Original article

Effectiveness of intra-operative and post-operative use of 5-Fluorouracil in trabeculectomy – a randomized clinical trial

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Abstract

Introduction: The success rate of trabeculectomy is limited by postoperative scarring.

Objective: To evaluate the effectiveness of intra-operative and post-operative use of 5-Fluorouracil (5-FU) in trabeculectomy

Materials and methods: Thirty consecutive eyes undergoing trabeculectomy were randomized systematically into 3 groups of ten patients each. Group A served as a control; in Group B intra-operative 5-FU was used, whereas Group C received post-operative sub-conjunctival 5-FU. The variables studied were pre- and post-operative intraocular pressure, post-operative bleb characteristics and complications.

Statistics: Data were evaluated using the SPSS ver 10.0 program. ANOVA, paired t test and chi^2 tests were performed.

Results: The means of age in years of patients in group A, B and C were 49 ± 9.23, 56.50 ± 8.39 and 52.10 ± 8.96 respectively (p = 0.222). The means of pre–operative IOP in groups A, B and C were 37.80 ±10 mmHg, 42.00 ± 11.22 mmHg and 29.40 ± 12.82 mmHg respectively. The medians of pre-operative anterior chamber depth (ACD) in groups B and C were 3 and 2 in group A according to van Herrick's grading. The mean values of final IOP were 11.90± 3.50, 11.70 ± 4.24, 11.00 ± 2.83 mmHg (p=0.841). The median post-operative anterior chamber depth in all the groups was similar compared to the pre-operative anterior chamber depth (p= 0.510). The final bleb scores in all the groups were similar (p=0.873).

Conclusion: The intra-operative and post-operative use of 5-FU in trabeculectomy is almost equally effective in terms of IOP control and bleb characteristics.

Keywords: trabeculectomy, 5-Fluorouracil, glaucoma

Introduction

The trabeculectomy has become the most commonly performed operation for glaucoma (Watkins & Brubaker, 1978). Unlike many other types of surgery in which complete healing of tissue with restoration of normal architecture would be a desirable outcome, glaucoma surgery seeks to achieve incomplete healing to allow aqueous to escape the eye. A completely healed trabeculectomy is a failed trabeculectomy (Lama & Fechtner, 2003).

The success rate of trabeculectomy unfortunately has been limited by postoperative scarring which occurs most commonly at the level of conjunctiva-tenon's capsule-episcleral interface leading to flap fibrosis and eventually bleb failure (Liebmann et al 1991). Scarring

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of a glaucoma filtering bleb is caused mainly by proliferation of sub-conjunctival fibroblasts and by their biosynthesis of collagen and other extra-cellular material. Inhibition of wound healing is a crucial factor in successful glaucoma surgery (Watkins & Brubaker, 1978; Lama & Fechtner, 2003).

In the early 1980s, 5- Fluorouracil (5-FU) and Mitomycin C were found to be effective in inhibiting fibroblastic activity and have tremendously impacted the success rate of trabeculectomy. The 5-Fluorouracil is a commonly used anti-fibrotic which inhibits fibroblast replication and is effective in achieving early filtration as well as enhancing bleb survival (Lama & Fechtner, 2003).

Antifibrosis regime is presently combined with trabeculectomy for high risk patients like aphakic, neovascular and inflammatory glaucomas which have poor prognosis and for patients in whom trabeculectomy has failed (Chen et al 1986, Sood et al 1990, Heuer et al 1996, Rockwood et al 1987, The Fluorouracil filtering surgery group, 1989, Lanigan et al 1994). Various authors have stated that anti-fibrosis regimen should be used adjunctively with trabeculectomy (Lanigan et al 1994; Goldenfeld et al 1994; Ophir et al 1992; Wilson, 1989; Wilson, 1990; Wilson, 1991; Wilson, 1992) in all cases routinely.

The 5-FU can be used as a single intra-operative application or as post-operative sub-conjunctival injections over a variable period. Subconjunctival injections of 5-FU can be toxic to the corneal epithelium and as this mode of administration is time consuming as well as uncomfortable both to patient and physician, intra-operative use is preferred ((Lama & Fechtner, 2003).

