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Bleb Morphology in MSICS with Trabeculectomy, with Subconjunctival Injection of Mitomycin C and 5-Fluorouracil with Respect To Conventional Subconjunctival Application – A Quasi Experimental Study At A Tertiary Care Center

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Abstract

Purpose: To compare the safety and efficacy of subconjunctival injection (MMC: 0.02%) to those with subconjunctival application of sponges soaked in Mitomycin C (MMC: 0.02%) and subconjunctival injection (5-FU: 0.1ml 0of 50 mg\ml) to those with subconjunctival application of sponges soaked in 5-Flurouracil (5-FU: 0.1ml 0of 50 mg\ml) intra-operatively in patients who underwent MSICS with trabeculectomy.

Methods: A total of 40 patients undergoing MSICS with trabeculectomy were randomized into four groups; for MMC the sponge group (10 eyes) received 0.02% MMC-soaked sponges, and the injection group (10 eyes) received subconjunctival injection of 0.02% MMC and for 5-FU the sponge group (10 eyes) received 0.1ML 5-FU-soaked sponges, and the injection group (10 eyes) received subconjunctival injection of 0.1ML 5-FU. The primary outcome was post-operative mean intra-ocular pressure reduction (IOP). The secondary outcomes were bleb morphology using Indiana Bleb Appearance Grading Score (IBAGS) and complications rates. These were compared at 1 week and 1, 3, and 6 months post-operatively. Complete success was defined as ≥30%

reduction in IOP without anti-glaucoma medications. **Results**: In sponge and injection groups, the mean pre-operative IOP was 29.1 ± 8.1 and 29.8 ± 8.8 mmHg, respectively. At 6 months, IOP in MMC (sponge group) and 5-FU(sponge) groups reduced by 65%(62%) (14 ± 3.6 mmHg, P < 0.001) and 50%(40%) (15.2 ± 4.1 mmHg, P < 0.001), respectively. Complete success was observed in 90.9% in the 5-FU group and 95.83% in the MMC group. Both groups had diffuse, shallow, relatively avascular blebs at 6 months using IBAGS. A few complications were seen in the sponge group during this period, which were not vision-threatening. **Conclusion**: Subconjunctival MMC injection is an effective, safe, convenient, and time-saving alternative to sponge-soaked delivery of MMC, and MMC continues to superior to 5-FU in maintainence the patency of filtring belb in MSICS with trabeculectomy.

Keywords: Filtering Blebs, Hyperemic, Subconjunctival Injection, Trabeculectomy

Introduction

Glaucoma is an ocular condition with multi-factorial etiology. The condition is most often bilateral. Progressive optic nerve damage resulting in blindness is the hallmark of untreated glaucoma. Intraocular pressure (IOP) is the only modifiable risk factor identified in the disease. Treatment modalities in glaucoma can be medical or surgical, both of which aim at lowering the IOP such that progressive loss of retinal ganglion cells (RGCs) is controlled and slowed down. At present, the first approach is use of topical medications that reduce either the production of aqueous humor or increase its drainage through the trabecular meshwork/uveo-scleral network. Failure to reduce IOP with maximal medical therapy (MMT) or loss of retinal ganglion cells loss despite MMT prompts an ophthalmologist to consider surgical intervention. At present, the gold standard approach in glaucoma surgery is trabeculectomy.

Trabeculectomy requires a track that diverts aqueous humour into the subconjunctival space thereby resulting in a filtering bleb which should ideally be diffuse and mildly elevated, with normal vascularity. To obtain such a good result, there should be a balance between aqueous production and drainage. The only modifiable risk factor in the management of glaucoma is the intraocular pressure (IOP) which is often achieved with medical therapy. Surgical treatment for glaucoma is usually considered when desired IOP control is not achieved with medical therapy or as a combined surgery along with cataract. Despite recent innovations in surgical treatment like glaucoma drainage devices or minimally invasive glaucoma surgeries, trabeculectomy is still the gold standard surgical treatment for glaucoma. Glaucoma filtering surgery is usually associated with an elevation of the conjunctiva over the sclerotomy site, that is the filtering bleb. Here, an alternate pathway is created for the exit of aqueous from the eye.

The morphologic characteristics of filtering blebs are variable. During the first week after trabeculectomy the conjunctiva and subconjunctival tissues are edematous and hyperemic. After several weeks the conjunctiva overlying the scleral flap usually shows the greatest elevation and a decreasing hyperemia. A late functioning bleb is slightly elevated, relatively avascular and show superficial microcysts – tiny spherical clear intraepithelial formations thought to indicate the current passage of aqueous across the conjunctival barrier. Poor filtration is indicated by increasing IOP and a bleb with one of the following appearances:

- Flat without vascularization.
- Vascularized bleb due to episcleral fibrosis.

- Encapsulated bleb, characterized by a localized, highly elevated, dome-shaped, fluid-filled cavity of hypertrophied Tenon capsule, often with engorged surface blood vessels

Filtering blebs can be described according to the following morphologic features: elevation, vascularization, and thickness of the wall, extent in clock hours, localized or diffuse, and presence or absence of micro cysts. However, this pathway is subject to various wound-healing processes. Though trabeculectomy has been reported to have an excellent initial success rate, about 30% of them fail in 3 years, and nearly 50% fail in 5 years. The most significant risk of failure still seems to be wound scarring, especially episcleral fibrosis, leading to bleb failure.

Wound healing occurs through three important overlapping phases: inflammatory, proliferative, and remodeling. The fibroblast is the effector cell and a key determinant of sub-conjunctival or episcleral fibrosis. This wound-healing response can be modified by using various anti-scarring agents, both in the intraoperative and postoperative periods. The most commonly employed agents include mitomycin C (MMC), 5-fluorouracil (5-FU), anti-vascular endothelial growth factors (anti-VEGF) such as bevacizumab. Each of these agents has its own risks and benefits. Careful selection of anti-scarring agents is critical in achieving the delicate balance between excess filtration and scarring that allows for appropriate IOP control. However, in literature, we found no studies prospectively evaluating the relationship between the postoperative bleb morphology and the intraocular pressure (IOP) with comparative use of different anti-scarring agents mentioned above.

The main purpose of this study was to prospectively study the effect of the postoperative morphologic appearance of filtering blebs on the IOP with use of different anti-scarring agents mentioned above.

Aims And Objectives

- To study safety and efficacy of subconjunctival use of MMC and 5-FU.
- To determine IOP reduction at 1 week,1 month ,3 months ,and 6 months postoperatively.
- To study the Bleb characteristics using the Indiana Bleb Appearance Grading Scale at 1 week, 1 month, 3 months and 6 months.
- To determine the success of surgery in terms of the necessity to use additional topical anti glaucoma at 3 months.
- To observe the rate of complications (hyphema, bleb leak, choroidal detachment, hypotony, blebitis, endophthalmitis) in post-operative period.

Material and Methods

Study Design – Quasi Experimental study

Study center – Dr. Shankarao Chavan Government Medical College, Vishnupuri. Nanded

Study population source - Patients visiting in Dr. Shankarao Chavan Government Medical College, Nanded.

