ORIGINAL ARTICLE

INTRAOPERATIVE MITOMYCIN-C, 5-FLUOROURACIL, RETROBULBAR TRIAMCINOLON ACETONIDE, IS IT EQUALLY EFFECTIVE TO DECREASE INTRAOCULAR PRESSURE AFTER TRABECULECTOMY?

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ABSTRACT

Objectives: *To evaluate the effect of mitomycin-C (MMC), 5-fluorouracil (5-FU), and retrobulbar triamcinolone acetonide (TA) on the surgical result of trabeculectomy*

Materials and Methods: *All consecutive trabeculectomies with releasable sutures performed in Sardjito General Hospital between January 2022 and December 2022 were retrospectively reviewed from medical records. Patients without any intraoperative metabolite (control group, n=5) were compared to those with retrobulbar TA (n=5), MMC group (n=19), and 5-FU group (n=11) in terms of surgical success. Successful surgery results were defined as IOP between 5 - 21 mm Hg without any further medications or surgical intervention and fewer complications.*

Results: *40 eyes of 35 patients (15 male, 25 female, mean age 52.4 years) were included in the study. The IOP pre operative in TCA group was 47.12 ±12.16 mmHg, in MMC group was 35.53 ± 17.05 mmHg, in 5-FU group was 34.54 ± 17.77 mmHg, and 43.80 ± 15.79 mmHg in group without any metabolite. The patient was observed until the post-operation day (POD) 90. There were no significant differences in intraocular pressure at POD 1, 7, 30, 60, and 90 between the control group compared to TCA, MMC, and 5-FU group. In TCA group, pre operative IOP was 47.12 ±12.16 mmHg then decreases to 15.60 ± 4.61 mmHg at POD 90. In MMC group, pre operative IOP was 35.53 ± 17.05 mmHg, 90 days later became 14.42 ± 5.71 mmHg. In 5-FU group, pre operative IOP was 34.54 ± 17.77 mmHg then decrease to 13.64 ± 4.08 mmHg. In group without metabolite, pre operative IOP was 43.80 ± 15.79 mmHg, then became 21.00 ± 6.81 mmHg at POD 90. The lowest mean intraocular pressure of POD 90 was in the 5-FU group (13.64 ± 4.08 mmHg).*
Complication after trabeculectomy in the TCA group was 21%, the MMC group was 27%, the 5-FU group was 10%, and the control group was 42%.

Conclusion: *MMC, 5-FU, and TCA in this study are equally effective to decrease IOP after trabeculectomy.*

Keywords: *mitomycin-C, 5-fluorouracil, retrobulbar triamcinolone acetonide, surgical success, trabeculectomy*

INTRODUCTION

Glaucoma is the leading cause of world irreversible blindness. The prevalence of glaucoma is increasing and is expected to affect 111.8 million people by 2040 universally.

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Glaucoma is neuropathy optic disturbance, which is marked by optic nerve head abnormalities and visual field defect. Intraocular pressure more than 20 mmHg is the main risk factor.

One of the treatments for glaucoma is trabeculectomy. Trabeculectomy decreases intraocular pressure (IOP) by the creation of a tunnel in which the aqueous humor can drain from the anterior chamber to the sub-Tenon's area.[1] Unlike other operations, the purpose of trabeculectomy is for the wound to heal postoperatively only partially. Truthfully, complete healing of the incision is considered a failed surgery. Bleb failure can arise after trabeculectomy for various reasons, but the most common cause changes in the conjunctiva and episclera.[2,3,4] Therefore, modulating wound healing has particular significance in trabeculectomy.

The normal ocular wound healing process begins with inflammation, extravasation of intravascular components, migration and proliferation of fibroblasts, extracellular matrix deposition, and scar formation occurs. An important factor in enhancing the success of glaucoma filtration surgery is the modification of the wound-healing process to minimize excessive fibroblast growth and scar formation.[5,6]

To reduce excessive scarring after glaucoma surgery, antimetabolites that can stop DNA or RNA replication, cell division, protein synthesis, and fibroblast proliferation are utilized as an additional therapy. Commonly used agents are mitomycin-C (MMC) and 5-Flurouracil (5–FU). Although their non-specific mechanisms may cause a variety of ocular problems, such as corneal toxicity, avascular blebs, endophthalmitis, hypotonia, and in other situations, they are simply ineffectual, they have increased the surgical success rate in trabeculectomy.[7]

