

Surgical Outcome of Trabeculectomy with Mitomycin - C Versus Trabeculectomy with Collagen Implant (Ologen), in Patients of Primary Open Angle Glaucoma: A Tertiary Centre Study

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Abstract

Purpose: To compare the surgical outcome of trabeculectomy with Mitomycin-C (MMC) versus trabeculectomy with collagen (ologen) implant in medically uncontrolled, primary open angle glaucoma patients of Bangladeshi population.

Methods: A Quasi experimental study; conducted at BIRDEM General Hospital, Dhaka from July, 2015 to June, 2021 consisting of 36 eyes of 24 patients (> 40 years of age) of medically uncontrolled primary open angle glaucoma (POAG). Study patients were randomly distributed between two comparison groups: namely; GROUP 1: Trabeculectomy with Mitomycin-C and GROUP 2: trabeculectomy with collagen (Ologen) implant. All the surgeries were performed by single surgeon. Total six Post operative follow-up was done up to 12 months after surgery. At each visit, BCVA, IOP, any post operative complications of surgery as well as requirement of any anti-glaucoma drug or possible need of second surgical intervention for lowering IOP were noted.

Results: Mean IOP reduction after surgery was significantly less at all time points in both groups ($p < 0.05$). Considering complete success criteria, survival probability in Ologen group was 94.8% at 6 months and 92.9% (95% CI: 59.1 - 99.0) at 12 months. The corresponding survival probability in MMC group was 95.2 and 93.8% (63.2 - 99.1) at 6 months and 12 months. There were no significant intra-operative complications in any of the eyes in either of the groups.

Conclusion: Surgical outcome of trabeculectomy with MMC was similar to that of trabeculectomy with Ologen implant.

Keywords: Trabeculectomy; Mitomycin-C; Collagen Implant; Surgical Outcome; Open Angle Glaucoma

Introduction

Trabeculectomy is considered to be the gold standard surgical procedure for reducing intraocular pressure (IOP) in patients with uncontrolled glaucoma till today. It was first introduced by Cairns in 1968 [1,2]. But, unfortunately sub-conjunctival tissue fibrosis sometimes interferes in the long term success of trabeculectomy as a result of bleb failure [3-5]. However, with the advent of adjunctive anti-metabolite substances as adjunctive of trabeculectomy,

namely: mitomycin-C (MMC) or 5-FU, the long term success rate of this surgery have increased significantly [6-9]. But at the same time, the use of these adjunctives have raised the incidence of post operative bleb-related complications as well, such as: hypotony, thin avascular bleb, blebitis, endophthalmitis etc. [10-12]. On the contrary, "Ologen" is a biodegradable, collagen implant, that was introduced to glaucoma surgeons very recently and is said to improve the long term success of trabeculectomy by decreasing the

sub-conjunctival scarring but with less post-operative, bleb-related issues ("Ologen" is produced by: OculusGen Biomedical Inc. Taipei, Taiwan) [13]. The implant helps to generate loose connective tissue matrix by acting as a scaffold for growth of fibroblast into the pores of the implant and also helps in tissue remodeling as well as to reduce scar formation. It keeps the conjunctiva and episcleral surface separate mechanically, thus preventing adhesion between them [14]. In some of the recent most studies, comparing trabeculectomy with or without Ologen implant [15], the researchers did not found any significant difference in IOP control between the ologen group compared to that of simple trabeculectomy. Where as in other comparative studies of trabeculectomy with MMC and Ologen in Caucasian eyes only, showed MMC group to have lowered IOP more than that of Ologen group at the end of study [16]. Success rate of trabeculectomy may differ between different ethnic entities due to separate scarring profile.¹⁷ Thus the purpose of this study was to compare the outcomes of trabeculectomy with MMC with trabeculectomy with Ologen implant in Bangladeshi, POAG patients which are medically uncontrolled.

Methods

It was a quasi experimental study, performed at BIRDEM General Hospital, Dhaka from July 2015 to June 2021. The study protocol was approved by the ethical committee of the institute and strictly followed the Declaration of Helsinki. All the study subjects were explained the benefits and risks of the trabeculectomy procedure as well as use of MMC and Ologen respectively (including the composition and source of collagen implant. An informed, written consent was taken from all the study patients.

