ORIGINAL ARTICLE

Outcome of Intraoperative Mitomycin C Injection in Trabeculectomy and Phacotrabeculectomy in Patients with Glaucoma

Saadia Farooq[1], Hajra Farooq[2], Momina Faisal[3]
[1]Shifa International Hospital, Islamabad, [2,3]The Aga Khan University, Karachi

ABSTRACT

Purpose: To determine the efficacy and safety of per-operative mitomycin C injection during trabeculectomy and combined phaco-trabeculectomy in different types of glaucoma.

Study Design: Interventional case series.

Place and Duration of Study: Shifa International, between January 2018 to July 2020.

Methods: Thirty one patients requiring trabeculectomy or Phaco-trabeculectomy with mitomycin C because of maximum tolerable anti-glaucoma treatment or poor compliance were included in the study. Out of these 15 in group A underwent simple trabeculectomy with intra-operative mitomycin C and 16 patients in group B underwent phacotrabeculectomy with intra-operative mitomycin C and IOL implantation. All patients underwent an eye examination (including IOP and visual acuity) before surgery and then afterwards at 1 week, 1 month, 2 months, 6 months and 1 year. Main outcome measures were best corrected visual acuity, intra-ocular pressure and number of medications at base line and post-operatively.

Results: Demographic results of the two groups were similar. Mean follow-up period was 1 year, mean IOP was 11 in group Aand 15.5 in group B in last follow-up.Mean IOP reduction at 1 year was significant in both group A and B ($p = 0.001$, $p = 0.022$ respectively). Hypotony, post-operative inflammatory membrane and bleb fibrosis were the main complications in group A and group B.

Conclusion: Trabeculectomy with mitomycin C and phaco-trabeculectomy with mitomycin C are equally successful at lowering IOP in common types of glaucoma permitting significant and safe reduction of anti-glaucoma medications for atleast 1 year after surgery.

Key Words: Mitomycin, Glaucoma, Intra ocular pressure.

How to Cite this Article: Farooq S, Farooq H, Faisal M. Outcome of Intraoperative Mitomycin C Injection in Trabeculectomy and Phacotrabeculectomy in Patients with Glaucoma. Pak J Ophthalmol. 2021, **37 (1):** 213-217.
Doi: http://doi.org/10.36351/pjo.v37i2.1204

INTRODUCTION

Mitomycin C (MMC) is a common wound modulator used in ophthalmology in glaucoma, pterygium surgery and refractive lasers.[1] In the past decade MMC has been routinely used in high risk "trabeculectomies" including young patients, African American or who had previous glaucoma surgery.[2] Traditionally MMC is applied per-operatively via soaked sponges for two minutes. With popularity and variety of anti-glaucoma medications as a first line management option, there has been a change in trend to use MMC in all trabeculectomies to improve the survival of bleb.[3] Moreover, shift to sub conjunctival

Correspondence: Hajra Farooq
Department of Ophthalmology, The Aga Khan University, Karachi
Email: hajrafarooq11123@gmail.com

Received: January 16, 2021
Accepted: March 3, 2021

injection of mitomycin C is found to be effective and results in more diffuse bleb formation.[4-6] This technique not only saves time, reduces conjunctival surface exposure to mitomycin with consequent less chances of wound leak, but is also proven as an effective modality with ideal bleb formation.[4]

Primary open angle glaucoma and chronic narrow angle glaucoma are the two most common causes of blindness among elderly Asian population. In hypermetropic eyes proportionately large lens plays a crucial role in the pathogenesis of angle closure.[7,8] Removal of lens not only reduces crowding in the anterior chamber but also improves vision by removing the lens with opacities. It reduces the need of sequential surgery which is needed with rapid progression of lens opacities into visually significant cataract post-trabeculectomy.[9-11] On the other hand, primary open-angle glaucomapatients are generally elderly with concurrent cataract and glaucoma. They need combined procedure. Phacotrabeculectomy again not only improves vision but reduces the need for sequential surgery.[12-14] However, some surgeons prefer separate procedures over combined. So there is lack of consensus on the best approach in such cases.[15,16] Long term data for the use of per-operative injection of MMC in phacotrabeculectomy and trabeculectomy is insufficient especially in South Asian population. We analyzed the effectiveness of trabeculectomy and phacotrabeculectomy with MMC (20 micro gram) in different types of glaucoma over an observation time of 1 year.

