

LONG TERM RESULTS OF INTRAOPERATIVE 5-FU IN GLAUCOMA FILTERING PROCEDURES

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Abstract - This prospective study evaluated the long term results of intraoperative 5-FU in glaucoma patients undergoing trabeculectomy. 14 patients categorized as high risk or medium risk underwent trabeculectomy with 5-FU and were followed for a mean period of 32 months. Patients were evaluated for visual acuity, cup-disc ratio and intraocular pressure (IOP); the number of medications was also taken into consideration. 78% (11) of patients achieved controlled IOP (< 21 mmHg) with or without medication. There was statistically significant reduction of IOP and number of medications after the operation. There were no significant complications observed during the follow-up period.

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Key Words: Glaucoma, 5-Fluorouracil (5-FU), cup disc ratio (C/D ratio), intraocular pressure (IOP)

INTRODUCTION

Usage of antimetabolites such as 5-Fluorouracil and Mitomycin-C for glaucoma surgery, especially high risk cases, is inevitable. In animal studies it has been shown that 5-FU hinders scar formation by inhibition of fibroblast proliferation (1). Repetitive injections of this agent postoperatively produce further reduction of intraocular pressure (2-7), however such injections cause great inconvenience for the patient and lead to local side effects such as punctate epithelial keratopathy. Intraoperative Mitomycin-C for high risk glaucoma patients, such as congenital glaucoma and aphakic glaucoma, is very effective, leading to significant reduction of IOP. But due to its potency complications are seen even with low dose and short term usage. The risk of hypotony maculopathy which may lead to irreversible visual loss is reported to occur in 0-36% of cases (8-11) and is related to dosage and exposure time of the drug during the operation. Another complication is thin-walled bleb and associated endophthalmitis which is reported to occur in 2-4% of cases (12,13).

In this study we used intraoperative 5-FU for glaucoma filtering procedures. The purpose was to evaluate the long term effectiveness, success and complications associated with such therapy.

MATERIALS AND METHODS

14 patients, 7 of either sex, with an age range of 30 days to 51 years (average 17 years) had one eye operated. Diagnostically these patients fitted into five categories as follows: congenital glaucoma (6 cases, 2.9%), juvenile glaucoma (3 cases, 21.4%), pigmentary glaucoma (2 cases, 14.3%), aphakic glaucoma (2 cases, 14.3%), primary open angle glaucoma (1 case, 7.1%).

Table 1. Glaucoma Subtypes

| Glaucoma Subtypes | No. | Percent |
|--------------------|-----|---------|
| Congenital | 6 | 42.9 |
| Juvenile | 3 | 21.4 |
| Pigmentary | 2 | 14.3 |
| Aphakic | 2 | 14.3 |
| Primary open angle | 1 | 7.1 |
| Total | 14 | 100 |

We divided our patients into two main groups, the high risk category (A) including congenital and aphakic glaucoma plus re-operations and the medium risk category (B) consisting of juvenile and pigmentary glaucoma.

We performed standard trabeculectomy on all patients as follows. First a limbus based conjunctival flap was made, after achieving hemostasis a rectangular half thickness scleral flap was fashioned; at this stage and just before entering the anterior chamber, the scleral and subconjunctival tissues were exposed to a 50 mg/ml 5-FU solution applied with a cellulose sponge for 5 minutes. The operation field was irrigated with 50 ml of Ringer's solution afterwards. Next, anterior chamber paracentesis was done followed by internal scleral block excision. The scleral flap was fixed with two 10.0 nylon sutures, the conjunctiva was also sutured continuously with the same material. At the conclusion of the operation 20 mg of gentamicin and 4 mg of betamethasone was injected subconjunctivally. Postoperative medications included topical antibiotic, steroid and cycloplegics.

After the mentioned procedure all patients were followed for a mean period of 32 months (range 12-42

months), measuring the IOP, visual acuity and cup-disc (C/D) ratio. IOP was mostly measured by applanation tonometry, however in congenital glaucoma cases the shiotsz device was used. We used standard snellen charts to evaluate the visual acuity; optic nerve head findings including the C/D ratio were evaluated and recorded in the files by figures and diagrams. Although we considered 4 variables (i.e IOP, C/D ratio, visual acuity, no. of medications) only IOP and medications defined our success criteria as follows:

Complete control, defined as IOP < 21 mmHg off medication or only on one drug. Relative control, defined as IOP < 21 mmHg with more than one medication. Cases not fulfilling any of these criteria were recognized as failures.

