Filtering Surgery with 5-Fluorouracil: A Second Course

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Summary

In five glaucoma patients, a previous filtering surgery that was followed by sub-conjunctival injections of 5-Fluorouracil (5-FU) failed, due to filtering bleb scarring. A repetition of the filtering surgery with subsequent sub-conjunctival injections of 5 mg of 5-FU, administered once daily for 8-14 days, was undertaken. At the end of 6-19 months of follow-up, IOP levels in all five eyes were 20 mmHg or less with medication. A repeated course of filtering surgery plus 5-FU treatment seems to be a favourable surgical option in refractory glaucoma.

Sub-conjunctival administration of 5 mg of 5-Fluorouracil (5-FU) following filtering surgery in aphakic/pseudophakic glaucomatous eyes and in cases of previously failed filtering surgery has been shown to be effective in the prevention of filtering bleb scarring.¹ In spite of this important adjunctive treatment, surgical failures occurred in 14%,² 16%³ and 27%^{1,4} of cases reported. In such situations, shunt implantation⁵⁻⁷ or cyclodestructive surgery procedures are usually tried. A repetition of the filtering surgery followed by 5-FU treatment has not been reported.

Materials and Methods

Five eyes of five patients were studied. Informed consent was obtained from all patients after the nature of the procedure had been fully explained. The age of the patients ranged from 27 to 72 years. The types of glaucoma and the different subsequent surgeries performed are listed in the Table. Prior to the surgery reported here each patient had undergone filtering surgery with sub-conjunctival injections of 5 mg of 5-FU, which had failed due to filtering bleb scarring.

Three to seven months after this filtering surgery, trabeculectomy was performed. In four of the cases, the surgery was performed inferiorly. At the end of surgery, sub-conjunctival dexamethasone was injected and topical 1% atropine sulfate was instilled. From the first post-operative day onwards, topical 0.1% dexamethasone and 1% atropine sulfate were administered four times daily. In addition, from the first post-operative day, 5 mg of 5-FU in 0.5 cc saline was injected once daily, 180° from the surgical site. Injections were continued as long as ocular inflammatory signs,³ judged by the anterior chamber reaction and/or hyperaemia at the area of the filtering bleb, were evident, altogether 8-14 days post-operatively (Table).

Patients were examined daily in the first week, twice to seven times in the second week, once in the third and fourth weeks, and again after the second, third, fourth, sixth, eighth, tenth and twelfth months.

Results

5-FU administration post-operation ranged

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Table *Data on trabeculectomy surgery with 5-FU after failure of previous filtering surgery with 5-FU treatment*

Age/ Gender	Original Glaucoma type	Previous surgeries	5-FU treatment (mg)	VA		IOP		No. of hypotensive medications	Length of follow-up (mos)	Corneal epithelial defects
				Pre-op.	post-op.	pre-op.	post-op.			
1 61F	Ps.P	Cat+IOL TRB+5-FU	45	20/40	20/40	28	16	2	11	absent
2 55F	Ps.P	Cat+IOL TRB+5-FU	40	20/-60	20/40	30	17	1	13	absent
3 72M	Ps.P	Cat+IOL TRB+5-FU	70	2m FC	3m FC	48	19	3	16	present
4 27F	JUV	TRO TRB Molteno shunt PLS+5-FU	55	20/200	20/200	34	20	4	19	present
5 30M	Steroid- induced	TRB TRB+5-FU	40	3m FC	3m FC	37	17	1	6	absent

Ps.P =Pseudophakia

JUV =Juvenile

Cat+IOL =Extracapsular Cataract extraction+IOL implantation

TRO =Trabeculectomy

TRB =Trabeculectomy

PLS =Posterior lip sclerectomy

from 40 to 70 mg. IOP fell from a pre-operative value of 35 ± 9.0 mmHg (range, 28 to 48 mmHg) to a post-operative value of 17.25 ± 1.26 mmHg (range, 16 to 20 mmHg), 13 ± 4.95 months (range, 6 to 19) after surgery (Table). Whereas pre-operatively all five eyes were treated by four hypotensive medications, a mean of 2.2 ± 1.3 medications were given post-operatively.

Side-effects included punctate corneal erosions in two (40%) eyes (Table) and conjunctival epithelial defects at the injection site in three (60%) eyes.

