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RESEARCH

Evaluation of Intraocular Pressure Changes Following Trabeculectomy with Mitomycin-C (MMC): A One-Year Follow-Up Study at Undaan Eye Hospital, Indonesia

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Abstract

Introduction: Trabeculectomy with mitomycin-C (MMC) is a widely used surgical intervention for the management of glaucoma. This study aimed to evaluate changes in intraocular pressure (IOP) before and after surgery, using statistical analyses of pre-operative and post-operative IOP measurements. **Purpose:** To determine the effectiveness of MMC in trabeculectomy and its role in enhancing surgical success. **Methods:** This retrospective observational study analyzed the medical records of 65 eyes from 52 glaucoma patients who underwent trabeculectomy with 2% MMC at Undaan Eye Hospital, Surabaya, Indonesia, between 2022 and 2023. Post-operative IOP was assessed at one, three, six, and twelve months. Statistical analyses were performed to identify patterns of IOP change over time. **Results:** A Kruskal-Wallis test, followed by Dunn's post hoc analysis ($p < 0.001$), revealed significant differences in IOP between the pre-operative and post-operative periods ($p < 0.05$). However, no significant differences were found among post-operative follow-up intervals ($p > 0.05$). Correlation analysis of IOP categories (< 20 mmHg vs. ≥ 20 mmHg) across observation points showed a negative correlation ($r = -0.491$, $p < 0.001$), indicating a tendency for IOP reduction over time. Regression analysis estimated that IOP decreased by approximately 1.141 mmHg per month. **Conclusions:** Significant reductions in IOP were observed post-operatively, with a sustained downward trend compared to pre-operative values. These findings provide valuable insights into the long-term effectiveness of trabeculectomy with MMC, emphasizing factors that optimize surgical outcomes for glaucoma management.

Keywords: intraocular pressure (IOP); mitomycin-C (MMC); trabeculectomy; glaucoma; surgical outcomes

Introduction

Reducing intraocular pressure (IOP) is the primary goal of glaucoma surgery, as sustained IOP reduction lowers the risk of progressive visual field loss. Trabeculectomy remains the gold standard surgical approach for achieving this goal, as it facilitates aqueous outflow by bypassing the trabecular meshwork, enlarging the suprachoroidal space, or creating full-thickness fistulae from the anterior chamber to the subconjunctival space.[1] However, post-operative management is critical, as complications and surgical failure can arise over time, necessitating continuous monitoring of IOP trends.

Although full-thickness filtration procedures significantly lower IOP, their long-term success can be hindered by fibrosis, which may lead to surgical failure. Mitomycin-C (MMC) has become the preferred antifibrotic agent in trabeculectomy, as it inhibits fibroblast proliferation by disrupting DNA synthesis and protein transcription.[2] These actions contribute to the cytotoxic effects of the compound as well as its potential to trigger apoptotic cell death in fibroblasts that are included in the Tenon capsule.[1] Historically, failure rates of trabeculectomy were reported to be as high as 30% within the first six months before antifibrotic agents were introduced, with even higher rates observed over longer follow-up periods.[3] Without adjunctive MMC, long-term monitoring has shown that while trabeculectomy remains effective in controlling IOP at one year, its success rates decline over time, stabilizing at approximately 67% by the tenth year.[4]

The use of MMC has significantly improved the long-term survival of trabeculectomy blebs, particularly in eyes at high risk of surgical failure.[4] A survey by the American Glaucoma Society reported an increase in MMC usage during trabeculectomy from 84% in 2008 to 97% in 2016, with the most common concentration being 0.4 mg/mL, administered via sponges or subconjunctival injection.[5] Despite the widespread adoption of MMC-enhanced trabeculectomy, there remains a notable gap in research regarding the long-term monitoring of post-trabeculectomy IOP trends, particularly within the first year following surgery. While the effectiveness of MMC in reducing early fibrosis is well established, limited studies have systematically evaluated the pattern of IOP changes at specific post-operative intervals. This study aims to address this gap by analyzing IOP fluctuations following trabeculectomy with MMC at one, three, six, and twelve months, providing insights into its sustained effectiveness and potential risk factors for surgical failure.

