Original Research Article

Comparative study of surgical outcome in patients with glaucoma treated with trabeculectomy done with and without the use of mitomycin C

Amod Bhaskarrao Gadikar

Assistant Professor, Department of Ophthalmology, Government Medical College, Latur, Maharashtra, INDIA.
Email: apurvaatharva@gmail.com

Abstract

Background: Glaucoma is the first cause of nonreversible blindness and the second overall, after cataract. Trabeculectomy remains the most performed glaucoma surgery. Mitomycin C (MMC) is a chemotherapeutic agent that has been widely used intraoperatively to enhance the success rate of glaucoma filtration surgery. In present study we compared surgical outcome in patients with glaucoma treated with trabeculectomy done with and without the use of mitomycin C at a tertiary hospital. **Material and Methods:** This was a prospective, interventional, comparative study carried out in patients of age more than 40 years, with primary open angle glaucoma/ primary angle closure glaucoma, intraocular pressure uncontrolled on anti-glaucoma medication with progressive visual field loss. Patient were randomly assigned into 2 groups for conventional trabeculectomy with trabeculectomy with mitomycin C. **Results:** During study period total 46 patients were operated for glaucoma. 23 patients were each randomly assigned to trabeculectomy only and trabeculectomy with mitomycin C groups. General characteristics such as age, gender, laterality and glaucoma type were comparable in both groups. In both groups statistically significant reduction was noted for intraocular pressure (IOP) and IOP lowering medications post-operatively. Characteristics such as preoperative intraocular pressure (IOP), IOP at 6 month, IOP at 1-year last visit and number of IOP lowering preoperative medications were comparable in both groups. Trabeculectomy with mitomycin C did not required any IOP lowering medications at 6 month and 1 year. A statistically significant difference was noted for number of IOP lowering medications at 6 month and 1 year between two groups. In present study 6 patients (26%) from trabeculectomy only group and 5 patients (22%) from trabeculectomy with mitomycin C group had complications. Post-operatively failed trabeculectomy and iritis were common complications in both groups. **Conclusion:** Mean intraocular pressure (IOP) was reduced significantly at 12 months in trabeculectomy with MMC group compared to trabeculectomy without MMC. No significant difference was noted in complications from both groups.

Key Words: glaucoma surgery, trabeculectomy, trabeculectomy with mitomycin C, primary open angle glaucoma.

*Address for Correspondence:
Dr Amod Bhaskarrao Gadikar, Assistant Professor, Department of Ophthalmology, Government Medical College, Latur, Maharashtra, INDIA.
Email: apurvaatharva@gmail.com

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INTRODUCTION

According to a review on blindness causes conducted by the World Health Organization, glaucoma is the first cause of nonreversible blindness and the second overall, after cataract.[1] The only known modifiable risk factor in open-angle glaucoma is the elevated IOP, and disease progression can be prevented by the control of IOP. Glaucoma is usually treated with medical therapy but in certain situations like poor compliance of the patient and disease progression, invasive interventions such as laser trabeculoplasty and surgery, becomes the first choice of treatment.[2] Trabeculectomy remains the most performed

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glaucoma surgery. The procedure consists in creating a scleral flap and a full-thickness removal of trabecular tissue, to drain the aqueous humor from the anterior chamber to the subconjunctival space, forming a conjunctival filtering bleb. [3] Factors associated with an increased risk of bleb failure include young age, aphakia, anterior segment neovascularization, inflammation, previously failed glaucoma filtering surgery, and prolonged exposure to ocular hypotensive agents.[4] Mitomycin C (MMC) is a chemotherapeutic agent that has been widely used intraoperatively to enhance the success rate of glaucoma filtration surgery.[5,6] However, it is frequently accompanied with short- and long-term postoperative complications such as hypotony, bleb leaks, cataract formation, avascular filtering blebs, thinning of the conjunctiva, subsequent blebitis, choroidal effusions, maculopathy, and endophthalmitis.[7] Despite the positive effect MMC has on filtering surgery success rates, its diffusion into adjacent ocular tissues may lead to toxic effects on cells not targeted during treatment. In present study we compared surgical outcome in patients with glaucoma treated with trabeculectomy done with and without the use of mitomycin C at a tertiary hospital.

MATERIAL AND METHODS

This was a prospective, interventional, comparative study carried out in department of Ophthalmology, XXX medical college and hospital, XXX. Study duration was of 2 years (November 2018 to October 2020). Institutional ethical committee clearance was obtained.

Inclusion criteria

- Patients of age more than 40 years, with primary open angle glaucoma/ primary angle closure glaucoma, intraocular pressure uncontrolled on anti-glaucoma medication with progressive visual field loss.

Exclusion criteria

- Patients requiring combined surgery for cataract and primary open angle glaucoma
- Patients with secondary glaucoma, juvenile glaucoma, congenital glaucoma, patients with previous ocular surgery, patients with conjunctival scarring, patients with previously failed filtering surgery.