Discussion

A repetition of filtering surgery followed by 5-FU treatment was performed in three pseudophakic glaucomous eyes, as a third filtering operation in one other eye, and a fourth filtering operation in a fifth eye. In all five eyes, IOP levels after six to 19 months follow-up were 20 mmHg or lower, all with hypotensive medication. Several theoretical reasons can be postulated for the success rate of the second rather than the first course of filtering surgery and 5-FU treatment. Among the possible explanations are undetectable bleeding or significant inflammation in the surgical area that promote scarring^{8,9} and lack of compliance of patients following the first operation.

The accepted options following failure of filtering surgery plus 5-FU treatment are aqueous shunt implantation or a cyclodestructive procedure, but both are probably more risky than the approach presented in this

report: Minckler and colleagues¹⁰ reported that 63% (26/46) of aphakic/pseudophakic glaucoma patients had final post-operative IOP of 21 mmHg or lower (at least six months follow-up), following a single-plate Molteno implantation. However, complications in a total of 90 patients included post-operative choroidal haemorrhage (8%), cataract (7%), tube block (6%), phthisis bulbi (2%), hypotony (2%), traction retinal detachment (2%), pupillary membrane (1%) and recurrent vitreous haemorrhage (1%). Schocket and associates implanted an anterior chamber tube shunt attached to an encircling band and reported on a successful outcome in four out of five eyes, with average IOP of 19.8 mmHg in non-neovascular refractory glaucoma. Due to corneal touch by the shunt, a retrocorneal membrane developed in the fifth eye, with resultant increased IOP and reduced visual acuity.⁶

Krupin and associates⁷ implanted a long Krupin-Denver valve attached to a 180° scleral explant in eyes in which prior filtration surgery had failed. After follow-up of 21 months (mean) IOP was less than 21 mmHg in 82% (27/33) of eyes; 56% of these eyes required additional medication. However, post-operative choroidal detachment with associated reduction in IOP and shallowing of the anterior chamber frequently occurred (11/33 of eyes = 33%). In eyes with a flat anterior chamber, the tube contacted the cornea or lens.

The effectiveness of cyclocryotherapy in lowering IOP to avoid further surgery is

reported as between 30-60% (11/12) depending on the type of refractory glaucoma being treated. The complications of cyclotherapy are well documented and include choroidal detachment with a flat anterior chamber, phthisis bulbi, loss of light perception, sympathetic ophthalmia, scleral thinning with resulting staphyloma, hyphaema, iritis, corneal oedema, iris atrophy, retinal detachment, cataract and vitreous haemorrhage. Brindley and Shields reported that after cyclocryotherapy, 60% of the eyes lost some vision with a phthisis bulbi rate of 12% (13).

The significant risks of phthisis and visual loss with cyclocryotherapy have led to the development of other techniques of cilioablation such as Neodymium:YAG cyclophotocoagulation (Nd:YAG-CPC), argon laser transpupillary or transiridectomy cyclophotocoagulation and therapeutic ultrasonography. It is the higher rate rather than the type of complications reported that distinguishes cyclocryotherapy from Nd:YAG-CPC.¹⁴

Trope and Ma¹⁵ reported that 30% of 28 eyes with good IOP control lost some vision after Nd:YAG-CPC, and the phthisis bulbi rate was 10.7%. Although this procedure appears to be effective, it is associated with significant complications.

Serious complications have also been described after the use of transscleral ruby laser cyclocoagulation.¹⁶ Currently, there are no studies comparing Nd:YAG-CPC or other forms of therapy, including cyclotherapy, to trabeculectomy with injections of antimetabolites.

First-time course of filtering surgery and 5-FU was only rarely accompanied by permanent complications,^{1,4} unless this treatment was administered in eyes with pre-operative bullous keratopathy¹⁷ or corneal oedema.¹ The second course of surgery with 5-FU was undertaken as early as three months after the preceding course (Case No. 5) and as late as seven months after the preceding course (Case No. 4). Side-effects following the second course of filtering surgery and 5-FU treatment reported here, were similar to those reported after a first course.¹⁻⁴ Neither serious side-effects nor permanent complications were observed following the second use of s.c. 5-FU reported here.

The small sample presented here precludes significance, however the results may have clinical importance: in the five poor-prognosis glaucomatous eyes, IOP levels were 20 mmHg or lower, although all with hypotensive medication. In addition, from this preliminary study it does seem that a second course of filtering surgery plus 5-FU treatment is safer than the alternatives mentioned above. A larger number of patients is needed to verify the results of this study.

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