Methods

The medical records of 65 eyes from 52 patients who underwent primary trabeculectomy with MMC between January 2022 and January 2023 were reviewed. Eyes with a post-operative follow-up period of less than one year were excluded. All surgeries were performed by a single surgeon (LA-operating operator).

A conjunctival flap was constructed with the limbus as its base, specifically over the insertion point of the superior rectus muscle. Subtenon's dissection was performed in all patients, followed by tenonectomy. A 2% MMC solution was applied to the sclera using a sponge applicator for two to four minutes, after which the area was thoroughly irrigated with a cool, balanced salt solution A trapezoidal scleral flap was marked and raised, measuring one-half to two-thirds of the scleral thickness, with its hinge located at the limbus. A Kelley Descemet's punch was used to create a sclerostomy in the middle third of the scleral bed, followed by a basal iridectomy. Post-operative care included the application of 1% prednisone eye drops four times daily during the first week, gradually tapering to three times daily in the second week, two times daily in the third week, and once daily in the fourth week. A topical antibiotic was also prescribed to be applied four times daily for eight days. Patients were instructed to gently press the conjunctival surface at the incision site on the sclera to facilitate aqueous outflow. Additionally, they were advised about potential complications, including bleb leakage and retinal detachment.

Data collected included age, sex, glaucoma diagnosis, operative eye, and pre-operative and post-operative IOP at one, three, six, and twelve months. This study received ethical clearance from the Health Research Ethics Committee of Faculty of Medicine, Universitas Airlangga, Surabaya (Letter No. 143/EC/KEPK/FKUA/2025). Statistical analysis began with a normality test using the Shapiro-Wilk test. Due to data heterogeneity, non-parametric tests were applied. Differences in IOP across follow-up intervals were analyzed using the Kruskal-Wallis test, while correlation analysis was performed using Pearson's test. A linear regression test was subsequently conducted to assess trends over time. Statistical analysis was performed using IBM SPSS Statistics 25 for Windows, with a significance level set at $p < 0.05$.

Results

A total of 65 eyes from 52 patients were included in this study, with a mean age of 55.19 ± 15.03 years. The cohort comprised 28 male patients (43.1%) and 37 female patients (56.9%). The most common glaucoma diagnosis was primary angle-closure glaucoma (PACG), accounting for 29.2% of cases, followed by acute glaucoma (18.5%)

Table 1. Characteristics of the sample.

Variable	N (%) / Mean±SD
Age	55.19 ± 15.03
Gender	
Male	28 (43.1)
Female	37 (56.9)
Patient diagnosis	
Absolute glaucoma	4 (6.2)
Acute glaucoma	12 (18.5)
Chronic glaucoma	3 (4.6)
PACG	19 (29.2)
POAG	4 (6.2)
Others	5 (7.7)
>1 diagnosis	18 (27.7)
Laterality	
Right eye	32 (49.2)
Left eye	32 (49.2)
Bilateral	1 (1.5)
Preoperative IOP	41.21 ± 12.73 mmHg
Post-operative	
One month	14.63 ± 8.24 mmHg
Three months	14.72 ± 8.66 mmHg
Six months	15.53 ± 10.23 mmHg
Twelve months	20.64 ± 14.65 mmHg

Table 2. Result analysis of IOP difference using Kruskal-Wallis.

Indicator	Signification	Conclusion
IOP	0.000	Significant

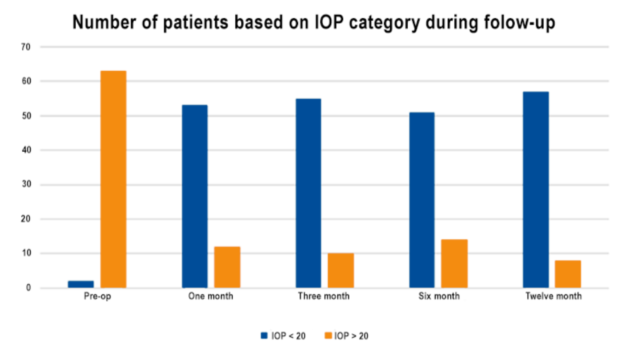

Figure 1. A bar chart to illustrate the number of patients based on IOP category during follow-up

