

Method Article

Collagen matrix implant (Ologen)TM in glaucoma surgeries; precautions for a better control of intraocular pressure

Abstract

Background: Collagen matrix implant (CM) is used in glaucoma surgery to regulate healing under the conjunctiva.

Purpose: To highlight the precautions that should be taken for a better intraocular pressure (IOP) control with CM in different glaucoma surgeries during and after the operation.

Methods: Thirty five cases of glaucoma were treated surgically with adjunctive OlogenTM.

- a) Fifteen subcleral trabeculectomies (SST): for adult Primary Open Angle Glaucoma(POAG).
- b) Five SST's for Primary Congenital Glaucoma(PCG).
- c) Fifteen Phaco-trabeculectomies for advanced POAG with cataract. One was converted to extracapsular cataract extraction with SST because of a subluxated (270 degree) cataractous lens with advanced glaucoma.

The number of 10/0 nylon stitches to close the scleral flap, the method of closure of the fornix based conjunctival flap and injection of Na hyaluronate at the end of the surgery were evaluated. Postoperatively: Anterior chamber(AC) depth, the need for ocular massage, any additional medications or further surgical intervention were assessed.

Results: Better IOP control was obtained with slightly shallow AC postoperatively and tight conjunctival closure. Ocular massage may be needed and medications for cases which experienced tight closures of the scleral flap. Four SST's and four phaco-trabeculectomies needed supplemental medications after surgeries. Failure in one SST and two phacotrabeculectomies was due to presence of additional risk factors in the patients. The rest of cases went successfully with IOP < 17 mm Hg without medications.

Conclusion: CM is a successful adjunct to glaucoma surgeries, intraoperative and postoperative precautions should be taken to maintain proper aqueous drainage and functioning blebs and improve the degree of success.

Intoduction

Glaucoma filtering surgery fails because of scarring of the filtering bleb. Fibroblasts proliferation from the episclera and Tenon's capsule play an important role in the scarring process. The use of antimetabolites in glaucoma filtering surgery has a beneficial effect on the lowering of intraocular pressure (IOP) especially in eyes at

poor surgery prognosis. They inhibit the fibroblasts proliferation and subsequent scarring of filtering bleb.⁽¹⁾

Mitomycin C (MMC) is currently the preferred antiproliferative agent.⁽²⁾ In addition to affecting DNA, it also affects RNA and protein synthesis. It thereby inhibits fibroblast proliferation and is toxic to endothelial cells. It introduces new complications of its own, including chronic hypotony with maculopathy, cystic avascular blebs, bleb leakage, bleb failure, bleb infections and endophthalmitis.⁽³⁾

OlogenTM is an artificial porcine extracellular matrix, which is made of atelocollagen cross-linked with glycosaminoglycan. It is a biodegradable scaffolding matrix that induces a regenerative wound-healing process in the absence of antifibrotic agents. It is designed to prevent episcleral fibrosis and subconjunctival scarring and minimize the random growth of fibroblasts, instead promoting their growth through the pores in the matrix. This implant is found to be biodegradable within 90–180 days.⁽⁴⁾

After degradation, this collagen matrix implant (CM) leaves behind a loose alignment of collagen fibers inside the bleb, which are remarkably similar to normal tissues.⁽⁵⁾

Two types of CM (Ologen, Aeon Astron Europe B.V., Leiden, The Netherlands) are used in glaucoma surgery, as per the manufacturer's design: the first is a disc of 6 mm diameter × 2 mm thickness and the second is a disc of 12 mm diameter × 1 mm thickness (Fig. 1a,b).

The advantages are claimed to be preventing episcleral fibrosis, subconjunctival scarring, risks of MMC (epithelial toxicity, hypotony, avascular blebs, late endophthalmitis). CM ensures as well a stable vascular bleb.

CM acts as a three dimensional porous scaffolding matrix. It promotes regenerative wound healing by allowing organised fibroblasts growth and physiological regeneration. Thus, a loosely structured filtering vascular bleb is formed. It has also a tamponade effect in the early postoperative course. This may promote long term IOP control.

CM is widely used in SST; according to Marey and co-workers, SST gave comparable successful results when assisted by OlogenTM as with adjunctive MMC.⁽⁶⁾

Ologen is getting to be assessed in phacotrabeculectomy by many surgeons, Narayanaswamy and his colleagues found it to be suboptimal in performance as compared with MMC in combined glaucoma and phacoemulsification.⁽⁷⁾ Biodegradable CM (Ologen) can be used to reduce the surgical risks and complications of SST with MMC in infants.⁽⁸⁾

Patients and methods

This is a retrospective study conducted from January 2011 to December 2013. The cases were done in the Department of Ophthalmology in Ain Shams University Hospitals and in Magrabi Eye Hospital in Cairo. All cases were operated upon by a

single surgeon (the first author). The primary objective was to evaluate the efficacy and safety of CM (Ologen, Aeon Astron Europe B.V., Leiden, The Netherlands).

