
ORIGINAL ARTICLE

A Comparative Study to Evaluate the Efficacy of Trabeculectomy with Pharmacologically Modulated Trabeculectomy Using Mitomycin - C in a Tertiary Health-Care Centre

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Abstract:

Purpose:

This study was undertaken to compare the effectiveness of conventional Trabeculectomy and the Trabeculectomy with Mitomycin-C (MMC) in Glaucoma patients.

Design:

Prospective randomised comparative clinical study.

Material and methods:

Sixty patients of primary open angle glaucoma (POAG) with positive indication for filtration surgery were selected during the study period of two years. Thirty patients were subjected to routine Trabeculectomy and other group of 30 patients to Trabeculectomy with MMC. Data on demographic profile, changes in the intraocular pressure (IOP), visual acuity, bleb characteristics, preoperative medications and postoperative complications were collected and analyzed in both the procedures.

Results:

Both the procedures are effective in reducing IOP in properly selected cases of POAG. The IOP reduction caused by both procedures is statistically significant ($P < 0.05$). Trabeculectomy with MMC appeared to be more effective in reducing IOP ($P < 0.05$) than the conventional trabeculectomy. Majority of the patients maintained the preoperative visual acuity after both the types of surgical procedures. It is also found that

the complications produced by use of MMC are not statistically significant than those with conventional trabeculectomy.

Conclusions:

Trabeculectomy with and without the use of MMC is an effective surgical procedure in controlling the IOP and arresting loss of vision and visual field in patients suffering from POAG. MMC showed good results with a few complications and hence should be used only in selective high-risk patients. As MMC prevents fibrosis, its use in high-risk cases is rewarding if due precautions are taken during the surgery and postoperative follow-up.

Key words:

Trabeculectomy, Primary open angle glaucoma, Mitomycin-C, Intra-Ocular Pressure.

Introduction:

Glaucoma is considered as one of the common causes of blindness in India. The insidious onset and the symptom free course of chronic simple glaucoma plays a devastating role in Indian community, especially in rural areas as the leading cause of painless blindness. Majority of poor rural population are illiterate and show a lack of concern for health problems in the background of their constant struggle to earn their livelihood in an era of perpetually rising cost of living.

Retrospective reports indicated that high percentages of patients treated medically subsequently

went on to surgery. Watson and Grierson¹ found 60 % within five years and Jay and murray² found 53% within four years required surgical intervention. In the latter study, patients treated medically had significantly greater visual field loss before surgery than those treated with early surgery². Of the patients having initial trabeculectomy, 90% had stable visual fields three years after diagnosis, compared to only 60% of those treated medically alone.

According to the Moorfields primary treatment trial in 1983, eyes undergoing surgery had the lowest intra-ocular pressure (IOP) and the greatest rate of prolonged control than those treated medically and with the Argon Laser Trabeculoplasty³⁻⁵. Trabeculectomy, first introduced by Cairns in 1968 has undergone subsequent modifications. It is the most frequently chosen surgical procedure for chronic simple glaucoma⁶. It is the standard procedure with excellent results for most forms of open angle glaucoma and chronic angle closure glaucoma. Aphakic, traumatic, inflammatory and other causes of secondary glaucoma are also managed well but with less success⁷. It can be combined with cataract extraction and with modern phacoemulsification.

Trabeculectomy is a guarded surgery as sclerostomy is covered by the scleral flap, which is in turn sutured to the scleral bed. The advantage of this technique is that the initial egress of aqueous from the anterior chambers prevents choroidal effusion. At the same time, guarded sclerostomy permits moderate reduction in IOP, which is around 16 mm of Hg.

This study was carried out to assess the effectiveness of conventional Trabeculectomy and the procedure modulated with the use of the Mitomycin-C (MMC) in terms of controlling the IOP, effect on visual acuity and associated complications in glaucoma patients during the immediate postoperative period and at the follow-ups are also assessed.

Materials and Methods:

All patients of primary open angle glaucoma (POAG) who had positive indication for filtration

surgery were selected during a study period of two years. The inclusion criteria for indication of the surgery: Patients with uncontrolled IOP even with medical treatment, who had poor compliance with medical treatment and had advanced glaucomatous cupping and field defects even with medical treatment. Newly diagnosed cases with advanced glaucomatous changes in the optic disc and visual field and Patients with POAG who could not afford medical treatment were included in the study. Criteria followed for use of MMC were, early onset open angle glaucoma, history of failed glaucoma filtration surgery, advanced cases of POAG with compromised optic nerve head where very low postoperative IOP was necessary to maintain optic nerve perfusion. The study was conducted after the approval of the institutional Ethical committee. Written consent from the patients was taken before inclusion of the patients in the study.

