

Comparative Study between Trabeculectomy and Trabeculectomy with Collagen Implantation

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Abstract

Background: To present the result of our study that compares the out-comes of trabeculectomy with collagen implant versus conventional trabeculectomy for uncontrolled intraocular pressure (IOP).

Methods: 60 eyes of 60 patients were randomly selected for trabeculectomy either with OloGen implant (study group) or without implant (control group). Preoperative history taking & examinations were done. Data included age, gender, glaucoma type, IOP and number of postoperative glaucoma medications were collected. Post operative IOP, number of post operative glaucoma medications & post operative complications were recorded. Each patient was followed up for at least 6 months.

Result: No significant differences were observed between the groups like preoperative IOP and number of pre operative anti glaucoma medications. Post operative IOP in both groups were significantly lower than preoperative level at all follow up. The number of glaucoma medications were reduced from a preoperative mean of 3.5 ± 0.5 to a 6-month postoperative mean of 0.2 ± 0.5 ($P < 0.001$) in the study group and from 3.5 ± 0.7 to $0.4 \pm .1$ ($P < 0.001$) in the control group. Collagen group had statistically significant less complications were observed in this study.

Conclusion: Trabeculectomy with OloGen does not show any significant advantages over the trabeculectomy alone in terms of Intraocular pressure but immediate post operative complications are less with Ologen implantation, that indicates Ologens safety profile. Large sample size & prolong follow up are needed to confirm the safety & long term out come of trabeculectomy with OloGen.

Key words: Trabeculectomy; Ologen; Glaucoma; Bleb; Intraocular pressure

Introduction

Cairns 1968 introduced trabeculectomy for the treatment of glaucoma. Trabeculectomy bleb can be failed by wound healing & fibrosis resulting obstruction of drainage fistula. Failure can be prevented by inhibition of fibrosis. Fibroblast growth beneath the conjunctiva (between 3rd -5th post operative day) plays an important role in bleb failure. [1] Adjunctive antimetabolites like 5-fluorouracil (5-FU) and mitomycin-C may enhance the success rate by preventing fibrosis. [2]

Antimetabolites increases the risk of post operative wound leak, hypotony & endophthalmitis [1.3] Studies in animal models show, the uses biodegradable collagen matrix implant beneath the conjunctiva helps in controlling wound healing process & maintain space for drainage with out post operative complications those are common with antimetabolites use. [4] The background of this study is to compare outcomes of trabeculectomy with ologen implant with the trabeculectomy without implant.

Materials & Method

This is a prospective randomized clinical trial that was done in the glaucoma department of Chittagong Eye Infirmary and Training Complex, Bangladesh. Randomly patients are divided into trabeculectomy (control group) and trabeculectomy & collagen (study group) 6x1 mm biodegradable, porous collagen matrix (atelocollagen plus glycosaminoglycans) were used for the implant.



Figure 1: A Piece of Collagen.

CEITC hospital review board approved the study following Helsinki declaration Informed consent was taken after detail explanation about the implant and operation. Explanation was done to Muslim people as Ologen is not halal origin.

2 Patients refused due to religious binding. No patient lost for follow up. Young age group (<18 yrs), neovascular glaucoma, history

of previous our surgery or laser & absolute complicated glaucoma were excluded from the study. Preoperative following data were collected age, gender, diagnosis, level of intraocular pressure (day before surgery), numbers of medications. All patients were under single future trabeculectomy. Post operative IOP, bleb condition & number of glaucoma medications, were also recorded in each follow up. IOP measurement was done with Goldmann applanation tonometry.

Success was defined with some criteria: (1) complete success when IOP of 21mmHg or less with out antiglaucoma medications & (2) qualified success when IOP of 21 mmHg with the use of antiglaucoma medication. Hypotony was defined as an IOP <6mmHg. Flat anterior chamber can be defined as peripheral iridocorneal touch with central at least I corneal thickness depth.