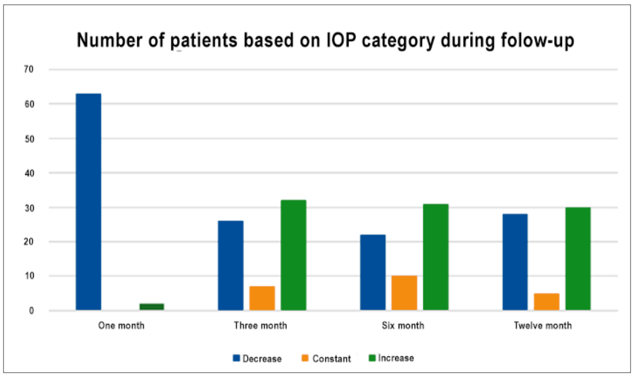

Figure 2. A bar chart to illustrate the number of patients based on the change in IOP during follow-up

and multiple glaucoma diagnoses in a single patient (27.7%). Other less frequent diagnoses included absolute glaucoma (6.2%), chronic glaucoma (4.6%), primary open-angle glaucoma (POAG) (6.2%), and other glaucoma subtypes (7.7%).

Regarding laterality, an equal distribution was observed between right and left eyes, with each constituting 49.2% of cases, while only 1.5% of cases involved bilateral glaucoma.

The mean pre-operative IOP was 41.21 ± 12.73 mmHg. Post-operatively, IOP showed a marked reduction, averaging 14.63 ± 8.24 mmHg at one month, 14.72 ± 8.66 mmHg at three months, and 15.53 ± 10.23 mmHg at six months. However, by the twelve-month follow-up, IOP had increased to 20.64 ± 14.65 mmHg, indicating a partial rebound in pressure over time.

These findings highlight the initial efficacy of trabeculectomy with MMC in achieving a significant reduction in IOP, with a trend toward stabilization over the first six months, followed by a slight increase at the one-year follow-up (Table 1).

Table 2 shows that the Kruskal-Wallis test revealed a significant difference in IOP across the follow-up period ($p = 0.000$, $p < 0.05$). Further pairwise comparisons using the Dunn test demonstrated that IOP was significantly lower at all post-operative follow-ups compared to pre-operative levels ($p = 0.000$). However, IOP comparisons between post-operative time points (one month, three months, six months, and twelve months) showed no statistically significant differences ($p > 0.05$).

Figure 1 illustrates the trend in IOP categories over time. Before surgery, the majority of patients (62 out of 63) had IOP > 20 mmHg. Following trabeculectomy, a significant reduction was observed, with most patients achieving IOP < 20 mmHg as early as one month post-operatively (52 patients). This trend remained stable over the next follow-ups, with 53, 50, and 58 patients maintaining IOP < 20 mmHg at three, six, and twelve months, respectively. By twelve months, the number of patients with IOP > 20 mmHg had decreased to just eight.

Overall, these results suggest a sustained reduction in IOP following trabeculectomy with MMC, with most patients maintaining an IOP < 20 mmHg throughout the follow-up period.

The IOP trend analysis reveals distinct patterns over the follow-up period, as shown in Figure 2. At one month post-surgery, nearly all patients (98.5%) experienced a decrease in IOP, with only one case of an increase. By three months, the trend shifted, with 43.1% showing a continued decrease, while 49.2% experienced an increase. This pattern persisted at six and twelve months, where approximately 46.2% of patients had an increase in IOP compared to earlier time points. However, a substantial proportion of patients still maintained a decreasing trend over time. These findings indicate an initial sharp drop in IOP post-operatively, followed by fluctuations in later months, emphasizing the importance of long-term monitoring for sustained pressure control.

The Pearson correlation analysis (Table 3) revealed a significant negative correlation between the follow-up period and intraocular pressure ($r = -0.34$, $p = 0.00$), indicating that IOP tended to decrease as the follow-up duration increased. In contrast, gender ($r = -0.54$, $p = 0.17$) and age ($r = -0.01$, $p = 0.42$) showed no significant correlation with IOP, indicating that these factors did not have a substantial impact on post-operative pressure changes. These findings highlight the importance of follow-up duration in maintaining lower IOP levels after trabeculectomy, while demographic variables appear to play a minimal role in influencing outcomes.