Sample size - Complete enumeration method, we studied all cases which occurred in data collection period with consideration of inclusion and exclusion criteria.

Convinient Sampling method - Purposive Sampling

Ethical Consideration: The study will be conducted after obtaining permission from the Institutional Ethics committee and department of ophthalmology.

Confidentiality: All the data collected as a part of this study will be kept strictly confidential and used for the

purpose of the study only.

Consent: The patients were informed about the design of the study and procedure, and written consent was obtained from all patients.

The study will be conducted in tertiary care hospital.

Ophthalmic history will be taken regarding the onset, course and duration of diminution of vision, history of drug intake for eye diseases, and history of previous eye surgery

Medical history was also taken regarding diabetes mellitus, hypertension, autoimmune disease (such as rheumatoid arthritis), cardiac diseases, and other relevant medical conditions.

Preoperative examination included uncorrected visual acuity (UCVA), refraction, best-corrected visual acuity (BCVA), colour vision testing, pupillary light reflex testing, slit-lamp examination of anterior segment, intraocular pressure measurement by the Goldman explanation tonometer, and posterior segment examination.

A keratometer will be used to detect the steepest and flattest meridian, and the difference between them will be the amount of corneal astigmatism and its axis will be the axis of the steepest meridian.

The information will be reviewed an documented in this study included patients' sex, age, preoperative and postoperative UCVA and BCVA, preoperative clinical diagnosis, preoperative Visual acuity measurement with the help of Snellen's Chart for distant vision all surgeries will be done by single surgeon.

- Visual acuity with pinhole.
- Sac syringing.
- Intra ocular pressure.
- Examination of anterior segment of eye with a slit lamp.
- Examination of fundus with direct and indirect ophthalmoscope.
- Keratometry.
- Autorefractometry.
- USG B scan as per indication

Probable Duration for the study completion – 18 months

Methodology in brief - MMC is available as a lyophilized powder of 2mg concentration, which is diluted with 10 ml balanced salt solution (BSS) to obtain a concentration of 0.2 mg/mL.[8] All procedures and surgeries were performed by a single highly trained glaucoma surgeon (R.N.W.). Patients randomized to the subconjunctival injection group received a subconjunctival injection of MMC (0.15 mL, 0.2 mg/mL, 30 µg total) at least 8 mm posterior to the limbus and just temporal to the superior rectus muscle using a 30-gauge needle in the preoperative area immediately before transportation to the operating room. The injected fluid was distributed nasally, temporally, and toward the limbus by gentle digital massage applied over the eyelid. Whereas in the sponge group the MMC drug absorbed weck-cels sponges were kept in contact with the same area for 2 mins.[9]

5-FU is available in ampoules, in the concentration of 50 mg/mL. 5-FU on the contrary acts as a competitive inhibitor of DNA formation and also by inhibiting thymidine synthetase, thus preventing the incorporation of thymidine into new DNA 5-FU therefore, needs to be applied repeatedly. It can be applied intraoperatively in the same way as MMC using weck-cel or PVA sponges on the episcleral surface, in a dose 0.1 ml of 50 mg/mL for 2 min.[10] It is often used in the form of repeated subconjunctival injections in the postoperative period, especially when the bleb shows signs of failure. It is

used as 5 mg in 0.1 mL and is injected 180° away from the bleb, with a maximum dosage of 25–50 mg. [11]

All patients underwent trabeculectomy with slight modifications in technique. 5-FU (50 mg/ml) subconjunctival injection was given between the conjunctiva and sclera, whereas in the sponge group drug absorbed weck-cels sponges were kept in the same area for 2mins. The area was then washed with 20 ml of balanced salt solution.

After which all groups folled a standard procedure as below. A fornix-based conjunctival flap was dissected. This was followed by dissection of a triangular or rectangular scleral flap. The exact dimensions of the scleral flap varied according to surgeon. A corneal tunnel was made. 2 Sideport incision made at 3 O'clock and 9O'clock. Trypan blue dye instilled, visco injected. Entry made into anterior chamber with keratome. Continuous curvilinear capsulorhexis done. Nucleus prechopped into two halves using Dr. Sohel Khan's Prechopper and delivered using viscoexpression. Pciol implanted and dialled. Irrigation and aspiration of the cortex done. Sideport hydrated. After the excision of a block of corneo-scleral tissue using a GASS punch, a peripheral iridectomy was done and the scleral flap was closed with one to five 10/0 nylon sutures. The conjunctival flap was closed with 6-0 vicyrl. Subconjunctival dexamethasone 1% and an antibiotic were given postoperatively. Patients used a topical steroid–antibiotic combination for at least 4 weeks postoperatively.

All surgeries were performed by highly trained glaucoma surgeon.

Inclusion Criteria

All cases attending ophthalmology OPD and casualty with Cataract and Glaucoma must understand the study and agree to participate which may include:

1. Patients older than 18 years of age.
2. Patients with medically uncontrolled glaucoma.
3. Patients with no previous incisonal glaucoma surgery.
4. Secondary glaucoma (uveitic, aphakic, post keratoplasty)
5. Failed trabeculectomy.
6. High preoperative IOP more than 35 to 40 mm Hg at presentation. However primary angle closure glaucoma (PACG) patients prior to peripheral iridotomy are an exception to this rule. If high pressures persist after a patent iridotomy, only then should MMC be considered for primary use in PACG eyes.
7. Patients with Cataract and glaucoma and with significant visual loss and uncontrolled IOP.

Exclusion Criteria

1. Patients with no light perception vision.
2. Patients with normal tension glaucoma and NVG glaucomas, secondary glaucoma other than PXF glaucoma.
3. Previous glaucoma surgery.
4. Patients with history of trauma.
5. Pregnant or nursing women.
6. Iris neovascularization or proliferative retinopathy.
7. Iridocorneal endothelial syndrome.
8. Chronic or recurrent uveitis.
9. Steroid-induced glaucoma.
10. Pathologic myopia or myopia of 6.00 diopters or greater.

11. Unwillingness or inability to give consent, or inability to return for scheduled protocol visits.
    Only one eye from eligible patients was included in the study.

Withdrawal & Drop-Out Criteria

The participants can withdraw anytime during study period.

1. Patients unwilling forgiving their consent
2. Patients who initially give their consent for the study but later on did not continue to follow up.

Statistical analysis

Collected data would be entered in MS Excel. Quantitative data expressed in mean and standard deviation. Non normal data expressed in Median and Inter quartile range. Qualitative data expressed in frequency and percentage. Use appropriate test of significance (statistical test). If data do not follow normal distribution, use Mann Whitney U test. If p

Details of Investigational Product

1. Mitomycin – C

MMC has been used in various concentrations ranging from 0.1 - 0.5mg/ml (0.01 to 0.05%), with 0.2 mg/ml (0.02%) being the most commonly used concentration.

The duration of application of MMC ranges from 1-5 minutes.