Although some surgeons have recommended intra-operative use of 5-FU as an alternative to it's post-operative use, a medline search of all relevant publications revealed a scarcity of reports comparing intra-operative and post-operative use of 5-FU. This study was conducted to compare the intra-operative and post-operative use of 5-Fluorouracil in trabeculectomy in terms of intraocular pressure control, bleb characteristics and complications.

Materials and methods

A randomized clinical trial was carried out to evaluate the effectiveness of intra-operative and post-operative use of 5-Fluorouracil in trabeculectomy. The variables studied were pre- and post-operative intraocular pressure, post-operative bleb characteristics and complications, if any.

Ethical clearance

The study proposal was approved by the institutional research committee and the ethical review board of the B P Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal. All the investigations and surgical procedures (including applications of 5-FU) were carried out after obtaining written informed consent from the patients.

Thirty consecutive eyes of patients with primary open angle or angle closure glaucoma undergoing trabeculectomy at the BPKIHS during the study period were prospectively included in this study. Indication for trabeculectomy was uncontrolled intraocular pressure despite maximal possible medical therapy.

The patients with the following diagnosis were excluded from the study.

i) Congenital glaucoma
ii) Secondary glaucomas
iii) Normal tension glaucoma
iv) Combined surgeries
v) Failed trabeculectomy

The patients undergoing trabeculectomy were randomized systematically into 3 groups of ten patients each. Group A served as a control; in Group B intra-operative 5-FU was used whereas Group C received post-operative sub-conjunctival 5-FU.

In all the patients, baseline demographic data such as name, age, gender and history of diabetes were recorded. Ocular history included duration of glaucoma since the time of diagnosis and the number and duration of anti-glaucoma medications used in the past and present. Ocular examination included the following: visual acuity measurement, slit lamp examination, fundus examination, intraocular pressure (IOP) measurement with Goldmann applanation tonometer and preoperative

visual field (automated) charting. Anterior chamber depth was measured using van Herrick's method.

van Herrick's slit-lamp grading of anterior chamber depthVan Herrick's slit lamp grading of anterior chamber depth

Grade 4 *PAC> 1**CT (wide open angle)
Grade 3 PAC= 1/4 to 1/2CT (mild narrow angle)
Grade 2 PAC = 1/4 CT (moderate narrow angle)
Grade 1 PAC < 1/4CT (extremely narrow angle)

* PAC= peripheral anterior chamber , **CT = corneal thickness

All intraocular pressure recordings were made between 11:00 am and 1:00 pm by the same investigator with the same instrument (PM). Visual field charting was done preoperatively using Humphrey automated perimeter whenever possible.

All surgeries were performed by ophthalmic surgeons with more than 5 years of experience using similar technique.

Trabeculectomy technique
Peri-bulbar anesthesia was used in all cases. Superior rectus bridle suture was placed. A Limbal-based conjunctival flap was prepared at 11 to 1 O' clock position by incising the conjunctiva and Tenon's capsule 8 mm posterior to the limbus. The dissection was carried out to the limbal zone. Hemostasis was obtained with bipolar cautery. A 4 x 4 mm rectangular scleral flap was created at 12 O'clock position to a depth of approximately one half of the scleral thickness, until the entire corneo-scleral limbus was exposed. In groups A and C no 5-FU was applied. In Group B 5-FU was applied over and below the scleral flap using two 3.0 mm X 3.0 mm cellulose sponge soaked in a 3 ml of 5-FU solution with a concentration of 50 mg/mL for 5 minutes. While doing so, the conjunctiva was elevated making sure that the margins did not come in contact with the 5-FU. Towards the end of the application time, slight pressure was exerted over the conjunctiva to the sponge to release the maximum amount of the 5 FU solutions in the underlying area. The area of application was then irrigated with 30-50 ml of normal saline.

Trabeculectomy was done by excising the deep rectangular block (1.5 x 3 mm) using Vannas scissors followed by peripheral iridectomy. The scleral flap was closed with 2 interrupted 10-0 nylon sutures. Tenon's capsule and the conjunctival layer were then closed in a single-layer in Groups A and C, and in two layers in Group B with running 8-0 Vicryl suture. Following surgery, dexamethasone sodium phosphate 4 mg and gentamicin 20 mg were injected sub-conjunctivally away from the bleb area.