Table 3. Result analysis of Pearson correlation.

Variable	Pearson correlation	p-value	Conclusion
Follow-up period	-0.34	0.00	Significant
Gender	-0.54	0.17	Not significant
Age	-0.01	0.42	Not significant

Table 4. Results of regression analysis.

Variable	B	SE	β	t	Sig.
Follow-up period	-1.14	0.18	-0.34	-6.42	0.00
Gender	-1.58	1.56	-0.05	-1.013	0.31
Age	-0.01	0.06	-0.01	-0.16	0.87

The regression analysis (Table 4) demonstrated that the follow-up period had a significant negative effect on intraocular pressure (B = -1.14, p = 0.00), indicating that IOP decreased by approximately 1.14 mmHg per month. In contrast, gender (B = -1.58, p = 0.31) and age (B = -0.01, p = 0.87) were not significant predictors of IOP reduction. The model explained 11.7% of the variance in IOP changes (R^2 = 0.117), indicating that while follow-up duration plays a crucial role in post-operative IOP reduction, other factors may also contribute to long-term outcomes.

Discussion

Open-angle glaucoma was more prevalent worldwide, while angle closure glaucoma was common in Asian people and those <40 years old.[6] In contrast to our study, research in India showed that 79% of patients had bilateral disease and were predominantly male (61%).[7]Glaucoma can be solved with an invasive or non-invasive procedure. Topical drugs, laser therapy, and surgery targeting lowering IOP were the primary focus of glaucoma management. Trabeculectomy is a popular option among ophthalmologists, classified as a bleb-based procedure, which also has several risks of complications.[8],[9],[10] Adjuvant agent, including MMC and 5-fluorouracil, was given to prevent subconjunctival fibrosis. Mitomycin-C, which is more potent than 5-fluorouracil, plays a crucial role in reducing the proliferative phase of the wound healing process after trabeculectomy by slowing the growth of fibroblasts and endothelial cells.[1],[11]

A previous meta-analysis[12] demonstrated that adding MMC to patients with glaucoma who underwent trabeculectomy resulted in a promising outcome regarding IOP measurement (MD = −11.31 mmHg, 95% CI −19.73 to −2.88 mmHg). It also had better filtering bleb formation compared to the placebo, with a smaller surgical failure rate. A recent study[13] found that MMC outperformed 5-fluorouracil in reducing the risk of corneal damage after surgery. In comparison with ologen implantation, adjuvant treatment with MMC among patients with trabeculectomy resulted in a higher reduction in IOP.[14] In contrast, a study in Indonesia found no significant difference between 5-fluorouracil and triamcinolone acetonide compared to MMC.[15]

In Japan, a long-term observation study[16] was conducted, and the results showed that IOP significantly decreased until the five-year post-operative follow-up, with fewer surgical complications. A Study in Korea reported that the surgery success rate after trabeculectomy with mitomycin-C at 10, 15, and 20 years accounted for 81.7%, 76.4%, and 74.7%, respectively. The IOP measured at one-year post-surgery strongly predicted the long-term success of the procedure.[17] This procedure yields nearly identical results in open-angle glaucoma and angle-closure glaucoma, with a complication rate of less than 3%, including hypotony, choroidal detachment, encapsulated bleb, and bleb leakage.[18] When assessing the complication rate, it is crucial to consider the dosage, application or delivery method, exposure duration, and the tissue area that comes into contact with MMC.[19]