The efficacy of use of MMC is dependent on numerous factors, which includes concentration of MMC used, surface area of exposure, duration of exposure and other tissue-related factors.

The method of MMC application using either subconjunctival sponge, sub-scleral flap sponge or subconjunctival injection influence the effectiveness and contributes to the morphology of the filtering bleb and its long-term survival.

2. 5- Fluorouracil

5-FU is used 0.1ml in the concentration of 50 mg/mL in the same way as MMC.

Result

In order to establish uniform clinical grading system of a trabeculectomy bleb, and to aid early recognition of bleb failure and to predict long term success of a trabeculectomy bleb, three bleb morphology grading systems are currently used in practice. They include

- the Indiana Bleb Appearance Grading scale (IBAGS)
- Moorefield's bleb grading system and
- The Wuerzburg classification.

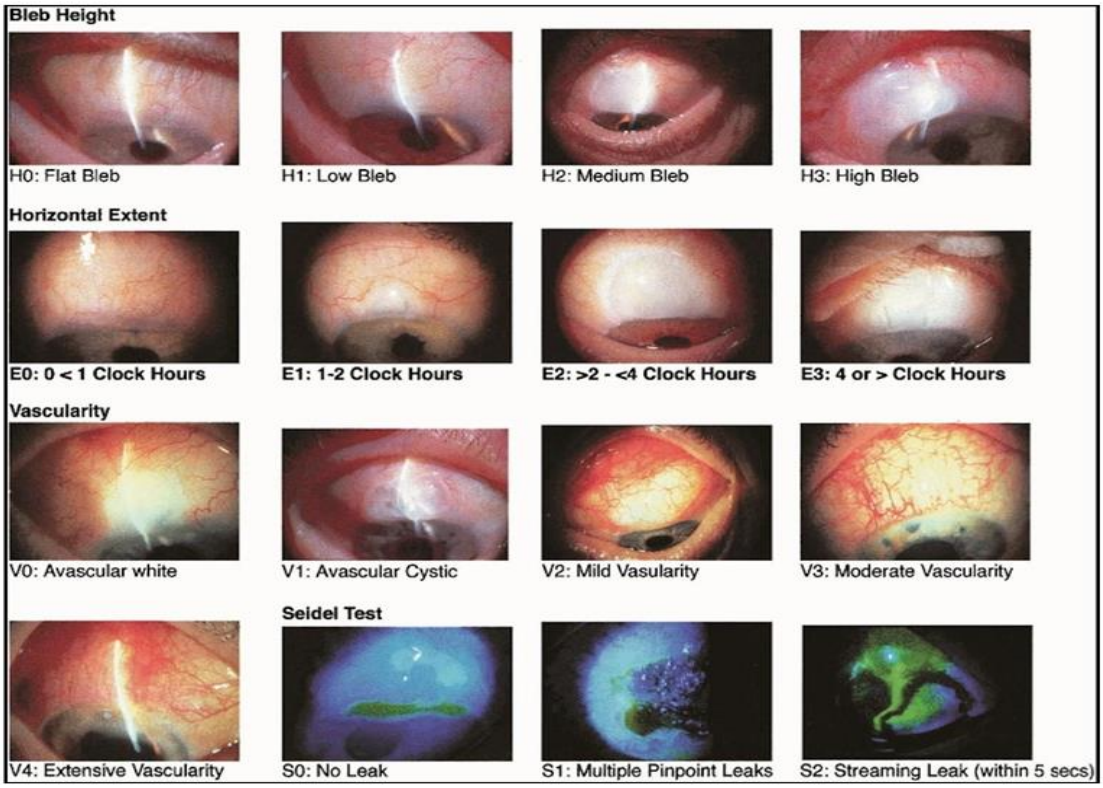
(For the purpose of this study, the IBAGS system of assessing bleb morphology was used.)

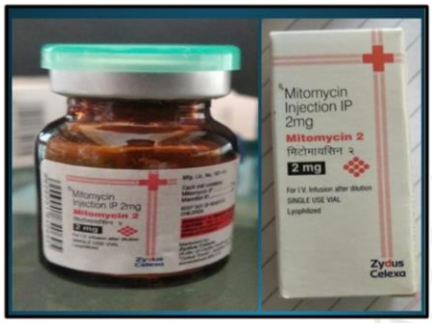
Indiana Bleb Grading System

This classification system characterizes the bleb using four criteria

i.e. Bleb height (H), Bleb extent (E), Bleb vascularity (V) and Seidel test (S)

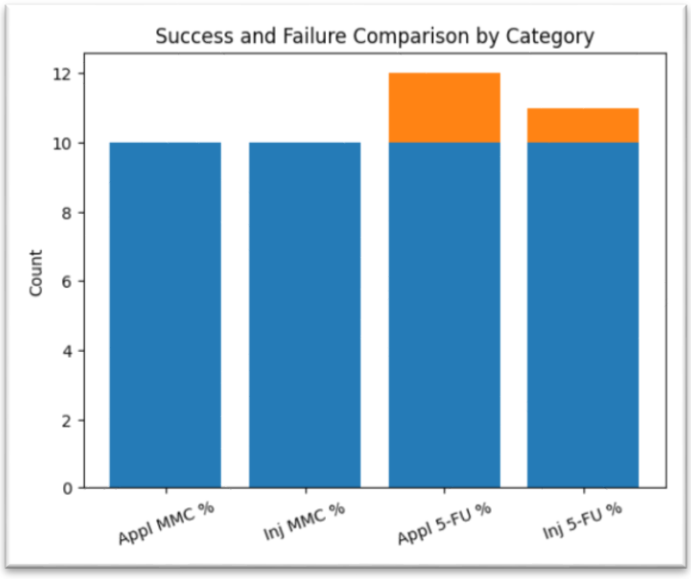
The height is graded as H0-H3 and is assessed based on the highest point of the conjunctival bleb from the scleral surface. The bleb extent is graded at E0-E3, Vascularity is graded as V0-V4 and it represents the extent of superficial and deep vessels visible over the site of the filtration bleb. Peri bleb conjunctival vessels are not considered for classification of vascularity. Seidel test is graded from S0-S2. It is used to assess the presence or absence of bleb leak.





