

5-Fluorouracil as an Adjunct in Glaucoma Filtration Surgery in Younger Age Group

Norin Iftikhar Bano, Tariq Mehmood Qureshi, Muhammad Tariq Khan, Harris Muzammil Ansari

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See end of article for authors affiliations

Correspondence to:
Norin Iftikhar Bano
LRBT Free Eye & Cancer
Hospital
436-A/I, Township
Lahore

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Purpose: To evaluate efficacy and complication of 5-Fluorouracil (5-FU) as an adjunct in trabeculectomy in young age group.

Material and Methods: 86 eyes of 62 patients were included in the study. There were 48 male patients (55.81%) and 38 female patients (44.18%). Age of patients were two year to fifteen year. Duration of study was four years with average follow up of two years.

Study was conducted at LRBT Eye Hospital Lahore. Trabeculectomy was performed with conventional method. First subconjunctival injection of 5-FU (50mg/0.2ml) was given at the end of the procedure, second at the end of 1st week and the third at the end of 2nd week. Additional 1-2 injections of 5-FU were given in more resistant cases.

Results: Target IOP was achieved in 83 (96.51%) of patients, 2 (2.32%) patients were given additional medication to achieve target IOP and 1 (1.16%) did not achieve target IOP. Visual acuity remained stable in 69 (80.23%) patients, improved in 13 (15.12%) patients, while it deteriorated in 4 (4.65%) patients due to late complications. Cup-to-disc ratio reversal was seen in 30% patients up to 14 years of age

Choroidal detachment occurred in 8 (9.30%) patients and was successfully treated with cycloplegics and pressure patching. Choroidal drainage was done in only one patient. Thin bleb was seen in 4 (4.65%) patients. Blebitis occurred in 1 (1.16%) patient that led to endophthalmitis. 2 (2.32%) patients had retinal detachment. Redo-trabeculectomy was done in 3 (3.48%) cases.

Trabeculectomy is a surgical procedure that lowers intraocular pressure (IOP) by creating a fistula which allows aqueous outflow from the anterior chamber to the sub-tenon space. This fistula is protected or guarded by a superficial scleral flap¹.

The surgical trabeculectomy has been prototype glaucoma filtering procedure over the last three decades². Primary trabeculectomy is still a preferred surgical approach all over the world for cases in which a larger reduction in IOP is the aim of treatment, especially when high IOP persists, despite maximum tolerable anti-glaucoma medication^{3,7}.

At times, certain co-existing risk factors (e.g. young age, uveitis, trauma) can result in failure in even the primary trabeculectomy⁴. Such cases

therefore rationalize the adjunctive use of anti-metabolites like mitomycin C, which has a proven efficacy in long term post trabeculectomy IOP control, although has some serious complications⁵. 5-Fluorouracil is a chemotherapeutic agent that specifically mediates its antiproliferative effect by antagonizing pyrimidine metabolism; hence is classified as an antimetabolite. 5-Fluorouracil is active on the synthesis phase of cell cycle. Fibroblastic proliferation is inhibited while fibroblastic attachment and migration are unaffected⁶.

We conducted this study to overview the efficacy and complications of 5-Fluorouracil as an adjunct in glaucoma surgery in younger age groups.

MATERIAL AND METHODS

This was a hospital based study conducted at the LRBT Free Eye and Cancer Hospital Lahore from January 2005 to June 2010. Patients with a minimum of two years follow up were included in this study. Eighty six eyes of 62 patients were included in this study.

Patients with Congenital glaucoma, glaucoma due to use of steroids, (responders), post traumatic glaucoma and those with previously failed trabeculectomy were included in the study.

Patients with neovascular glaucoma, active iritis or scarred superior fornix were excluded from the study.

Preoperative evaluation; For those upto six years of age 90% of examination was carried under sedation with Chloral hydrate (500mg/5ml). During examination IOP was measured with Perkins applanation tonometer, corneal diameter with calipers and detailed fundus examination especially cup-disc ratio was done with indirect or direct ophthalmoscope. Older cooperative children were examined routinely on slit lamp.

Preoperatively the intraocular pressure was controlled with topical beta blockers and topical carbonic anhydrase inhibitor, however in some cases a third topical anti-glaucoma drug like alpha agonist above the age of two year was also used. In some cases preoperative intravenous Mannitol was used for rapid control of IOP.

