

## Original Research Article

## A Prospective Intervention Study to Compare the Results of Trabeculectomy with Ologen Implantation and Other Methods of Trabeculectomy in Managing Glaucoma in a Medical College in West Bengal

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### ABSTRACT

#### Background

While performing trabeculectomy in glaucomatous patients, application of mitomycin C or implanting ologen showed significantly improved long term outcomes.

**Objective:** To compare the results of trabeculectomy with or without ologen implant and trabeculectomy with mitomycin C in glaucoma patients.

#### Methods

Ninety glaucomatous eyes were selected after matching for the operative suitability in each case and distributed into 3 groups. Group 1 underwent trabeculectomy, Group 2 had trabeculectomy with mitomycin C and Group 3 underwent trabeculectomy with ologen implant. Data was analyzed using one-way ANOVA and Kruskal-Wallis tests at 5% significance level.

#### Results

At 6 month postoperatively, significantly higher mean intraocular pressure (IOP) was found in Group 1 ( $p = .000$ ). However, it did not vary significantly among Group 2 and Group 3 ( $p = .25$ ). In comparison to the other groups significantly higher mean bleb height was found in group 3 ( $p = .000$ ). In Group 3 the incidence of anterior chamber reaction was significantly lower when compared to Group 1 ( $p = 0.021$ ) and Group 2 ( $p = .024$ ). In comparison to other two groups, thin cystic bleb was found to occur less significantly in Group 3 ( $p = .031$ ). Significantly lower incidence of shallow anterior chamber was found in Group 3 in comparison to Group 2 ( $p = .024$ ), though not in Group 1 ( $p = .34$ ).

#### Conclusion

Considering safety and effectiveness, implantation of ologen in trabeculectomy could

provide a promising alternative to the use of mitomycin C.

**Keywords:** Glaucoma, trabeculectomy, adjunctive anti-metabolites, ologen.

## INTRODUCTION

More than 67 million persons across the world are affected by glaucoma leading to blindness in around 10%,<sup>1</sup> being the second most common cause after cataract.<sup>2,3</sup> India has an estimated prevalence of 11.9 million cases of glaucoma of whom 12.8% are reported to be blind.<sup>4</sup>

Introduced by Cairns in 1968, trabeculectomy has still remained the standard surgical intervention for reducing intraocular pressure (IOP) in glaucoma patients unresponsive to usual medications.<sup>5,6</sup> In cases of primary open angle glaucoma (POAG), primary trabeculectomies had more than 75% reported success rate reaching even up to 100%.<sup>7</sup> Trabeculectomy is done with the aim of lowering IOP and thus slowing the progression of glaucoma induced optic neuropathy and visual loss.<sup>8,9</sup>

This procedure is carried out to successfully create a functioning aqueous drainage shunt with the formation of a filtering bleb. However there may be a risk of scarring of the structures at the site of trabeculectomy resulting in inadequate control of IOP. Hence all care must be given to prevent scar formation during wound healing.<sup>10,11</sup>

Mitomycin C (MMC), an adjunctive antimetabolite, has been found to inhibit the scarring of the subconjunctiva postoperatively. It thus enhances the chance of success of trabeculectomy in the long run.<sup>12-15</sup>

Ologen, a recently introduced structurally porous, biodegradable collagen matrix of porcine origin, is used as an implant in trabeculectomy to prevent subconjunctival scarring with lower incidences of complications related to bleb.<sup>16</sup> At the end of trabeculectomy, this implant is placed over the sclera flap, sub-conjunctivally. It provides a scaffolding for development of a matrix of loose connective tissue due to growth of fibroblast in its pores and thereby remodeling tissue resulting in decrease scar formation. Apart from acting as a reservoir, this implant also prevents adhesions between the conjunctiva and the episcleral surfaces by separating them mechanically.<sup>16,17</sup>

In this backdrop the present study was conducted with the objective to compare the results of trabeculectomy with or without ologen implant and trabeculectomy with mitomycin C in glaucoma patients.