Additionally, corticosteroids are frequently administered after glaucoma surgery to lessen inflammation. Although the exact cause is unknown, it is generally accepted that inflammation causes fibrosis, which in turn accelerates the creation of scars. Injectable suspension of the corticosteroid triamcinolone acetate (TA) is already used to treat neovascular, proliferative, and edematous conditions in ophthalmology. Its anti-inflammatory potential is approximately five times that of cortisol.[8,9] MMC and 5-FU are usually only available at tertiary hospitals that have cancer centers, meanwhile, TCA may be available in primary and secondary hospitals. This research is going to compare the effect of MMC, 5-FU, and TCA intraoperative in lowering IOP after filtering surgery trabeculectomy.

MATERIAL AND METHODS

All consecutive trabeculectomies with releasable sutures performed in Sardjito General Hospital between January 2022 and December 2022 were retrospectively reviewed from medical records. Patients without any intraoperative metabolite as the control group (control

group, n=5) were compared to those with retrobulbar TA (n=5), MMC group (n=19), and 5-FU group (n=11) in terms of surgical success. Successful surgery results were defined as IOP between 5 - 21 mmHg without any further medications or surgical intervention and fewer complications. By following the Declaration of Helsinki, all patients were informed about the surgical procedures and postoperative period, and written informed consent forms were obtained from all participants.

The patients followed for at least 3 months were included in the study. Patients with secondary glaucoma and re-trabeculectomy were excluded.

The following data were recorded from patients' charts: age, gender, diagnoses; preoperative corrected visual acuity (CVA), pre and postoperative IOP values,
and complications.

Patients were evaluated before the surgery; at 1st day, 1st week, and 1st, 2nd and 3rd months after surgery.

Visual acuity was measured using a Snellen chart and converted to decimal for statistical analysis. A non-contact tonometer was used for all IOP measurements.
At the final examination, an unmedicated IOP of less than 21 mmHg was considered 'success'; and an IOP of 21 mmHg or higher was 'failure'. IOP under 5 mmHg was considered hypotony.

Surgical Technique

Following stabilization of the globe with a 6/0 vicryl traction suture placed in the superior limbus, a conjunctival flap was created based on the fornix. MMC was applied to the scleral surface at a concentration of 0.2 mg/mL for 2 min, then washed with at least 10 mL of saline solution in the MMC group. Hemostasis was achieved by cauterization when necessary. A half-thickness, 3x4 mm rectangular scleral flap was created. Paracentesis was performed through a side port opened with a 15° blade. Peripheral iridectomy was performed after removing a 1x2 mm corneoscleral block using Kelly punch. The scleral flap was closed at 2 corners with 10/0 nylon sutures and 1 releasable suture. After checking the aqueous drainage, additional sutures were placed when necessary. The conjunctiva was closed with 10/0 nylon sutures in the limbus and checked for leakage. In patients receiving retrobulbar TA, the procedure was concluded with the administration of 0.1-0.3 mL of 10 mg/mL TA into the retrobulbar through the floor orbital. In the 5FU group, 0.1 subconjunctival of 5FU (Curacil© Fluorouracil 500mg/10ml) was done after suturing the conjunctival flap.

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All patients were treated postoperatively with a topical antibiotic (levofloxacin 5 mg/ml) 6 times a day for 2 weeks and topical 1 mg Betamethasone dihydrogen phosphate disodium starting at 6 times a day for the first 2 weeks and decreasing each week for a total of 6 weeks.

Statistical Analysis

SPSS version 22.0 software was used in all statistical analyses. Numerical variables are expressed as mean ± standard deviation (SD). Categorical variables are expressed as frequency and percentage (%). The Saphiro-wilk was used to know the normality distribution of the data less than 50. The Wilcoxon test was used for dependent intergroup comparisons of numerical variables. Results with P values less than 0.05 were accepted as statistically significant.

Patients without any intraoperative metabolite (control group, n=5) were compared to those with retrobulbar TA (n=5), MMC group (n=19), and 5-FU group (n=11) in terms of surgical success. Successful surgery results were defined as IOP between 5 - 21 mmHg without any further medications or surgical intervention and fewer complications. Analysis of variance was used to compare statistical significance between pre- and postoperative IOP values.