The study included 24 patients

Inclusion criteria:

- Age: >40 years(both male and female).
- Medically uncontrolled primary open angle glaucoma (using at least 4 antiglaucoma medication).
- No previous history of intraocular surgery, ocular inflammation or trauma.

Exclusion criteria

- Age: < 40 years.
- Angle closure glaucoma or any category of secondary glaucoma.
- Any H/O: Ocular- trauma, inflammation, neovascularization or surgery.

POAG was defined as

- IOP > 21 mmHg
- Open anterior chamber angle on gonioscopy
- Glaucomatous optic disc damage on fundoscopy
- Corresponding glaucomatous field defect on Humphrey (30-2) visual field examination.

IOP was measured using Goldmann Applanation Tonometer, and gonioscopy was performed using a Sussman's 4 mirror, non indentation, gonioscope. Visual field defects were considered to be glaucomatous if at least 2 out of the 3 Anderson's criteria were fulfilled. Age, gender, associated systemic conditions (eg: diabetes mellitus, hypertension), IOP on enrollment, number of anti-glaucoma medications on enrollment and visual field defect parameter (Mean deviation) were noted.

After enlistment, study patients were randomly distributed between the 2 groups; namely:

- Trabeculectomy with MMC: Group 1 (MMC group) and
- Trabeculectomy with Ologen implant: Group 2 (Ologen group).

Surgical technique

- All surgeries were performed by a single surgeon.
- Prior to surgery peribulbar anesthesia was applied to all the patients.
- A corneal bridle suture was applied with 6-0 vicryl. o A fornix-based conjunctival flap at the superior limbus was made. o A 4 × 4 mm, rectangular, partial thickness scleral flap was fashioned. o A trabeculectomy of appx. 2 × 2 mm was done with Descemet's punch and o a peripheral iridectomy was made as well.
- The scleral flap was closed with two fixed sutures with 10-0 Nylon, o (one each at the two edges of the scleral flap).
- The conjunctiva was then secured with two 8-0 Vicryl sutures.
- The basic procedure was the same for both the MMC and Ologen groups.

The MMC Group had 3 small pieces of MMC soaked weck-cell sponges, placed sub-conjunctivally over the scleral flap area for 2 minutes before making the superficial scleral flap. Concentration

of MMC used was 0.2 mg/ml. After removing the sponges, the area was copiously irrigated with 30 cc of BSS.

The Ologen group had a 6× 2 mm, Ologen implant, placed over the top of the sutured sclera flap, before closing the conjunctiva.

After surgery all the patients were prescribed: prednisolone acetate 1% eye drops: in tapering doses for 6 weeks, antibiotic eye drops: 6 hourly for 4 weeks and atropine 1% eye drops: 8 hourly for 1 week, postoperatively.

Post-operative follow up was done at: day 1, day 7, 1st month, 3rd month, 6th month, and 12th month. At each visit, BCVA, IOP, complications of surgery as well as requirement of any anti-glaucoma drug or IOP lowering procedure was noted.

Primary outcome measure was designated as: Complete success when the IOP was 10 -20 mm Hg; without any anti glaucoma medication. Qualified success was termed as IOP of <21 mm Hg with antiglaucoma medication.

Secondary outcome measures were: Surgery associated complications in between the MMC and Ologen group. Failed surgery was defined as an IOP > 22 mm Hg despite use of anti glaucoma medications or <6 mm Hg with occurrence of hypotony maculopathy or necessity of additional procedure like bleb needling or bleb revision or repeat trabeculectomy to reduce the IOP or if there is complete loss of light perception while recording post operative vision.

Statistical analysis

Was performed using commercial software. Both the study groups were compared using student's t test. Kaplan-Meier survival curves were used to assess cumulative probability of success. A P value of ≤ 0.05 was considered statistically significant.