## MATERIALS AND METHODS

The present study was a prospective intervention study conducted after receiving approval from the institutional ethics committee. The glaucoma clinic at the Regional Institute of Ophthalmology, Medical College and Hospital, Kolkata was the place where the study was carried out for a period of twelve months (June 2018 to June 2019). Convenient and purposive sampling method was used to select ninety eyes of patients affected either with primary open-angle glaucoma (POAG) or by primary angle-closure glaucoma (PACG) after matching for the operative suitability in each case. All patients submitted written informed consent forms. They were then grouped into Group 1 including 30 eyes for trabeculectomy, Group 2 with 30 eyes found suitable for trabeculectomy with mitomycin C (MMC), and Group 3 with 30 eyes found suitable for undergoing trabeculectomy with ologen implantation (having a diameter and height of 6 mm and 2 mm respectively).

All the acute and chronic PACG patients, and patients of POAG with progressive loss of visual field and/or uncontrolled IOP levels even with standard medical intervention were included in the study. Those patients who were  $\leq 18$  years or those diagnosed with neovascular or normal tension glaucoma or those found to be suffering from any acute or chronic diseases that could confound the outcomes of the study namely immunodeficiency

disorders, connective tissue diseases, diabetes, hypertension etc. and patients with past history of ocular trauma or previous ocular surgery (with the exception of cataract surgery) and patients known to be allergic to collagen, were excluded from the present study after proper history taking and thorough physical and laboratory examinations as required.

A single experienced competent surgeon performed all the surgeries. The implants, in Group 3 patients, were placed on top of the scleral flap before conjunctival closure.

Postoperative follow-up reviews were done on day 1, 2<sup>nd</sup> week, 1<sup>st</sup>, 3<sup>rd</sup> and 6<sup>th</sup> month. Successes of the interventions were assessed at the last follow-up i.e. 6<sup>th</sup> month post operatively. Absolute success was defined as an IOP less than 18 mm of Hg without the use of any other topical medication. While qualified success was defined as an IOP of 18 mm of Hg or more without the application of any topical medication in addition.

### Statistical Analysis

Statistical package for the social sciences (SPSS) version 20.0 was used to analyze data. One-way ANOVA with Bonferroni post-hoc tests and Kruskal-Wallis with Dunn-Bonferroni post-hoc tests were applied at 5% significance level.

## RESULTS

The mean age in Group 1 (trabeculectomy) was  $56.74 \pm 11.48$  years. Among them half (15/30) was male and the other half (15/30) was female. The same in Group 2 (trabeculectomy with MMC) was  $55.31 \pm 11.86$  years. Among them 53.3% (16/30) was male and 46.7% (14/30) was female. The mean age in Group 3 (trabeculectomy with ologen) was  $56.17 \pm 9.47$  years. Among them 63.3% (19/30) was male and 36.7% (11/30) was female.

No significant difference was found across the three groups with regard to age ( $p = 0.87$ ) or gender ( $p = 0.67$ ).

Group 1 included 17 (56.7%) left eyes and 13 (43.3%) right eyes. In Group 2, there were 9 (30.0%) left eyes and 21 (70.0%) right eyes. Group 3 had 15 (50.0%) left eyes and 15 (50.0%) right eyes. PACG affected eyes in Group 1, Group 2 and Group 3 were 56.7% (17/30), 70.0% (21/30) and 56.7% (17/30) respectively. While POAG affected eyes were in Group 1, Group 2 and Group 3 were 43.3% (13/30), 30.0% (9/30) and 43.3% (13/30) respectively. No significant difference was found across the three groups with respect to type of glaucoma ( $p = 0.53$ ).

The proportions of eyes that underwent trabeculectomy with phacoemulsification were 90.0% (27/30), 73.3% (22/30) and 70.0% (21/30) in Group 1, Group 2 and Group 3 respectively. While the proportions of eyes that underwent only trabeculectomy were 10.0% (3/30), 26.7% (8/30) and 30.0% (9/30) in Group 1, Group 2 and Group 3 respectively. No significant difference was found across the three groups with respect to type of surgery ( $p = 0.27$ ).

