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COMPARISON OF OUTCOME OF TRABECULECTOMY WITH MITOMYCIN C VERSUS TRABECULECTOMY WITH OLOGEN IMPLANT IN PRIMARY OPEN ANGLE GLAUCOMA.

Ophthalmology

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ABSTRACT

PURPOSE- To study the efficacy of Ologen implant with Mitomycin-C, in the form of post-operative intraocular pressure reduction, post-operative visual acuity, safety in terms of intra-operative and post-operative complications and success rates. **METHODS -** It was a comparative study in 38 patients undergoing trabeculectomy surgery in Mahatme eye bank eye hospital, Nagpur from August 2016 to December 2017. After enrollment, patients were randomized into 1 of the 2 groups; Trabeculectomy with MMC in Group A (MMC group) and trabeculectomy with ologen in Group B (Ologen group). Post-operative evaluations were performed on Day 1 and at 1st week, and then at 1st, 3rd and 6th month. Data analysis was done with the help of JASP 0.8.3.1 and MS-Excel 2013. **RESULTS-** The mean age was 63.74 ± 5.23 in Group A and 60.11 ± 6.64 in Group B respectively. Group A had 5 male patients (26%) and 14 female patients (73%), while Group B had 10 male (52%) and 9 female patients (47%). The difference between the two was statistically significant (P=0.01). There was a statistically significant difference in mean IOP reduction from baseline between Ologen and MMC Groups, with a mean IOP of 13.4 ± 1.8 mm Hg in MMC and 12.2 ± 2.4 mm of Hg in Ologen eyes, respectively at the end of 6 months. Statistically significant improvement in IOP was seen from preoperative to 6 month postoperative level, p<0.001 for MMC group, <0.001 for Ologen group. **CONCLUSION-** The Ologen implant is a new, safe, and effective alternative to MMC for improving the long-term success rate of trabeculectomy surgery and it avoids the side effects associated with the use of MMC.

KEYWORDS

Trabeculectomy, Ologen, Mitomycin-c, Glaucoma, Iop.

INTRODUCTION

Worldwide, the most common cause of irreversible blindness is glaucoma. Early glaucoma is treated medically, whereas advanced glaucoma requires surgical treatment. Trabeculectomy is generally recommended for those patients with glaucoma that continues to progress despite use of medications and/or laser treatment.[1]

Trabeculectomy as the standard procedure for the surgical management of glaucoma is widely performed since 1968. Successive rates for primary trabeculectomies ranges from 67% to 84%. In trabeculectomy, a new drainage site is created to facilitate the drainage of fluid from the eye. Instead of draining into the normal drainage site of the eye (the trabecular meshwork), the fluid is drained into a new space (a "bleb") that is completely covered by the conjunctiva. This lowers the intraocular pressure.[2]

Episcleral fibrosis & sub-conjunctival scarring remain the most common reason for the failure of trabeculectomy. To resolve this problem, the method was developed further over subsequent decades. In 1990's, anti-fibrotic agents such as Mitomycin-C (MMC) improved the success rate and produced lower IOP when applied intra-operatively during trabeculectomy. Trabeculectomy with MMC is still considered the gold standard in glaucoma surgery.[2]

But, Mitomycin-C, when used in high risk patients like high myopia with thin sclera, severe dry eye, repeat trabeculectomy, was accompanied by increased adverse events. The use of MMC is hence contraindicated in such patients. There is an urgent requirement for a safer alternative to MMC for fibrosis control.[2]

Various modifications and newer techniques have been developed in an attempt to reduce or avoid the adverse effects of MMC like reducing the concentration and the duration of MMC used intraoperatively during trabeculectomy, glaucoma drainage devices, various implants, amniotic membrane transplantation, lasers etc.[3]

Tissue engineering, nowadays has achieved great progress in creating biomedical devices which prevent scar formation by modifying process of wound healing. It takes advantage of micro technology and tissue bioengineering by having a molecular structure that permits the formation of a spongy filtration bleb without the use of anti-fibrotic agents. The implant is a 3-D disc shaped porcine-derived biodegradable collagen-glycosaminoglycan copolymer matrix implant (Ologen®) that has been proposed. It is used as a spacer to mechanically separate the subconjunctival and episcleral tissues in order to prevent fibrosis and, also to help in reorganizing the subconjunctival scar formation.

Ologen, a collagen-based scaffold, has been used to create a healthy vascular bleb following trabeculectomy. It degrades within 90~180 days after implantation, over scleral flap. Ologen modifies the healing process by allowing fibroblasts and myofibroblasts to grow into its pores. Theoretically this implant can decrease scar formation and improves surgical success of trabeculectomy performed without the adjunctive use of anti-fibrotic agent.[4] What results is an elevated bleb with dynamic flow of aqueous humor from anterior chamber to sub-conjunctival space, without the thin walled, cystic bleb associated with anti-fibrotic.