Technique of 5-fluorouracil application
Group A: Control. No 5-FU was used.
Group B: 5-Fluorouracil was applied intra-operatively in the concentration of 50 mg/ml by simultaneous episcleral and subscleral application of sponge soaked in it. The sponge was kept for 5 minutes after which it was removed and the operation field was washed with about 30 ml of ringer lactate solution.

Group C: Post-operatively, sub-conjunctival injections of 0.1 ml 5-Fluorouracil were given using 26 G needle at the site, 180 degrees away from the filtration bleb at a concentration of 50 mg/ml for 4 consecutive days starting from 1st postoperative day.

Post-operative treatment
All patients were treated with 1 % predisolone acetate 1 hourly (waking hours), tropicamide 8 hourly and ciprofloxacin eye drops 4 hourly for a week. The dosage of steroids was tapered according to the anterior chamber inflammatory response and all medications were stopped 3 weeks after the surgery.

In cases of patients with IOP > 21 mm Hg, digital massage was done first to decrease the IOP, when not controlled anti-glaucoma medications were started.

Failure was defined as IOP > 21 mm Hg with medications or when further glaucoma surgery would be indicated.

Post-operative assessment and follow-up
All patients were evaluated every day on the first week, then weekly for 2 weeks, then every three weeks for three months and at the last available follow-up.

Ocular assessment included record of number of medications used post operatively, best corrected visual acuity, slit-lamp examination and intraocular pressure. Intraocular pressure was determined at a fixed time (11:00 am -1:00 pm) and an average of 3 readings was

taken. Eyes having IOP of less than 6 mmHg were classified as hypotony. Slit-lamp examination was done to record the corneal (corneal oedema, epithelial defects, keratitis) and conjunctival (chemosis, defects, hemorrhage) complications.

Shallow anterior chambers were graded according to the description of Costa et al (1993). Grade1= peripheral irido-corneal touch

Grade 2 = peripheral and central irido-corneal touch
Grade 3 = totally flat, including lens-corneal touch.

In cases with hyper filtering bleb and grade 3 shallow anterior chamber, anterior chamber re-formation was done with viscoelastic (2 % hydoxymethyl cellulose) on the same day. Examination of the bleb was performed to look for type of bleb (bleb score according to Migdal and Hitching's classification, 1983) and any evidence of bleb leak.

Bleb score according to Migdal and Hitching's (1983) classification

Bleb score	Bleb characteristics
1	Flat bleb
2	Elevated engorged conjunctiva
3	Pale elevated area within engorged conjunctiva
4	Residual conjunctival engorgement around suture line
5	Pale and diffusely elevated
6	Pale cystic conjunctival elevation

Leniticular examination was done to note the grade of cataract. Fundus examination was done to rule out any macular edema or choroidal detachment.

Criteria for success

Intraocular pressure of 21 mmHg or lower with or without medication was considered a success. These eyes were further classified as follows.

i) complete surgical success when the IOP was 21 mmHg or less without any medication,

ii) qualified surgical success when the IOP was 21 mmHg or less with anti-glaucoma medications.

Statistical analysis

Data were evaluated using the SPSS ver 10.0 program. ANOVA was used to evaluate the difference between the preoperative characteristics. IOP during follow-up in the three groups was evaluated using ANOVA and in the same group using paired t test. Success rate was evaluated using the Chi square test. To test for potential confounding variables, ANOVA was used.

Results

In group A the age of the patients ranged from 35 to 65 years. In group B the age range was from 40 – 65 years and in group C the range was from 40 – 67 years. Most of the patients, i.e. four in each group, were in the age group 51 – 60 years.

The means of age of patients in group A, B and C were 49 ± 9.23 years, 56.50 ± 8.39 years and 52.10 ± 8.96 years respectively. The three groups were comparable for age (P = 0.222).