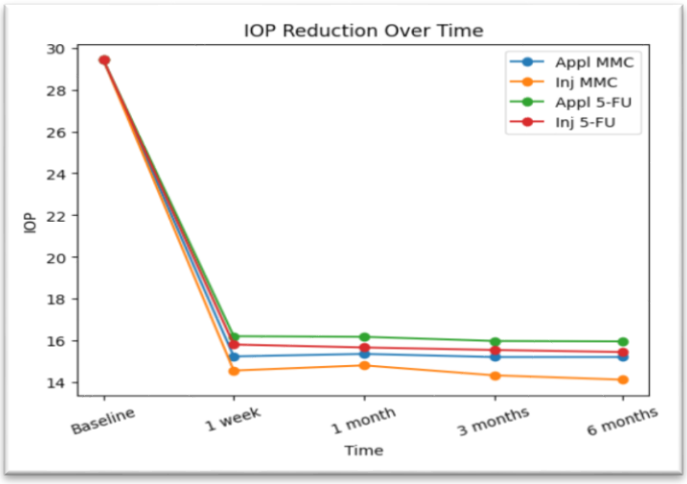
Success and Failure at the End of 6 Months

		Subconj. Appl of MMC %	Subconj. Inj. Of MMC %	Subconj. Appl of 5-FU %	Subconj. Inj. Of 5-FU %
6 Months	Success	10	10	8	9
	Failure	0	0	2	1
	Total- 40	10	10	10	10



The baseline IOP was compared with post operative IOP. at 1 week, 1 month, 3 months and 6 months postoperatively

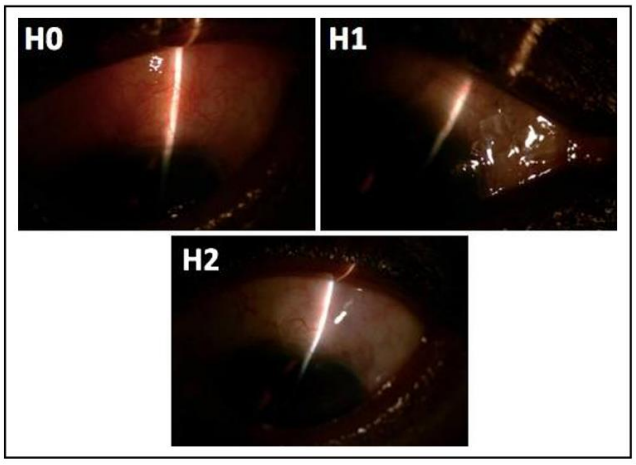
IOP	Subconj. App of MMC	Subconj. MMC Inj.	Subconj. App of 5-FU	Subconj. 5-FU inj
Baseline	29.42 +/- 5.48	29.42 +/- 5.48	29.42 +/- 5.48	29.42 +/- 5.48
1 week	15.24 +/- 1.64	14.56 +/- 1.78	16.21 +/- 1.71	15.81 +/- 1.67
1 month	15.36 +/- 1.53	14.81 +/- 1.26	16.18 +/- 1.64	15.67 +/- 1.26
3 months	15.21 +/- 1.47	14.33 +/- 1.14	15.98 +/- 1.21	15.55 +/- 1.18
6 months	15.21 +/- 1.37	14.12 +/- 0.99	15.96 +/- 1.32	15.45 +/- 1.01

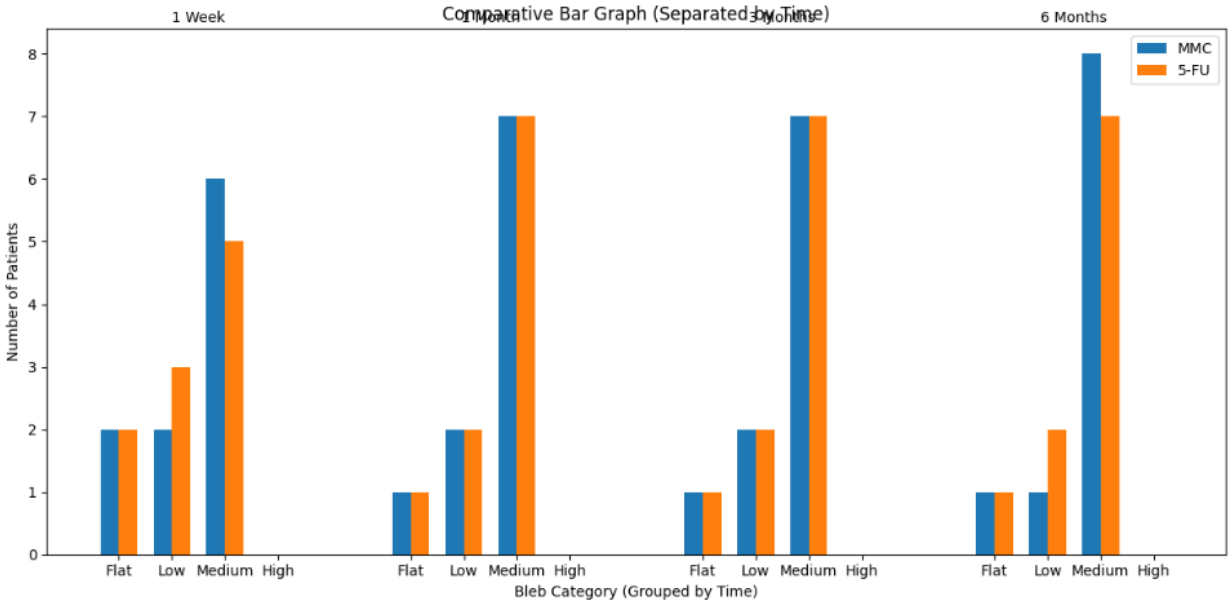


Grading of Bleb Height Using IBAGS Classification At 1 Week, 1 Month, 3 Month, And 6 Month

Bleb height	Subconj. MMC Inj. (Subconj. Appl of MMC)				Subconj. 5-FU Inj. (Subconj appl of 5-FU)			
	At 1 week	At 1 month	At 3 months	At 6 months	At 1 week	At 1 month	At 3 months	At 6 months
Total Patients	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)
0 – Flat bleb	2 (2)	1 (2)	1 (2)	1 (2)	2 (3)	1 (2)	1 (2)	1 (2)
1- Low Bleb	2 (3)	2 (3)	2 (3)	1 (2)	3 (4)	2 (4)	2 (3)	2 (3)
2 – Medium bleb	6 (5)	7 (5)	7 (5)	8 (6)	5 (3)	7 (4)	7 (5)	7 (5)
3 – High Bleb	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

