World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
Original Article

Trabeculectomy with ologen implant versus trabeculectomy with mitomycin-C in primary open angle glaucoma: A 2-year study

[1]Dr. Ashok Madan and [2]Dr. Kavita Dhabarde and [3]Dr. Karishma Shah

[1]Professor & HOD, [2]Associate Professor and [3]Junior Resident, Department of Ophthalmology, Government Medical College, Nagpur, Maharashtra, India

Received: 17-10-2017 / Revised Accepted: 27-11-2017 / Published: 02-12-2017

ABSTRACT

Aim: The aim of this study is to assess the efficacy and safety of trabeculectomy with Ologen implant *versus* trabeculectomy using Mitomycin-C (MMC) in patients of open-angle glaucoma.
Study design- Hospital based, prospective, comparative study at a tertiary eye care centre in central India.
Materials and Methods: 40 eyes of 40 patients with primary open angle glaucoma (POAG), were randomly assigned into two groups: trabeculectomy with Ologen implant (group A) or trabeculectomy with Mitomycin – C (group B). Assessment of intraocular pressure (IOP), intra-operative complications, anti-glaucoma medications required post – operatively was done for a period of 6 months.
Results: The mean IOP in the Ologen Group was reduced to 12.89$\pm$2.43 mm Hg from 26.17 $\pm$ 3.01 mm Hg and in the MMC group was reduced to 14.05$\pm$4.02 mm Hg from 26.72 $\pm$ 3.067 mm Hg after 6 months. No significant inter-group difference was noticed at any visits. The complete success rate in Group A was 85% and in Group B was 80%.
Conclusion: In this study, the success of trabeculectomy and complications were similar in both Ologen and MMC groups at the end of 6 months.

Keywords: Trabeculectomy, Ologen implant, Mitomycin-C, glaucoma

Address for Correspondence: Dr. Ashok Madan, Professor & HOD, Department of Ophthalmology, Government Medical College, Nagpur, Maharashtra, India; E-mail: dr.ashokmadan@gmail.com

How to Cite this Article: Ashok Madan, Kavita Dhabarde and Karishma Shah. Trabeculectomy with ologen implant versus trabeculectomy with mitomycin-C in primary open angle glaucoma: A 2-year study. World J Pharm Sci 2017; 5(12): 139-145.

INTRODUCTION

Glaucoma is the most common cause of irreversible blindness worldwide. Treatment of glaucoma begins with medical management but often requires surgical intervention. Trabeculectomy as the standard procedure for the surgical management of glaucoma is widely performed since 1968. The reported success rates for primary trabeculectomies range from 67% to 84%. [1-2] 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, antifibrotic 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. But, Mitomycin-C, when used in high risk patients like high myopia with thin sclera, severe dry eye, previous failed trabeculectomy, was accompanied by increased adverse events such as the formation of avascular filtering blebs, corneal endothelial cell loss, hypotony, bleb leaks, cataract formation, thinning of the sclera, subsequent blebitis, and endophthalmitis. Therefore, use of MMC is contraindicated in such patients and hence there still is an urgent need for the development of a safer alternative for fibrosis control. [3-4]

Recently, tissue engineering has achieved great progress in creating biomedical devices for preventing scar formation by modifying the well-organized process of wound healing. A 3-D disc shaped porcine-derived biodegradable collagen-glycosaminoglycan copolymer matrix implant (Ologen®) has been proposed as an alternative adjuvant, used as a spacer to mechanically separate the sub conjunctival and episcleral tissues to preventing fibrosis, and also helps in reorganizing the subconjunctival scar formation. It consists of a collagen-based scaffold containing multiple microscopic pores. It has been used to create a prominent and healthy vascular bleb following trabeculectomy. Ologen completely degrades within 90~180 days after its implantation. The implant is placed directly over the scleral flap and influences the healing process by forcing fibroblasts and myofibroblasts to grow into the pores and secrete connective tissue in the form of a loose matrix. Theoretically this implant can decrease scar formation and improves surgical success of trabeculectomy performed without the adjunctive use of anti-fibrotic agent. [5-6]

Objective - The aim of this study is to assess the efficacy and safety of trabeculectomy with a biodegradable implant (Ologen implant) *versus* trabeculectomy using Mitomycin-C (MMC) in patients of open-angle glaucoma. We explored the hypothesis that the Ologen implant may be a viable alternative to the use of antimetabolite agents for trabeculectomy procedures and may provide a new, safe, simple, and effective therapeutic approach for treating glaucoma

MATERIALS AND METHODS

Study period: 2 years
Study design: Hospital based, prospective, randomised, comparative study at a tertiary eye care centre in central India.