METHODS

Out of 31 eyes, 15 underwent trabeculectomy with MMC whereas 16 patients underwent phaco-trabeculectomies with intra-operative MMC. All surgeries were performed by one surgeon at Shifa International Trust, between January 2018 to July 2020 and followed up for one year. Patients who had progressive damage with maximum tolerable anti-glaucoma treatment or poor compliance with topical drugs and with or without lens changes were included. Exclusion criteria were patients who underwent previous glaucoma lasers or glaucoma valve surgeries or patients who were lost in follow-up in less than 6 months.

Institutional ethical board approved this study and informed consent was obtained from every patient. Data was collected pre-operatively and post-operatively at 1 week, 1 month, 3-months, 6-months and 1 year. Assessment included best corrected visual acuity, GoldmanApplanation tonometry, cup-disk ratio, number of anti-glaucoma medications, post-operative interventions and outcomes. Complete successwas defined as IOP 6 – 18 mmHg without anti-glaucoma treatment and improved or stable visual acuity compared to pre-operative visual acuity. Conditional success was defined as IOP less than 18 mmHg with 1 or 2 anti-glaucoma medications with stable visual acuity as compared to pre-operative. Failure was defined as IOP higher than 23 mmHg with 2 or more anti-glaucoma medications, severe co-morbidity such as choroidal detachment, recurrent encysted bleb needing revision more than 3 times. Similar protocol was followed for phaco-trabeculectomy.

Same surgeon performed all procedures under local anesthesia.Following sub-Tenon's or peribulbar anesthesia, 7 – 0 silk stay suture was placed in the superior cornea. Standard dosage of MMC 0.2 mg/ml (0.1 cc) was used as an intra-operative sub-conjunctival injection, 8mm from limbus at the beginning of procedure. Injection xylocaine with adrenaline was used to dissect conjunctiva and tenon at surgical site. The exposed sclera under the conjunctival flap was cleaned with gentle bipolar diathermy. Partial thickness scleral flap (4x3 mm 2/3rd thickness) was made and advanced to 2mm into clear cornea. Internal window was marked and completed after paracentesis. BSS was injected through paracentesis to confirm the patency of fistula. Scleral flapwas stitched with 10/0 nylon at the ends of flap. Conjunctiva and tenon were stitched.

Combined phaco-trabeculectomy was done with the same standard steps till the marking of internal window. Keratome (2.2mm) was used to make a phaco-incision temporal to the scleral flap. Capsulorhexis, hydrodissection, phaco chop or flip and lens matter aspiration was done. After IOL implantation in bag, Miochol was used to constrict the pupil, internal scleral window was removed, PI done and Conjunctival flap was stitched as described above. Subconjunctival injectionof Dexamethasone was given at the end of combined procedure.

Post-operative Predforte eye drops were given 02 hourly for two weeks then 5 times a day. Eye drops were reduced by 1 drop every week and discontinued after 7 weeks. In case of bleb vascularization or increase in IOP, digital massage was introduced from

2nd week onwards and steroid frequency was increased to 2 hourly for 3 days. No bleb needling was performed post-operatively. Vigamox was continued for 02 weeks. Cyclopentolate was given in phaco-trabeculectomy for 05 days.Considering the sample size, the significance level was set to 0.5 and confidence coefficient to 0.95. Statistical analysis was performed with SPP software (version 21).

RESULTS

The meanpreoperative IOP at the baseline was 25.59± 8.69 mmHg. Post-operatively the mean IOP had decreased to 8.14 ± 3.25 mmHg at 1 month, 12.30 ± 3.94 mmHg at 6 months and 12.39 ± 3.94 after 1 year. The IOP reduction after surgery was statistically significant at the end of observation period. No significant difference of IOP was found in different types of glaucoma and different sex.