RESULTS

Preoperative findings of 40 eyes of 35 patients (15 males, 25 females, mean age 52.4 years) were included in the study. The demographic data of the study group (n=19) and control group (n=21) are summarized in Table 1. Patient was observed until post-operation day (POD) 90. The pre-operative intraocular pressure until post operation day 90 was summarize in Table 2.

Table 1. Patients' demographic characteristics and preoperative findings

	Triamcinolon (N=5)	**Mitomycin-C (N=19)**	**5-Fluorouracil (N=11)**	**Without metabolite (N=5)**
Age (years) (mean ± SD)	56.40 ± 8.08	51.58 ± 19.06	51.91 ± 11.06	52.60 ± 8.08
Gender				
Male	2	8	4	5
Female	3	11	7	0
Glaucoma Type				
POAG (eye)	0	3	2	1
CCAG (eye)	1	6	2	1
PACG (eye)	4	8	5	3
Others (eye)	0	2	2	0
UCVA (decimal) (mean ± SD)	0.03 ± 0.04	0.18 ± 0.22	0.10 ± 0.19	0.14 ± 0.29
IOP pre operative (mmHg)	47.12 ±12.16	35.53 ± 17.05	34.54 ± 17.77	43.80 ± 15.79

Categorical data are given in number (%); numerical values are expressed as mean ± standard deviation (SD). POAG: Primary open angle glaucoma, CCAG: Chronic closed angle glaucoma, PACG: Primary angle closure glaucoma; UCVA: Uncorrected visual acuity, IOP: Intraocular pressure.

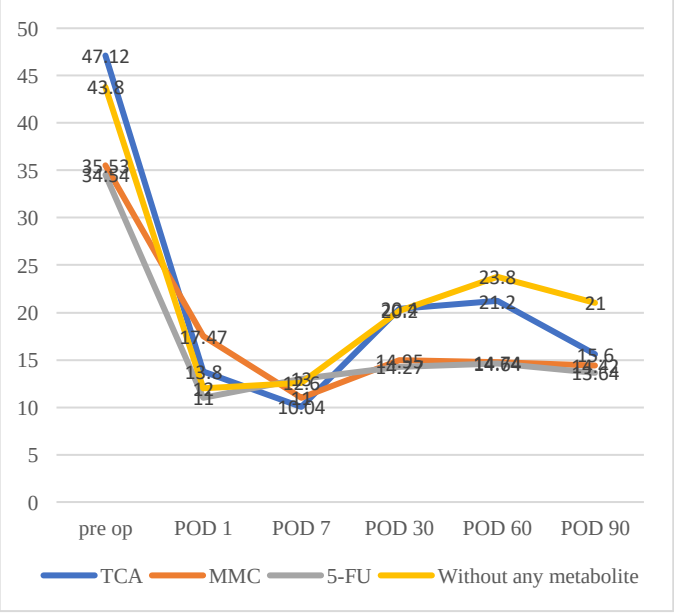
Table 2. The pre-operative intraocular pressure until post operation day 90

	IOP Pre Op (mmHg)	IOP POD 1 (mmHg)	IOP POD 7 (mmHg)	IOP POD 30 (mmHg)	IOP POD 60 (mmHg)	IOP POD 90 (mmHg)
TCA group	47.12 ±12.16	13.80 ± 7.85	10.04 ± 2.88	20.40 ± 14.84	21.20 ± 21.70	15.60 ± 4.61
MMC Group	35.53 ± 17.05	17.47 ± 11.81	11.00 ± 4.58	14.95 ± 5.92	14.74 ± 6.47	14.42 ± 5.71
5-FU group	34.54 ± 17.77	11.00 ± 4.33	13.00 ± 6.60	14.27 ± 5.06	14.64 ± 6.23	13.64 ± 4.08
Wihtout metabolite group	43.80 ± 15.79	12.0 ± 5.96	20.20 ± 6.07	20.20 ± 14.65	23.80 ± 12.32	21.00 ± 6.81

There were no significant differences of intraocular pressure at POD 1, 7, 30, 60, and 90 between control group compared to TCA, MMC, and 5-FU group.