It was observed on the day 1 of post-operative follow-up that as per the critical difference (CD), among all three groups the mean IOP of Group 1 was significantly the highest ( $p = 0.000$ ). Whereas it was significantly lesser in Group 3 in comparison to Group 2 ( $p = .000$ ). Similar observation was also made in the day14 of post-operative follow up. (**Table 1**)

During the post-operative follow-up at one month, as per the CD, among all three groups the mean IOP of Group 1 was significantly the highest ( $p = 0.000$ ). But this did not vary significantly between Group 2 and Group 3 ( $p = 0.23$ ). Also at the 3<sup>rd</sup> post-operative month as per the CD, among all three groups the mean IOP of Group 1 was significantly the highest ( $p = 0.000$ ). But this did not vary significantly between Group 2 and Group 3 ( $p = .32$ ). (**Table 1**) Similarly during the follow-up at 6<sup>th</sup> month, among all three groups the

mean IOP of Group 1 was significantly the highest ( $p = 0.000$ ). But again this did not vary significantly between Group 2 and Group 3 ( $p = .25$ ). (**Table 1**)

The mean bleb height on each of day 1 and 14 and on 1<sup>st</sup>, 3<sup>rd</sup> and 6<sup>th</sup> month varied significantly across the three groups ( $p = .000$ ). Post-hoc test showed that in comparison to Group 1 and Group 2, significantly higher mean bleb height was observed in Group 3 ( $p = .000$ ). This was also significantly higher in Group 2 than in Group 1 ( $p = .000$ ). (**Table 2**)

The total number of uncomplicated cases were found to be significantly more ( $p = .042$ ) in Group 3 (86.7%) than in the other two groups (63.3% in each). Anterior chamber reaction was found to be 13.3% in Group 1, 10.0% in Group 2 and 3.3% in Group 3. Statistical significance was observed for this difference ( $p = .035$ ). Post hoc test showed that the incidence of anterior chamber reaction was significantly less in Group 3 than in both Group 1 ( $p = 0.021$ ) and Group 2 ( $p = .024$ ). However this difference was not significant between Group 1 and Group 2 ( $p = .34$ ). (**Table 3**) No significant difference was noted in the incidences of choroidal detachment across the three groups ( $p = .63$ ). In comparison to both Group 1 and Group 2, thin cystic bleb was found to occur less significantly in Group 3 ( $p = .031$ ). The incidence of shallow anterior chamber varied significantly across the three groups ( $p = .033$ ). Post-hoc test revealed that this was significantly lower in Group 3 than in Group 2 ( $p = .024$ ) but not in Group 1 ( $p = .34$ ). However no such significant difference existed between Group 1 and Group 2 ( $p = .53$ ). (**Table 3**)

Follow-up	IOP (Mean $\pm$ SE)			p
	Trabeculectomy (Group 1) (n <sub>1</sub> =30)	Trabeculectomy+MMC (Group 2) (n <sub>2</sub> =30)	Trabeculectomy + Ologen (Group)(n <sub>3</sub> =30)	
Day 1	17.72 $\pm$ 0.61	15.83 $\pm$ 0.34	14.04 $\pm$ 0.05	.000
Day 14	17.63 $\pm$ 0.58	15.57 $\pm$ 0.22	13.91 $\pm$ 0.04	.000
Month 1	17.54 $\pm$ 0.58	15.11 $\pm$ 0.07	13.83 $\pm$ 0.03	.000
Month 3	17.51 $\pm$ 0.55	14.04 $\pm$ 0.73	14.13 $\pm$ 0.68	.000
Month 6	16.92 $\pm$ 0.28	14.44 $\pm$ 0.59	13.63 $\pm$ 0.55	.000

**Table 1: Mean IOP during postoperative follow-ups**

Follow-up	Bleb height (Mean $\pm$ SE)			p
	Trabeculectomy (Group 1) (n <sub>1</sub> =30)	Trabeculectomy+MMC (Group 2) (n <sub>2</sub> =30)	Trabeculectomy + Ologen (Group 3)(n <sub>3</sub> =30)	
Day 1	0.46 $\pm$ 0.02	0.87 $\pm$ 0.04	1.05 $\pm$ 0.04	.000
Day 14	0.45 $\pm$ 0.02	0.86 $\pm$ 0.03	1.06 $\pm$ 0.04	.000
Month 1	0.41 $\pm$ 0.02	0.80 $\pm$ 0.04	0.99 $\pm$ 0.03	.000
Month 3	0.39 $\pm$ 0.02	0.78 $\pm$ 0.03	0.99 $\pm$ 0.04	.000
Month 6	0.37 $\pm$ 0.02	0.76 $\pm$ 0.03	0.96 $\pm$ 0.04	.000