Surgical Technique

Surgeries were done by single surgeon (SMN). After peribulbar anesthesia & proper drapping, fornix based incision was given around 12'O Clock. Triangular, superficial scleral flap (4x4mm) was produced facing apex towards 12 O' clock position. 2x1 mm deep sclerectomy & a peripheral iridectomy was performed thereafter. Scleral flap was closed with a single suture (10/0 nylon). Ologen was placed over the apex of the triangular flap beneath the conjunctiva after making the operation area dry. Conjunctiva was closed like a wing with 2 sutures by 10/0 nylon. Post operative all patients were treated with Atropin 1%, 3 times daily for 2 weeks, Moxifloxacin 4 times daily for 1 week & Prednisolone acetate eye drop 6 times daily for 3 weeks then tapered gradually.

Statistical analysis was done with windows SPSS. Pre operative & demographic data & IOP comparison were analyzed with students T test. Surgical failure success & complications were analyzed with the χ^2 test. With long rank test, Kaplan-Meier survival analysis for surgical success were calculated.

P values < 0.05 were taken as statistically significant.

Results

60 eyes were enrolled in the study & randomly divided into two groups of Trabeculectomy with or without ologen implant.

Table 1 describes demographic & diagnostic data before operation. There were no significant differences between the groups in terms of age, gender, eye laterality, diagnosis, pre operative IOP and number of topical & systemic anti glaucoma medications. 8 patients

from the study group and 9 patients from control group needed systemic carbonic anhydrase inhibitors.

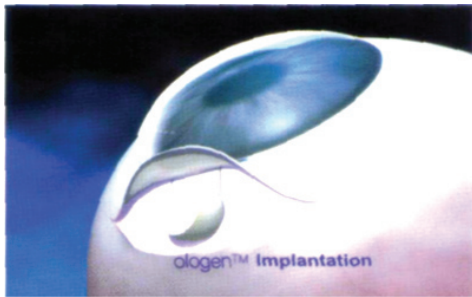


Figure 2: Collagen Implantation under Conjunctiva.

	Study group	Control group	P-value
No. of eyes	30	30	
Age (years)			
Mean (\pm SD)	61.3 (\pm 18.5)	70.9 (\pm 12.9)	0.188
Range	20–80	32–86	
Median	65	74.5	
Gender			
Male	17 (55%)	18 (60%)	
Female	13 (45%)	12 (40%)	0.759
Eye laterality			
Right	12 (40%)	17 (55%)	
Left	18 (60%)	13 (45%)	0.17
Diagnosis			
POAG	15 (50%)	15 (50%)	
PXG	6 (20%)	6 (20%)	
PACG	3 (10%)	6 (20%)	
IG	6 (20%)	3 (10%)	0.838
Preoperative IOP (mmHg)			
Mean (\pm SD)	27.5 (\pm 4.3)	34 (\pm 10.6)	0.289
Range	20–35	21–51	
No. of preoperative medications			
Mean (\pm SD)	3 (\pm 0.5)	3.5 (\pm 0.7)	0.613
Range	2–4	1–4	
Time of preoperative medications (months)			
Mean (\pm SD)	45.15 (\pm 37.34)	43.35 (\pm 35.96)	0.180

Table 1: Operations were uncomplicated in both groups.

** SD, standard deviation; IOP, intraocular pressure; POAG, primary open-angle glaucoma; PXG, pseudoexfoliative glaucoma; PACG, primary angle closure glaucoma; IG, inflammatory glaucoma.

Mean IOPs for both groups are listed in Table-2 No difference is observed in IOP measurement 6 month after operation between two groups. Post operative IOP levels in both groups is significantly lower than preoperative one. ($P < 0.05$) None of the eyes in the study group developed high IOP > 21 mmHg post operatively where 2 eyes of control group developed so at the six month visit.

Post operatively in control group mean number of antiglaucoma medications was dropped from (3.5 ± 0.7) to (0.4 ± 0.1) ($P < 0.001$). Where in the study group from (3.5 ± 0.5) to (0.2 ± 0.5) ($P < 0.001$). There is no significant difference in their reduction between & groups.