Visual acuity significantly improved (in both groups) from 32.3% (6/12-6/6) preoperatively to 64.5% (6/12-6/6) post operatively. Applying the success/failure criteria, complete surgical success was achieved in 73.3% in A, 62.5% in B. Qualified success was 18.75% in group B. Failure was seen in 12.5% in group B and in 6.67% in group A. Loss of 1 year follow up was observed in 6.25% in group B and 20% in group A. A decrease in number of medications was observed in post-operative period up to 1 year. Post-operatively the number of medications were significantly decreased to 3.22 (p value less than 0.005) and digital massage was needed in 6.45 patients.

Intraoperative and post-operative complications were evaluated in all surgeries. Most common complications were hypotony in 9.67% and post-operative inflammatory membrane in 6.45% and bleb fibrosis in 3.22%.

Table 1: *Different types of glaucoma and their frequency.*

	Diagnosis	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Secondary angle glaucoma	3	9.7	10.0	10.0
	Open angle glaucoma	13	41.9	43.3	53.3
	Narrow angle glaucoma	1	3.2	3.3	56.7
	Steroid induced glaucoma	3	9.7	10.0	67.7
	Drug allergy	4	12.9	13.3	80.0
	Advanced glaucoma	3	9.7	10.0	90.0
	PXF glaucoma	2	6.5	6.7	96.7
	Post vitrectomy	1	3.2	3.3	100.0
	Total	30	96.8	100.0	
Missing System		1	3.2		
Total		31	100.0		

Table 2: *Pre-Operative and post-operative visual acuities in the patients.*

		Frequency	Percent	Valid Percent	Cumulative Percent
Pre-op vision					
Valid	C.F. – 6/36	11	35.5	36.7	36.7
	6/24 – 6/12	9	29.0	30.0	66.7
	6/12 – 6/6	10	32.3	33.3	100.0
	Total	30	96.8	100.0	
Missing System		1	3.2		
Total		31	100.0		
Post-op vision					
Valid	C.F. – 6/36	7	22.6	22.6	22.6
	6/24 – 6/12	4	12.9	12.9	35.5
	6/12 – 6/6	20	64.5	64.5	100.0
	Total	31	100.0	100.0	

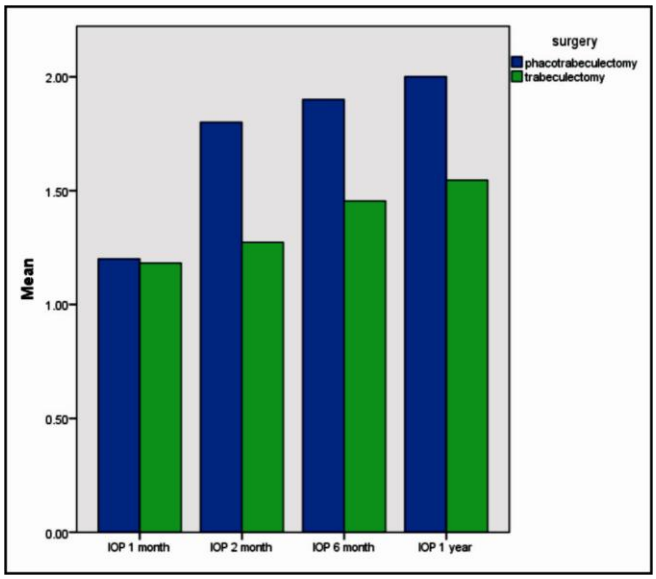

Fig. 1: Comparison of IOP in both groups till 1 year post-operative.

DISCUSSION

Injection of mitomycin is comparable to sponge application with less need of visits and bleb intervention. Efficacy of MMC injection in trabeculectomy and phaco-trabeculectomy is comparable. In the current study, complete treatment success was73.3% in trabeculectomy group and 62.5%in phacotrabeculectomy group over the time of 1 year.