Ten (41.66 %) patients were female and 14(58.33 %) were male. In group A, 50 % were males and 50 % were females whereas the male and female patients in group B and C were 40 % & 60 % and 70 % &30 % respectively. While comparing the groups in terms of gender, they were comparable (P= 1.000).The most common type of glaucoma among the 30 eyes operated was chronic angle closure glaucoma (Table 1). The 3 groups were comparable in this regard (p = 0.992). Four patients in each group had visual acuity between 0.3 to 0.6 in log MAR i.e. from 6/12 to 6/24 (Table 2). The difference in visual acuity between the 3 groups was not statistically significant (p= 0.943).

The mean pre–operative IOP in group A was 37.80 ± 10 mmHg, group B was 42.00 ± 11.22 mmHg and group C was 29.40 ± 12.82 mmHg. The low IOP in group C was attributable to the topical and systemic anti-glaucoma medications. Six of the patients in this group had been commenced on those drugs prior to the surgery.

Table 1
Distribution of patients and types of glaucoma

Group	No. of patients	Chronic ACG	Acute ACG	POAG
A	10	5	2	3
B	10	4	1	5
C	10	5	1	4
P Value	0.992			

Table 2
Pre-operative visual acuity in logMAR

Group	No. of patients	0.00 - + 0.2	+0.3 - + 0.6	+0.7 - + 1.0	+1.1 - + 1.4	+2.0 or <
A	10	0	4	1	2	3
B	10	1	4	1	1	3
C	10	1	4	0	1	4
P Value			0.943			

Pre-operative anterior chamber depth
The median pre-operative anterior chamber depth in group B and C was 3 according to van Herrick's grading and 2 in group A.

Post-operative evaluation
The post-operative IOP on the first post-operative day was lowest in group A and the final IOP was lowest in group C. Mean IOP was lowest during the first day to first week in group A which later on was seen to rise to 11.9 mm Hg ± 3.5SD. In group B and C the means of final post-operative IOP were 11.7 ± 4.24 SD and 11.00 mm Hg ± 2.83 SD respectively (Table 3). The IOP in the 3 groups on day 1, 1st week, 6 weeks and final follow-up were more or less the same and the difference was not statistically significant.

The IOP reduction following trabeculectomy was highest in group B, i.e. 72.14% and lowest in group C i.e. 28.57% (Table 4). The percentage reduction in group A was 68.52%. In all the groups the IOP reduction following surgery was statistically significant.

Table 3
Post-operative intra-ocular pressure

Group	Day 1	1st Week	6 Week	Final
A	5.30 ± 4.00	7.10 ± 4.89	11.40 ± 4.88	11.90 ± 3.50
B	6.80 ± 4.83	7.20 ± 3.39	10.50 ± 4.30	11.70 ± 4.24
C	5.70 ± 3.43	5.80 ± 3.65	10.10 ± 5.24	11.00 ± 2.83
p Value	0.705	0.690	0.828	0.841

Table 4
Pre-operative and post-operative intraocular pressure and reduction percentage

Group	Mean ± SD IOP		Reduction	P Value (paired t test)
	Pre-OP	Post-OP		
A	37.80 ± 10.00	11.90 ± 3.51	68.52%	0.001
B	42.00 ± 11.22	11.70 ± 4.24	72.14%	0.001
C	29.40 ± 12.82	11.00 ± 2.83	28.57%	0.001

Table 5
Median post-operative anterior chamber depth

Group	Day 1	1st Week	6 Week	Final
A	1	1	2	2.5
B	2.5	2	3	3
C	2	2	2	2.5
p value (Kruskal Wallis ANOVA)	0.062	0.199	0.519	0.510

Median post-operative anterior chamber depth (Table 5) in all the groups was similar compared to the pre-operative anterior chamber depth. Median AC depth was significantly low in group A in the 1st post-operative day as compared to other groups (p= 0.062) but the final AC depth in all the groups was similar (p= 0.510).

The mean bleb scores (Table 6) on day 1 in all the groups were similar, ie, 1.5 ± 0.53 in group A, 1.4 ± 0.52 in group B and 1.6± 0.52 in group C. Subsequently, in 1st week, 6 weeks and in the final bleb scores in all the groups were similar (p=0.873). Grade 6 blebs were observed in 2 patients in group A, 4 patients in group B and 5 patients in group C.

