

# Mitomycin C versus Ologen Implant in Primary Trabeculectomy: A Comparative Study

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**Abstract:** Aim: To assess and compare the efficacy of mitomycin c versus ologen implant in trabeculectomy. Methods: In this study, 21 patients of POAG underwent trabeculectomy with ologen implant (group A) and 21 patients of POAG underwent trabeculectomy with MMC (group B). Postoperative IOP, BCVA, need for antiglaucoma medications, complications were noted at day 1 and 7, 4 week, 12 week and 6 month. Results: The mean pre operative IOP in group A was  $27.05 \pm 4.30$  mm Hg and  $26.72 \pm 4.47$  mm Hg in group B. At six months follow up the post operative mean IOP was  $13.23 \pm 4.28$  mm Hg in group A and  $13.66 \pm 4.39$  mm Hg in group B which was not statistically significant. Post operative complications in the two groups was found to be not significant ( $p = 0.198$ ). Postoperative mean BCVA (in log mar) in group A was 0.6 and 0.68 in group B which was not significant. Conclusion: The success and complications rate of trabeculectomy were similar in both Ologen and MMC groups at the end of 6 months.

**Keywords:** MMC, Trabeculectomy, ologen implant

## 1. Introduction

Glaucoma is a leading cause of irreversible blindness worldwide and is second only to cataracts as the most common cause of blindness overall<sup>[1]</sup>.

Trabeculectomy as the standard procedure in penetrating anti-glaucoma surgery was introduced by Cairns in 1968.<sup>[2]</sup> Wound healing and scar formation causing fibrosis and the obstruction of aqueous outflow remain the most common reason for the failure of trabeculectomy<sup>[3], [4]</sup>.

Mitomycin C is used as an anti-metabolite during trabeculectomy. MMC is an antitumor antibiotic isolated from *Streptomyces caespitosus*. However, it is frequently accompanied by short- and long-term complications such as hypotony, bleb leaks, cataract formation, avascular filtering blebs, thinning of the conjunctiva, subsequent blebitis, and endophthalmitis.

The current focus is on the development of less toxic agents and implants to inhibit cicatrization without adverse effects of antimetabolites. One approach is the development of biodegradable implants to serve as a placeholder to prevent conjunctiva-sclera adhesion. The Ologen implant was developed aiming at replacing MMC for trabeculectomy. It is a disc-shaped porcine-derived biodegradable collagen matrix that has been developed to prevent excessive scarring after trabeculectomy<sup>[5], [6]</sup> Ologen when inserted under the conjunctiva it acts as an absorbent and also helps separate mechanically the conjunctiva and episcleral surface and thereby prevent adhesions between them<sup>[7], [8]</sup>

## 2. Methods

This study was conducted in compliance with the tenets of declaration of Helsinki and Institutional ethics committee approval had been obtained ahead of the study.

This prospective randomised comparative case study included patients scheduled for trabeculectomy at anand hospital and eye centre jaipur. 42 adult patients were enrolled in the study. After explaining the study, surgical procedures and possible complications, an informed consent was obtained and patients were assigned to two groups;

Group A ( $n = 21$ ) who underwent trabeculectomy with ologen implant

Group B ( $n = 21$ ) who underwent trabeculectomy with MMC.

### Eligibility Criteria

#### Inclusion Criteria

Patients with an IOP >20 mmHg with maximal tolerated anti glaucoma drugs, Patients having intolerable side effects of anti glaucoma drugs, Patients with POAG and having poor compliance for anti glaucoma drug use, Patients who couldn't afford anti glaucoma medicine, Patients willing for surgery, Patients willing for follow ups were included in study.

#### Exclusion Criteria

Age less than 18 years, Any glaucoma other than primary glaucoma, Recent ocular infection or inflammation, Previous intraocular surgery, anterior segment laser surgery, History of IOP altering events such as retinal detachment or prolonged corticosteroid administration, Corneal or retinal pathology, History of presence of uveitis, Those who were not willing to participate, Those who were not able to come for follow up were excluded.