In our study, we compared the outcomes of trabeculectomy augmented with either Ologen implant and intraoperative low-dose MMC. We tried to test efficiency of the Ologen implant against antimetabolite agents like MMC in trabeculectomy surgery. Ologen may thus provide a new, safe, simple and effective therapeutic approach for treating glaucoma.[5]

METHODOLOGY

It was a prospective, randomized comparative study in 38 patients undergoing trabeculectomy surgery in Mahatme eye bank eye hospital, Nagpur from August 2016 to December 2017. Adult patients (>18 years) with uncontrolled primary open glaucoma undergoing trabeculectomy were included. Exclusion Criteria were patients with known allergic reaction to mitomycin C or porcine collagen, Angle closure glaucoma, secondary glaucoma, Traumatic glaucoma, Juvenile glaucoma, Repeat trabeculectomy, uncontrolled Diabetics and Uncontrolled Hypertensives. Study was approved from Institutional ethics committee.

Informed consent were taken from the patients who fulfill the inclusion criteria. After enrollment, patients were randomized into 1 of the 2 groups; Trabeculectomy with MMC in Group A (MMC Group) and

trabeculectomy with ologen in Group B (Ologen Group).

Detailed history regarding any pre-existing ocular inflammations and all the aforesaid ocular and systemic conditions in the inclusion and exclusion criteria were taken. Measurement of best corrected visual acuity (BCVA) by LogMAR chart was done both pre and post operatively. Ophthalmological examination was done using slit lamp. Dilated fundus examination using +90D and +20D was done to rule out any posterior segment pathology. IOP was measured using Goldmann Applanation Tonometer. Optic disc changes that were considered to be glaucomatous were focal or diffuse neuroretinal rim thinning, localized notching or nerve fiber layer defects.

Visual field defects were considered glaucomatous if at least 2 of the 3 Anderson's criteria (3 or morenon-edged points in a cluster depressed to P < 5% and 1 of which is depressed to P < 1%, Glaucoma Hemifield Test outside normal limits and Pattern Standard Deviation depressed to P <5%) were fulfilled.Age, gender, type of glaucoma, presence of any systemic diseases (diabetes mellitus and systemic hypertension in particular), highest recorded IOP, number of anti-glaucoma medications and visual field parameters were noted. All the surgeries were performed under microscope by the experienced surgeon, in the same OT settings, under all aseptic precautions. All subjects were operated under local peribulbar anaesthesia.

Post-operative treatment were topical steroid i.e. Prednisolone acetate 1% 6 times for four weeks and antibiotics i.e. Moxifloxacin 0.5% eye drop 4 times a day, which were then tapered over a time span of one month , and cycloplegic drops i.e. homatropine 2% twice a day for 15 days. Post-operative evaluations were performed on Day 1 and then at 1st week, and then at 1st, 3rd and 6th month. Best corrected visual acuity (BCVA), Intraocular pressure (IOP) & the need for any anti-glaucoma medications, Slit lamp examination, Ophthalmoscopy, Perimetry & OCT were repeated at the end of 6 months.

The definitions used to evaluate the efficacy of both surgical techniques were as follows:

- Complete success was defined as an IOP of > 5 mm of Hg & ≤ 21 mmHg without anti-glaucoma medication.
- Relative success was defined as IOP of >5 mm of Hg & ≤ 21 mmHg with anti-glaucoma medication.
- OVERALL SUCCESS = COMPLETE + RELATIVE SUCCESS
- Failure was defined as IOP of < 5 mm of Hg or > 21 mm of Hg with addition of anti-glaucoma medications.

Data analysis was done with the help of JASP 0.8.3.1 and MS-Excel 2013. Descriptive statistics such as mean, standard deviation (SD), 95% confidence intervals (CI) were analyzed. Chi-square, repeated Anova and Student's T-test were used. P value less than 0.05 was considered significant.

RESULT

Mean age was 63.74 ± 5.23 in Group A and 60.11 ± 6.64 in Group B respectively. The difference was statistically insignificant between the two groups (P =0.07). Patients were in the age group of 50-75 years in both the groups.Group A had 5 male patients (26%) and 14 female patients (73%), while Group B had 10 male (52%) and 9 female patients (47%). The difference between the two was statistically significant (P=0.01, chi-square test).

Pre-operative mean best corrected visual acuity (BCVA) in Group A and Group B was 0.53 ± 0.2 logMAR units and 0.77 ± 0.6 log MAR units respectively. The difference between mean BCVA in both the groups was statistically insignificant (P =0.31). Pre-operative mean intraocular pressure in Group A 29.8 ± 8.81 and Group B 26.6 ±3.9 was mm Hg and mm Hg respectively. The difference in pre-operative mean intraocular pressure in the two groups was statistically insignificant (P=0.55).

