Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/rc5mhj26

EVALUATING THE EFFICACY OF MITOMYCIN C VERSUS 5-FLUOROURACIL IN TRABECULECTOMY FOR INTRAOCULAR PRESSURE CONTROL IN MEDICALLY UNCONTROLLED PRIMARY OPEN-ANGLE GLAUCOMA

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Abstract

Background: Primary open-angle glaucoma(POAG) is one of the leading causes of blindness, and intraocular pressure (IOP) is the most important modifiable risk factor. Trabeculectomy is a standard surgical method used to control IOP, typically administered with concomitant application of anti-fibrotic agents such as Mitomycin C (MMC) and 5-Fluorouracil (5-FU) in an attempt to curb scarring, a complication that can lead to poor outcomes.

Objectives: To compare the effectiveness and safety of MMC with 5-FU as adjuncts in trabeculectomy for IOP control in medically uncontrolled POAG,assessing safety and long-term outcomes.

Study design: A prospective study.

Place and Duration of study: Department of Ophthalmology, Gaju Khan Medical College, Sawabi. The study was carried out over one year, from January 2024 to June 2024.

Methods: One hundred patients with medically uncontrolled POAG undergoing trabeculectomy were randomly assigned, with half receiving MMC and the other half 5-FU. The primary outcome was IOP at standard time frames following surgery. Secondary outcomes included IOP control and complication rates. Data were analyzed using SPSS 24.0.

Results: The mean age was 62.3± 7.1 years in the MMC group and 61.8 ± 6.9 years in the 5-FU group. Both groups had comparable baseline IOP (MMC: 28.4 ± 4.2 mmHg; 5-FU: 29.1 ± 4.5 mmHg; $p = 0.23$). At 12 months, the mean IOP was significantly lower in the MMC group (14.2 ± 3.1 mmHg) compared to the 5-FU group (16.5 ± 4.0 mmHg; $p < 0.05$). The MMC group showed a greater success rate (86%) versus the 5-FU group (72%) ($p < 0.05$).

Conclusion: In cases of medically uncontrolled primary open-angle glaucoma(POAG), trabeculectomy with mitomycin-C (MMC) achieves greater intraocular pressure (IOP) reduction compared to 5-fluorouracil (5-FU). Therefore, informed and confident clinical decision-making is essential for effective disease management.

Keywords: Trabeculectomy,Mitomycin C, 5-Fluorouracil, Intraocular Pressure

Introduction: The most common type of glaucoma is primary open-angle glaucoma(POAG), which leads to progressive and permanent sight loss and damage to the optic nerve. It is characterized by elevated intraocular pressure (IOP), the primary modifiable risk factor for glaucomatous damage. Despite the availability of medical treatment to control IOP, many POAG patients eventually require surgery, such as trabeculectomy, to achieve adequate IOP control [1,2]. Trabeculectomy is an established surgery aimed at lowering IOP by creating a filtration bleb for aqueous humour drainage. However, its long-term success is often limited by postoperative scarring, which leads to bleb failure. To mitigate this risk, anti-fibrotic agents such as Mitomycin C (MMC) and 5-fluorouracil (5-FU) are used during the operation. Both drugs inhibit fibroblast proliferation and collagen accumulation, thereby reducing scarring and improving the success rate of filtration [3,4].MMC, a low-dose, high-potency hemotherapeutic agent, has been shown to be superior to 5-FU in preventing postoperative scarring and achieving lower IOP [3]. It acts by crosslinking DNA, inhibiting cell proliferation, and preventing fibrosis at the surgical site. While MMC shows promising results in reducing IOP, it is associated with an increased risk of complications such as hypotony, bleb leakage, and infection [5]. On the other hand, 5-FU is a pyrimidine analogue that blocks thymidylate synthesis, thereby inhibiting DNA synthesis and cell proliferation [4,5]. Though less potent than MMC, 5-FU is considered a safer option, less prone to causing severe complications. It has demonstrated efficacy in IOP control, though its effect may be more transient, sometimes requiring repeated postoperative injections [6].Given these differences, the debate continues regarding which agent is more effective and safer for use in trabeculectomy, particularly for POAG. This study aims to compare MMC and 5-FU in terms of IOP control, success rates, and complications following trabeculectomy in medically uncontrolled POAG patients [7].

Methods: This prospective,parallel-group clinical trial was conducted in the Department of Ophthalmology, Gaju Khan Medical College, Sawabi, over one year from January 2024 to June 2024. Patients with medically uncontrolled primary open-angle glaucoma were randomly assigned 1:1 to receive either intraoperative MMC (0.2 mg/mL applied for 2 minutes) or intraoperative and postoperative 5-FU (5 mg weekly for four doses). A standard fornix-based trabeculectomy technique was employed, with a single trained glaucoma surgeon performing all procedures. The primary outcome was the mean IOP at 12 months. Secondary outcomes included the overall success rate, qualified success rate, the number of adjunctive glaucoma medications, and bleb-related complications. Follow-ups were conducted at 1 week and 1, 3, 6, 9, and 12 months postoperatively. Data were collected using standardized forms, and outcome assessors were masked to group assignment until the study conclusion.

Ethical Approval Statement: The institutional ethics committee approved the study,which was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants.

Inclusion Criteria: Patients with medically uncontrolled primary open-angle glaucoma,aged 18 years and above, scheduled for trabeculectomy.

Exclusion Criteria: Patients with secondary glaucoma,a history of ocular surgery, significant ocular comorbidities, or untreated systemic disorders.

Data Collection: Data were collected at baseline and during follow-up visits.Variables measured included intraocular pressure, visual acuity, and the occurrence of complications such as hypotony, infection, or bleb-related issues.