#### Pre operative evaluation

Baseline information, such as, age, gender, number of anti-glaucoma medications and medical history were recorded. All patients received a complete preoperative examination, including best corrected visual acuity measurement (Snellen chart), slit lamp examination, tonometry

(Goldmannapplanation tonometry), gonioscopy, dilated fundus examination, a Humphrey visual field (24-2, or 30-2) examination

### Surgical technique

All surgeries were performed by the same surgeon under peribulbar anesthesia.

Group A: The eye was prepared with Povidone Iodine 5% solution. Controlled gentle digital massage with the hand was given. Trabeculectomy was performed in the superotemporal or superonasal quadrant trying to avoid sites of perforating scleral vessels. The conventional superior rectus suture placed. A fornix based conjunctival flap was prepared. Haemostasis was achieved by adequate wet field cautery. A 4 x 4 mm triangular scleral flap one third of the thickness dissected to within 1 mm of clear cornea with a Bard Parker knife. After creating a paracentesis opening, inner sclerostomy block was dissected out with the blade in the dimensions 2mm x 3 mm, at the base of the hinge of the superficial scleral flap. Peripheral iridectomy performed through the inner sclerostomy with a vannascissor and a single toothed fine forceps. Scleral flap closure with an apical suture using 10-0 nylon and one releasable suture at one side. A 6 mm x 2 mm Ologen implant was placed on top of the sclera and the conjunctiva was then closed water tight by 10-0 nylon suture.

Group B: The eye was prepared with Povidone Iodine 5% solution. Controlled gentle digital massage with the hand was given. Trabeculectomy was performed in the superotemporal or superonasal quadrant trying to avoid sites of perforating scleral vessels. The conventional superior rectus suture placed. A fornix based conjunctival flap was prepared. Haemostasis was achieved by adequate wet field cautery. Subconjunctival Mitomycin C 0.2 mg/ml applied for 3 minutes with 3 merocel sponges. Subconjunctival space copiously irrigated with 30 ml Ringer Lactate. A 4 x 4 mm triangular scleral flap one third of the thickness dissected to within 1 mm of clear cornea with a Bard Parker knife. After creating a paracentesis opening, inner sclerostomy block was dissected out with the blade in the dimensions 2mm x 3 mm, at the base of the hinge of the superficial scleral flap. Peripheral iridectomy performed through the inner sclerostomy with a vanna scissor and a single toothed fine forceps. Scleral flap re-approximated with an apical 10-0 nylon suture and one releasable suture. Conjunctival flap closed water tight by 10-0 nylon suture.

Postoperatively patients were prescribed combination of antibiotic-steroid [Tobramycin 0.3%+Dexamethasone 0.1%] eye drops every 2 hours for one week and tapered over the following 5 weeks. Cycloplegic-mydratic [Homatropine 2%] eye drops used when signs of early inflammation, shallow A/C, hypotony were present. The number, frequency and duration of the anti-glaucoma drugs, if required, was carefully noted down and compared in the above two groups.

Postoperatively subjects examined at days 1 and 7 then at 4 weeks, 12 weeks and 6 months for:

- Intra ocular pressure (Applanation tonometry)
- Unaided visual acuity

- Best corrected visual acuity
- Slit lamp examination to assess : condition of filtering bleb
- Anterior chamber depth, Inflammatory reaction, Hyphaema etc.
- Gonioscopy
- Fundoscopy :

Any change in cup disc ratio postoperatively Cystoid macular edema

- Complications (if any)

**Surgical success** defined in terms of IOP measurement according to the following criteria:

- 1) Complete success – final IOP <14mm Hg without medication
- 2) Qualified success – final IOP <14mm Hg with medication
- 3) Failure – IOP >14 mm Hg with medication.