Post-operative visual acuity in most of the patients in all the groups were from +0.3 to +0.6 logMAR. Visual acuity was seen to improve in some patients in each group.

In group A, 5 patients had improved in Snellen's acuity by 2 or more lines and 5 had no change. In group B, 2

patients had improvement and 8 had no change, whereas in group C, 4 patients had improvement and 6 had no change.

Success rate of trabeculectomy

Complete surgical success, that is IOP <21mm Hg without medication was noted in 80 % of patients in group A, and 90 % of patients in group B and C. Percentage of qualified success i.e. IOP < 21mm Hg on anti-glaucoma drug was noted in 20 % of patients in group A, 10 % in group B and C. No case of failure (IOP > 21mm Hg on anti glaucoma drugs) was noted in any of the groups.

Complications

Six of the patients in group A had immediate post-operative hypotony. This was associated with 4 (40%) of the patients with shallow AC. Five (50 %) of the patients had hypotony in group B but shallow AC was not noted. In group C, 3 (30 %) patients had immediate post-operative hypotony and shallow AC was present in 1 (10 %) patient (Table 7). The complications other than hypotony and shallow AC were also noted. Hyphema was seen in 3 (30 %) patients in group A only. Sub-conjunctival hemorrhage was noted in 3 (30 %) patients in group C. Choroidal detachment was seen in 2 (20 %) patients in group A and 1 (10 %) in group C in immediate post-operative period. Though cataract progression was seen in 1 patient each in group A and B and 2 patients in group C, it was not visually significant except in one patient in the post-operative period, who underwent cataract surgery through temporal approach. None of the patients had any of the corneal complications. Though hypotony was quite common in the early post-operative period in all the groups, none of the patients had hypotony maculopathy.

Table 6
Post-operative bleb score

Group	Day 1	1st Week	6 Week	Final
A	1.50 ± 0.53	2.40 ± 0.52	3.50 ± 0.71	5.10 ± 0.57
B	1.40 ± 0.52	2.50 ± 0.53	3.38 ± 0.48	4.90 ± 1.10
C	1.60 ± 0.52	2.30 ± 0.67	3.60 ± 0.70	5.00 ± 0.82
p Value (ANOVA)	0.694	0.743	0.571	0.873

Table 7
Post-operative complications in various groups

Complications	Group A	Group B	Group C
Hyphema	3	0	0
Choroidal detachment	2	0	1
Sub-conjunctival hemorrhage	0	0	3
Immediate post-operative hypotony	6	5	3
Immediate post-operative shallow anterior chamber	4	0	1
Qualified success	2	1	1

Discussion

Anti-fibrosis regimen is presently combined with trabeculectomy for aphakic, neovascular and inflammatory glaucomas which have poor prognosis and for patients in whom filtration surgery has failed (Heuer et al 1996, Rockwood et al 1987, The Fluorouracil filtering surgery group, 1989). Though primary glaucoma in adults has been reported to be more common after 60 years of age, it is not uncommon for the glaucoma to occur in < 60 years as other factors like gender and race also attribute to the occurrence of glaucoma (Goldenfeld et al 1994). In our study, patients of less than 40 years of age were also encountered. All those patients were diagnosed as having angle closure glaucoma. This is explainable by the reported prevalence of angle closure glaucoma to be relatively more common in eastern and south Asian people (Shen SY et al, 2008). Angle closure glaucoma with pupillary block can occur in patients of any age including children (Apply et al 1971).

In our study population males (58.33 %) outnumbered the females (41.66 %). Most studies have reported that primary angle closure glaucoma occurs 2 to 3 times more commonly in women than in men (Palimkar et al, 2008), whereas in several studies, males had a higher prevalence of primary angle closure glaucoma (Kaha et al 1980). The most common type of glaucoma diagnosed in our study population was angle closure glaucoma. The incidence of angle closure glaucoma in Caucasians has been reported as 0.1-0.2 % and in East

Asians as 0.3-3.2 % (Yanoff M, 2004). Following closely to this, primary open angle glaucoma patients were 30 % in group A, 50 % in group B and 40 % in group C. The prevalence of POAG varies according to the study population. In most studies, in Europe and US, the prevalence is reported as 0.5 to 1 % above the age of 40 years.