Patients included in the study were explained about the procedure and expected results and risks were informed. Written and informed consent was taken. Patients underwent history taking, detailed ocular examination. Grading for anterior chamber depth was done on the basis of Van Herrick's protocol. IOP was recorded on goldmann applanation tonometry. Gonioscopy was performed using Volk 4 mirror. Perimetry of each patient was performed on Humphrey field analyzer. Eyes with glaucoma progression was described with a mean deviation loss of 3dB or more from 'baseline' VFs to the most recent test. Open angle was diagnosed on gonioscopy with angles open, POAG was defined in the presence of an IOP > 21 mmHg, open anterior chamber angle on gonioscopy, glaucomatous optic disc damage on clinical examination, and corresponding glaucomatous visual field defects. PACG was defined in the presence of an occludable angle on gonioscopy (posterior trabecular meshwork not seen in at least 180° of the total circumference of the angle in primary position), glaucomatous optic disc damage, and corresponding glaucomatous visual field defects. Patient were randomly assigned into 2 groups for conventional trabeculectomy with trabeculectomy with mitomycin C. Conventional trabeculectomy done with limbal based conjunctival incision. A limbus based rectangular graft was created, an inner rectangular scleral flap was excised with help of 11 no blade and vannas scissors so as to make an opening in the anterior chamber. A peripheral button hole iridectomy was done. The superficial flap was then closed. For eyes in MMC group, after preparing scleral flap, MMC (0.2 mg/ml) was applied by multiple thin sponges under the conjunctiva and scleral flap for 3 minutes. The area was then irrigated thoroughly with 50 cc balanced salt solution. Then sclerectomy and peripheral iridectomy was performed and scleral flap was closed. Post-operatively all patients were started on topical prednisolone eye drops 6 to 8 times a day, moxifloxacin eye drops 4 times a day, homatopine eye drops, 2 times a day. Antiglaucoma medications were continued in the other eye. All patients were examined in outpatient department on, 1st day, 5th day, weekly for 1 month, then each patient was followed every month for 3 months and then every 3 monthly up to 1 year. Patients were assessed on visual acuity, intraocular pressure, anterior chamber depth, immediate complications, anterior chamber depth, post-operative lens changes. Anterior chamber depth was assessed on slit lamp, central distance between anterior surface of lens and cornea. Data was collected and entered in Microsoft Excel for statistical analysis. Results of trabeculectomy only were compared with trabeculectomy with mitomycin C. The significance was calculated by paired 't' test and Fisher Exact test. p value less than 0.05 was considered as statistically significant.

RESULTS

During study period total 46 patients were operated for glaucoma. 23 patients were each randomly assigned to trabeculectomy only and trabeculectomy with mitomycin C groups. General characteristics such as age, gender, laterality and glaucoma type were comparable in both groups.

Table 1: Patients characteristics

Characteristics	Trabeculectomy only (n=23)	Trabeculectomy with mitomycin C (n=23)
Age in years (Mean ± SD)	61.3 ± 9.4	60.9 ± 10.1
Gender		
Male	10 (43%)	11 (48%)
Female	13 (57%)	12 (52%)
Laterality		
Right eye	9 (39%)	12 (52%)
Left eye	14 (61%)	11 (48%)
Glaucoma type		
Primary open angle (No. eyes)	20 (87%)	18 (78%)
Primary angle closure glaucoma	3 (13%)	5 (22%)

In both groups statistically significant reduction was noted for intraocular pressure (IOP) and IOP lowering medications post-operatively. Characteristics such as preoperative intraocular pressure (IOP), IOP at 6 month, IOP at 1-year last visit and number of IOP lowering preoperative medications were comparable in both groups. Trabeculectomy with mitomycin C did not required any IOP lowering medications at 6 month and 1 year. A statistically significant difference was noted for number of IOP lowering medications at 6 month and 1 year between two groups.

Table 2: Comparison of preoperative and postoperative characteristics

Characteristics	Trabeculectomy only (Mean ± SD)	Trabeculectomy with mitomycin C (Mean ± SD)	p value
Preoperative IOP	21.4 ± 4.12	20.17 ± 3.89	0.53
IOP at 6 month	13.38 ± 3.11	12.03 ± 3.25	0.20
IOP at 1 year	15.19 ± 3.99	12.49 ± 3.51	0.34
No. of IOP lowering preoperative medications	3.14 ± 0.37	2.86 ± 0.89	0.23
No. of IOP lowering medications at 6 month	0.9 ± 1.1	0.0	0.001*
No. of IOP lowering medications at last visit	0.7 ± 1.22	0.0	0.001*

(* - statistically significant)

In present study 6 patients (26%) from trabeculectomy only group and 5 patients (22%) from trabeculectomy with mitomycin C group had complications. Post-operatively failed trabeculectomy and iritis were common complications in both groups. Other complications were hyphema , hypotony and hypopyon.