However, when evaluating the complication profile of MMC, it is essential to consider factors such as dosage, method of administration, exposure duration, and the extent of tissue contact. Beyond its well-documented benefits, MMC is also associated with rare but serious adverse effects. These include corneal complications such as corneal melting, perforation, edema, and calcification, as well as secondary glaucoma. Additionally, some patients may experience prolonged hyperemia, chemosis, excessive tearing, lid edema, ptosis, wound dehiscence, corneal blood staining, and photophobia. Other reported complications include superficial punctate keratitis, pigment accumulation, and delayed wound healing. In cases of ocular surface tumor treatment, MMC may also induce periocular allergic contact dermatitis and limbal stem cell deficiency, underscoring the importance of careful patient selection and post-operative monitoring.[19] The lack of association between demographic factors and decreased IOP in the current research is inconsistent with a previous study.[20] A study showed that age at surgery and glaucoma drug prescription correlated significantly with complete success criteria post-surgery based on IOP reduction.[21] In our research, the linear regression model revealed that the influence of age, observation time, and gender on IOP is 11.7%. At the same time, the remaining 88.3% is influenced by other factors. Expanding the time for one month of eye examination can decrease the IOP by 1.14 mmHg. Previous studies[22] showed that patients diagnosed with juvenile open-angle glaucoma who were younger than 40 years had superior surgical results and higher rates of long-term success following trabeculectomy. This implies that if aqueous humor filtering is maintained consistently and inflammatory and fibrotic responses are successfully inhibited during surgery, younger patients, despite having more Tenon's capsule can develop long-lasting functional blebs. Similarly, elderly individuals with high IOP who had trabeculectomy without long-term glaucoma medication showed blebs that resembled those of younger patients, with thin walls, transparency, and little vascularization.[23]

A previous study[20] showed that other factors may interfere with the outcome of trabeculectomy in glaucoma. Pre-operative factors such as family history and higher IOP were associated with surgical outcome.[17] Comorbid conditions, such as hypertension, encapsulated bleb, and more pre-operative topical medications, are associated with surgical failure.[24] There are some limitations in this study. The small sample size used in the study might not accurately reflect the general population. Consequently, the results might not be generalizable to other demographic groups. The study was unable to account for every possible confounding variable because of time and budget limitations. Therefore, those associated factors recorded need to be further studied.

Conclusions

Our study highlights the significance of MMC as an adjuvant drug in trabeculectomy for glaucoma patients based on the results. It could be a suggestion for ophthalmologists to incorporate mitomycin-C into their daily practice.

References

[1] Bell K, de Padua Soares Bezerra B, Mofokeng M, Montesano G, Nongpiur ME, Marti MV, et al. Learning from the past: Mitomycin C use in trabeculectomy and its application in bleb-forming minimally invasive glaucoma surgery. Surv Ophthalmol 2021;66:109–123. https://doi.org/10.1016/j.survophthal.2020.05.005.

[2] Khan SA, Whittaker K, Razzaq MA, Arain UR. National survey of intraoperative mitomycin C use during trabeculectomy surgery in the UK. Int Ophthalmol 2021;41:1309–1316. https://doi.org/10.1007/s10792-020-01688-8.

[3] Zaidi AA. Trabeculectomy: A review and 4-year follow-up. Br J Ophthalmol 1980;64:436–439. https://doi.org/10.1136/bjo.64.6.436.

[4] Edward D, Al Habash A, Aljasim L, Owaidhah O. A review of the efficacy of mitomycin C in glaucoma filtration surgery. Clinical Ophthalmology 2015:1945. https://doi.org/10.2147/OPTH.S80111.

[5] Vinod K, Gedde SJ, Feuer WJ, Panarelli JF, Chang TC, Chen PP, et al. Practice preferences for glaucoma surgery: A survey of the American Glaucoma Society. J Glaucoma 2017;26:687–693. https://doi.org/10.1097/IJG.0000000000000720.

[6] Allison K, Patel D, Alabi O. Epidemiology of Glaucoma: The past, present, and predictions for the future. Cureus 2020. https://doi.org/10.7759/cureus.11686.

[7] Seth PK, Senthil S, Das AV, Garudadri C. Prevalence of glaucoma types, clinical profile and disease severity at presentation: Tertiary Institute based cross-sectional study from South India. Indian J Ophthalmol 2023;71:3305–3312. https://doi.org/10.4103/IJO.IJO_3305_22.

[8] Wagner IV, Stewart MW, Dorairaj SK. Updates on the diagnosis and management of glaucoma. Mayo Clin Proc Innov Qual Outcomes 2022;6:618–635. https://doi.org/10.1016/j.mayocpiqo.2022.09.007.

[9] Schuster AK, Erb C, Hoffmann EM, Dietlein T, Pfeiffer N. The diagnosis and treatment of glaucoma. Dtsch Arztebl Int 2020. https://doi.org/10.3238/arztebl.2020.0225.

[10] Cvenkel B, Kolko M. Devices and treatments to address low adherence in glaucoma patients: A narrative review. J Clin Med 2022;12:151. https://doi.org/10.3390/jcm12010151.