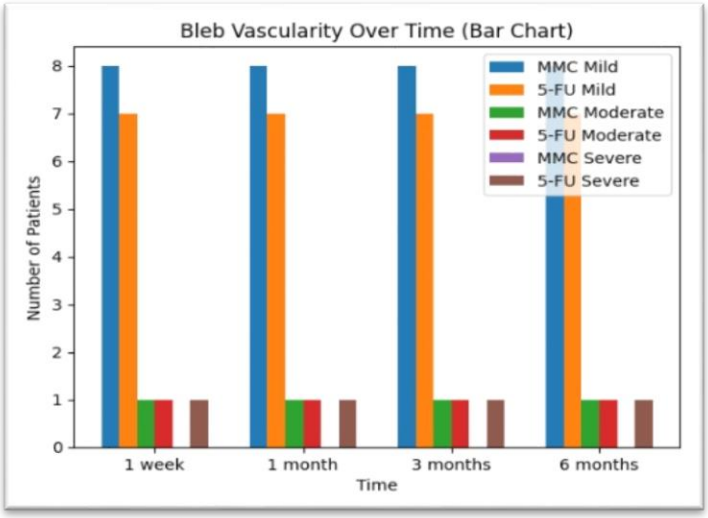
1) BLEB HEIGHT



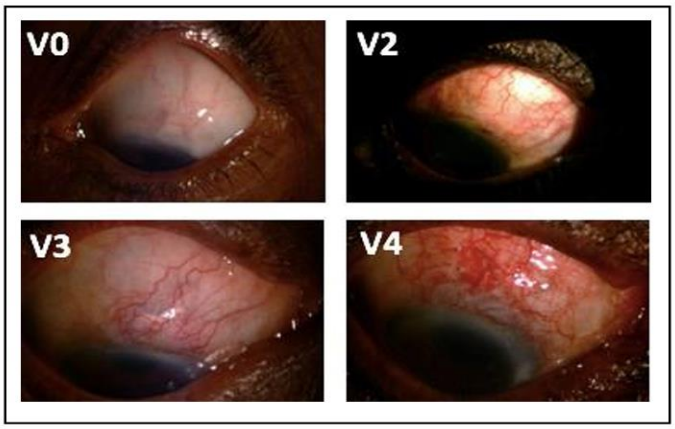


Bleb Vascularity Using IBAGS Classification at 1 Week, 1 Month, 3 Months And 6 Months

Bleb Vascularity	Subconj. MMC Inj. (Subconj. Appl of MMC)				Subconj. 5-FU Inj. (Subconj appl of 5-FU)			
	At 1 week	At 1 month	At 3 months	At 6 months	At 1 week	At 1 month	At 3 months	At 6 months
Total Patients	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)
0- Avascular white	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
1- Avascular Cystic	1 (2)	1 (2)	1 (2)	1 (2)	1 (2)	1 (2)	1 (2)	1 (2)
2- Mild Vascularity	8 (7)	8 (7)	8 (7)	8 (7)	7 (6)	7 (6)	7 (6)	7 (6)
3- Moderate Vascularity	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
4- Severe vasuclarity	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	1 (1)	1 (1)

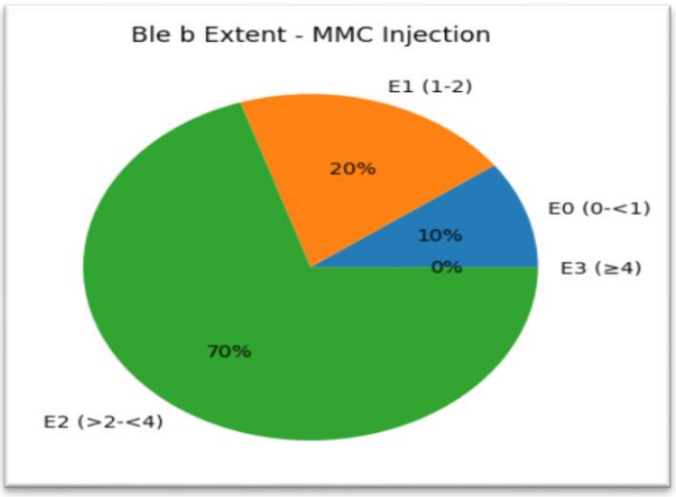


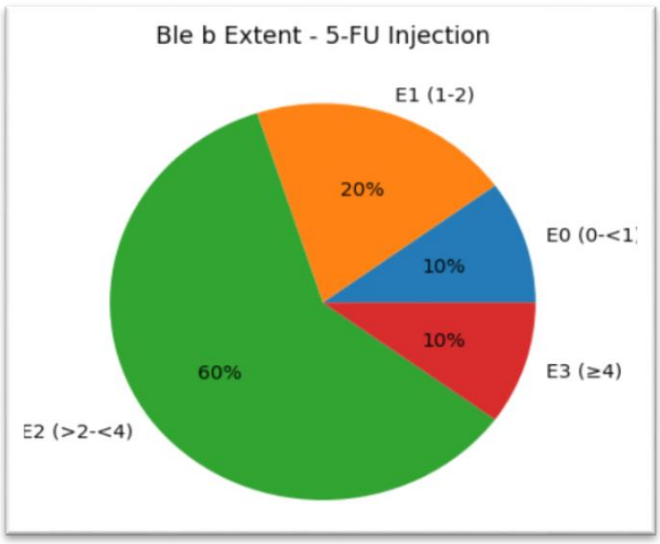
3) BLEB VASCULARITY



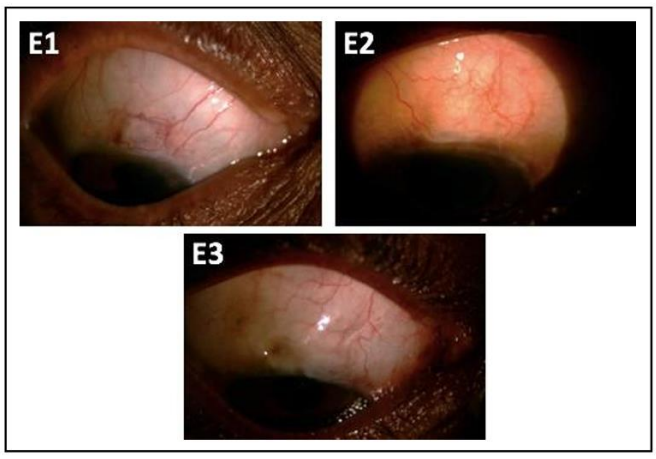
Bleb Extent Using IBAGS Classification at 1 Week, 1 Month, 3months and 6 Months

Bleb Extent	Subconj. MMC Inj. (Subconj. Appl of MMC)				Subconj. 5-FU Inj. (Subconj appl of 5-FU)			
	At 1 week	At 1 month	At 3 months	At 6 months	At 1 week	At 1 month	At 3 months	At 6 months
Total Patients	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)
E0: 0 to <1	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
E1: 1 to 2	2 (3)	2 (3)	2 (3)	2 (3)	2 (3)	2 (3)	2 (3)	2 (3)
E2: >2 to <4	7 (6)	7 (6)	7 (6)	7 (6)	6 (5)	6 (5)	6 (5)	6 (5)
E3: 4 or >	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	1 (1)	1 (1)