Patient criteria: In this study, 40 eyes of 40 patients with primary open angle glaucoma (POAG), who were candidates of trabeculectomy were included and randomly assigned into two groups; Trabeculectomy with Ologen implant (group A) or Trabeculectomy with Mitomycin –C (group B).

Inclusion criteria was all patients of age >18 years who are diagnosed as primary open angle glaucoma and with an IOP > 21mm of Hg which is uncontrolled on maximal medical management; unacceptable side effects of anti-glaucoma medications; Poor compliance to medical treatment of glaucoma.

Exclusion criteria was patients with Previous ocular surgery, Previous anterior segment laser therapy, Presence of ocular inflammation, Presence of advanced cataract, Congenital glaucoma, Secondary glaucomas, Patients having neurological lesions affecting the optic nerve. A written informed consent was taken from every patient after explaining to them about the benefits & risks of the procedure, composition & source of collagen implant (Ologen).

Financial support and sponsorship - nil

Before surgical intervention all patients underwent a baseline examination, which included thorough history of the patient, BCVA (Snellen's chart), IOP (Goldmanns applanation tonometer), slit lamp biomicroscopy, gonioscopy, visual field examination (Humphrey perimetry 30-2 program), pachymetry, SD-OCT for RNFL and GCC. The trial was approved by the local Ethics committee.

Ologen implant: The Ologen implant (version 1) (Aeon Astron Europe BV, Leiden, The Netherlands) is a porous implant comprising >90% lyophilised porcine collagen and <10% lyophilised glycosaminoglycan with a pore size of 10–300 μm.

In our study, we used a 6 x 2 mm sized disc of Ologen implant.

Procedure: Surgical technique: All subjects were operated under local- peribulbar anaesthesia & by the same surgeon.

GROUP A -Trabeculectomy with Ologen implant
Wire speculum was applied and superior rectus stay suture was taken. Fornix based conjunctival flap was made and Tenon's capsule was dissected. Haemostasis was achieved using cautery.A 4 x 4 mm partial thickness rectangular scleral flap was made at 12 o 'clock to within 0.5 mm of the limbus using a 15 number blade and then with crescent knife. The crescent knife was used to fashion the flap and is then further advanced into the clear cornea for about 1 mm. Anterior chamber paracentesis made with the help of lancetip. A 2 X 2 mm sclerolimbal block dissection was done with the help of vanna's scissor. Peripheral iridectomy was done with the help of section enlarging scissors. Anterior chamber was formed with air and the scleral flap closed with the help of 2 loose fitting 10-0 nylon suture. Before closing the conjunctiva, a 6 x 2 mm OLOGEN IMPLANT (model 830601) was placed above the fornix-based sclera flap. The conjunctiva was then closed with 10-0 nylon sutures. No sutures were required to secure the implant; as soon as it touched the sclera, it absorbed aqueous fluid and molded to the scleral tissue. The collagen matrix did not need to be presoaked or prepared in any way.

GROUP B - Trabeculectomy with Mitomycin-C
The procedure was same for the 2 groups except that MMC Group had MMC (0.2 mg/ml) soaked sponges placed sub-conjunctivally for 3 minutes (just prior to making the superficial scleral flap). The sponges were removed, and the area was copiously irrigated with 20 cc of ringer lactate.

Postoperative management: Postoperatively; Patients were started on topical Prednisolone acetate 1% eyedrop 6 times for 4 weeks and Moxifloxacin 0.5% eyedrop 4 times a day; which was then tapered over the next month. Postoperatively, patients were examined on Day 1 and then at 1,4,6 weeks and then at 3 and 6 month interval. At each visit, full ocular examination was performed, including BCVA, slit lamp biomicroscopy including bleb status, tonometry and fundoscopy. Visual field assessment & OCT was repeated at 6 months after surgery.

