

A prospective comparative study between trabeculectomy alone versus trabeculectomy with Ologen for patients with open angle glaucoma two years follows up.

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Abstract: **Subject:** A prospective comparative study between trabeculectomy alone versus trabeculectomy with Ologen for patients with open angle glaucoma two years follows up. **Introduction:** Recent studies reported that the use of a biodegradable collagen glycosamino-glycan matrix (ologen) implant in the subconjunctival space offers an alternative method for wound healing modulation of MMC after glaucoma surgery. Ologen is composed of a three-dimensional disc-shaped porous structure that implanted over scleral flap before closure of conjunctiva during trabeculectomy. Ologen regulate aqueous flow by keeping pressure on top of the scleral flap and by acting as a reservoir, as aqueous gets absorbed into its porous structure. **Patient and Methods:** A prospective randomized clinical study was done in Al-Azhar university hospitals. Thirty-two eyes were presented by POAG or PEX glaucoma included in this study. 16 eyes treated by trabeculectomy alone (control group) and the other 16 eyes treated by trabeculectomy with subconjunctival implant of ologen (ologen or study group). Follow up for 2 years were done. Statistical analysis was performed using SPSS program and Student's test. **Results:** It is found that; mean IOP in ologen group was 13.16 ± 1.68 mmHg and in the control group mean IOP 16.47 ± 3.56 mmHg. Regarding to postoperative antiglaucoma medications, in ologen group, the mean was 0.31 ± 0.48 compared to control group 1.06 ± 0.85 drugs, p-value is 0.05. Success rate was 15/16 eyes (93.75%) in the ologen group, in comparison to control group, success rate was 12/16 eyes (75%). **Conclusion:** This new degradable collagen implant (ologen) improves and normalizes filtering surgical wound healing with more loosely organized bleb tissue and healthy than that unaugmented blebs.

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1. Introduction

Trabeculectomy operation was introduced by Cairns since 1968¹. Nowadays, it is the most common operation for treatment of glaucoma all over the world². Mitomycin-C and 5-Fluorouracil has been introduced since more than 20 years ago to reduce wound healing and enhance surgical success for trabeculectomy operation^{3,4}.

The rule of these antifibrotic agents is to inhibit fibroblast proliferation in wound healing process, and thus preventing scar formation and bleb failure⁵⁻⁷. However, the use of antimetabolites increases the risks of bleb leakage, hypotonousmaculopathy, endophthalmitis and other many dangerous ophthalmic complications⁸⁻¹⁰.

Recent studies in animals reported that the use of a biodegradable collagen-glycosamino-glycan matrix (ologen) implant in the subconjunctival space offers an alternative method for wound healing modulation after glaucoma surgery. This material (ologen) implant is composed of a three-dimensional disc-shaped porous structure that implanted over the scleral flap before closure of conjunctiva during trabeculectomy operation^{11,12}.

This implant aims to regulate aqueous flow by keeping pressure on top of the scleral flap and by acting as a reservoir, as aqueous gets absorbed into its porous structure¹³. This implant, also, should prevent the collapse of the subconjunctival space and creation of microcysts with collagen deposition¹⁴.

The aim of this study is to compare between surgical outcomes of trabeculectomy versus trabeculectomy with Ologen regarding IOP, postoperative medications, bleb function and postoperative complications.

2. Patient and Methods:

A prospective randomized clinical study was done in Al-Azhar university hospitals. Thirty-two eyes of 32 patients were presented by primary open angle glaucoma or pseudo-expholiation glaucoma included in this study. Sixteen eyes treated by trabeculectomy alone (control group) and the other 16 eyes treated by trabeculectomy with subconjunctival implant of Ologen (Ologen or study group) over the closed scleral flap. Ologen (a collagen matrix of 1% collagen/C-6-S copolymer–OculusGen Biomedical Inc. Taipei, Taiwan). The selected size is the

recommended size by the company which is 7mm length, rounded disc-shaped with 4mm thickness for all cases.

Informed consent and procedure explanation were analyzed for each patient. Inclusion criteria are

age more than 18 years old, with primary open angle glaucoma or exophthalmia glaucoma only. Follow up was done for all eyes for two year as follows, 1st postoperative day, 1, 2 weeks, 1, 3, 6, 12, 18 and 24 months.

Table (1): Demographic data of all patients.