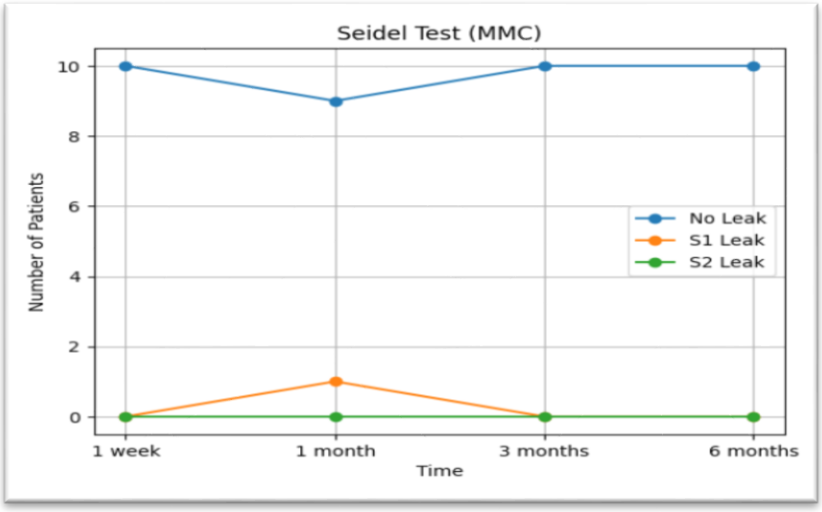


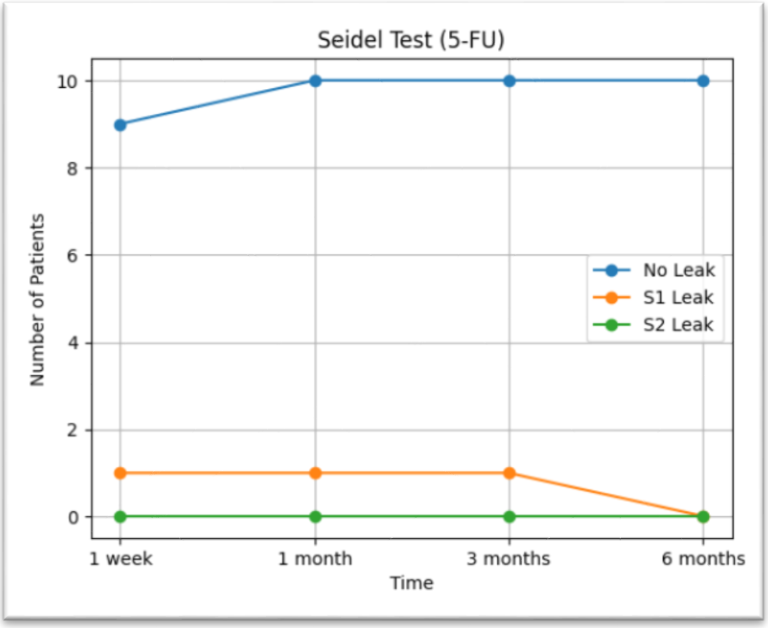
2) BLEB EXTENT



Seidel Test Grading Using IBAGS Classification At 1 Week, 1 Month, 3 Months And 6 Months

Seidel test	Subconj. MMC Inj. (Subconj. Appl of MMC)				Subconj. 5-FU Inj. (Subconj appl of 5-FU)			
	At 1 week	At 1 month	At 3 months	At 6 months	At 1 week	At 1 month	At 3 months	At 6 months
Total Patients	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)	10 (10)
S0: No Leak	10 (9)	9 (9)	10 (10)	10 (10)	9 (7)	9 (8)	9 (8)	10 (9)
S1: Multiple pinpoint leaks	0 (1)	1 (1)	0 (0)	0 (0)	1 (2)	1 (2)	1 (2)	0 (1)
S2: Streaming leak (within 5 sec)	0 (0)	0 (0)	0 (0)	0 (0)	0 (1)	0 (0)	0 (0)	0 (0)



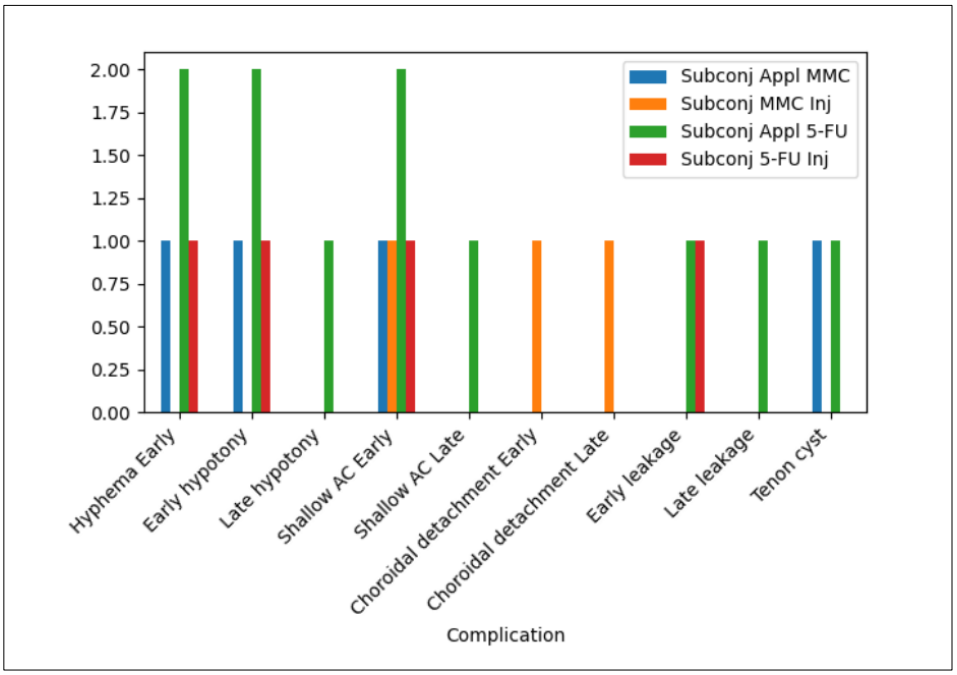


Complications Present

MMC blebs are often thin walled and avascular, with higher incidence of transconjunctival filtration through the thin wall of the bleb. This can also lead to development of bleb related endophthalmitis as it may act as a conduit for micro-organisms to gain entry into the eye. Thin blebs can lead to ocular hypotony as a result of inadequate resistance to the outflow of aqueous humor. Ocular hypotony may lead to development of choroidal effusion, hypotonic maculopathy, retinal hemorrhages, anterior chamber shallowing with increased likelihood of endothelial cell decompensation. Other complications related to the use of MMC with trabeculectomy published in the literature include scleromalacia, scleritis, corneal endothelial toxicity. The most frequent complication encountered was superficial punctate keratopathy, followed by shallowing of the anterior chamber, choroidal detachment, and hyphema which was managed conservatively. The conventional method of applying MMC and 5-FU sponge has been associated with specific complications such as losing sponges in the orbit, breaking off of a sponge fragment and accidental retention of the broken fragment, which may result in scleral necrosis and perforation with related complications.