IOP was the primary outcome measure.
Complete success - was defined as an IOP of > 5 mm of Hg & ≤ 21 mmHg without anti-glaucoma medication or re-surgery.

Relative success was defined as IOP of >5 mm of Hg & ≤ 21 mmHg with anti-glaucoma medication (maximum number of IOP lowering medication should not be more than preoperative)

The combination of complete and relative success was labeled as overall success: Failure was defined as IOP of < 5 mm of Hg or > 21 mm of Hg with addition of anti-glaucoma medications.

RESULTS

Patient Demographics: The patient demographics are shown in Table 1. Baseline characteristics were similar in both groups. There were no statistically significant differences between the Ologen group and the MMC group with regard to the gender, mean age, Pre-operative IOP and Pre-operative medication. Total number of patient were 40 with 40 eyes with 20 patients in each of the trabeculectomy with Ologen implant (Group A) and trabeculectomy with MMC (Group B) groups. (Table: 1).

Table 2 demonstrated that the mean IOP decreased from 26.17 + 3.01 mmHg to 12.89 + 2.43 mmHg in the Ologen group and from 26.72 + 3.067 mmHg to 14.05 +4.02 mmHg in the MMC group at 6 months follow-up. The post-operative mean intraocular pressure (mmHg) between the two groups was found to be statistically insignificant on every follow-up.

The success rate of the two Groups is described in Table 3. After 6 months, the percentage of eyes with complete success was 85% in Ologen group and 80% in MMC group. But this difference was not statistically significant. The overall success rate in both Groups was 100%. Table 4 provided an overview of all the recorded side effects. During the postoperative follow-up visits, we did not detect any side effects directly attributable to the Ologen implant, such as allergy or translocation of the implant. The complications included hyphaema, shallow AC, wound leak & hypotony. Complications were not significantly different between the two groups. Table 5 shows mean reduction in anti-glaucoma medication. At the 6^{th} month follow up visit, the mean number of anti-glaucoma medications per treated eye was 0.5 ± 0.60 for both the groups with no significant difference between the mean drug number reduction.

DISCUSSION

Glaucoma is one of the major causes of blindness and cannot yet be cured [1-2]. Trabeculectomy has been used since 1960's and still is the most

common incisional surgery for glaucoma. Achieving and maintaining good IOP control is the main aim of trabeculectomy in primary open-angle glaucoma. Several augmentation modifications (e.g. antimetabolites, amniotic membrane transplantation, drainage devices, implants have been tried, in order to prevent sub-conjunctival fibrosis & scarring which is the main reason for its failure. [3-6]

In 1990's, antifibrotic agents such as Mitomycin-C (MMC) improved the success rate and produced lower IOP when applied intra-operatively and since then is considered GOLD STANDARD in glaucoma surgery. Yet, MMC-related complications such as prolonged wound leaks, hypotony, choroidal effusions, maculopathy, thin avascular blebs, or bleb leaks with late infection are frequently reported due to its toxicity. [7-10].

Our study "TRABECULECTOMY WITH OLOGEN IMPLANT VERSUS TRABECULECTOMY WITH MITOMYCIN-C IN PRIMARY OPEN ANGLE GLAUCOMA: A 2 YEAR STUDY " is a hospital-based, prospective, randomized, comparative study of the effectiveness of operational methods and it included patients planned for trabeculectomy surgery and those who met the criteria for inclusion in the study. In this study, out of 40 patients with primary open angle glaucoma (POAG), 20 patients underwent trabeculectomy with Ologen implants (Group A) and the rest 20 patients underwent trabeculectomy with Mitomycin-C (Group B).

We compared the efficiency in the form of visual outcome, intraocular pressure control, reduction in the number of anti-glaucoma drugs used and safety in the form of intraoperative and postoperative complications between trabeculectomy with Ologen implant and Mitomycin-C.

