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Trabeculectomy with Mitomycin and Ologen Implant Are Equally Effective in Reducing Intraocular Pressure in Primary Open Angle Glaucoma

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ABSTRACT

Trabeculectomy is a surgical procedure performed to treat glaucoma, specifically primary open-angle glaucoma (POAG). As subconjunctival fibrosis is found to be the common cause of bleb failure, different wound modulation agents are being tried as adjuvants to improve the long-term success of trabeculectomy. The objective of the current investigation is to compare the efficacy of mitomycin C (MMC) and Ologen implant (Olo) in trabeculectomy in patients with POAG in eastern India. The duration of the investigation was 18 months, from November 2019 to April 2021. It was a hospital-based prospective randomized parallel group comparison. Group A patients underwent MMC trabeculectomy, while Group B patients underwent Olo implant type 830601 trabeculectomy. The mean pre-operative IOP for the Olo group was 34.0 (IQR: 30.75-38.0), while for the MMC intervention group it was 36.50 (IQR: 31-42). The difference in IOP between the two groups was insignificant (p = 0.24). On the first postoperative day, the IOP in the MMC group was 10.05±3.65 mmHg and in the Olo group it was 10.35±2.13 mmHg. Seven days after surgery, the mean IOP in the MMC group was 9.45±3.0 mmHg, while it was 11.50±2.52 mmHg in the Olo group. One month after surgery, the mean IOP in the MMC group was 11.15±4.25 mmHg, whereas it was 11.50±5.02 mmHg in the Olo group. At 3 months post-operatively, the mean IOP in the MMC group was 12.25± 5.17 mmHg, while it was 12.70±1.84 mmHg in the Olo group. Six months after surgery, the mean IOP in the MMC group was 10.55±2.72 mmHg, whereas in the Olo group it was 13.35±2.94 mmHg. In trabeculectomy surgery on POAG eyes, the MMC and Olo implants both successfully lower intraocular pressure. Between the two groups, there was no statistical significance in the success rates.

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Key Words
Glaucoma, POAG, mitomycin C, ologen implant: IOP

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INTRODUCTION

Intraocular pressure (IOP) increase is a major risk factor for a group of diseases characterized by unique optic neuropathy and concurrent visual field loss which is termed glaucoma[1]. Primary open-angle glaucoma (POAG) is the most common subtype of glaucoma worldwide[2-4]. In primary glaucoma, IOP is the only established modifiable risk factor and multiple clinical trials have demonstrated that lowering IOP slows the progression of visual field loss in glaucoma patients[5-10]. A range of therapeutic approaches, including medications (topical and systemic), laser therapy and surgery, can be used alone or in combination to achieve target IOP in glaucoma patient[11]. In POAG, although medical management is the first line of treatment, surgery indicated when IOP is not well controlled with maximal medical therapy.

Trabeculectomy continues to be the most preferred surgical procedure for lowering IOP in primary glaucoma patients[12,13]. Although, the first successful trabeculectomy was first documented by Cairns[15], different modifications at some steps are still being carried out today in consideration of its safety and efficacy. Trabeculectomy with mitomycin C (MMC) and trabeculectomy with Ologen implant (Olo) are two methods used to improve surgical success rates by reducing scarring at the operative site and improving long-term outcomes[16-19]. The antimetabolite medication MMC is used in the trabeculectomy with MMC method. It can be used topically or subconjunctivally to the surgical site to inhibit fibroblast proliferation and reduce scarring[20]. This approach improves trabeculectomy success rates and aids in maintaining the desired IOP drop by minimizing scar tissue formation[21]. Trabeculectomy with Olo, on the other hand, employs a biodegradable, porous and collagen-based implant Olo. It is considered as a viable alternative for patients contraindicated to antimetabolites[22]. The Olo not only acts as a spacer to reduce wound contraction but also acts as a scaffold for the growth of fibroblasts to help in tissue remodelling and reduce subconjunctival scar formation, thereby improving the long-term success of trabeculectomy with fewer bleb-related complications[23].

Subconjunctival fibrosis, continues to be the main reason for trabeculectomy failure and is more frequently seen in Asian and Afro-Caribbean eyes[24-26]. When comparing the efficiency of MMC or Ologen implants, studies undertaken all across the world have yielded inconsistent results[16,27-30]. The current study's goal is to determine the outcomes of trabeculectomy with MMC or Olo implant in patients with POAG in the eastern part of India.