Complication	Subconj. Appl of MMC	Subconj. MMC Inj.	Subconj appl of 5-FU	Subconj. 5-FU Inj.
Hyphema Early	1	0	2	1
Early hypotony	1	0	2	1
Late hypotony	0	0	1	0
Shallow anterior chamber Early Late	1 0	1 0	2 1	1 0

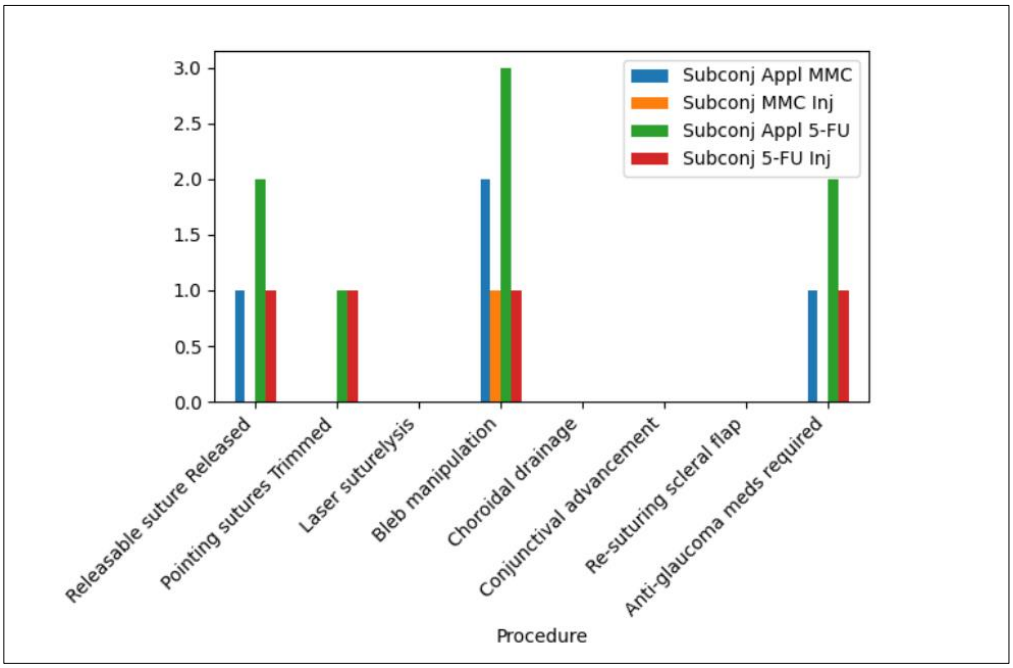
Choroidal detachment Early Late	0 0	1 1	0 0	0 0
Early leakage	0	0	1	1
Late leakage	0	0	1	0
Tenon cyst	1	0	1	0

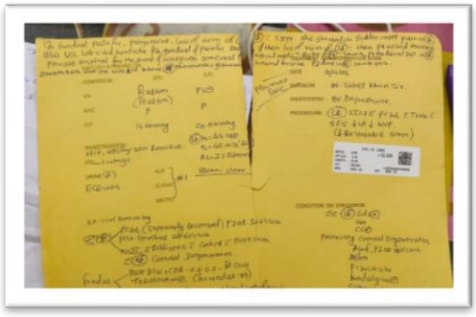


Post-Operative Additional Procedures

Post Operative Procedures	Subconj. Appl of MMC	Subconj. MMC Inj.	Subconj appl of 5-FU	Subconj. 5-FU Inj.
Releasable suture Released	1	0	2	1
Pointing sutures Trimmed	0	0	1	1
Laser suturolysis	0	0	0	0
Bleb manipulation	2	1	3	1
Choroidal drainage	0	0	0	0
Conjunctival advancement	0	0	0	0
Re-suturing of scleral flap	0	0	0	0
Anti-glaucoma medications required	1	0	2	1

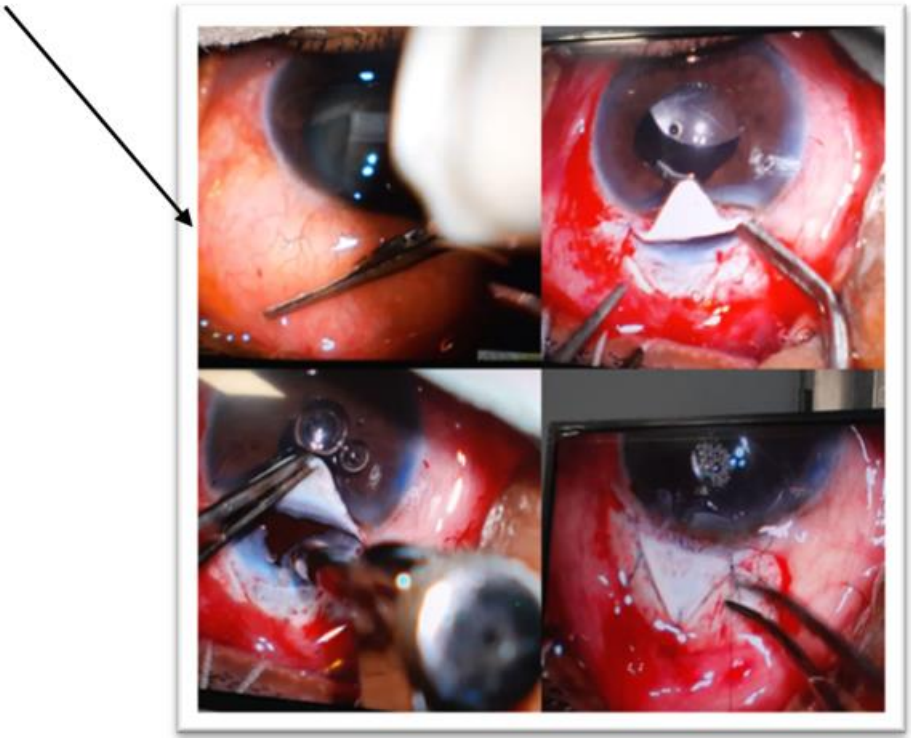
Releasable sutures were taken in patients with chronic angle closure glaucoma.