- In our study, total number of patients were 40 with 40 eyes consisting of 20 patients in Ologen (Group A) and 20 patients in Mitomycin-C (Group B) respectively (Table 1).
- The patients were in the age group of 50-70 years.
- Mean age was 61.85 ±5.48 years and 62.8 ±3.92 years in the Ologen and Mitomycin-C group respectively. (Table 2)
- The Ologen group had 9 male patients and 11 female patients, while the Mitomycin-C group had 6 male patients and 14 female patients.

A study by A. Rosentreter et al. [11](2010) on comparing the success rate of Ologen implant in trabeculectomy with that of Mitomycin-C, evaluated a total of 20 eyes, with 10 in each group. Out of 20 patients, 12 (60%) were female and 8 (40%) were male. The mean age was 62.8 + 9.5 years. A study by S Cilino et al. [12] (2011) on Ologen versus Mitomycin-C augmented trabeculectomy in the management of POAG, evaluated 40 eyes from 40 patients, which included 23 males(57.5%)and 17 females(42.5%). Their mean age was 63.2 +7.2 yrs and 65.8 + 6.4 yrs, respectively.

A study by Senthil S et al.[13](2013) on comparing the outcomes of trabeculectomy with Mitomycin-C vs Ologen implant in primary open angle glaucoma, evaluated a total of 39 eyes of 33 patients out of which, 20(51.2%) were males and 19 (48.8%) were females.

Intraocular Pressure: In our study, the pre-operative intraocular pressure in Group A and Group B was 26.7 ± 3.010 mm Hg and 26.6 ± 3.067 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 11.1 ± 1.02 mmHg (Group A) and 11.5 ±1.0 (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 15.3 ± 3.62 mmHg in Group A and 15.7 ± 2.84 mmHg in Group B, with the difference being statistically insignificant.

In a study by Rosentreter A. et al. [11] 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.

In a study by Cilino S et al. [12] (2011), 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).

In a study conducted by Mitra et al. [14] in 2012, the mean post-operative reduction in IOP was from 28.4 ± 8.4 mm of Hg to 13.3 ± 3.4 mm of Hg in the Ologen group and from 30.2 ± 3.4 mm of Hg to 14.3 ± 4.5 mm of Hg in the MMC group.

Reduction in number of anti-glaucoma medications: In our study, the pre-operative mean number of antiglaucoma medications used in Group A and Group B was 2.2 ± 0.3 and 2.3 ± 0.4 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 0.5 ± 0.60 for both the groups. This difference was statistically insignificant (p>0.99).

Our results were comparable to a study by S Senthil. Et al.[13](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).

In a study conducted by Mitra et al.[14] in 2012, the mean number of anti-glaucoma medications was reduced to 0.4 ± 0.7 from 3.4 ± 0.6 in MMC group and 0.5 ± 0.6 from 3.2 ± 0.3 in Ologen group. The drop in the number of anti-glaucoma medication used at the end of study was statistically significant in both groups (P < 0.001).

Complications: In the 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. [13] (2013) on a comparative study of trabeculectomy with Ologen implant versus trabeculectomy with MMC in the management of POAG, the incidence of post-operative complications were similar in 2 groups except hyphaema, which was significantly more in the Ologen group. A total of 12/19 eyes experienced one or the other complication in the Ologen group as compared to 7/20 in MMC group.

In a study by Cilino et al.[12] in 2011 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.

In a study by Rosentreter A. et al.[11] (2010) 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.

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.

Table 1: PRE-OPERATIVE DATA OF PATIENTS WHO UNDERWENT TRABECULECTOMY

	OLOGEN GROUP (n = 20 eyes)	MMC GROUP (n = 20 eyes)	P value
Sex (M: F)	14:7	14:5	0.62
Age (years) (mean ± SD)	63.15 ± 5.20	63.35 ± 5.04	0.90
Pre-operative IOP (mm of Hg) (mean ± SD)	26.17 ± 3.01	26.72 ± 3.067	0.92
Pre-operative medications	2.2 ± 0.3	2.3 ± 0.4	0.22