Acute angle closure glaucoma patients were also included in our study population. Though trabeculectomy is not considered to be the first line of management for acute angle closure glaucoma, it has been recommended that some eyes with pupillary block eventually require filtration surgery for control of IOP, particularly those presenting late (Krupin et al 1978). Therefore, after reducing the IOP with systemic and topical anti-glaucoma drugs, those patients were considered for trabeculectomy. Moreover, considering the financial status and poor compliance in our part of the world, trabeculectomy is thought to be the best option for control of IOP.

In all the groups, most patients had visual acuity between 0.3 to 0.6 in Log MAR.

Decrease in visual acuity in cases of glaucoma is attributed to corneal edema in cases of acute angle closure glaucoma, optic nerve atrophy in all forms of glaucoma and in associated cataract. In our study, almost all the patients who had angle closure glaucoma, had better visual acuity following surgery.

The mean pre-operative IOP was highest in group B, i.e. 42.00 ± 11.22 and lowest in group C, i.e. 29.40 ± 12.82 mm of Hg. The low IOP in group C is attributable to the use of anti-glaucoma drugs the patients were on prior to the trabeculectomy. In a similar study by Lamba et al, the mean pre-operative IOP was 42.3± 2.4 mmHg in the control group (Lamba et al 1997).

The median pre-op AC depth in group A was 2 and it was 3 in groups B and C.

As most of the patients (70 %) in group A had angle closure glaucoma, the low mean AC depth in this group is explainable. The IOP reduction in all the groups following surgery on the 1st post-operative day was statistically significant (p= 0.001) but the difference in IOP among the three groups was not. The levels of IOP in the 1st week, 6th week and in the final visit in the 3 groups were significantly less compared to the pre-operative IOP but the difference in IOP within the groups was not statistically significant at any point.

The IOP reduction percentage at 3 months or last follow up was noted to be 68.52 % in group A, 72.14 % in group B and 28.57 % in group C. This reduction doesn't relate to the findings in other studies. In a study carried out by Lamba et al (1997) in 33 patients randomized to 3 groups as control, intra-operative 5-FU and post-operative 5-FU, the IOP fall in 3 months following surgery was 56.6% in the control group, 62.5 % in the intra-operative group and 62.4 % in the post-operative group. In another study carried out by Dastur et al (1994), IOP reduction percentage one year after the conventional trabeculectomy was 65 % while sub-conjunctival injections of 5-FU following trabeculectomy led to 80 % reduction in IOP. The low reduction percentage in group C in our study is because of the lower preoperative IOP in this group compared to the other groups. In spite of the low reduction percentage, the mean IOP at last follow up in this group C was the lowest. This complements to the fact that post-operative 5-FU injections do lead to a good control of IOP.

The median post-operative AC depth was lowest in group A which is likely due to the lower AC depth in this group pre-operatively, owing to high number of ACG patients in this group. In our study, five of the patients had shallow AC in the immediate post-operative period. The shallow AC was graded according to the grading of Costa et al (1993). All the patients had grade 1 shallow AC, i.e. peripheral irido-corneal touch which was managed conservatively. None of the patients required AC reformation.

The final median post-operative AC depth was 2.5 in group A and C and 3 in group B and the difference was not statistically significant.

The mean bleb score in post-operative day 1 was similar in all the groups. Similarly in the 1st week, 6th week and in the final, bleb scores were more or less similar in all the groups.

Bleb resulting after conventional trabeculectomy has been described as diffusely elevated with varying degree of residual vascularization, whereas blebs following use of anti-metabolites have been described

to range from low diffuse to frankly cystic, avascular blebs. But in our study, such significant difference in the type of bleb was not noted. However, grade 6 blebs or pale cystic blebs were noted in 2 patients in group A, 4 in group B and 5 in group C.

The post-operative visual acuity in most of the patients in all the groups was from +0.3 to +0.6 in log MAR. In contrast to the reported studies, trabeculectomy with adjunctive 5-FU did not result in loss of vision in comparison with eyes subjected to trabeculectomy alone. As mentioned in the studies, patients treated with trabeculectomy and 5-FU have low tension and consequently have fluctuating and seriously blurred vision (Wilson, 1989; Wilson, 1990; Wilson, 1992).