	Study group	Control group	P-value
Preoperative	27.5 (\pm 4.3)	34 (\pm 10.6)	0.269
Range	20–35	21–51	
Postoperative visits			
6 months	16 (\pm 4)	15.5 (\pm 3)	0.950
Range	11–21	10–21	

Table 2:

Figure 3 shows Kaplan-Meier survival analysis for both groups using complete success definition. No statistical differences observed between survival curves.

At the 6 month 27 (90%) eyes in both groups showed complete success. All eyes in the study groups 100% & 29 (97%) of 30 eyes in the control group showed qualified success. ($P > 0.66$)

No statistical significance difference was observed in post operative patients in terms of post operative complication (Table-3).

In the first post operative day 2 eyes in the control group & 2 eyes in the study group developed hypotony those were improved within one month.

Two eyes in the control group & two eyes in the study group developed flat anterior chamber with out positive Seidel test those were resolved spontaneously after giving patching for two days. 1 Patient from the control group & 1 patient from the study group

developed encapsulated bleb. No patient developed cataract in the study group where as 1 patient developed cataract in the control group at the end of the 5th month. No patient develop endophthalmitis in either groups.

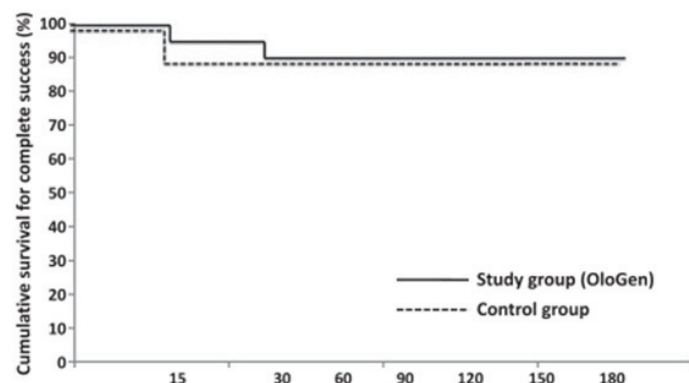


Figure 3:

	Study group (%)	Control group (%)	P-value
Hypotony	2 (5)	2 (5)	1
Flat anterior chamber	2 (10)	2 (5)	0.548
Hyphaemas	4 (5)	3 (15)	0.179
Encapsulated bleb	1 (10)	1 (25)	0.211
Cataract	0	1	0.311

Table 3:

Discussion

Penetrating glaucoma surgical procedures allow a powerful reduction of IOP. The pressure reducing effect of penetrating surgery is probably still higher than that of non penetrating strategies, particularly in the long run. [5, 6, 7].

Trabeculectomy is the most standard procedure in penetrating anti glaucoma surgery was introduced by Cairns in 1968 [8].

The method was developed further over subsequent decades to address various problems. In 1990, MMC was applied as an anti metabolite during trabeculectomy [9]. Various studies demonstrated significant enhancement of success rates and post operative IOP through intra operative use of MMC [10] this is associated with an increase in adverse effect such as cataract formation, avascular blebs, thinning of the conjunctiva, subsequent blebitis and end ophthalmoties. [11-13]

The current focus is on the development of less toxic agents & implants to inhibit cicatrization with out adverse effects.

One approach in the development of biodegradable implants to serve as a place holder and prevent conjunctiva and scleral adhesion.