MATERIALS AND METHODS

The current study was conducted in a tertiary eye care center of eastern India, from November 2019 to April 2021, for a period of 18 months. It was a hospital based randomized prospective parallel group comparative study, approved by the hospital's ethics committee and carried out as per the tenets of the Declaration of Helsinki. Informed consent was signed from all participants and their confidentiality was maintained throughout the study.

Patients with POAG, attending outpatient department of the hospital, aged between 18 and 80 years were enrolled in the study. Inclusion criteria was patients with inadequate IOP control (IOP >21 mm Hg) or progression of visual field loss despite the maximum tolerated medical therapy. We excluded patients with normal tension glaucoma, advanced glaucoma with split fixation of the visual field and history of any intraocular surgery or ocular trauma. Patients with history of any acute or chronic diseases e.g., immunodeficiency, connective tissue disorders and use of any systemic or topical medication that can affect the study outcome were excluded from study. Forty eyes of the forty patients were included in the study and divided into two groups of twenty. MMC or Olo was used as per randomization, using GraphPad random number generator. We used MMC in a concentration of 0.4 mg mL^{-1} and the Ologen implant model 830601 in this study.

Each patient was assigned a registration number. Along with the demographic profile, detailed systemic and treatment history, including the number and types of antiglaucoma medications, were recorded. Best corrected visual acuity (BCVA) was recorded using Snellen's visual acuity chart. Each patient underwent comprehensive eye examination with slit lamp biomicroscope. A regularly calibrated Goldman applanation tonometer was used to measure the IOP. Gonioscopy with Sussmann four mirror gonioscope was performed to ensure cases included in the study were open anterior chamber angle. Fundus examination by 90 D lens and standard automated perimetry (Humphrey Field Analyzer, HFA II 750; Carl Zeiss Meditec, Inc.) using 24-2 SITA standard protocol and 10-2 programme where indicated, was performed in each patient.

Preoperatively all patients received an intravenous infusion of 20% mannitol as per body weight. All the patients were operated by a single surgeon under local peribulbar anaesthesia. A superior rectus bridle suture was applied. The fornix-based conjunctival flap was made superiorly with blunt tipped Westcott scissors. After light cauterization with bipolar cautery, a partial thickness triangular scleral flap (4×4 mm) was

constructed, encompassing approximately two-thirds of the scleral thickness. In the MMC group, sponges soaked with 0.4 mg mL^{-1} MMC were applied over a wide area under the conjunctiva. After two minutes, the sponges removed and the area was thoroughly washed with 25 cc of a balanced saline solution. A side port was created with a 15-degree angled knife. A trabecular block of 2×4 mm was removed under the scleral flap using the side port knife and Kelly Descemet's punch. Through the trabeculectomy opening, a broad-based peripheral iridectomy was done parallel to the limbus with Vanna's scissors. The scleral flap was closed using two 10-0 monofilament nylon sutures with minimal tension, one at each arm and one releasable suture (Kolker's technique) at the apex. In patients randomly assigned to receive Ologen, trabeculectomy was made similarly without MMC. A cylindrical Ologen implant (6 mm in diameter by 2 mm in height) placed on top of the sutured scleral flap, under the conjunctiva. In both the groups, the conjunctival flap was secured to the limbus with the 8-0 vicryl suture (one at each extremity and one in the center). At the end of the procedure, bleb titration was performed via side port wound to ensure water tight suturing. Postoperatively all eyes were treated with Moxifloxacin 0.5% eye drops six times per day for four weeks, Homide eye drops twice daily for one week and Prednisolone acetate one percent eye drops were applied eight times daily for the first week, then tapered over the course of six weeks. On the first post postoperative day and at subsequent follow ups at one week, one month, three months and six months after surgery, BCVA, IOP and any complications encountered were recorded.

Statistical analysis: The collected data were organized in an Excel spreadsheet and analysed using "R" software 4.0.3 and R-studio. The quantitative variables were represented by the mean and standard deviation, while the qualitative data were represented by percentages and proportions. Statistical significance was defined as a p-value of 0.05 or less.

RESULTS

Forty patients were involved in the current study (Table 1). The Mean age of the patients in MMC group was 64.80±9.81 years while for Olo group mean age was 64.55±8.12 years. The age distribution between the two groups was almost similar. This indicates a homogenous distribution of study participants between two groups. Among the patients, many of them were aged 61-70 years old (45.00%) followed by more than 70 years old (27.50%). Only 2 patients (5.00%) were aged 41-50 years old. In our study, twenty-eight (seventy percent) patients were males and twelve (thirty percent) patients were females.