Operative procedure: Trabeculectomy was performed in each eye according to a modification of the technique developed by Watson and Cairns. After making a fornix based conjunctival flap, partial thickness rectangular scleral flap (4mm wide by 3mm long.) was made, block of deep sclera (2mm wide by 1.5mm long) was excised and peripheral iridectomy performed. The superficial scleral flap was approximated; Conjunctiva and tenon were sutured separately. Subconjunctival injection of 5-FU (50mg/0.2ml) was given in a separate plane directed away from the fistula. Eye washed thoroughly to remove any released 5-FU to prevent epithelial toxicity which was reported to be very high with 5-FU.

Second injection of 5-FU was given after first week and third after second week. Additional 1-2 injections of 5-FU were given if found necessary.

Postoperative care: On the first postoperative day, intraocular pressure was recorded with computed air-

puff tonometer. In cases of shallow anterior chamber a cycloplegic was used and if the anterior chamber was not formed properly, a pressure bandage with antibiotic eye ointment was used for another twenty four hours.

Postoperatively topical antibiotic and steroid eye drops were used every two to four hours in waking hours and antibiotic eye ointment at bed time if necessary. The treatment was tapered off according to condition of the eye on follow up visits. Postoperative follow-up was at week 1, 2, 6 and at the 3rd month and then 6 monthly. At each visit visual acuity was recorded and slit lamp biomicroscopic examination was carried out to evaluate the condition of conjunctiva, cornea, anterior chamber, vitreous, macula and optic disc. Applanation tonometry was done and corneal diameter was recorded. Special emphasis was given at the condition of bleb i.e. which type of bleb is established and the vascularisation of the bleb, and to decide how many postoperative subconjunctival injections of 5-FU should be given.

5-FU used in concentration of 50mg/0.2ml with 27 gauge needle on insulin syringe, given 10 to 12 mm away from the bleb. Total dose of 5-FU ranged from 15 to 25mg per patient. In 90% of the cases only three injections were required.

RESULTS

Eighty six eyes of 62 patients were included in the study. There were 48 male patients (55.81%) and 38 female patients (44.18%) (Table 1). Duration of study was four years with average follow up of two years.

Table 1:

Age (Years)	Number of Eyes		Total eyes
	Male	Female	
2-5	18	15	33
6-10	17	10	27
11-15	13	13	26
Total	48	38	86

Target IOP was achieved in 83 (97%) of patients, additional 2 (2%) patients also achieved target IOP with AGT and 1 (1%) did not achieve target IOP (Fig. 1). Vision remained stable in 69 (80%) patients, in 13

(15%) patients it improved while in 4 (5%) it deteriorated (Fig. 2).

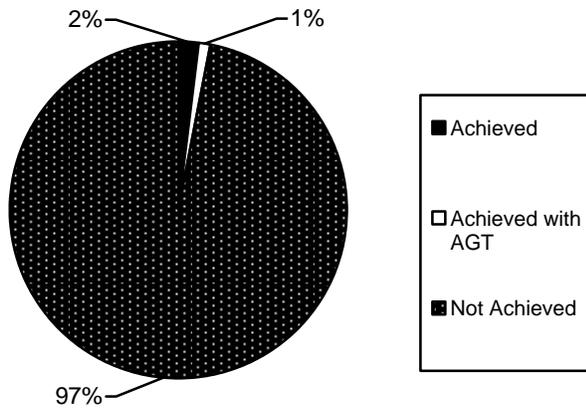


Fig. 1: Target IOP

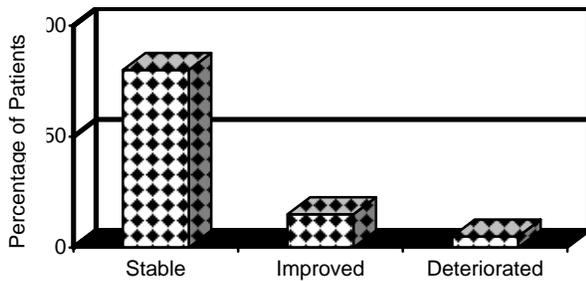


Fig. 2: Post Trabeculectomy Visual Acuity

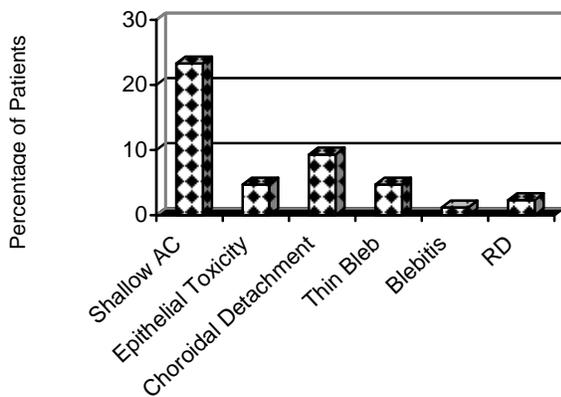


Fig. 3: Complications

Cup-to-disc ratio reversal was seen in 30% of the patients. Shallow anterior chamber was seen in 20 eyes, treated with cycloplegics and pressure patching. Epithelial toxicity was found in 4 patients that was reduced with the application of ointment for three days after injection of 5-FU. Choroidal detachment