Results

We enrolled 36 eyes of 24 subjects into 2 groups: 20 eyes to trabeculectomy with MMC group and 16 eyes to trabeculectomy with Ologen group. Among these, 4 patients of the MMC group failed to complete 12 months of follow-up and were excluded from the study. For the final outcome analysis, there were 16 eyes of 12 patients in MMC group and 16 eyes of 12 patients in Ologen group.

All the pre-operative conditions nearly were similar between the 2 groups, except severity of disease prior surgery, which was

worse in MMC group (mean MD in MMC group was -24.46 ± 8.13 as compared to -18.84 ± 7.42 in Ologen group).

Compared to the pre-operative IOP, the mean IOP after surgery was significantly less at all time points in both the groups ($P = 0.05$). Although the MMC group showed a little bit better IOP lowering effect in long term follow up. The post-operative features between the 2 groups are shown in table 1. The postoperative IOP was nearly similar in the 2 groups at post-operative visits, except at 3rd month and 6th month where the IOP in the MMC group was significantly lower ($P = 0.01$) than in Ologen group.

Figure 2 shows post-operative bleb appearance following trabeculectomy with Ologen at 2nd week.

The number of anti-glaucoma medications post-surgery was similar between the 2 groups.

Considering complete success criteria, survival probability in Ologen group was 94.8% at 6 months and 92.9% (95% CI: 59.1 - 99.0) at 12 months. The corresponding survival probability in MMC group was 95.2 and 93.8% (63.2 - 99.1) at 6 months and 12 months. Considering qualified success criteria, survival probability in Ologen group was 100% at 6 months, 92.9% (59.1 - 99.0) at 12 months. The corresponding survival probability in MMC group was 100.0% at 6 and 12 months. The difference in the success rates (complete as well as qualified) was not statistically significant between the groups. Number of eyes achieving an IOP of less than or equal to 18 mm Hg at 6 months follow-up were higher in the MMC group (11/16 in Ologen vs. 13/16 in Trab MMC group).

There were no intra-operative complications in any of the eyes in both the groups. The early post-operative complications in the 2 groups are shown in table 2. The incidences of early post-operative complications were similar in the 2 groups, except hyphema, which was significantly more in Ologen group. The number of eyes, which experienced one or more of the complications, was 6 out of 12 in the Ologen group and 5 out of 14 in the MMC group. However, most of the complications were managed within 2-4 weeks after surgery, with conservative management. Except hypotony in 1 eye in MMC group, which resolved by 6 weeks. 2 of the eyes in Ologen group required intervention for the management of early post-operative complication. Among them one case needed resuturing for hypotony and the other one needed resuturing for bleb leak. None of the

eyes from any group suffered any significant loss of visual acuity in long term. Only one of the patient from MMC group developed cataract after surgery. But, none of the patients encountered blebitis or endophthalmitis.

Parameters	MMC group (n = 16)	Ologen Group (n = 16)	P value
Age (yrs)	59 ± 8	56 ± 5	
Sex (M:F)	11:5	10:6	
BCVA (pre operative)	6/60 -6/36	6/60-6/24	
Mean pre-operative IOP (mmHg)	28.2 ± 10.4	24.8 ± 8.6	
Mean post- operative IOP (mmHg)	14.4 ± 6.6	16.2 ± 4.2	0.05
No. of antiglaucoma drugs prior to trabeculectomy	3.2 ± 0.8	3.2 ± 0.8	
No. of antiglaucoma drugs after trabeculectomy	0.3 ± 0.2	0.4 ± 0.1	0.05
Visual field parameter: MD (dB)	-24.46 ± 8.13	-18.84 ± 7.42	0.05
Systemic disease	Diabetes mellitus	3	2
	Hypertension	4	3

Table 1: The post-operative features between MMC and OLOGEN group.

Post operative complication	MMC group n = 16 (%)	Ologen group n = 16 (%)
Shallow anterior chamber	1(7.1)	1(8.3)
Anterior chamber reaction	2(14.2)	1(8.2)
Hypotony	1(7.1)	2(16.6)
Hyphaema	1(7.1)	2(16.6)
Bleb leak	1(7.1)	1(8.2)
Cataract	1(7.1)	0

Table 2: Post operative complication in MMC and Ologen group.