Cataract progression has been reported frequently after trabeculectomy and anti-metabolites (Wormald et al 2003). In our study, a few patients did have progression of cataract, which was not visually significant, except for one patient who underwent cataract surgery through the temporal approach. A longer follow-up period would be required to ascertain this complication. In all the groups, there were a few patients who had improvement in Snellen's acuity by 2 or more lines. None of the patients had deterioration of vision.

The improvement seen in those patients was probably due to the pre-operative corneal edema in patients with angle closure glaucoma which resolved leading to significant improvement in vision following surgery and control of IOP.

Complete surgical success, i.e. IOP less than 21mm Hg without anti-glaucoma drugs was seen in 80 % of patients in group A, 90 % each in group B and C. In a similar study by Lamba et al (1997), IOP was maintained <22 mmHg at 3 months of follow up in 66.7 % in the control group, 90.9 % in the intra-operative 5-FU group and 80 % in the post-operative 5-FU group. In a study by Dietz & Gross (1992), an 84 % success rate defined as an IOP of <21mmHg or 20 % reduction, was noted following intra-operative use of 5-FU. Goldenfeld et al (1994) reported the outcome of 62 patients in a prospective randomized study in primary trabeculectomy with sub-conjunctival 5-FU. IOP less than 20mmHg was seen in 94 % compared to 73 % in the control group. A similar study by Ophir & Ticho (1992) reported IOP < 20mmHg in 96 % of patients compared to 76 % in the control group. Our study is consistent with the findings in the literature (Goldenfeld et al 1994; Ophir & Ticho 1992; Dietz et al 1992). Qualified success defined as IOP <21mmHg on anti-glaucoma medications was seen in 20 % in group A and 10% each in group B and C.

Immediate post-operative hypotony was noted in some of the patients in all the 3 groups. Associated shallow AC was present in a few of those patients. In none of the patients in group B was shallow AC present. Hypotony without shallow AC could have been due to the systemic anti-glaucoma medications most of the patients were on for IOP control in the other eye. Among the intra-operative and the post-operative groups, hypotony was more common in the intra-operative group. This is similar to that reported in a similar study by Lamba et al (1997) where hypotony was seen commonly.

Though immediate post-operative hypotony was quite common, none of the patients in our study had hypotony maculopathy. The final IOP in all the patients was >6 mmHg. Associated choroidal detachment was seen in 3 of the patients with hypotony. They resolved spontaneously by the 1st week and one patient was given oral steroid which led to a rise in pressure and deepening of AC by the end of 1st month. Hyphema was seen in 3 of the patients in the 1st post-operative day, which resolved by 1st week. As expected, sub-conjunctival hemorrhage was present in 3 of the patients in group C, which is similar to 3 patients with sub-conjunctival hemorrhage in the post operative 5-FU group in a study in 33 patients (Lamba et al 1997). Cataract progression which is said to be a common complication following trabeculectomy especially with anti-metabolite (Wormald et al 2003), cataract-requiring surgery was seen in 1 patient only in our study.

Corneal complications as superficial punctuate keratopathy are reported exclusively with post-operative anti-metabolite use (Shapiro et al 1985). None of the patients in our study had this complication. This could have been due to the antibiotic ointment applied following each sub-conjunctival injection of 5-FU.

Bleb related infections are commonly reported with anti-metabolite use (Wolner et al 1991). However, as none of the patients in this study developed a bleb related infection such as blebitis or endophthalmitis, it is probable that thicker, more vascularized blebs seen with

5-FU use are less likely to develop infection as compared to the thinner avascular blebs of MMC. Moreover, as our follow-up duration in the majority of patients was for 3 months only, perhaps a longer follow-up would be required to comment on such complications.

Conclusion

The intra-operative and post-operative use of 5-FU in trabeculectomy is almost equally effective in terms of IOP control and bleb characteristics. Considering the time and patient-comfort of one-time use, intra-operative use can be recommended. A study with a larger sample size and a follow-up for a longer duration would be required to confirm these findings.

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