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Original Research Article

Effect of trabeculectomy with mitomycin C versus ologen implant in reducing intraocular pressure: A comparative study in patients with primary open-angle glaucoma

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ABSTRACT

Aim and Objective: To compare the efficacy of mitomycin C (MMC) and Ologen implant (OLO) as adjuvants in Trabeculectomy in patients with POAG in eastern India.
Materials and Methods: It was a hospital based prospective randomized parallel group comparative study from November 2019 to April 2021. Forty eyes of forty patients of POAG with inadequate intraocular pressure (IOP) control were enrolled and randomly divided them into two groups of twenty. Group A (MMC) patients underwent MMC trabeculectomy, while Group B (OLO) patients underwent OLO trabeculectomy. All the cases were followed up post-operatively for six months, and the recorded IOP of each visit was analyses using software R 4.0.3 and R-studio.
Results: The preoperative IOP for the OLO group was 34.0 mmHg (IQR: 30.75 – 38.0), while for the MMC intervention group it was 36.50 mmHg (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 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 OLO group. At 3 months postoperatively, 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 10.50± 2.72 mmHg, whereas in the OLO group it was 13.35± 2.94 mmHg. In both the groups, there was significant reduction of IOP (p value < 0.05) observed in all postoperative visits.
Conclusion: In trabeculectomy surgery on POAG eyes, the MMC and OLO implants both successfully lower IOP. Between the two groups, there was no statistically significant difference in the success rate.

1. 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 sub type 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 patient.[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

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medical therapy.

Trabeculectomy continues to be the most preferred surgical procedure for lowering IOP in primary glaucoma patients.[12–14] 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 rate by reducing scaring at the operative site and improving long term outcomes.[16–19] The anti metabolite medication MMC is used in the Trabeculectomy in MMC method. It can be used topically or sub conjunctival 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 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 to patient 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 fibroblast to help in tissue remodeling 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 Asia and Afro-Caribbean eyes.[24–26] When comparing the efficiency of MMC or OLO implants, studies undertaken all across the world have yielded inconsistent results.[16,27–29] The current study's goal is to determine the efficacy of Trabeculectomy with MMC and OLO implant in patients with POAG in the eastern part of India.

2. 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 participant and their confidentiality was maintained throughout the study.

Patients with POAG, attending out-patient department of the hospital, aged between 18 and 80 years were enrolled in the study. Inclusion criteria was patient with inadequate IOP control (IOP >21 mmHg) 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 Graph Pad random number generator. We used MMC in a concentration of 0.4 mg/mL and the OLO 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 anti glaucoma 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 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 2×2 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 mono filament 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

1% 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 followups at one week, one month, three months and six months after surgery, BCVA, IOP and any complications encountered were recorded.

2.1. Statistical analysis

The collected data were organized in an Excel spreadsheet and analyzed 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.

3. 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 homogeneous 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 (Table 1) preoperative IOP was shown in MMC group and in OLO group participants. The mean preoperative IOP among MMC intervention group was 36.95±6.68 mmHg and for OLO group was 34.70±5.24 mmHg. There was slight difference of IOP between two groups, however, this did not show statistical significance ($p = 0.24$).

The postoperative IOP of both groups at each visit is shown in (Table 2). 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 postoperative, the 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 postoperative mean IOP in MMC group was 10.50±2.72 mmHg while in OLO group it was 13.35±2.94 mmHg.

In this study, the mean IOP at all postoperative visits was similar in two groups, except at day 7 and at 6 months where the IOP in the OLO group was significantly high. In both the MMC and OLO groups, the IOP recorded at all postoperative visit was significantly lower than the preoperative IOP ($p < 0.05$) (Table 2).

4. Discussions

Subconjunctival scarring is the well accepted limitations in preserving the hypotensive effect of trabeculectomy in glaucoma. Mitomycin C and Ologen are two adjuvants used in trabeculectomy to reduce the scarring postoperatively.[19] 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 followup 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 observed between OLO and MMC groups. Senthil et al.[16] in their 24 months followup comparative prospective study, observed that IOP was significantly lower at 6 months in MMC group but the difference between two groups was not so on subsequent follow up visits.

In supposition with the studies of Cillino et al.[30] and Ji et al.[31] the current pilot study found that the success rate of trabeculectomy was comparable in MMC and OLO groups at all follow-ups. In this hospital based, randomized, prospective, parallel group trial, although the mean postoperative IOP was significantly lower in the MMC group at the 6-month followups ($p<0.05$), IOP found to be significantly reduced from baseline at all postoperative follow-ups in the both groups. Add to this observation, Tanna et al.[32] in their prospective randomized multi centre clinical trial found no difference in success rate between MMC and Ologen in both trabeculectomy and combined phacoemulsification with trabeculectomy.

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. Consistent to these observations, Kassem et al.[33] found that although reduction of IOP was significant in trabeculectomy with MMC at all postoperative visit, it was not so until 4 months in OLO group, which explains the resistance to aqueous outflow by the OLO implant in early postoperative period.

Helmers et al.[28] studied the additional benefit of OLO, considering trabeculectomy with MMC the gold standard in glaucoma surgery, in their retrospective comparative

Table 1: Demographic details and preoperative intraocular pressure (IOP) of the participants of the present study

Parameters	MMC (n=20)	OLO (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%)	
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				>0.05
Female	5 (12.50%)	7 (17.50%)	12 (30.00%)	
Male	15 (37.50%)	13 (32.50%)	28 (70.00%)	
Preoperative IOP (mmHg)	36.95±6.68	34.70±5.24	35.83±6.03	>0.05

Table 2: Postoperative intraocular pressure (mean±SD in mmHg) during the follow up period in the two groups

Follow-up period	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
1 month	11.15±4.25	11.50±5.02	0.81
3 months	12.25±5.17	12.70±1.84	0.72
6 months	10.50±2.72	13.35±2.94	<0.01

study and found that both procedures significantly lower the IOP, and the addition of the OLO was considered superior to the standard trabeculectomy with MMC. Aiding to this, Paul et al.[34] 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 followup period.

5. Conclusions

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. This study limits the statistical comparison of the long-term outcomes due to shorter followup period. Additional larger studies with a longer follow-up period are needed to address the long-term efficacy of Ologen over MMC in trabeculectomy.

6. Source of Funding

None.

7. Conflict of Interest

None.

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