In Fig. 1 preoperative IOP was shown in MMC group and in Olo group participants. The mean pre-operative IOP among MMC intervention group was 36.50 (IQR:31-42) and for Olo group was 34.0 (IQR:30.75-38.0). There was slight difference of IOP between two groups, however, this did not show statistical significance (p = 0.24).

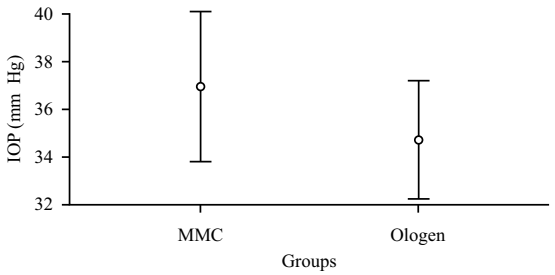

Fig. 1: Comparison of preoperative intraocular pressure (IOP) in the study participants

Table 1: Demographic and medical history details of the participants of the present study

Parameters	MMC (n = 20)	Ologen (n = 20)	Total (n = 40)	p-value
Age (mean±SD) (years)	64.80±9.81	64.55±8.12	64.67±8.89	>0.05
Age groups				
40-50	2 (5.00%)	0 (0.00%)	2 (5.00%)	>0.05
51-60	3 (7.50%)	6 (15.00%)	9 (22.50%)	
61-70	9 (22.50%)	9 (22.50%)	18 (45.00%)	
>70	6 (15.00%)	5 (12.50%)	11 (27.50%)	
Sex				
Female	5 (12.50%)	7(17.50%)	(30.00%)	>0.05
Male	15(37.50%)	13 (32.50%)	28 (70.00%)	
Medical history				
Diabetes mellitus	0 (0.00%)	3 (7.50%)	3 (7.50%)	
Hypertension	6 (15.00%)	6 (15.00%)	12 (30.00%)	

Table 2: Postoperative intraocular pressure (IOP) during the follow-up period in the two groups

Postoperative IOP (mean±SD) (mmHg)	MMC (n = 20)	Olo (n = 20)	p-value
Day 1	10.05±3.65	10.35±2.13	0.75
Day 7	9.45±3.00	11.50±2.52	0.02
Month one	11.15±4.25	11.50±5.02	0.81
Month three	12.25±5.17	12.70±1.84	0.72
Month six	10.502.72	13.35±2.94	<0.01

On postoperative day 1, the mean IOP in MMC group was 10.05±3.65 mmHg while in Olo group it was 10.35±2.13 mmHg. At day 7, the mean IOP in MMC group was 9.45±3.0 mmHg while in Olo group it was 11.50±2.52 mmHg. At 1-month postoperative, the mean IOP in MMC group was 11.15±4.25 mmHg while in Olo group it was 11.50±5.02 mmHg. At 3-month post-op, mean IOP in MMC group was 12.25±5.17 mmHg while in Olo group it was 12.70±1.84 mmHg. At 6-month post-op, mean IOP in MMC group was 10.55±2.72 mmHg while in Olo group it was 13.35±2.94 mmHg.

DISCUSSIONS

This hospital-based, randomized, prospective, parallel group trial included patients with POAG who were scheduled for trabeculectomy. Patients were separated into two groups for trabeculectomy and were given either MMC treatments or Olo implants as adjunct. The effect on IOP and complications, if any, were recorded and compared.

Numerous studies comparing these two augmentation procedures for trabeculectomy have been published. In a prospective trial comparing Olo with MMC in POAG, Rosentreter *et al*.[29] found that, Olo group had higher mean IOP at 1 month postoperatively, which was statistically significant and this difference remained for up to 12 months over the follow-up period. They observed that, both the IOP lowering effect and absolute success rate was significantly less in Olo group. On the other hand, Cillino *et al*.[30] found no difference in the IOP between two groups during their follow up period. In a detailed meta-analysis trial that comprised of six studies including 224 patients, comparing Ologen and MMC in trabeculectomy, did not observe statistical significance in IOP reduction between the groups[31]. There were no noticeable differences in success rate, reduction in glaucoma medications and the incidence of adverse events existed between Olo and MMC groups.

Inconsistent to these observations, Kassem *et al*.[32] found that although the IOP in both groups continues to be stable over 12 months of follow-up, the IOP rise was noticed in the Ologen group at 4 weeks postoperative visit. Senthil *et al*.[16] in their 24 months followed-up prospective study, observed that IOP was significantly lower at 6 months but not on subsequent follow up visits in the MMC group.