### Outcome Analysis

Best corrected visual acuity, Intra ocular pressure, Post operative use of anti glaucoma medication of both the groups will be assessed in mean +/- SD. Post operative complications of both the groups will be expressed in Percentage and Proportions. Significance of difference in means will be inferred by unpaired 't' test. Significance of difference in proportions will be inferred by chi-square test. For significance P value equal to or less than 0.05 will be considered significant.

### 3. Result

42 eyes of 42 patients were evaluated in our study with the aim to study and assess the efficacy of mitomycin C versus ologen implant in patients undergoing trabeculectomy with ologen implant (group A) and trabeculectomy with MMC.

The mean age of patients in group A was 56.05 years and in group B was 54.0 years (p = 0.000).

In group A, patients who had POAG alone were 13 and associated with Nuclear Sclerosis grade 1 and 2 media opacity were 1 each where as in group B, patients with POAG alone were 14 and associated with NS grade 2 were 2. This distribution was not found to be significant.

The pre operative mean BCVA (in log mar) in group A and group B was found to be 0.72 and 0.87 respectively. The post operative mean BCVA (in log mar) in group A was 0.6 and 0.68 in group B. The change in the mean BCVA in both the groups individually post operatively was found to be 0.15 and 0.2 in group A and group B respectively and was found to be not significant. (TABLE 1, 2, 3) (FIGURE 1, 2, 3)

In present study mean pre operative IOP was 27.05 ± 4.30 mm Hg in group A and 26.72 ± 4.47 mm Hg in group B (t = 0.244 with 40 degrees of freedom, p = 0.809). which was found to be not significant. In our study the mean post operative IOP in group A (trab with Ologen) was 13.23 ± 4.28 mm Hg and in group B (trab with mmc) was 13.66 ± 4.39 mm Hg at six month follow up. (t = -0.321 with 40

degrees of freedom,  $p = 0.750$ ). The comparison of mean changes in the pre and post operative IOP in group A ( $13.82 \pm 3.49$  mm Hg) and group B ( $13.06 \pm 4.12$  mm Hg) was not significant statistically ( $t = 0.645$ , with 40 degrees of freedom,  $p = 0.523$ ). (table 4, 5, 6, 7, 8) (figure 4, 5, 6, 7, 8)

The mean number of pre operative anti glaucoma medications used in our study in group A was  $2.7 \pm 0.73$  SD and in group B was  $2.6 \pm 0.6$  SD. This was not significant statistically ( $p = 0.630$ ).

The mean number of post operatively anti glaucoma drugs used was  $0.28 \pm 0.56$  SD and  $0.33 \pm 0.48$  SD in group A and B respectively. In both the groups there was highly significant reduction in the mean number of drugs required to control IOP. Among the groups the difference was not significant ( $p = 0.758$  with 40 degrees of freedom). (table 9, 10) (figure 9, 10)

In our study we observed shallow AC, hyphaema, choroidal detachment, bleb leakage as early complications. In group A (trabeculectomy with ologen) three patients (14.28%) had complications during first week of post operative follow up. Two patients had shallow AC with hypotony and one patient had hyphaema. In group B (trabeculectomy with MMC) out of six patients (28.5%) who had complications, shallow AC with hypotony and hyphaema was seen in two patients each respectively. One patient had choroidal detachment and another had bleb leakage in first week of follow up with positive seidel's test. The comparison of post operative complications in both the groups was found to be not significant statistically (chi square = 1.725 with 4 degrees of freedom,  $p = 0.786$ ) (table 11) (figure 11)

In our study at six months, we achieved complete success (IOP < 14.0 mm Hg without medication), in 76.19% in group A, and 66.67% in group B. The difference between the two groups in success rate was not significant statistically  $P = 0.733$ . (table 12) (figure 12)

Qualified success was achieved (IOP < 14.0 mm Hg with medication) 19.05% in group A and 14.28% in group B. The difference between the two groups in success rate was not significant statistically  $P = 0.999$ . Overall success rate (complete success and qualified success) at six months was 95.24% in group A and 80.95% in group B. The difference between the two groups in success rate was not significant statistically (with 2 degrees of freedom,  $P = 0.656$ ).