occurred in 8 (9.30%) patients, most of these patients had microspheric lens. Choroidal drainage was done in two cases, other six responded well with pressure patching, cycloplegics and steroids. Thin bleb was seen in 4 (4.65%) patients. Blebitis occurred in 1 (1.16%) patient that led to endophthalmitis. Retinal detachment occurred in 2 (2.32%) patients. Redo trabeculectomy was done in 3 (3.48%) cases because stitches were not released in time due to poor follow up (Fig. 3).

DISCUSSION

The main cause of failure of filtering surgery is scarring of the filtering bleb. Antimetabolites like 5-FU and MMC originally found to inhibit scarring through their inhibitory effect on fibroblasts, are efficacious after filtering surgery in preventing bleb fibrosis in eyes with poor surgical prognosis¹⁰.

The prognosis of glaucoma surgery is poor in complicated cases such as previous failed trabeculectomy, inflammatory glaucoma, angle recession glaucoma, combined procedure, younger age group, history of topical anti glaucoma medication for more than three years, previous history of conjunctival surgery and individuals with dark skin.

This effect is caused by inhibition of fibroblast proliferation or inhibition of cell migration and extracellular matrix production. As a result of its prolonged cytological toxicity, MMC is associated with development of potentially severe side-effects and complications as compared to 5-FU. It may lead to development of thin walled avascular bleb which may results in over filtration. Late onset focal bleb leaks are three times more frequent with Mitomycin C than with 5-FU¹³. Such blebs are strongly associated with endophthalmitis. The posterior choroid becomes thickened in acute hypotony followed by choroidal detachment. Scleritis is also reported in some patients¹³. Although MMC is an effective antifibrotic adjunct with glaucoma surgery but there is a growing concern with hypotony, leaky ischemic blebs, and potentially increased risk of endophthalmitis. This has led us to re-evaluation of the use of 5-FU.

In our study, a complete surgical success was considered to be an intraocular pressure of less than 21 mm Hg without any anti-glaucoma medication after trabeculectomy with 5-FU. We also studied the safety of use of 5-FU.

Pressure rose in those cases in which we were unable to give inj. 5-FU due to choroidal detachment

or poor follow up of the patient. We had to redo in these cases in spite of 3- 5 injections of 5-FU.

Chronic hypotony was seen in only one case in which the cause of glaucoma was angle recession, Intravitreal C₃F₈ was injected, that brought the IOP to 12mmHg but vision did not improve due to maculopathy.

Thin cystic bleb was seen in 4 cases that were managed with postoperative lubricants. Blebitis was seen in one case, that child had iridocorneal endothelial syndrome. The present study has clearly demonstrated that 5-FU improves the surgical prognosis for patients at low to moderate risk as well as high risk for failure and indicates that 5-FU facilitates filtering bleb formation as well as with less complications.

There is a significant benefit of 5-FU, in terms of bleb survival and clinical success as determined by IOP. According to national survey of antimetabolite 93% of consultants are using 5-FU rather than MMC in United Kingdom¹⁴. There are some differences between success rates of different studies yet our study results are comparable to that demonstrated in some of the previous studies.

Among previous studies, the pilot study of Heuer and colleagues with postoperative subconjunctival injections daily for up to two weeks showed the success rate in previous failed trabeculectomy was found 81%¹⁶. Although the results of these studies are comparable with our study yet the number of postoperative injections was quite higher compared to our study¹⁷. Leibmann showed 77.8% 5 years success rate¹⁸.

Our complications with the use of 5-FU were less as compared with other studies. The cause seems to be less number of subconjunctival injections.

CONCLUSION

The use of 5-FU as an adjunctive has a significant efficacy and low complication rate in glaucoma filtration surgery.

Author's affiliation

Dr. Norin Iftikhar Bano
LRBT Free Eye & Cancer Hospital
436-A/I, Township
Lahore

Dr. Tariq Mehmood Qureshi
LRBT Free Eye & Cancer Hospital
436-A/I, Township
Lahore

Dr. Muhammad Tariq Khan
LRBT Free Eye & Cancer Hospital
436-A/I, Township
Lahore

Dr. Harris Muzammil Ansari
LRBT Free Eye & Cancer Hospital
436-A/I, Township
Lahore

Dr. Khalid Mehmood
LRBT Free Eye & Cancer Hospital
436-A/I, Township
Lahore

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