Table.1: Comparison Of Postoperative Complications

Complications	MMC	Ologen	Total
Bleb Leak	2	0	2
Hyphema	0	2	2
Hypotony	1	1	2
Shallow Anterior Chamber	1	0	1
No Complications	15	16	31
Total	19	19	38

Most of the complications were minor and they subsided within 3-4 weeks after surgery. 2 cases in Group A developed leak after surgery. None of the eyes in either groups required any intervention for management of the complications (Table 1).

There was a statistically significant difference in mean IOP reduction from baseline between Ologen and MMC Groups, with a mean IOP of 13.4 ± 1.8 mm Hg in MMC and 12.2 ± 2.4 mm of Hg in Ologen eyes, respectively at the end of 6 months. Statistically significant improvement in IOP was seen from preoperative to 6 month postoperative level, p<0.001 for MMC group, <0.001 for Ologen group, Repeated measures ANOVA.

Table 2: Evaluation Of Success

	MMC (n=19)	Ologen (n=19)
Complete Success	16	16
Qualified Success	3	3
Failure	0	0

Complete success i.e IOP <21 mm Hg at the end of follow up. Relative success: IOP <21 mm Hg with medication at the end of follow up. Failure: IOP >21 mm Hg with medication at the end of follow up (Table 2).

Table 3: Comparison Of Anti-glaucoma Medications From Preoperative To Postoperative Stage.

	MMC (n=19)	Ologen (n=19)
No. of eyes with 2 anti-glaucoma medications	14	14
Anti-glaucoma medications continued postop	3	1
No anti-glaucoma medications postop	11	13
No. of eyes with 3 anti-glaucoma medications	5	5
Anti-glaucoma medications continued postop	0	2
No anti-glaucoma medications postop	5	3

The post-operative mean number of antiglaucoma medications reduced significantly from 2.3 to 0.2 in group A and from 2.3 to 0.15 in group B (Table 3).

DISCUSSION

Mean age was 63.74 ± 5.23 years and 60.11 ± 6.64 years in the mitomycin c and ologen group respectively. The mitomycin c group had 5 male patients and 14 female patients, while the ologen group 10 had male patients and 9 female patients. Our study was compared with similar studies as mentioned in table 4 below

Table 4: Comparison Of Mean Age With Similar Studies

	Rosentreter A et al.[6]	Cillino S et al.[7]	Senthil S et al.[8]	Eldaly ZH et al.[9]	Our study
Male:Female	8:12	23:17	20:19	17:13	23:15

In our study, the pre-operative intraocular pressure in Group A and Group B was m 29.8 ± 8.81m Hg and 26.6 ± 3.9 mm Hg respectively. The difference in pre-operative mean intraocular pressure in both groups was found to be statistically insignificant. Post-operatively, the intraocular pressure showed a decrease in value on each subsequent follow-up visit, but there was no statistically significant difference seen in the mean postoperative IOP at any point of follow up between the two groups.

At 6 months postoperatively, the IOP was 13.4 ± 1.8mmHg (Group A) and 12.2 ± 2.4 (Group B) in both the groups. The difference between the two was statistically insignificant. Also the mean decrease in the intraocular pressure postoperatively after 6 months was 16.4 mmHg in Group A and 14.4 mmHg in Group B, with the difference being statistically insignificant.

In a study by Rosentreter A. et al [6] in 2010, the mean preoperative IOP was 24.8 ± 8.9 mm of Hg for all patients enrolled. After 1 year of surgery, the mean IOP was 15.6 ± 2.4 mm of Hg in the Ologen group (43% reduction) and 11.5 ± 4.1 mm of Hg in the MMC group (50 % reduction). The results were comparable to those of our study.

Another study by Cilino S et al. [7], the mean pre-operative IOP (± SD) in the 2 groups was 26.5 (±5.2) in MMC eyes and 27.3 (± 6.0) in the Ologen group, without significant intergroup difference. In both the groups, there was a decrease in IOP at every post-operative visit, but the mean IOP did not differ between the two groups. The decrease in

mean IOP was 16.0 ± 2.9 (39.6%) mmHg in the MMC group compared to 16.5 ± 2.1(39.5%) mmHg in the Ologen group, at the end. This difference was not statistically significant (P = 0.5).