	Trab with Ologen group	Trab only	p-value
No of eyes	16 eyes	16 eyes	-
Age (mean±SD)	(56.13±8.82) years	(59.19±4.86) years	0.23
Gender:			
Male	6 (37.50%)	9 (56.25%)	-
Female	10 (62.50%)	7 (43.75%)	-
Glaucoma type			
POAG	13 (81.25%)	12 (75%)	-
PEX	3 (18.75)	4 (25%)	-
Preop. IOP	(33.13±2.85) mmHg	(35.38±2.36) mmHg	0.21
No.preop drugs	(3.81±0.40)	(3.56±0.51)	0.14

Surgical technique:

All surgeries were done by two surgeons with the same identical techniques. After local (peri-bulbar anesthesia) and betadine sterilization, a superior rectus bridle suture using 6/0 silk was taken and then a limbal-based conjunctival flap 8mm from limbus. Good dissection of the tenon's capsule with episcleral mild cauterization. Half-thickness scleral flap dissection 4x3.5mm, paracentesis, trabecular meshwork block removal 2x1.5mm, peripheral iridectomy and closure of the scleral flap using 10/0 silk sutures. One or two stitches are just approximating and not tight. Guarding filtration using microsponge was done.

Ologen implant application before closure of tenon's and conjunctiva for 16 eyes of the study. Closure of tenon's and conjunctiva in two separate layers using 8/0 virgin silk sutures was done. Postoperative treatment in the form of topical antibiotics, corticosteroids and mydriatic eye drops was given for all eyes. Follow up visits were labeled for each patient for 2 years. Statistical analysis was performed using SPSS program for demographic data, preoperative and postoperative data were analyzed with Student's test.

3. Results:

All patients included in this study completed the period of follow up (two years). There is no statistically significant difference between two groups regarding to demographic data as shown in table (1). Among operative procedure "subconjunctival-trabeculectomy" there is no recorded intra-operative complications in both groups.

Mean postoperative IOP was calculated in all postoperative visits and as reported in table (2),

shows also no statistically significant difference between two groups. It is found that; mean IOP in ologen group 13.16±1.68mmHg and in the control group mean IOP 16.47±3.56mmHg. Also, mean of last visit IOP for both groups was, ologen group 14.06±1.91mmHg and control group 18.69±3.05mmHg, p-value 0.46. Regarding to postoperative antiglaucoma medications, in ologen group, the mean was 0.31±0.48 compared to control group 1.06±0.85 drugs, p-value is 0.05.

Next figure shows serial photos of the conjunctival bleb, postoperatively after one week, 3 weeks, 12 and 24 months, and after one year. Notice the elevated diffuse polycystic relatively avascular bleb. Success rate was 15/16 eyes (93.75%) in the ologen group, as ologen matrix was removed in one eye that complicated by severe hypotony, in spite of interferences by viscoelastic injection in anterior chamber twice and tighten the sutures of scleral flap. In comparison to control group, success rate was 12/16 eyes (75%) as there is 3/16 eyes (18.75%) of encapsulated bleb with high IOP, flat bleb in 1/16 eye (6.25%) with high IOP at the 6 month follow up visit, in spite of different methods of interferences.

Postoperative complications was reported in both group as in table (2), in ologen group two eyes 2/16 (12.50%) were complicated by severe hypotony with flat anterior chamber, interference by viscoelastic injection done for both, one eye respond, other eye not responding even with repeated injection of viscoelastic, until ologen was removed with multiple sutures of the scleral flap. Transient shallowing of the anterior chamber was seen in 4/16 eyes (25%), which improved within few days postoperatively. Hyphema was recorded in 2/16 eyes only (12.5%) that is resolved in 2-3 days

postoperatively. Cataract progression was reported in 2/16 eyes (12.5%), but as it is low grade, so no interferences done. No other major complication was seen as endophthalmitis, bleb leakage, cataract or encapsulated bleb.

Postoperative complications in the control group was hypotony in 2/16 (12.5%) with shallow anterior chamber, but one eye improved by excessive fluid drinking by the patient. Other eye improved by viscoelastic injection in anterior chamber. Hyphema was reported also in 2/16 eyes (12.5%), it was transient and disappeared gradually within few days

postoperatively. Bleb encapsulation after first follow up visit was reported in 3/16 eyes (18.75%) that lead to increased IOP and failed to turn back to normal levels in spite of needling with multiple 5-FU injection. Flat bleb with high IOP was reported in 1/16 (6.25%) eyes at the 6 month follow up visit, with antiglaucoma medications again. Cataract was progressed in 2/16 (12.5%) and two eyes was planned for phaco at the end of the follow up visit. No endophthalmitis or bleb leakage was reported in the group.