In supposition with the studies of Cillino *et al*.[30], Ji *et al*.[31] and Kassem and Esmael[30] the current pilot study found that the success rate of trabeculectomy was comparable in MMC and Olo groups at all follow-ups. IOP reduced considerably from baseline in both groups. Although, the IOP was significantly lower in the MMC group at the 1-week and 6-month follow-ups ($p<0.05$), the same trend was not found at all follow-up visits. In this study, we observed, on day 7 the IOP was significantly higher in the Olo group, compared to the subsequent scheduled postoperative visits. This disparity could be explained by the reservoir effect of the Ologen matrix absorbing aqueous humor and pressing on the scleral flap, which provides valvular-like physical resistance to over-filtration. Aiding to this, Paul *et al*.[33] observed that Ologen and MMC were both effective adjunctive in their recent study on combined phaco-trabeculectomy and noted that the IOP between the two groups did not differ during the follow-up period.

CONCLUSION

During trabeculectomy surgery, the MMC and Olo implants both successfully lower intraocular pressure. Between the two groups, there was no statistical significance in the success rates.

REFERENCES

1. Safa, B.N., C.A. Wong, J. Ha and C.R. Ethier, 2021. Glaucoma and biomechanics. Curr. Opin. Ophthalmol., 33: 80-90
2. Zhang, N., J. Wang, Y. Li and B. Jiang, 2021. Prevalence of primary open angle glaucoma in the last 20 years: A meta-analysis and systematic review. Sci. Rep., Vol. 11. 10.1038/s41598-021-92971-w
3. Tham, Y.C., X. Li, T.Y. Wong, H.A. Quigley, T. Aung and C.Y. Cheng, 2014. Global prevalence of glaucoma and projections of glaucoma burden through 2040. Ophthalmology, 121: 2081-2090.
4. Kapetanakis, V.V., M.P.Y. Chan, P.J. Foster, D.G. Cook, C.G. Owen and A.R. Rudnicka, 2015. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): A systematic review and meta-analysis. Br. J. Ophthalmol., 100: 86-93.
5. Heijl, A., M.C. Leske, B. Bengtsson, L. Hyman, B. Bengtsson, M. Hussein, Early Manifest Glaucoma Trial Group, 2002. Reduction of intraocular pressure and glaucoma progression. Arch. Ophthalmol., 120: 1268-1279.
6. Jay, J.L. and S.B. Murray, 1988. Early trabeculectomy versus conventional management in primary open angle glaucoma.. Br. J. Ophthalmol., 72: 881-889.
7. Collaborative Normal-Tension Glaucoma Study Group, 1998. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. Am. J. Ophthalmol., 126: 487-497.