Table 2: COMPARISON OF POST-OPERATIVE MEAN INTRA OCULAR PRESSURE BETWEEN GROUP A AND GROUP B

Groups	**Day 1**	**1 week**	**4 weeks**	**6 weeks**	**3 month**	**6 month**
Group A	12.15±8.1	14.1±6.01	14.4±4.34	15.05±4.65	15.9±3.26	12.89±2.43
Group B	12.05±8.12	14.15±5.97	14.45±4.52	16.95±4.54	15.8±3.29	14.05±4.02
p VALUE	0.97	0.98	0.97	0.95	0.92	0.18

Table 3: EVALUATION OF SUCCESS

Results	No. of cases		P- value
	Group A	Group B	
Complete success	17(85%)	16(80%)	0.6
Relative success	3 (15%)	4 (20%)	0.07

Complete success – 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 4: COMPARISON OF COMPLICATIONS BETWEEN THE OLOGEN GROUP & MMC GROUP.

Complications	Group A	Group B	P - value
Hyphaema	2 (10%)	1(5%)	0.26
Shallow AC	2 (10%)	3 (15%)	0.05
Wound leak	1 (5%)	3 (15%)	0.17
Hypotony	1 (5%)	2 (10%)	0.1

Table 5: MEAN REDUCTION IN NUMBER OF ANTI-GLAUCOMA MEDICATIONS.

	GROUP A	**GROUP B**
Preoperative	2.2 ± 0.3	2.3 ± 0.4
Postoperative (6 months)	0.5±0.60	0.5±0.60
Mean drug number reduction	1.8±0.132	1.7±0.230.

REFERENCES

1. Cairns JE. Trabeculectomy. Preliminary report of a new method. Am J Ophthalmol 1968;66:673-9.
2. Watson PG. Surgery of the glaucomas. Br J Ophthalmol 1972;56:299-306.
3. M. R. Razeghinejad, S. J. Fudemberg, and G. L. Spaeth, "The changing conceptual basis of trabeculectomy: a review of past and current surgical techniques," *Survey of Ophthalmology*, 2012; 57(1):1–25.
4. Sihota R, Gupta V, Agarwal H. Long-term evaluation of trabeculectomy in primary open angle glaucoma and chronic primary angle closure glaucoma in an Asian population. Clinical and Experimental Ophthalmology. 2004; 32(1):23-28.
5. C. H. Lee, A. Singla, and Y. Lee, "Biomedical applications of collagen," *International Journal of Pharmaceutics*, 2001; 221(1-2): 1-22.
6. W.-C. Hsu, R. Ritch, T. Krupin, and H. S.-L. Chen, "Tissue bioengineering for surgical bleb defects: an animal study," *Graefe's Archive for Clinical and Experimental Ophthalmology*, 2008; 246(5), 709–717.
7. Anand N, Atherley C. Deep sclerectomy augmented with mitomycin C. Eye. 2005;19:442–50.
8. Anand N, Arora S, Clowes M. Mitomycin C augmented glaucoma surgery: evolution of filtering bleb avascularity, transconjunctival oozing, and leaks. Br J Ophthalmol. 2006; 90:175–80.
9. Lama PJ, Fechtner RD. Antifibrotics and wound healing in glaucoma surgery. Surv Ophthalmol. 2003; 48:314–46.

10. Beckers HJ, Kinders KC, Webers CA. Five-year results of trabeculectomy with mitomycin C. Graefes Arch Clin Exp Ophthalmol. 2003;241:106–10.
11. Rosentreter A, Schild AM, Jordan JF, Krieglstein GK, Dietlein TS. A prospective randomised trial of trabeculectomy using mitomycin C vs. an ologen implant in open angle glaucoma. Eye (Lond) 2010;24:1449-57.
12. Cillino S, Di Pace F, Cillino G, Casuccio A. Biodegradable collagen matrix implant vs.mitomycin-C as an adjuvant in trabeculectomy: A 24-month, randomized clinical trial. Eye (Lond) 2011;25:1598–606.
13. Senthil S, Rao HL, Babu JG, Mandal AK, Garudadri CS. Comparison of outcomes of trabeculectomy with mitomycin C vs. ologen implant in primary glaucoma. Indian J Ophthalmol. 2013;61:338–42.
14. Mitra A (2012) To Compare the Outcome, Complications and Management of Complications of Trabeculectomy with Ologen Implant Versus Trabeculectomy with MMC. Glaucoma-II Free Papers: 330.