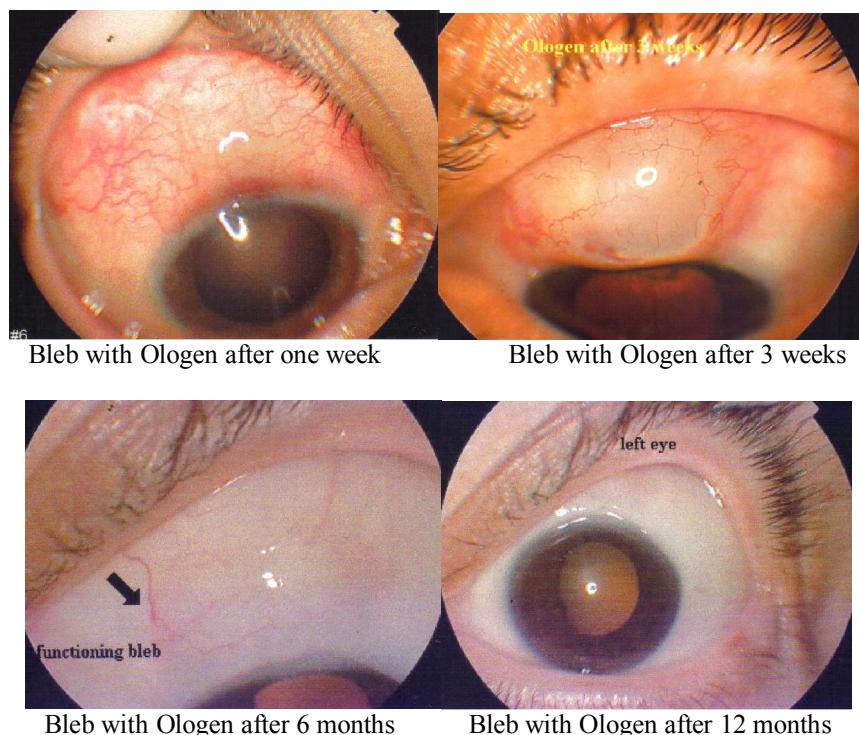


Table (2): Postoperative data.

	Study (Ologen) group	Control group	p-value
Hypotony	2/16	6/16	
Encapsulated bleb	0/16	3/16	
Flat bleb	0/16	1/16	
Ologen removal	1/16	0/16	
Mean postop IOP	$13.16 \pm 1.68 \text{ mmHg}$	$16.47 \pm 3.56 \text{ mmHg}$	0.46
Mean postop drugs	0.31 ± 0.48	1.06 ± 0.85	0.05
Success rate	93.75%	75%	

4. Discussion:

It is known that postoperative scarring is a major problem compromising postoperative surgery success in trabeculectomy operation¹⁴. Wound healing and scar formation could cause fibrosis and obstruction of aqueous outflow, which is one of the

most common reasons for the failure of glaucoma surgery¹⁵⁻¹⁷.

Since introduction of MMC in 1990, there is significant enhancement of success rate but adverse effects such as cataract formation, avascular filtering blebs, thinning of the conjunctiva, blebitis and endophthalmitis were increased^{14,18,19}. Another anti-

scar agents as growth-factor inhibition and amniotic membrane have been applied to enhance success rate of glaucoma surgery with limited results^{20,21}.

The ologen implant is a possible alternative to antimetabolite use in trabeculectomy surgery because of its modulatory effect on wound healing. The aim of this porous collagen polymer is to allow random proliferation of fibroblasts through the collagen matrix, hence decreasing collagen deposition and scarring. A literature suggests that ologen degradation time is about 30-60 days¹². But Boey et al find that ologen implant residue to be still present in up to 40% at 90 days¹³.

The clinical applications of ologen have been presented at conferences (European congress of Ophthalmology, Vienna, June 2007 and world glaucoma congress, Singapore, July 2007)²². Dimitris et al concluded that, there were no statistical significant difference between trabeculectomy and trabeculectomy with ologen regarding to mean postoperative IOP, mean of antiglaucoma drugs and postoperative complications²². In comparison to our study, it is found that, mean postoperative IOP is more controlled with trabeculectomy with ologen than control group, at the same time, mean postoperative antiglaucoma drugs and complications are lower in ologen group than in control group.

A recent experimental studies^{23,24} revealed that, the use of anti-scar materials like solid hyaluronic acid-carboxymethyl cellulose film (Seprefilm) significantly reduced postoperative conjunctival-scleral adhesion. In this study, ologen implant was used to get same idea of anti-scarring after its use in animals too.

Although, more studies with large sample designs are necessary to evaluate the effectiveness of ologen matrix with trabeculectomy operation, our study has demonstrated a high success in comparison to trabeculectomy alone for two years follow up. Another two recent studies reported that, ologen is will effective and helps in scarring regression as reported by Rosentreter et al¹⁴. Other study²² revealed that a non-significant differences in postoperative IOP after trabeculectomy with ologen and sole trabeculectomy. In this study, no postoperative infection, no implant extrusion or conjunctival erosion was reported same as previous studies reported^{14,22}.

In comparison to trabeculectomy with MMC, it is found that, MMC is more effective on conjunctival healing, getting marked reduction of fibrosis and transparent polycystic blebs, but with high incidence of complications. In this study, no case of endophthalmitis reported, in another study²² they reported one case of endophthalmitis but after culture, it was not due to ologen. The limitation of this

study is the small sample size of the patients included.

In conclusion, this new degradable collagen implant (olen) improves and normalizes filtering surgical wound healing with more loosely organized bleb tissue and healthy than that unaugmented blebs.

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