Intraocular pressure pre- and post-operation in each group was significantly different (p<0.05). In TCA group, pre operative IOP was 47.12 ±12.16 mmHg then decreases to 15.60 ± 4.61 mmHg at POD 90. In MMC group, pre operative IOP was 35.53 ± 17.05 mmHg, 90 days later became 14.42 ± 5.71 mmHg. In 5-FU group, pre operative IOP was 34.54 ± 17.77 mmHg then decrease to 13.64 ± 4.08 mmHg. In group without metabolite, pre operative IOP was 43.80 ± 15.79 mmHg, then became 21.00 ± 6.81 mmHg at POD 90.

The lowest mean intraocular pressure of POD 90 was in 5-FU group (13.64 ± 4.08 mmHg) as shown in graph 1.



Graph 1. Intraocular pressure pre and post operation up to POD 90 in the groups

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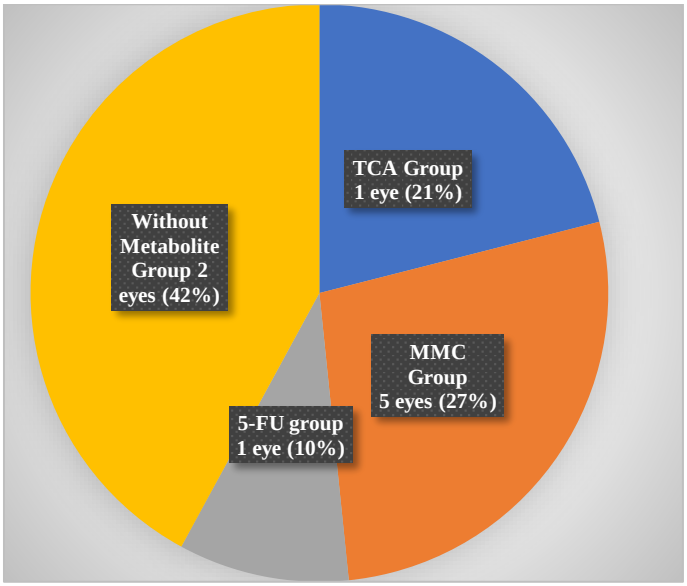

Graph 2. Complication in the groups

DISCUSSION

In the last 20 years, the use of antimetabolites has become increasingly popular. Ninety-three percent of antimetabolite users preferred using 5-FU in some cases rather than MMC (41%). This is in contrast with the United States, where MMC appears to be the preferred antimetabolite over 5-FU. The use of intraoperative MMC in first-time trabeculectomy ranged from 33 to 52% in 1996 and was found to be 68% in the 2002 Survey of the American Glaucoma Society.[16]

In this study, the intraocular pressure after trabeculectomy in control group were compared to TCA group, MMC group, and 5-FU group. The injection of retrobulbar TCA, application of MMC and subconjunctival injection of 5FU at the end of surgery did not result in any significant differences in lowering intraocular pressure rates in our study. At the final examination after follow-up period of 90 days, the IOP was 15.60 ± 4.61 mmHg in retrobulbar TCA group, 14.42 ± 5.71 mmHg in patients treated with MMC, 13.64 ± 4.08 mmHg and 21.00 ± 6.81 mmHg in the 5FU group and control groups, respectively. The final IOP patients in the study group was 18 mmHg or lower at final follow-up.

At the previous study, injection of TA retrobulbar was show statistically significant at POD 1 ,7, 30 and 90 without hypotensive drops. TA is commonly used in ocular disease and surgery, usually in the form of an intravitreal or sub-Tenon injection. TA applied intracamerally during pediatric cataract surgery has been reported to provide superior control of anterior segment inflammation and fewer inflammation related complications.[11,12] It has also been shown that the use of intracameral TA does not change the IOP profile or lead to major complications

in the postoperative period.[13,14]

Intraocular pressure pre- and post-operation in each group was significantly different (p<0.05). The lowest mean intraocular pressure of POD 90 was in 5-FU group (13.64 ± 4.08 mmHg). Complication after trabeculectomy in TCA group was 21%, MMC group was 27%, 5-FU group was 10%, and control group was 42%.

Further studies will be needed, in a prospective and randomized fashion, to better delineate the utility of steroids and anti-metabolite in increasing the efficacy of trabeculectomy procedures.

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