Instruments/material used were Snellen's visual acuity chart, Applanation tonometer, Slit lamp Biomicroscope, Gonioscopy with single mirror Goldman's gonio lens, Ophthalmoscope, Operating microscope, Lister's perimeter.

All cases were operated under standard peribulbar anesthesia. Along with routine steps of trabeculectomy, after a 5 mm square partial thickness scleral flap three times application of a sponge (5x5 mm size) soaked in 0.4 mg/ml concentration of MMC between the two scleral lamellae and followed by copious irrigation of the intra-lamellar area of dissection as well as rest of ocular surface. The dressing was opened on the first postoperative day. Antibiotic steroid drops and cycloplegics were instilled and the eye was dressed again. The dressing was reopened on the second postoperative day. Conjunctival sutures were removed on the 14th postoperative day. The schedule for postoperative follow up was weekly for 6 weeks then every 15 days till 3 months postoperative period. The surgery was considered to be successful if the post operative IOP was less than or equal to 21 mm of Hg without any glaucoma medication and if there was no further

loss of visual field. However in eyes with markedly low vision, visual field assessment could not be performed.

All data were processed and analysed using SPSS (SPSS Inc, Chicago version v.23.0) software package. Paired ‘t’ test was done to assess the statistical significance.

Observations and Results:

Out of 60 eyes, 45 eyes (75%) were of male patients and 15 eyes (25%) were of female patients. The maximum numbers of patients were in age group of 50-60 years. The youngest patient was 22 years old and the oldest patient was 70 yrs old.

Table No. 1: Etiological classification of the patients

Etiology	No. of cases	Percentage %
POAG without high risk for surgical failure and advanced field change	30	50.00
Early onset glaucoma	03	5.00
POAG with previously failed trabeculectomy	04	6.67
POAG with advanced glaucomatous field changes	23	38.33

Table No. 2: Type of surgery performed and IOP

Type of surgery	n	Pre-operative	Post-operative	% change
Trabeculectomy alone	30	28.82 ± 4.85	15.05 ± 4.26	↓ 13.77 *
Trabeculectomy with MMC	30	35.25 ± 4.28	11.83 ± 3.75	↓ 23.42 **

IOP = Intra-Ocular Pressure in mm of Hg; Values are mean ± SD; *P<0.05. P<0.001 **

Table No. 3: Overall success of controlling IOP

Type of Surgery	Successful cases	Failure cases	% of Success
Trabeculectomy alone	27	03	90.00
Trabeculectomy with MMC	29	01	96.67

Table No. 4: Post operative complications

Sr.No	Complications	Trabeculectomy	Trabeculectomy with MMC
1	Hypotony	2 (6.67%)	4 (13.33%)
2	Delayed AC Formation	2 (6.67%)	4 (13.33%)
3	Iritis	3 (10.00%)	3 (10.00%)
4	Raised IOP	4 (13.33%)	3 (10.00%)
5	Cataract formation	2 (6.67%)	4 (13.33%)
6	Decreased Visual Acuity	5 (16.67%)	4 (13.33%)

The complications like anterior synechie, hyphema and wound leak were not observed in present study

Discussion:

The present study was undertaken to compare the outcome of surgical management in eyes with POAG by two different methods. The standard Watson procedure was undertaken in 30 eyes, while equal numbers of eyes were subjected to the intra-operative exposure of the antimetabolic agent MMC in the intrascleral flap area. In later procedure, the basic steps of the surgery remained same.

Trabeculectomy is a very safe procedure, but it is not effective to reduce IOP beyond a certain limit. In addition, there is a risk of failure with subsequent conjunctival fibrosis. Use of MMC is not advised in all cases of POAG, it is restricted to only high-risk cases, which are likely to go into failure with plain trabeculectomy.

Changes in IOP:

In this study, the trabeculectomy group shows mean preoperative IOP of 28.82 mmHg, while mean postoperative IOP was 15.05 mmHg and the difference or change of IOP was 13.77 mmHg. Therefore, the average fall of IOP was 13.77 mmHg, which is statistically significant ($P < 0.05$). IOP reduction after trabeculectomy in the present study is comparable with other published studies. The figures were higher by Watson & Barnett⁸ (13.5-14.8), Kaur and Singh⁹ (20.5), and Kupin et al¹⁰. Whereas in some studies it is little lower than the present study such as Yamamoto et al¹¹ and Spaeth et al¹². This difference could be attributed to the differences in surgery procedure or by various complications of surgery or it could be due to variations in the responses of the patients.