Intra-operative injection offers several advantages over conventional procedures. It provides large area and longer surface area exposure reducing diffusely elevated blebs.[17] There is also increased long term success with minimal complications.[18] Another advantage is predictable dose delivery as compared to sponge application.[19] The main complications of MMC are bleb leak, hypotony, corneal epithelial toxicity and overhanging blebs.[20] Some of these are related to unpredictable MMC concentration in deep scleral and sub scleral layers,[21] whereas others are related to exposure of MMC to edges of the wound and small area of exposure with thin walled bleb.[17]

In a prior study of injection of MMChypotony and serous choroidal detachment were seen as the commonest complications.[4] In our study, hypotony was found in 13.4% and serous choroidal detachment in 6.7% which resolved spontaneously with time.We have seen effective control of IOP and lesser need of anti-glaucoma medication with per-operative injection of MMC. This is consistent with an earlier study in which similar results were reported regarding IOP decrease and need of fewer anti-glaucoma medications after injection of MMC in trabeculectomy.[1]

We analyzed the efficacy of intraoperative MMC in combined phaco-trabeculectomy and found it to be a safe and effective procedure for control of glaucoma with complete success in 62.5% and need of fewer medication in 18.75%. Data related to MMC injection during phaco-trabeculectomy is scarce. In a previous study it was shown that two site phaco trabeculectomy with MMC (sponge application) in West Indian patientsproved to be a safe and effective treatment.[22] Contrary to that other authors have reported that trabeculectomy and single site phacotrabeculectomy with intraoperative sponge MMC was safe and effective treatment for IOP control.[23] Reported results of inject mitomycin in trabeculectomy and phacotrabeculectomy are rarely seen together in literature. We have found it to be safer than conventional and equally comparable to sponge mmc application with predictable results in variety of glaucoma patients at 1-year follow-up.

Limitations of this study includes relatively small sample size and follow-up limited to 1 year. Future studies in prospective long term and larger cohort are necessary to further confirm its safety and efficacy as a modality. Additional influencing risk factors to be considered include number of anti-glaucoma medications, duration of treatment, pre-operative conjunctival injection, previous eye surgeries with and without conjunctival injections, active skin disease, intraocular inflammation, races, and thinness of conjunctiva to standardize risk factor adjusted protocol for MMC application.

Ethical Approval

The study was approved by the Institutional review board/ Ethical review board **(IRB#335-1155-2020).**

Conflict of Interest

Authors declared no conflict of interest.

REFERENCES

1. **S Khouri A, Huang G, Y Huang L.** Intraoperative Injection vs Sponge-applied Mitomycin C during Trabeculectomy: One-year Study. J Curr Glaucoma Pract. 2017; **11 (3):** 101–106.