Table 3: Post-operative complications

Complications	Trabeculectomy only		Trabeculectomy with mitomycin C	
	No. of patients	%	No. of patients	%
Iritis	3	13%	1	4%
Failed trabeculectomy	3	13%	2	9%
Hyphema	2	9%	1	4%
Hypotony	1	4%	2	9%
Hypopyon	1	4%	2	9%

DISCUSSION

Aggressive medical therapy increases the number of inflammatory cells and enhances the risk of external bleb scarring and filtration surgery failure. There are many factors which can adversely affect the outcome of trabeculectomy including: history of previous incisional surgery involving the superior conjunctiva, prolonged use of topical anti-glaucoma medication and young ages (<50 years). Other factors are associated with increased risk of failure after glaucoma filtration surgery like, aphakia, uveitis, rubeosis iridis, angle recession and angle closure glaucoma.[9] Mitomycin C (MMC) is activated via enzymatic reduction into metabolites that inhibit cell replication by inhibiting DNA synthesis, RNA transcription, and protein synthesis. MMC prevents scarring by inhibiting the multiplication of cells that produce scar tissue.[10] The dose and duration of MMC used in the literature have varied from 0.1 to 0.5 mg/ml and from

0.5 to 5 minutes. Low-dose MMC successfully achieves low target IOPs and results in significantly less thinning of the blebs.[11] Long-term follow-up of primary trabeculectomy without adjunctive MMC indicates that despite successful control of intraocular pressure (lOP) at 1 year, the probability of success decreases with time and stabilizes at 67% by 10 years.[12] A Cochrane database review of eleven clinical trials evaluating 698 patients concluded that MMC reduced the risk of surgical failure in eyes undergoing primary trabeculectomy and high-risk eyes. The best evidence for the benefits of MMC comes from a 2010 Cochrane review that assessed the effects of intraoperative MMC compared with no antifibrosis agent. The authors found that mean intraocular pressure (IOP) was reduced significantly at 12 months in high-risk and first-time surgery eyes when trabeculectomy with MMC was compared with trabeculectomy without MMC. Aside from an increased risk of cataracts, the meta-analysis did not detect a difference in other adverse effects, such as rates of wound leak, hypotony, or endophalmitis.[13] Trabeculectomy with adjunctive MMC application intraoperatively increases surgical success. The efficacy of 0.2 mg/mL of MMC applied for a period of 2–3 minutes during surgery appears to be quite effective in clinical trials.[14] Napoli PE *et al.*, [15] compared filtering blebs with optical coherence tomography noted that blebs following MMC trabeculectomy had good functionality with low index of reflectivity and cystoid pattern. On the other hand, in trabeculectomies without MMC, mixed optical coherence tomography patterns (layer or diffuse pattern) were associated with high infrared and poor functionality. The success rate of trabeculectomy was 81.8% in eyes treated with mitomycin-C compared with 63.6% in eyes not receiving this drug. Rates of intraocular pressure reduction were 57.9% and 42.9% respectively. Mitomycin-C, as adjunctive treatment during trabeculectomy offers great benefit in lowering IOP, but with a substantial high risk of complications.[16] Similar findings were noted in present study. While, Ayala M.,[17] in the no-MMC group, noted that IOP decreased from preoperative average 28.78–13.91 mmHg postoperatively and IOP reduction was significant. In the MMC group, IOP decreased from preoperative average 27.80–12.72 mmHg postoperatively and IOP reduction was significant. The IOP reduction comparing both groups (no MMC vs MMC) showed to be no significant. Hypotony, defined as IOP ⩽5 mmHg, was of 24.1% in the no MMC meanwhile in the MMC group the frequency was 46.4% and difference was statistically significant. Hypotony was probably induced by an excessive filtration due to the use of MMC. The frequency of cataract operation was higher in the MMC group (35%) than in the no-MMC group (19%).[17] Another study noted that the complications occurred in 36.3% of the eyes managed with mitomycin-C against 9% in the control eyes.[16] Progressive visual field loss after trabeculectomy was reported to be 50-60% after 10-22 years in a study conducted by Sihota *et al.*[18] However, insignificant visual field loss was noted at final visit in a study with three years follow-up.[4] Reibaldi A *et al.*,[19] noted that for MMC, long-term follow-up of a randomized clinical trial of trabeculectomy with MMC vs no MMC revealed no difference in safety outcomes, including leaks, hypotony, blebitis, and endophthalmitis. Sihota R *et al.*,[20] found greater corneal endothelial cell loss at three months in patients getting trabeculectomies with mitomycin than in those undergoing trabeculectomy without mitomycin. In addition to the benefits of lowering IOP, MMC-assisted trabeculectomy may have an impact on the patient's quality of life (QoL) At 5 years follow-up, both medical and surgical therapy were effective in reducing IOP, but initial surgery led to lower visual field progression in subjects with advanced visual field loss at baseline.[21] Limitations of present study were single center based, small sample size study with only 1 year follow up. Larger, multicentric trials are required to confirm our findings.

CONCLUSION

Mean intraocular pressure (IOP) was reduced significantly at 12 months in trabeculectomy with MMC group compared to trabeculectomy without MMC. No significant difference was noted in complications from both groups.

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