In the present study, trabeculectomy with MMC group showed mean preoperative IOP 35.25 mmHg and mean postoperative IOP 11.83 mmHg. The difference is average fall of IOP after trabeculectomy with MMC was 23.42 mmHg. This is found to be higher and statistically significant ($p < 0.05$) than the

trabeculectomy alone group. The IOP reduction with MMC appears to be more effective than that with conventional trabeculectomy alone ($p < 0.05$). IOP reduction after trabeculectomy using MMC reported by Palmer¹³ (9.7), Gaspar et al¹⁴ (14), Annen & Sturmer¹⁵ (15.4), Zacharia et al¹⁶ (12.3 ± 11.5) are comparable with the present study. Therefore, MMC is indicated in high risk and complicated cases with due precautions.

Postoperative effect on visual acuity:

In this study, amongst the cases undergoing trabeculectomy alone, 3 cases had improvement of visual acuity, 5 cases had deterioration of visual acuity, and in the remaining cases the visual acuity remained unchanged. Majority of cases selected for MMC application during trabeculectomy had very poor visual acuity preoperatively and their postoperative visual acuity remained unchanged except in 1 case where it improved. Four cases in the MMC group with fairly good visual acuity preoperatively showed loss of 1 snellen's line postoperatively (Table-4).

In our study, reasons for decrease in visual acuity in a few patients could be explained. In trabeculectomy group there was uveitis in 3 cases and inadequate lowering of IOP in 2 cases. While in Trabeculectomy with MMC group 2 cases were with uveitis and cataract formation / progression was seen in 2 cases.

The reported percentage of decrease in visual acuity in trabeculectomy group by some studies varied widely and it is comparable with present study. It is 18% by Watson & Barnett⁸, 46.15% by Spaeth & Poryzees¹², 11% by Drance & Vargas¹⁷, 13% by Ramkrishnan et al¹⁸. In contrast to these studies, Mirza et al reported 6-20% decrease in visual acuity in trabeculectomy with MMC group¹⁹. The visual acuity produced by trabeculectomy with MMC in the present study (13.33%) is marginally better than that produced by conventional trabeculectomy, as it is statistically non-significant ($p > 0.05$). Kirwan et al in their prospective study in South Africa, reported 26-28% of the patients lost more than 0.25 log MAR units (approximately 2 Snellen lines) after a mean follow-up of about two

years after beta-irradiation and trabeculectomy²⁰.

Overall success of the surgical procedure:

The success of the filtration surgery is defined as the ability to keep IOP less than or equal to 21 mmHg without additional anti-glaucoma medications and stabilization of visual fields and visual acuity. MMC is an anti-metabolite, it serves to decrease the post-operative fibrosis by inhibiting the fibroblast. The use of MMC during trabeculectomy is one of the modifications of the filtration procedure. In this study, the patients were followed up for a period of three months postoperatively in evaluation of the success. Only IOP control was considered primarily in the success evaluation. The criterion of visual field could not be included because of advanced form of C glaucomatous damage, concomitant cataract and due to poor reliability in same illiterate patients.

In the present study, 'trabeculectomy alone' group showed 90% overall success rate. Of the three failure cases, one has raised IOP at 12 weeks post-operatively with fibrosis over the bleb and progression of field changes. Patients required repeat surgery. The second case with increased IOP was controlled with antiglaucoma drug and the third case was lost in follow up. The variable success rates are reported in earlier other studies. Waston and Barnett⁸ (84%), Spaeth et al¹² (84.16%), Mills²¹ (87%), which were little lower than or comparable to our study. While in some other studies, Yamashita et al²² (60.8%), Martini et al²³ (73.3%), Kupin et al¹⁰ (56%), D'Ermo et al²⁴ (71%), it is much lower as compared to the present study. This could be because of differences in criteria of patient selection in earlier studies.