2. **Swogger J, Conner IP, Rosano M, Kemmerer M, Happ-Smith C, Wells A, et al.** Injected Versus Sponge-Applied Mitomycin C (MMC) During Modified Trabeculectomy in New Zealand White Rabbit Model. Transl Vis Sci Technol. 2020; **9 (11):** 23. Doi: 10.1167/tvst.9.11.23.
3. **Ya Y, Ys G, Ct F, Xq M.** Long-term effects of simultaneous subconjunctival and subscleral mitomycin C application in repeat trabeculectomy. J Glaucoma. 2002; **11 (2):** 110–118.
4. **Lee E, Doyle E, Jenkins C.** Trabeculectomy surgery augmented with intra-Tenon injection of mitomycin C. Acta Ophthalmol (Copenh). 2008; **86 (8):** 866–870.
5. **Al-Habash A, Aljasim LA, Owaidhah O, Edward DP.** A review of the efficacy of mitomycin C in glaucoma filtration surgery. Clin Ophthalmol. 2015; **9:** 1945-1951. Doi: 10.2147/OPTH.S80111.
6. **Sisto D, Vetrugno M, Trabucco T, Cantatore F, Ruggeri G, Sborgia C.** The role of antimetabolites in filtration surgery for neovascular glaucoma: intermediate-term follow-up. Acta Ophthalmol Scand. 2007; **85 (3):** 267–271.
7. **Dietlein TS, Widder RA, Jordan JF, Jonescu-Cuypers C, Rosentreter A.** Combined cataract and glaucoma surgery. Current options. Ophthalmol Z Dtsch Ophthalmol Ges. 2013; **110 (4):** 310–315.
8. **Khandelwal R, Bijlani M, Raje D, Rathi A.** Evaluating the efficacy of short duration Mitomycin C in safe surgery system trabeculectomy combined with cataract surgery. Clin Ophthalmol. 2019 May 22; **13:** 849-857. Doi: 10.2147/OPTH.S192044.
9. **Alsagoff Z, Aung T, Ang LP, Chew PT.** Long-term clinical course of primary angle-closure glaucoma in an Asian population. Ophthalmology, 2000; **107 (12):** 2300–2304.
10. **Morgan WH, Yu D-Y.** Surgical management of glaucoma: a review. Clin Experiment Ophthalmol. 2012; **40 (4):** 388–399.
11. **Tan AM, Loon SC, Chew PTK.** Outcomes following acute primary angle closure in an Asian population. Clin Experiment Ophthalmol. 2009; **37 (5):** 467–472.
12. **Vijaya L, David RL.** Safety and Efficacy of Single-site Phacotrabeculectomy with Mitomicin C Using Nylon and Polyglactin Suture for Scleral Tunnel Closure. J Glaucoma. 2015; **24 (5):** e64-68.
13. **Rao HL, Maheshwari R, Senthil S, Prasad KK, Garudadri CS.** Phacotrabeculectomy without mitomycin C in primary angle-closure and open-angle glaucoma. J Glaucoma. 2011; **20 (1):** 57–62.
14. **Augustinus CJ, Zeyen T.** The effect of phacoemulsification and combined phaco/glaucoma procedures on the intraocular pressure in open-angle glaucoma. A review of the literature. Bull Soc Belge Ophtalmol. 2012; **(320):** 51–66.
15. **Emanuel ME, Parrish RK, Gedde SJ.** Evidence-based management of primary angle closure glaucoma. Curr Opin Ophthalmol. 2014; **25 (2):** 89–92.
16. **Li H-J, Xuan J, Zhu X-M, Xie L.** Comparison of phacotrabeculectomy and sequential surgery in the treatment of chronic angle-closure glaucoma coexisted with cataract. Int J Ophthalmol. 2016; **9 (5):** 687–692.
17. **Cordeiro MF, Constable PH, Alexander RA, Bhattacharya SS, Khaw PT.** Effect of varying the mitomycin-C treatment area in glaucoma filtration surgery in the rabbit. Invest Ophthalmol Vis Sci. 1997; **38 (8):** 1639–1646.
18. **Onol M, Aktaş Z, Hasanreisoğlu B.** Enhancement of the success rate in trabeculectomy: large-area mitomycin-C application. Clin Experiment Ophthalmol. 2008; **36 (4):** 316–322.
19. **Maheshwari D, Kanduri S, Rengappa R, Kadar MA.** Intraoperative injection versus sponge-applied mitomycin C during trabeculectomy: One-year study. Indian J Ophthalmol. 2020; **68 (4):** 615-619. Doi: 10.4103/ijo.IJO_963_19
20. **Holló G.** Wound healing and glaucoma surgery: modulating the scarring process with conventional antimetabolites and new molecules. Dev Ophthalmol. 2012; **50:** 79–89.
21. **Georgopoulos M, Vass C, Vatanparast Z.** Impact of irrigation in a new model for in vitro diffusion of mitomycin-C after episcleral application. Curr Eye Res. 2002; **25 (4):** 221–225.
22. The Safety and Efficacy of Two-site Phacotrabeculectomy with Mitomycin C under Retrobulbar and Topical Anesthesia [Internet]. [cited 2020 Oct 15]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4875729/
23. **Murthy SK, Damji KF, Pan Y, Hodge WG.** Trabeculectomy and phacotrabeculectomy, with mitomycin-C, show similar two-year target IOP outcomes. Can J Ophthalmol. 2006; **41 (1):** 51–59.

Author's Designation and Contribution

Saadia Farooq; Consultant Ophthalmologist: *Concepts, Design, Data acquisition, Manuscript preparation, Manuscript review.*

Hajra Farooq; MBBS Student: *Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review.*

Momina Faisal; MBBS Student: *Literature search, Manuscript editing, Manuscript review.*