A few different biodegradable implants are due to be tested in animal models. With a poly (L-lactide-co-epsilon-caprolactone) film, designed to work as an adhesion barrier in filtration surgery, a significantly lower postoperative IOP was found in relation to control eyes and no significant difference to outcome in MMC-treated eyes was detected. [14] A solid hyaluronic acid-carboxymethyl cellulose film significantly inhibited sub conjunctival scar formation and prevented adhesions of conjunctiva and sclera.[15] The use of seprafilm (sodium hyaluronate and carboxymethylcellulose) reduced postoperative conjunctiva-sclera adhesion. A porous collagen-glycosaminoglycan matrix (ologen implant) was tested in animal models. This implant was designed to prevent collapse of the subconjunctival space, for example, the conjunctive-sclera adhesion. It led to a randomised collagen deposition and microcyst formation after penetrating anti-glaucomatous surgery in contrast to the negative control and decreased early postoperative scarring [16, 17]. Moreover, the ologen implant will also be adjuvant in repairing postoperative bleb leaks [17]. In human subjects, the ologen implant was tested non augmentation in deep sclerectomy. This study revealed that deep sclerectomy with ologen implantation is an effective and well-tolerated method for reduction of IOP. [18] A further pilot study revealed non-significant differences in postoperative IOP after trabeculectomy with ologen and sole trabeculectomy. [19] In summary of the previous studies, the use of the ologen implant promises comparable IOP reduction after trabeculectomy and a lower risk profile in comparison with the use of anti-metabolites, for example, MMC and 5-fluorouracil, although the use of ologen implant does not seem to offer a significant advantage compared with trabeculectomy alone in a pilot study. [19]

Recent studies in animal models reported that, the use of a bio-engineered biodegradable, porous collagen implant offers the potential for a new method of providing controlled resistance seteven the anterior chamber and the subconjunctival space in the early post operative period, as well as maintaining long term IOP control by avoiding loosely structured filtering bleb [4]. According to the manufacturer, the Ologen implant used in our study may normalize sub conjunctival wound healing and maintain good filtration & biodegrade within 30-90days.

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Figures 4-7: Some Implanted Collagen in filtration surgery.)

Our study reveals that trabeculectomy with implantation of an ologen implant is a safe method for penetrating anti-glaucomatous surgery. We did not detect any ologen-specific side effects, such as translocation of the implant or erosion of the conjunctiva. No allergy was detected and corkscrew vessel scores were comparable in the two interventional groups.

In the early post operative period, excessive aqueous filtration could cause low IOP. Severe hypotony could result in severe complications such as choroidal detachment, gradual bleb failure, cataract & corneal edema & can be associated with maculopathy and loss of visual acuity. [19]

In our study, there was no vision threatening complications were observed except temporary hypotony & shallow anterior chamber (same number of patients in both groups) those were improved with conservative management gradually.

Post operative IOP levels were significantly lower than pre operative levels with both groups at 6 months after operation.

The mean number of antiglaucoma medications used in both groups was significantly reduced after surgery, there was no significant difference between the two groups in terms of either the mean post operative IOP with the mean number of antiglaucoma medications used. This result is very much similar with the study of Papaconstantinou et al. [19] There were non statistically significant differences between the two groups in terms of post operative complications. That is very similar with other study [19].

Papconstantenour et al [19] experienced one case of endophthalmitis with 2 cases of positive Seidel test in the study group. In our study we did not face such complications in either groups.

One patient from the control group developed cataract at the end of 5th month after filtration surgery. He underwent cataract surgery with implantation. Still bleb Morphology & IOP are normal limit in that patient.

4 eyes from the control groups & 2 eyes from the study groups developed hyphema at immediate post operative period (1st to 3rd).

This is probably due to leaking of blood from the scleral flap angle to the anterior chamber. In the study group probably it is less due to relative tight sealing due to pressure of the ologen.

Even though there were no statistically significant differences between the two groups in terms of post operative complications, there may be clinical significance in the fact that 4 eyes from the control group developed hyphaema & one eye developed cataract which needed cataract surgery.

Ologen did not show any allergy to anybody in our study. But biodegradation is slower than the mentioned period of 60-90 days. Even in all eyes of the ologen group the implant degraded partially even at the end of 6 month after filtration surgery.

Conclusion

In conclusion of their study we can say that, trabeculectomy with ologen implantation have not significant advantage over trabeculectomy only. Additionally there were no statistically significant differences between the two groups in terms of complications.

Large sample sizes, prolong follow up are needed to confirm those outcomes with safely as well as efficacy of ologen in filtration surgery.

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