th>
<th>Mean final IOP (mmHg)</th>
<th>Mean Follow-up (months)</th>
<th>Mean of complete success time (months)</th>
<th>Mean % of IOP reduction</th>
<th>Mean of formed bleb duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formed bleb (52 eyes)</td>
<td>64±13</td>
<td>43±13</td>
<td>15±5</td>
<td>20±7</td>
<td>33±22</td>
<td>17.5±23</td>
<td>49±21*</td>
<td>33±21</td>
</tr>
<tr>
<td>Failed bleb (20 eyes)</td>
<td>62±12</td>
<td>42±12</td>
<td>18±4</td>
<td>28±18</td>
<td>32±21</td>
<td>7.6±16</td>
<td>33±370</td>
<td>16±15</td>
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<tr>
<td>P-value</td>
<td></td>
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<td></td>
<td>0.027</td>
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* & ◊: ANOVA
POAG: Primary open angle glaucoma
DSMMC: Deep sclerectomy with Mitomycin C

Intraoperative anterior chamber micro perforation happened in four cases. Immediate postoperative complications were hypotony with IOP of four to six mmHg in six cases, shallow anterior chamber in eight cases, hyphema in two cases, and bleb failure in two cases. Early postoperative complications were subconjunctival hemorrhage in 14 cases and severe conjunctival injection in 10 cases. No iris incarceration was observed. Late postoperative complications included cystic bleb formation in 12 cases, progression of preexisting cataract in 18 cases (20%). Cataract progression was observed in 41% of eyes with the preexisting senile lens opacity. In three cases the postoperative IOP values were found to increase higher than the corresponding preoperative ones, this was detected at 12-, 21-, and 30-month steps of follow-up of these three cases respectively.

Discussion

According to the results of this study, the high mean preoperative IOP value of 42 mmHg was markedly reduced to the mean value of 15.5 mmHg at the first postoperative day and then increased by the time during the follow-up with a significant rise during the first postoperative month, which indicates a rapid progression of out flow resistance. This progressive resistance could be at the level of trabeculo-descemet’s membrane or distal to it. Formed bleb anatomy was found in 98% of eyes at the first postoperative day. About 25% of eyes had a failed bleb at the end of the follow-up. Bleb failure was found to be accompanied by IOP rise in phakic eyes. Significantly lower complete success time in eyes with anatomical failure of the bleb indicates that some part of aqueous filtration in this NPGS might have been achieved by the absorption of aqueous through the bleb; therefore, some part of the developed progressive outflow resistance could be attributed to the process of wound healing which can end up with bleb failure. Intraoperative application of mitomycin and loose suturing of the scleral flap in this study were done to delay the process of wound healing and probably improve the success rate of deep sclerectomy. Intraoperative use of Mitomycin was found to increase the success rate of deep sclerectomy. Intraoperative use of Mitomycin was found to increase the success rate of deep sclerectomy by some authors; that is why they used postoperative subconjunctival injection of antimetabolites and employed needling when the filtering bleb showed signs of fibrosis. Loose suturing of the scleral flap in deep sclerectomy was employed by some authors probably to facilitate the outflow filtration through the bleb. Wishart PK et al found large or cystic drainage blebs after deep sclerectomy but no drainage bleb after viscocanalostomy. They concluded that tight closure of scleral flap in viscocanalostomy might have discouraged aqueous drainage under the conjunctiva. The rate of cystic fibrotic bleb was 13.3% in this study that may be attributed to the use of mitomycin and loose suturing of scleral flap. Bleb fibrosis was found in 13.3% of eyes being treated by DSMMC with loose scleral suture, which also received multiple postoperative injections of 5-FU in 29% of eyes. Bleb fibrosis was found in 22.2% of eyes being treated by DSMMC with loose scleral suture which also received...
multiple postoperative injection of 5fu in 34% of eyes. Cystic fibrotic bleb was found in 4.7% of eyes who underwent deep sclerectomy without intraoperative mitomycin.

The results of this study might have been improved by subsequent yag laser goniopuncture. Yag laser goniopuncture was not employed in this study because no properly functioning yag instrument was available at the beginning of the study. Detry-Morel M found complete and qualified success rates of 27% and 77% after DSMMC with subsequent yag laser goniopuncture which was found to be necessary in 54% of their cases. The most important complication they had to manage was iris incarceration, which happened in 11% of their cases after yag laser intervention.

Different results were obtained from the two previous studies of DSMMC with loose scleral flap suture and without subsequent yag laser goniopuncture. One is the older study by Kozobolis VP et al in Greece obtaining high qualified and complete success rates of 50% and 95%. The other is the more recent study by Mielke C et al on black Africans obtaining low complete and qualified success rates of 13% and 38%; they also noticed extensive subconjunctival and episcleral fibrosis in eyes that underwent surgical revision. The effect of race and ethnicity on the response to glaucoma surgery is a subject for consideration that might have affected their results.

Another factor that might have affected the wide range of success rates could be the technique of the deep sclerectomy, which had been actually performed by different authors, like the depth of sclerectomy, the extent of schlemms unroofing, removal of juxtacanalicular trabeculum and the schlemm's endothelium. The overall effect of the fine technical differences may be mostly projected on IOP levels at the first postoperative day. Shaarawy et al noticed that studies with poor results on NPGS were accompanied by higher first postoperative IOPs. However Mielke et al could not show any significant effect of low first day IOP on their success rates. In this study, the success time duration was found to be significantly higher in eyes with lower IOPs at the first postoperative day. The IOP means at the first postoperative days in the above mentioned studies of deep sclerectomy ranged between 6 mmHg to 15 mmHg, the mean of the IOP at the first postoperative day in this study was found to be 15.5 mmHg. Two factors could have affected the results of this study and indeed make it to be different from the previous studies. One is the mean preoperative IOP value of 42 mmHg which is considerably higher than the mean preoperative IOP values of 23-29 mmHg in other reports, and the other is unemployment of any postoperative augmenting procedures, which was performed in most of the above mentioned studies.

The surgical technique which was employed in this study decreased the out flow resistance by exposing the schlemm's canal to the subscleral and subconjunctival space, but the extent of resistance release at the level of trabeculo-descemet's membrane induced by this NPGS is otherwise not clear. Recent studies did not show any difference between deep sclerectomy compared with very deep sclerectomy.

The limited number of intra and postoperative complications in this study is almost similar to the previous reports of DSMMC. No eye with a primary clear lens developed cataract during this follow-up study. Shallow anterior chamber, hypotony, and hyphema were resolved during the early postoperative days.

**Conclusion**

Low rate of operative complications and 71% qualified success rate for an IOP of ≤21 mmHg are positive points for choosing this surgical procedure. Low complete success rate of 35% for IOP of ≤21 mmHg indicates that this NPGS is not fair for patients who want to get rid of antiglaucoma drops. Very low complete success rate of 11% for IOP of ≤16 mmHg indicates that DSMMC is not a fair procedure whenever low target IOPs are required. Since trabeculectomy was found to lower the IOP more than deep sclerectomy, trabeculectomy might be a better choice in this regard. Randomized trials are necessary to define the IOP lowering effect of each fine technical variation.

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References