The failure (IOP > 14.0 mm Hg with medications) was noted 4.76% in group A (one case) and 19.05% (four cases) in group B, which was not significant statistically  $P = 0.341$ . If the target IOP was taken to be 20mmHg, the success rate would have been 100.0% in both the groups.

#### 4. Discussion

The present study was undertaken with the aim to assess and compare the efficacy of MMC versus Ologen implant in trabeculectomy for the management of POAG. There was no significant difference in pre-operative parameters of the two

groups in terms of age, sex, average number of anti glaucoma drugs and IOP being used.

IOP reduction was more in group A but the difference was not statistically significant. The comparison in the mean change of pre and post operative IOP at six months in both groups was statistically not significant ( $p = 0.523$  with 40 degrees of freedom) which was comparable to a study done by Papaconstantinou Det al (2010)<sup>(9)</sup>. In their study of 40 patients, 20 in each group (A – trabeculectomy, B- trabeculectomy with ologen implant) found that mean post operative IOP for both the groups was significantly lower than pre operative levels ( $p < 0.05$ ). The study shows that trabeculectomy with ologen does not seem to offer significant advantage compared with trabeculectomy alone in terms of the IOP reduction.

The change in the mean BCVA in both the groups individually post operatively was found to be not significant. Salvatore Cillino et al (2011)<sup>(10)</sup> studied 40 glaucoma patients, 20 in each group (MMC and Ologen). In their study they found that the visual acuity was stable post operatively in both the groups.

Post operative complications were observed more in group B. Shallow AC (two in each group), hyphaema (one in group A and two in group B), choroidal detachment (one case in group B), bleb leakage (one case in group B). The difference in post operative complications in the two groups was found to be not significant ( $p = 0.198$ ), which was comparable to a study done by Marey HM et al (2013)<sup>(11)</sup> who studied eyes of sixty patients of two groups (group 1 – SST augmented with intraoperative MMC, group 2- SST using Ologen implant) and reported one case in each group who had hyphaema and four cases in group 1 and two cases in group 2 had shallow AC. In group 1 one case had blebitis. There was no significant difference regarding the complications between both the groups.

Complete success was achieved in 76.19% cases of group A and 66.67% cases in group B which was found to be non significant ( $p = 0.733$ ). Qualified success was achieved in 19.05% in group A and 14.28% in group B which was non significant (0.999). Overall success at six months was 95.24% in group A and 80.95% in group B which was non significant ( $p = 0.656$ ). Failure was 4.76% (one case) in group A and 19.05% (four cases) in group B which was non significant. ( $p = 0.341$ ). Sirisha Senthil et al<sup>(12)</sup> in their study found probability of success using Kaplan-meier graphs. Considering complete success criteria, survival probability in Ologen group was 100% at six months – 92.9% (95% CI, 59.1 – 99.0) at 12 months and 82.5% (45.1 – 95.1) at 24 months. The corresponding survival probability in MMC group was 93.8% (63.2 – 99.1) at 6 months, 56.3% (13.1 – 85.0) at 24 months. The difference in the success rates (complete and qualified) was not statistically significant, ( $p > 0.5$ ).

Though the results of this study has been encouraging. Since MMC is observed to have late post operative bleb related problems, we believe a longer duration follow up will be more informative in deciding whether Ologen is superior to MMC in the long term management of glaucoma.

## 5. Limitations of the Study

- 1) Small population size: The study would have been more informative if the sample size were larger.
- 2) Smaller follow up duration: If a longer follow up duration were given, the results could have been more informative specially with regard to the late bleb complications associated with MMC.
- 3) This study had undertaken patients with primary open angle glaucoma alone. Further research on other types of glaucoma like angle closure glaucoma, secondary glaucomas, juvenile glaucoma is required.

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