RESULTS

According to the above mentioned definitions, out of 14 cases 11 (78%) were successful, including 9 cases complete success and 2 cases with relative success. For 3 patients this method has not been successful. The success rate differs in the 2 different groups of our patients. In the high risk group (A) we achieved 70% success, whereas the medium risk group (B) enjoyed a 100% success rate. In each group there has been one case of relative success. All failures belong to the high risk category.

Table 2. Summary of Results

| | Pre-op IOP (mmHg) | Post-op IOP (mmHg) | Pre-op med | Post-op med | Success | Failure |
|---------|-------------------|--------------------|------------|-------------|---------|---------|
| Overall | 29.47 | 17.63 | 1.9 | 1.2 | 78% | 22% |
| Group A | 31.36 | 19.14 | 1.8 | 1.5 | 70% | 30% |
| Group B | 24.75 | 13.87 | 2.2 | 0.5 | 100% | 0 |

Overall, the average pre-op IOP was 29.74 mmHg while receiving 1.9 medications. The average post-op IOP has been 17.63 mmHg on 1.2 drugs. Statistically both reductions in IOP ($p=0.0001$) and number of required medications ($p=0.01$) have been significant. In group A mean pre-op IOP was 31.36 mmHg falling to 19.14 mmHg. Corresponding figures for group B were 24.75 and 13.87 respectively. Average number of medications for group A was 1.8 before and 1.5 after the operation. Similar figures for group B are 2.2 and 0.5.

Changes in C/D ratio were subject to evaluation in 11 cases, the remaining 3 eyes had hazy media obscuring view of the fundus. In 9 patients the C/D ratio remained constant; six high risk patients and 3 medium risk patients belonged to this group. However,

2 of the patients suffered increased cupping during the follow-up period, both belonging to the high risk group.

Table 3. Changes in C/D ratio

| | Overall | Group A | Group B |
|---------------------|---------|---------|---------|
| Increased C/D ratio | 2 | 2 | - |
| Unchanged C/D ratio | 9 | 6 | 3 |
| C/D ratio unknown | 3 | 2 | 1 |

Changes in visual acuity could be assessed in only 9 patients, the remaining 5 were too young to cooperate. 6 patients showed no significant change in their acuity (4 high risk, 2 medium risk) but 3 experienced deterioration (2 medium risk, 1 high risk).

Table 4. Changes in visual acuity (VA)

| | Overall | Group A | Group B |
|-----------------|---------|---------|---------|
| No change in VA | 6 | 4 | 2 |
| Decreased VA | 3 | 1 | 2 |
| VA not known | 5 | 5 | - |

It should be stressed that during the follow-up period all patients were carefully and systematically examined; except mild choroidal effusion in 3 cases which resolved with conservative management, no other significant complications occurred in the anterior or posterior segment.

Table 5. Post-operative complications

| Post operative Complication | Number |
|-----------------------------|--------|
| Flat AC | 0 |
| Choroidal effusion | 3 |
| Hypheama | 0 |
| Epithelial defect | 0 |
| Wound leakage | 0 |
| Endophthalmitis | 0 |
| Persistent hypotony | 0 |

DISCUSSION

The effectiveness of 5-FU as an antimetabolite has been proved in many previous studies (2,14). Trabeculectomy in primary open angle glaucoma can achieve high success and significant IOP lowering if supplanted with multiple postoperative 5-FU injections (14,15), however this mode of usage causes inconvenience and discomfort. Three year follow-up in the Fluorouracil Filtering Surgery Study (FFSS) showed that intraoperative usage of this substance led to

suitable control of IOP and reduced the need to reoperate(16).

In other studies the effectiveness of intraoperative 5-FU and Mitomycin-C have been compared. The effect on IOP reduction has been almost the same, however there have been more instances of persistent hypotony in the Mitomycin group (17,18,19).

Our results also conform to that of others and show that while achieving a success rate of 78% and reducing the number of required medications, intraoperative 5-FU is safe with no significant or long term sequelae. It's worth reminding that in the high risk group we had 30% failure, in contrast to no failure in the medium risk group. This fact shows the possible need for a more potent antimetabolite such as Mitomycin-C in high risk patients such as congenital glaucoma. Of course more complications both in number and severity are to be anticipated. Like any other study we are aware of some strong and weak points. Although we have the advantage of variety in our patients and also a good, long-term follow-up, the rather small number of cases in our study is a disadvantage. Further studies of patients in larger numbers in a randomized double blind fashion comparing different antimetabolites is needed to help glaucoma surgeons make the optimum choice, especially in high risk patients. The final word; referring to our results and many others it is evident that intraoperative 5-FU can give excellent results in lower risk patients who require adequate IOP reduction while avoiding severe complications such as hypotony maculopathy.

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