IOP (mmHg)	MMC group (n = 16)	Ologen group (n = 16)	P value
At 1 st POD	9.8 ± 6.5	13.6 ± 4.2	0.05
At 1 st week	14.4 ± 4.3	16.5 ± 4.1	0.05
At 3 rd month	12.9 ± 2.9	14.7 ± 2.8	0.05
At 6 th month	14.3 ± 3.5	17.2 ± 5.1	0.05
At 12 th month	15.6 ± 3.9	18.1 ± 4.4	0.05

Table 3: Post operative IOP in MMC and Ologen group.

Figure 1: Demographic distribution of study population.

Figure 2: IOP in two groups during follow up.

Figure 3: Mechanism of tissue activity of Collagen (Ologen) implant.

Figure 4: Post-operative appearance of Ologen implant.

Discussion

Compared to the outcome of trabeculectomy without MMC, the post surgical outcome of trabeculectomy with MMC is quite impressive in terms of lowering IOP and bleb viability in the long run which has made it a preferred option in primary trabeculectomy surgery for medically uncontrolled glaucoma.^{8,9} But application of MMC is also related with higher rate of some long-term, bleb-related complications.^{10,12} Whereas, use of Ologen is aimed at reducing those specific; bleb related issues of MMC.

In this prospective, interventional, randomized study, we found the outcome of trabeculectomy with MMC group at 6th months was quite similar as that of trabeculectomy with Ologen group (success rate 95.8% in the MMC group, 94.2% in the Ologen group with $P > 0.5$). But, notably, the IOP at 3rd and 6th months follow up were significantly lower in MMC group ($P = 0.01$), and it continued dur-

ing the follow-up visits at 12th months as well. The complete and qualified success rate differed only to a very small extent, between the two groups. So the study outcome needs to be observed very carefully with further studies with bigger sample size and longer follow-ups than that of the current one to reach a substantial end-point.

There are several studies regarding the use of Ologen implant during trabeculectomy. Rosentreter, *et al.* [16] compared 10 eyes each in trabeculectomy with MMC and Ologen groups and reported significantly higher complete success rate (IOP ≤ 18 mm Hg and at least 20% reduction of pre-operative IOP) at the end of 12 months in trabeculectomy with MMC group (100% with MMC vs. 50% with Ologen, $P = 0.01$). Boey, *et al.* [14] in their prospective case-control study comparing phacotrabeculectomy with MMC and Ologen implants, have reported significantly greater ($P < 0.001$) IOP control in MMC group at 3 months follow-up. The complications noted in the study by Papaconstantinou, *et al.* [15] were bleb leaks (2 eyes in Ologen group, which resolved on re-suturing), encapsulated blebs (2 eyes in Ologen group and 5 eyes in trabeculectomy group needing 2 to 7 5FU injections), and endophthalmitis (1 eye in the Ologen group).

We have observed nearly similar post-operative complications in the 2 groups, except for a case of hypotony, and a case of bleb leak in Ologen group. The possible explanation is a loose scleral suture in both the cases. Both of the two eyes required re-suturing. We had to perform bleb needling in two of the eyes (one case from each group). One eye required re-trabeculectomy (due to failed trabeculectomy; from Ologen group) during the study.

According to literature there is a theoretical risk of inflammation with Ologen implant as it is non-human porcine in origin (due to foreign body reaction related to the porcine cross-linked collagen). But we did not notice any such inflammation in this study.

Limitation of the Study

- Some patients were lost during follow-up at 24 months,
- If sample size was bigger, the statistical outcome would have been more efficient.
- A longer duration of follow-up would be required to establish any remarkable significance of the collagen implant over MMC as an adjunct of trabeculectomy.

Conclusion

The study found the surgical outcome of trabeculectomy with MMC to be quite similar to that of trabeculectomy with collagen (Ologen) implant in most of the aspects. Except that, the MMC group showed higher reduction of IOP in the long term. However, the rate of occurrence of post surgical complications appeared to be somewhat similar in both groups.

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