8. Ederer, F., D.A. Gaasterland, L.G. Dally, J. Kim and P.C. VanVeldhuisen, 2004. The advanced glaucoma intervention study (AGIS): 13. Comparison of treatment outcomes within race: 10-year results. Ophthalmology, 111: 651-664.
9. Caprioli, J. and A.L. Coleman, 2008. Intraocular pressure fluctuation. Ophthalmology, 115: 1123-1129.
10. Holló, G., 2012. Wound healing and glaucoma surgery: Modulating the scarring process with conventional antimetabolites and new molecules. Glaucoma Surg., 50: 79-89.
11. Garg, A. and G. Gazzard, 2019. Treatment choices for newly diagnosed primary open angle and ocular hypertension patients. Eye, 34: 60-71.
12. European Glaucoma Society Terminology and Guidelines for Glaucoma, 2017. Classification and terminology supported by the EGS foundation. Br. J. Ophthalmol., 101: 73-127.
13. Wells, A.P., C. Bunce and P.T. Khaw, 2004. Flap and suture manipulation after trabeculectomy with adjustable sutures: Titration of flow and intraocular pressure in guarded filtration surgery. J. Glaucoma, 13: 400-406.
14. Rao, A. and R.D. Cruz, 2022. Trabeculectomy: Does it have a future? Cureus, Vol. 14. 10.7759/cureus.27834
15. Cairns, J.E., 1968. Trabeculectomy. Am. J. Ophthalmol., 66: 673-679.
16. Senthil, S., H. Rao, J. Babu, A. Mandal and C. Garudadri, 2013. Comparison of outcomes of trabeculectomy with mitomycin C vs. ologen implant in primary glaucoma. Indian J. Ophthalmol., 61: 338-342.
17. Perez, C.I., F. Mellado, A. Jones and R. Colvin, 2017. Trabeculectomy combined with collagen matrix implant (ologen). J. Glaucoma, 26: 54-58.
18. Chelerkar, V., D. Agrawal, V.S. Kalyani and M. Deshpande, 2021. Comparison of bleb morphology by anterior segment optical coherence tomography and clinical outcome after phacotrabeculectomy with mitomycin C or ologen implant. Indian J. Ophthalmol., 69: 2734-2739.
19. Song, D.S., J. Qian and Z.J. Chen, 2019. Ologen implant versus mitomycin-C for trabeculectomy. Medicine, Vol. 98. 10.1097/md.0000000000016094
20. Wagdy, F.M., H.G. Farahat, A.F. Ellakwa and S.S. Mandour, 2021. Evaluation of conjunctival autografting augmented with mitomycin C application versus ologen implantation in the surgical treatment of recurrent pterygium. J. Ophthalmol., Vol. 2021. 10.1155/2021/8820926
21. Wilkins, M., A. Indar and R. Wormald, 2005. Intraoperative mitomycin c for glaucoma surgery. Cochrane Database Syst. Rev., Vol. 2010. 10.1002/14651858.cd002897.pub2
22. Bhattacharyya, M., K. Singh, A. Mutreja and S. Dangda, 2018. Trabeculectomy with subconjunctival collagen implant in Indian eyes: Long-term results. Indian J. Ophthalmol., 66: 1429-1434.
23. Chen, H.S.L., R. Ritch, T. Krupin and W.C. Hsu, 2006. Control of filtering bleb structure through tissue bioengineering: An animal model. Invest. Opthalmol. Visual Sci., 47: 5310-5314.
24. Husain, R., J.C.K. Clarke, S.K.L. Seah and P.T. Khaw, 2004. A review of trabeculectomy in East Asian people-the influence of race. Eye, 19: 243-252.
25. AGIS Investigators, 2001. The advanced glaucoma intervention study (AGIS): 9. Comparison of glaucoma outcomes in black and white patients within treatment groups. Am. J. Ophthalmol. 12: 311-320.
26. Nguyen, A.H., N. Fatehi, P. Romero, A. Miraftabi and E. Kim *et al*., 2018. Observational outcomes of initial trabeculectomy with mitomycin C in patients of African descent vs patients of European descent. JAMA Ophthalmol., 136: 1106-1113.
27. Sen, M., N. Midha, T. Sidhu, D. Angmo, R. Sihota and T. Dada, 2018. Prospective randomized trial comparing mitomycin c combined with ologen implant versus mitomycin C alone as adjuvants in trabeculectomy. Ophthalmol. Glaucoma, 1: 88-98.
28. Helmers, G., C. Munteanu, U. Löw and B. Seitz, 2022. Trabekulektomie mit mitomycin c und ologen®-implantat im vergleich zur klassischen trabekulektomie. Die Ophthalmologie, 120: 20-26.
29. Rosentreter, A., A.M. Schild, J.F. Jordan, G.K. Krieglstein and T.S. Dietlein, 2010. A prospective randomised trial of trabeculectomy using mitomycin C vs an ologen implant in open angle glaucoma. Eye, 24: 1449-1457.
30. Cillino, S., A. Casuccio, F.D. Pace, C. Cagini, L.L. Ferraro and G. Cillino, 2016. Biodegradable collagen matrix implant versus mitomycin-C in trabeculectomy: Five-year follow-up. BMC Ophthalmol., Vol. 16. 10.1186/s12886-016-0198-0.
31. Ji, Q., B. Qi, L. Liu, X. Guo and J. Zhong, 2015. Efficacy and safety of ologen implant versus mitomycin C in primary trabeculectomy. J. Glaucoma, 24: e88-e94.
32. Kassem, R.R. and A.F. Esmael, 2023. Subscleral Trabeculectomy with ologen implant versus mitomycin C in primary infantile glaucoma: up to 103 months' follow-up., 10.21203/rs.3.rs-2734611/v1, https://www.researchsquare.com/article/rs-2734611/v1
33. Paul, C., J. Divya, R. Kamal and A. Paul, 2022. Ologen implant versus mitomycin C in combined trabeculectomy and phacoemulsification. Indian J. Ophthalmol., 70: 1248-1252.