[11] Almobarak FA, Alharbi AH, Morales J, Aljadaan I. The influence of mitomycin C concentration on the outcome of trabeculectomy in uveitic glaucoma. Int Ophthalmol 2018;38:2371–2379. https://doi.org/10.1007/s10792-017-0737-6.

[12] Song ZH, Xu SS, Li GY, Wang ET, Li Y, Zhang C. Efficacy and safety of the intraoperative application of mitomycin in glaucoma patients with trabeculectomy: A systematic review and meta-analysis. J Clin Pharm Ther 2023;2023:1–11. https://doi.org/10.1155/2023/5249552.

[13] He M, Wang W, Zhang X, Huang W. Ologen implant versus mitomycin C for trabeculectomy: A systematic review and meta-analysis. PLoS One 2014;9:e85782. https://doi.org/10.1371/journal.pone.0085782.

[14] Song D-S, Qian J, Chen Z-J. Ologen implant versus mitomycin-C for trabeculectomy. Medicine 2019;98:e16094. https://doi.org/10.1097/MD.0000000000016094.

[15] Sari YP, Ekantini R, Gani TT, Jati KDP. Intraoperative mitomycin-c, 5-fluorouracil, retrobulbar triamcinolon acetonide, is it equally effective to decrease intra ocular pressure after trabeculectomy? Ophthalmol Indones 2024;49. https://doi.org/10.35749/4e85px09.

[16] Yuasa Y, Sugimoto Y, Hirooka K, Ohkubo S, Higashide T, Sugiyama K, et al. Effectiveness of trabeculectomy with mitomycin C for glaucomatous eyes with low intraocular pressure on treatment eye drops. Acta Ophthalmol 2020;98. https://doi.org/10.1111/aos.14195.

[17] Romero P, Hirunpatravong P, Alizadeh R, Kim E-A, Nouri-Mahdavi K, Morales E, et al. Trabeculectomy with mitomycin-C: Outcomes and risk factors for failure in primary angle-closure glaucoma. J Glaucoma 2018;27:101–107. https://doi.org/10.1097/IJG.0000000000000842.

[18] Maheshwari D, Kanduri S, Kadar M, Ramakrishnan R, Pillai M. Midterm outcome of mitomycin C augmented trabeculectomy in open angle glaucoma versus angle closure glaucoma. Indian J Ophthalmol 2019;67:1080. https://doi.org/10.4103/ijo.IJO_1328_18.

[19] Cumurcu T. Mitomycin-C use and complications in ophthalmology. Inter J Clin Exp Ophthalmol 2017;1:29–32. https://doi.org/10.29328/journal.hceo.1001004.

[20] Musch DC, Gillespie BW, Niziol LM, Cashwell LF, Lichter PR. Factors associated with intraocular pressure before and during 9 years of treatment in the collaborative initial glaucoma treatment study. Ophthalmology 2008;115:927–933. https://doi.org/10.1016/j.ophtha.2007.08.010.

[21] Hoang TKH, Kim YK, Jeoung JW, Park KH. Relationship between age and surgical success after trabeculectomy with adjunctive mitomycin C. Eye 2018;32:1321–1328. https://doi.org/10.1038/s41433-018-0071-x.

[22] Birla S, Varshney T, Singh A, Sharma A, Panigrahi A, Gupta S, et al. Machine learning-assisted prediction of trabeculectomy outcomes among patients of juvenile glaucoma by using 5-year follow-up data. Indian J Ophthalmol 2024;72:987–993. https://doi.org/10.4103/IJO.IJO_2009_23.

[23] Lee S, Park DY, Huh MG, Cha SC. Influence of preoperative glaucoma medication on long-term outcomes of trabeculectomy. Sci Rep 2024;14:28341. https://doi.org/10.1038/s41598-024-79637-z.

[24] Qin Z-X, Han Q, Wang L, Tan L, Xu Y-F, You Q-X, et al. Outcomes and risk factors for failure of trabeculectomy in glaucomatous patients in Southwest China: A 325 eyes analysis. Int J Ophthalmol 2023;16:367–374. https://doi.org/10.18240/ijo.2023.03.06.