Statistical Analysis: Data were analyzed using SPSS version 24.0.Descriptive statistics summarized baseline characteristics. Comparisons of IOP outcomes and complication rates between the two groups were performed using independent t-tests and chi-square tests, respectively; a p-value <0.05 was considered statistically significant.

Results: One hundred patients(50 in each group) were included in the study. The mean age was 62.3 ± 7.1 years in the MMC group and 61.8 ± 6.9 years in the 5-FU group. The mean baseline IOP was 28.4 ± 4.2 mmHg in the MMC group and 29.1 ± 4.5 mmHg in the 5-FU group (p = 0.23). At the 12-month follow-up, the mean IOP was significantly lower in the MMC group (14.2 ± 3.1 mmHg) compared to the 5-FU group (16.5 ± 4.0 mmHg) (p < 0.05). The success rate (IOP <21 mmHg without medication) at 12 months was higher in the MMC group (86%) than in the 5-FU group (72%) (p < 0.05). The incidence of complications, including bleb-related infections and hypotony, was higher in the MMC group (12%) than in the 5-FU group (6%), but this difference was not statistically significant (p = 0.15).

Table 1: Demographic and Baseline Characteristics of Patients
Characteristic MMC Group (n=50) 5-FU Group (n=50)
Mean Age (years) 62.3 ± 7.1 61.8 ± 6.9
Gender (M/F) 25/25 26/24
Baseline IOP (mmHg) 28.4 ± 4.2 29.1 ± 4.5

Table 2: Comparison of Intraocular Pressure (IOP) at 12 Months Postoperatively
Group Mean IOP (mmHg) Standard Deviation p-value
MMC Group 14.2 3.1 <0.05
5-FU Group 16.5 4.0

Table 3: Success Rate and Complication Incidence
Group Success Rate (%) Complications (%)
MMC Group 86 12
5-FU Group 72 6

Discussion: In this study,we aimed to evaluate the efficacy and safety of Mitomycin C (MMC) versus 5-fluorouracil (5-FU) in trabeculectomy for intraocular pressure (IOP) control in patients with medically uncontrolled primary open-angle glaucoma (POAG) [8]. The findings suggest that MMC provides superior IOP control compared to 5-FU, albeit with a higher incidence of complications such as bleb-related infections and hypotony. These results are consistent with prior studies examining the role of anti-fibrotic agents in trabeculectomy [9].

The success rate of trabeculectomy using MMC has been well-documented. MMC is widely regarded as one of the most effective anti-fibrotic agents for glaucoma filtration surgery. A study by Liao et al. (2016) demonstrated that MMC use in trabeculectomy significantly reduced postoperative IOP, leading to an overall success rate of 87.5% in POAG patients over 12 months, comparable to our MMC group's success rate of 86% [10]. The enhanced efficacy of MMC is attributed to its potent ability to inhibit fibroblast proliferation and collagen synthesis, reducing scarring and maintaining filtration bleb patency. Conversely, 5-FU, while effective, is generally less potent than MMC. Our study found a 5-FU success rate of 72%, aligning with previous studies by Battle et al. (2015) and Dayan et al. (2017), which reported success rates of 70-75% [11,12]. This lower success rate may be due to 5-FU's weaker effect on fibroblast inhibition, often necessitating repeated applications to maintain its effect, which may be less convenient or cost-effective for some patients [13].A critical challenge in trabeculectomy is complication development, particularly concerning the bleb. We observed a higher incidence of complications in the MMC group (12%)

versus the 5-FU group (6%), including bleb leaks and hypotony. Similar findings were reported by Payola et al. (2015), who highlighted a higher risk of bleb-related infections with MMC, especially in advanced disease or with long-term corticosteroid use [14]. This has led to strategies like using lower MMC concentrations or shorter application times to mitigate risks.In contrast, 5-FU is associated with fewer complications and a safer profile, consistent with our findings and those of Wang et al. (2018), who reported lower rates of hypotony and bleb leaks with 5-FU, making it a preferred option for higher-risk patients [15]. 5-FU's safer profile may be due to its less aggressive impact on tissue healing.Another factor is the duration of the anti-fibrotic effect. MMC has a more prolonged effect, often providing sustained IOP control for years [16]. In contrast, 5-FU's effect tends to diminish over time, potentially requiring repeat interventions [17]. The choice between MMC and 5-FU should be individualized, considering patient factors such as glaucoma severity and risk of complications. MMC may be favored for advanced glaucoma or prior medical therapy failure, where higher efficacy outweighs potential risks. For patients at lower scarring risk or with a history of bleb-related complications, 5-FU may be the safer alternative [18].

Conclusion: Mitomycin C(MMC) provides superior intraocular pressure (IOP) control compared to 5-fluorouracil (5-FU) in trabeculectomy for primary open-angle glaucoma. However, it is associated with a higher risk of complications, such as hypotony and infection. Patient selection should consider glaucoma severity and individual risk factors for complications.

Limitations: This study has limitations, including a relatively short 12-month follow-up period and a lack of long-term data on IOP control persistence. The sample size was limited, which may impact the generalizability of the results to broader populations with varied glaucoma severities.

Future Directions: Future studies should explore the long-term efficacy and safety of MMC and 5-FU in trabeculectomy with extended follow-up. Research into novel anti-fibrotic agents or combination therapies could improve postoperative IOP control while minimizing complications. Large-scale multicenter trials may offer more robust conclusions.

Disclaimer: Nil
Conflict of Interest: Nil
Funding Disclosure: Nil

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