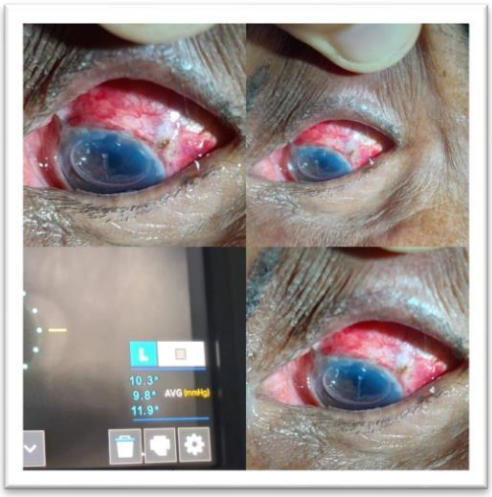


PT. With Subconj. INJ. OF MMC

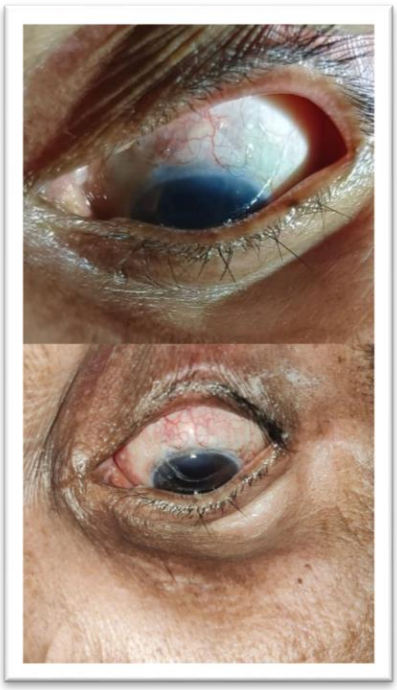
Subconjunctival INJ. OF 5-FU



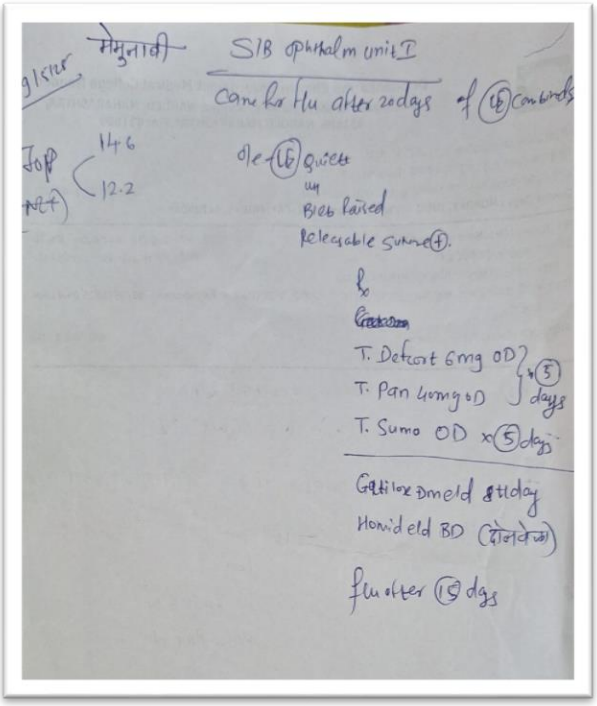
Intraoperative Pictures of Pt. With Use of 5-Fu



Post Op Day 1



Post Op Day 7



Post Op Day 30 (1 Month)

Discussion

MMC soaked sponges applied under the conjunctival space is the most widely used method of patients undergoing trabeculectomy[6,7]. The application of MMC should involve MMC delivery in a broader area, to help achieve a diffuse and ideal functional filtering bleb. With the use of MMC and 5-FU soaked sponges the volume of MMC and 5 -FU delivered at the desired area may differ depending on the size of the sponges used, number of sponges used, the amount of soakage of the sponge and adequate coverage of the sub-conjunctival area. These factors may influence the morphological and functional characteristics of the filtering bleb. Additionally although rare, this method has been associated with the dreaded complication of losing the sponge into the orbit, and its sequelae. Hence, it is considered important to standardize the surgical procedure using a technique which can be exactly replicated and also ensure delivery of uniform dosage and concentration of MMC and 5-FU. By giving sub-conjunctival injection, drug delivery is more widespread and its exact amount and concentration can be controlled, thereby theoretically providing an improved filtering bleb morphology and functionality. In this study, we seek to compare the two modes of delivery of MMC and 5-FU during trabeculectomy with MSICS surgery. Patients diagnosed to have either POAG, CACG, PACG or combined mechanism glaucoma with cataract planned to undergo trabeculectomy with MSICS with subconjunctival injection of MMC and 5-FU. All patients in this study underwent surgery. The concentration of MMC used was 0.02% (0.2mg/ml) and 5-FU was 0.1ml of 50mg/ml and the surgical procedure was uniform throughout the study duration. All patients were followed up as per regular post- operative follow up schedule, and if needed more frequent follow-ups

were advised, based on the glaucoma specialist's clinical judgment. As per study protocol, patients were examined at 1 week, 1, 3 months and 6 months post-surgery. At each follow-up bleb images were taken by the PI.

The blebs were graded clinically as per the Indiana Bleb Appearance Grading Scale by the PI at each of the assigned follow-up visits. In the follow up period the need for injection 5- FU, additional needling procedure, decision on either releasing the releasable suture or trimming it was assessed and executed based on the IOP and bleb appearance. Patients showed decrease in IOP following trabeculectomy. Although, the IOP on follow-up was significantly lower than the baseline IOP. In result produced significant reduction in IOP on follow-up when compared to baseline. We defined 'Complete Success' of surgery as more than or equal to 30% reduction in IOP without anti-glaucoma medication at each study visit. Those with less than 30% reduction in IOP without anti-glaucoma medications were considered failure. Post-operative hypotony was defined as IOP less than 6.0 mm Hg. Though there seems to be a better success rate at 3 months follow-up , the difference was not statistically significant. At 3 months follow-up the blebs had low height, mild vascularity and diffuse extent. This result is in accordance with the data published by Pakravan et al., who also classified blebs as per IBAGS and showed that the blebs in the injection tend to assume a more diffuse, shallow and less vascular characteristic at 6 months' follow-up. The 6 months and 1 year follow up on our patients will give us a better idea of any difference in bleb morphology. Analysis of the bleb morphology over a period of 6 months showed 22.5% patients had flat bleb at 1 week, which reduced to 15% at 6 months. 20% patients had low bleb at 6 months' follow-up. 65% of patients had medium bleb height at 6 months although these results were statistically insignificant. The extent of the bleb at 1 week, 1 month, 3 months and 6 months was found to be of the E2 grade (bleb extent from more than 2 to less than 4 clock hours) in majority of the patients. 70% had mild vascular blebs at 1 week. This bleb morphology changed over the course of follow-up. At 6 months, majority of the patients had blebs with mild vascularity (70%).

Our results show that, the appearance as well as functionality of the filtering bleb is good. In the 5-FU group One showed presence of hyphaema which was managed conservatively. One showed early hypotony and one early shallow anterior chamber. At 3 months' follow-up, none of the patient had any conjunctival or bleb leak. One patient had shallow anterior chamber in the early post-operative period in both groups. One patient showed presence of early leakage from the conjunctival edge. One patient was found to have choroidal detachment in the subconjunctival injection group of MMC. None Of these two patients had bleb leak at 1month follow up .1 patient developed tenon cyst at 3 months follow up in both in application of antimetabolite group. The complications were too small to be analyzed statistically.

Releasable suture release is a common procedure in the post-operative management of filtering blebs. Five patients underwent release of the releasable suture .This result may indicate a minimally better bleb morphology attained after MMC injection use, that defers the need to improve further aqueous outflow by removing a suture. Two patients had pointing sutures causing discomfort to patients which were trimmed. During the 3 months' follow-up period, bleb manipulation was required in 1 patients 5-FU injections and in one patient in MMC

subconjunctival injection group, also bleb manipulation was demonstrated to patient and their relatives.

One patient of 5- FU subconjunctival Injection Required anti glaucoma drugs at the end of 6 months with none in MMC injection group. Although statistically insignificant, this outcome can be considered clinically relevant in the management of glaucoma.

Conclusion

In conclusion, subconjunctival injection of MMC (0.02%) and 5-Fu injection is a safe, effective convenient in combined manual small incision cataract and glaucoma surgeries. MITOMYCIN C WAS FOUND TO BE SUPERIOR TO 5-FU and helps in longtime maintenance of patency of filtering bleb WHEN USED IN THE FORM OF SUBCONJUNCTIVAL INJECTION.

Limitations

Limitations of the Study: Lack of endothelial cell count study and lack of long term follow ups.(> 6 months)

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