In the present study, trabeculectomy with MMC group showed 96.67% of success rate. One patient with failure had fibrosis of bleb 3 months after the surgery. Success rate reported in other studies for trabeculectomy augmented with MMC are, Chen²⁵ 100% (at 1yr) and 78% (at 3yrs), Palmer¹³ 84%, Annen & Sturmer¹⁵ 88.2%, Martini et al²³ 96.6%, Kupin et al¹⁰ 85% is comparable to our study. A study

of primary trabeculectomy with low-dose MMC reported that IOP was maintained at 15 mmHg or less in more than 80% of patients after 1 year and in 60% of patients after 6 years²⁶. This suggests the usefulness of MMC in the long-term period. Another study by Zhang Z et al²⁷ have suggested intrascleral MMC application using a standard dose of 0.4 mg/mL which seems to be more effective without increasing the complication rate compared to subconjunctival MMC application and it can be considered as an alternative approach in filtering surgery for clinically advanced glaucoma. This approach was followed and therefore much higher success rate (96.67%) was achieved in this study than the earlier published studies.

Complications:

In Trabeculectomy, complications like hypotony, cataract formation, hyphaema, iritis and others can be prevented by taking adequate precautions while performing surgery and with careful postoperative follow-ups. Some of the complications of MMC like hypotony, cataract formation, shallow anterior chamber may sometimes occur in spite of all precautions and hence proper selection of cases is a must, after ruling out contraindications for its use. With advances in glaucoma surgery, safer alternatives to anti-fibrotic agents are being developed that augment success rates of trabeculectomy but with fewer complications. Various agents like biodegradable collagen implants (Ologen), amniotic membrane and anti-vascular endothelial growth factors are currently being investigated^{28,29}. The study by Sen et al indicated that the addition of biodegradable collagen implant (Ologen) to trabeculectomy with MMC did not offer any advantage over conventional trabeculectomy with MMC alone²⁹. IOP lowering effect of MMC plus ologen is inferior compared with that of MMC alone in Asian eyes with advanced primary glaucoma and there seems no merit in adding this implant to trabeculectomy with MMC²⁹. Another study by Kaushik J et al suggested adjunctive bevacizumab in trabeculectomy is effective and comparable to MMC for controlling IOP in POAG

patients for the first year³⁰.

In present study, the complications produced by use of MMC are not statistically significant than those with conventional trabeculectomy. This can be attributed to small sample size and selection bias, which was inevitable, since only high-risk cases were considered for MMC use, as it was the basic criterion in the study.

Summary:

Trabeculectomy is not a very difficult procedure to perform and its pharmacological modulation requires just an extra step of keeping MMC soaked sponge intrasclerally. It has inherent flexibility in flap size, flap shape and suturing technique which allows it to modify the surgical steps as per the patient's requirement for reduction of IOP. Both the procedures are effective in reducing IOP in selected cases of POAG. The IOP reduction caused by both of the procedures is statistically significant ($P < 0.05$). However, Trebeculectomy with MMC was found to be more effective in reducing IOP ($P < 0.001$) than conventional trabeculectomy alone. The change in the preoperative visual acuity caused by trabeculectomy with MMC is not statistically significant than the conventional trabeculectomy and majority of the patients maintained the preoperative visual acuity after both the types of surgical procedures. Trabeculectomy with MMC is economical and cost effective procedure. Mitomycin C vial (2 mg) is available at low price and the same vial can be used for many patients operated on the same day. This aspect is important in treating economically poor patients in underdeveloped healthcare setup.

Conclusions:

Trabeculectomy is a very safe and effective procedure and results are good if proper selection of cases is done. Trabeculectomy with and without the use of MMC is an effective surgical procedure in controlling the IOP and arresting further loss of vision and visual field in patients suffering from POAG. In our experience, it fulfills the criteria for an ideal filtration

procedure to a large extent because of high success rate, low frequency of complications. The procedure is easy to perform and can be modified as per the convenience of the operating surgeon. In a tertiary health care centre set up, MMC showed good results with a few complications, it is cost-effective and hence should be used only in selective high-risk patients. It is advisable that routine use of MMC as a primary procedure in patients without high-risk criteria should be avoided. It has advantage in high-risk cases if due precautions are taken during the surgery and postoperative follow-ups.

Sources of Support - Nil

Conflict of Interest – Nil

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Received date: 29/07/2020

Revised date: 31/07/2020

Accepted date: 03/08/2020

How to cite this article: Kashinath Choudhary, Deepali Gawai, Vinod Bhagwat, Asma Fahreen and Panse A. A Comparative Study to Evaluate the Efficacy of Trabeculectomy with Pharmacologically Modulated Trabeculectomy Using Mitomycin - C in a Tertiary Health-Care Centre. Walawalkar International Medical Journal 2020; 7(2):1-8. <http://www.wimjournal.com>