Johnson MS et al. [10] (2014) compared outcomes between patients undergoing trabeculectomy with an Ex-PRESS mini glaucoma device using Mitomycin-C (MMC) to those undergoing the same procedure using a subconjunctival collagen matrix implant (Ologen). A total of 49 eyes received Ologen, and 50 eyes received MMC and postoperative data were reviewed over 12 months. The mean preoperative IOP was 24.98 mm Hg for the MMC group, and 23.24 mm Hg for the Ologen group. At 12 months postoperatively, the mean IOP was 12.1 mm Hg for the MMC group, and 13.12 mm Hg for the Ologen group

A study conducted by Senthil S et al [8] revealed that Mean IOP reduction at 6 months was significantly lower (P = 0.01) in the Mitomycin c group (11.9 ± 2.9 mm Hg) as compared to Ologen group (14.6 ± 2.7 mm Hg). However, at 12 months (P = 0.81) and 24 months (P = 0.32), the mean IOP was similar between the 2 groups. Complete success probability at the end of 6 months in Ologen group was 100% (95% confidence interval: 59.1 - 99.0) was similar (P = 0.53) to that in Mitomycin C group (93.8%, 95% CI: 63.2 - 99.1). The incidences of early post-operative complications were similar in the 2 groups, except hyphema, which was significantly more in Ologen group.

In our study, the pre-operative mean number of antiglaucoma medications used in Group A and Group B was 2.3 and 2.3 respectively. Post-operatively, there was a decrease in the mean number of antiglaucoma medications at every subsequent visit, with the difference being statistically insignificant at every visit. At the end of 6 months, the mean number of antiglaucoma medications was 0.2 in Group A and 0.15 in Group B. This difference was statistically insignificant.

Our results were comparable to a study by Senthil. S et al [8] (2013). In their study the mean number of pre-operative anti glaucoma medication was 3.2 0.9 in both the groups. The number of medication reduced to 0 in Group A and 0.1 0.3 in the last follow-up. This reduction in the number of medications was statistically insignificant among the two groups (P= 0.33).

A study by Cilino S et al (7) (2011), found that the number of anti-glaucoma medication reduced significantly at the end in both groups after surgery. It was reduced from 2.6 ± 0.2 to 0.9 ± 0.2 in Ologen group and from 2.5 ± 0.3 to 0.8 ± 0.2 in MMC group, without significant intergroup differences (P=0.122).

So, on comparing our results with the above studies, we found that the post-operative decrease in the number of antiglaucoma medications achieved in both Ologen and MMC groups are comparable and was statistically significant.

In our study, the pre-operative mean best corrected visual acuity (BCVA) Group A and Group B was 0.53 ± 0.2 logMAR units and 0.77 ± 0.6log MAR units respectively, which was statistically insignificant. After surgery, the visual acuity in both the groups improved significantly. However, there was no statistically significant difference seen in mean BCVA at any point of follow-up between the two groups. The postoperative mean BCVA at 3 months was 0.57 + 0.18 in Group A and 0.78 ± 0.65 in Group B. The difference was statistically insignificant. The postoperative mean BCVA at 6 months was 0.54 ± 0.18 in Group A and 0.78 ± 0.65 in Group B. The difference was statistically insignificant.

Senthil S et al (8) (2013) showed that the mean BCVA changed from 0.33 ± 0.43 to 0.44 ± 0.66 in Ologen group and from 0.29 ±0.46 to 0.20 ± 0.24 in the MMC group, at the end of 6 weeks.

In this study, a total of 2 (10%) cases of hyphaema were noted in OLO group, 2 (10%) cases of hypotony (1 in each group), 2 cases with bleb leak and 1 case with shallow AC in the MMC group. All of these complications resolved without any intervention for its management.

Similarly, in the study conducted by Senthil S et al [8] (2013), a total of 12/19 eyes experienced one or the other complication in the Ologen group as compared to 7/20 in MMC group. Rosentreter A. et al [6] (2010), reported that hypotony was seen in both groups equally. However, a shallow anterior chamber occurred in only two cases in the Ologen group. No significant difference between the two groups was detectable. In two cases in the ologen group, Tenon's cysts built up after 4 weeks postoperatively and needling was necessary. In the MMC group revision, surgery was necessary because of a prominent bleb cyst and a subsequent late leakage in one case. Cillino et al [7] revealed that the frequency of postoperative complication did not significantly differ between the two groups. Early bleb leakage was more frequent in the OLO than in the MMC group (3 vs 1 eye, respectively, P=0.604), while early hypotony was more frequent in MMC than in OLO group (8 vs 4 cases, respectively, P=0.300), with an increased frequency of choroidal detachment in the former (5 vs 2 cases, respectively, P=0.407). No adverse reaction to the OLO, matrix extrusion, or conjunctival erosion was noted in OLO group.

CONCLUSION

In conclusion, trabeculectomy augmented with Ologen implant has efficacy and safety comparable to that of trabeculectomy augmented with Mitomycin-C. The Ologen implant has comparable visual outcomes, reduction in intraocular pressure and post-op number of antiglaucoma medications required to that with MMC, if any. The Ologen implant is a new, safe, and effective alternative to MMC for improving the long-term success rate of trabeculectomy surgery and it avoids the side effects associated with the use of MMC.

Conflict Of Interest- No

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