Complications	Trabeculectomy (Group 1) (n <sub>1</sub> =30)	Trabeculectomy+MMC (Group 2) (n <sub>2</sub> =30)	Trabeculectomy + Ologen (Group 3) (n <sub>3</sub> =30)
Anterior chamber	4 (13.3)	3 (10.0)	1(3.3)

reaction			
Choroidal detachment	2 (6.7)	2 (6.7)	1(3.3)
Thin Cystic bleb	3 (10.0)	3 (10.0)	1 (3.3)
Shallow AC	2 (6.7)	3 (10.0)	1 (3.3)
Uncomplicated	19 (63.3)	19 (63.3)	26 (86.7)
<b>Table 3: Postoperative complications in the three groups</b>			

## DISCUSSION

The present study aimed at comparing the results of trabeculectomy with or without ologen implant and trabeculectomy with mitomycin C in glaucoma patients.

In this study it was observed that the mean IOP of Group 1 was significantly higher than that in Group 1 & 2. However the mean IOP of Group 2 and Group 3 did not vary significantly in the later months of follow-up. Similar observations were reported by Ciflino et al<sup>18</sup> and Papaconstantinou et al<sup>19</sup> in their respective studies. However Rosenteter et al<sup>20</sup> reported significantly greater reduction of IOP during follow-up at the end of 12 months in trabeculectomy with MMC group than in ologen group. However all were POAG cases and each group comprised of ten cases only.<sup>20</sup>

Ji et al<sup>21</sup> in their meta-analysis revealed that trabeculectomy with ologen implant resulted in lower but non-significant reduction in IOP in comparison with MMC. No significant difference was found in terms of reduction of glaucoma medication, incidence of complications or success rate.<sup>21</sup>

The present study showed that the mean bleb height on each follow up varied significantly across the three groups. Significantly higher mean bleb height was observed in Group 3 compared with both Group 1 and Group 2. This was also significantly higher in Group 2 than in Group 1. These findings indicated that filtration was significantly better in Group 3 than in Group 1 and Group 2. Even this was significantly better in Group 2 when compared to Group 1.

Min et al<sup>22</sup> observed the nature of wound healing of a filtering bleb after trabeculectomy using ologen soaked with MMC and found no synergistic effect in reduction in IOP. But a comparatively stable IOP was achieved. Also it did not aggravate scarification.<sup>22</sup> Boey et al<sup>23</sup> found non-significant difference in mean bleb height at one and two months follow up (Ologen vs. MMC). However, a significantly lower mean bleb height was noted at 3 month in the ologen group in comparison to the MMC group.<sup>23</sup>

Group 3 had significantly more uncomplicated cases in the present study than the other two groups. Significantly lesser number of anterior chamber reaction was found in Group 3 than both Group 1 and Group 2. The incidences of choroidal detachment did not vary significantly across the groups. Thin cystic bleb was found to occur less significantly in Group 3. Also the incidence of shallow anterior chamber was found to be significantly lower in Group 3 than Group 2 but not Group 1. However Group 1 and Group 2 did not vary significantly in this respect. Papaconstantinou et al<sup>19</sup> were not in agreement with our results since it showed ologen to have longer amount of complications than simple trabeculectomy. The lower success rate and bleb functionality in ologen cases when compared with MMC showed a higher complication rate later as reported in 2 studies.<sup>20, 23</sup>

## LIMITATIONS

There were a few limitations in this study. It was not a randomized controlled trial. The sample size was arbitrary and selected purposively which had limited the power of statistical comparison between the groups. Affordability of ologen was also an important limitation.

## CONCLUSION

It can be concluded from the present study that considering the safety and effectiveness, implantation of ologen in trabeculectomy could provide a promising alternative to the use of mitomycin C with more or less similar success rate. The postoperative complications were much less with ologen group. This implant might be preferred in cases where antimetabolite related risks would be needed to be avoided.

Well organized randomized controlled trials would provide us with higher level of evidence on safety and efficacy of this implant in the long run.

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