All patients were operated upon after taking informed consent from them if adults or from their parents in cases with PCG.

Thirty-five cases were studied including the following:

- Fifteen subsclear trabeculectomies (SST) : for adult Primary Open Angle Glaucoma (POAG).
- Five SST's : for Primary congenital glaucoma (PCG).
- Fifteen phaco-trabeculectomies:
 - Fourteen for advanced POAG with cataract.
 - One converted to extracapsular cataract extraction with SST (asubluxated (270 degree) cataractous lens with advanced pseudo-exfoliative glaucoma).

Subscleral trabeculectomy (SST):

SST started with a fornix based conjunctival flap, cauterization of the episcleral blood vessels was done then a scleral flap measuring 3 mm × 4 mm was performed. The scleral flap was sutured with one or two loose 10.0 nylon stitches and CM was placed over it. A watertight closure of the fornix based conjunctival flap with buried 10.0 nylon stitches at the limbus was performed (2 peripheral stitches or 2 peripheral + 1 middle continuous stitch). * A combination of steroid–antibiotics (dexamethasone–tobramycin) eye drops q.i.d. was prescribed for six weeks then tapering over the following two weeks.

Phaco trabeculectomy:

Phaco trabeculectomy was performed using two different sites: a temporal clear corneal incision for the phacoemulsification and a superior scleral flap measuring 2 mm × 3 mm. Fornix based conjunctival flap was used and episcleral blood vessels were cauterised. The scleral flap was sutured with one or two loose 10.0 nylon stitches and CM was placed over it. A watertight closure of the fornix based conjunctival flap with buried 10.0 nylon stitches at the limbus was performed (2 peripheral stitches or 2 peripheral + 1 middle continuous stitch). * A combination of steroid–antibiotics (dexamethasone–tobramycin) eye drops q.i.d. was prescribed for 6 weeks, tapering over the following two weeks.

One phaco trabeculectomy was converted to extracapsular cataract extraction with SST (asubluxated (270 degree) cataractous lens with advanced glaucoma). The capsulorrhexis failed, the cataractous lens was retrieved by a scoop after enlarging the temporal corneal incision, limited anterior vitrectomy was done. Anterior chamber IOL was implanted and the corneal incision was closed by four interrupted 10.0 nylon stitches. The glaucoma surgery was continued as described.

Intraoperative measures to be evaluated:

- number and tightness of 10/0 nylon stitches to close the scleral flap (one or two).
- Method of the fornix based conjunctival flap closure with 10/0 nylon stitches (2 peripheral stitches or 2 peripheral+1 middle continuous stitch).
- Na hyaluronate injection in AC at the end of surgery.
*As the cases enrolled in this study were considered the beginning of the learning curve using CM, closure of the scleral flap was done by one loose stitch in some cases or two in others. Closure of the fornix based conjunctival flap as well by two or three stitches was due to the same reason.

Postoperative evaluation :

- Anterior chamber(AC) depth.
- Need for ocular massage.
- Need for supplemental steroids .
- Additional IOP lowering medications.

The definition of success was as follow for SST treating POAG and phacotrabeculectomies:

- Full success (IOP < 17 mm Hg without medications).
- Qualified success (IOP < 21 mm Hg with IOP lowering medication(s)).
- Failure (IOP > 21 mm Hg not responding to medications).

The definition of success was as follow for PCG:

- Full success: IOP less than 15 mmHg without medications; clear cornea.**
- Satisfactory success: IOP less than 21 mmHg without medications; clear cornea.
- Poor success: IOP less than 21 mmHg with medications.
- Failure: IOP more than 21 mmHg.
** Full success in PCG was considered 15 mmHg rather than 17 mmHg as this level might be more suitable for better corneal clarity and the target IOP for such young age group should be lower than adults with POAG.
***Some of the cases with SST for PCG were discussed in a paper by the first author as a preliminary report , this was published in 2013.⁽⁸⁾

Figure 1



(a)



(b)

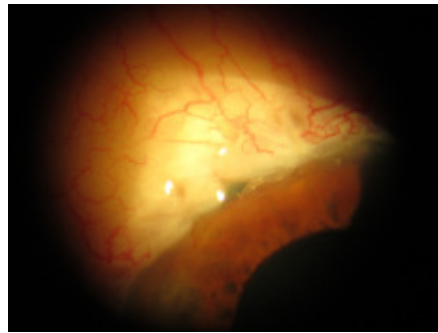
Results

SST for POAG:

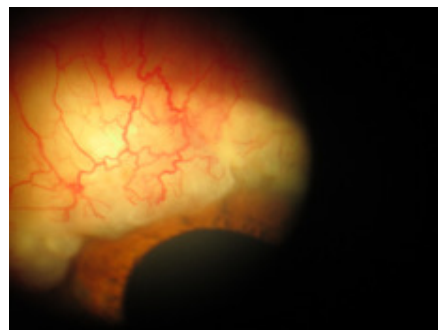
Regarding the fifteen SST with CM done for POAG the following remarks and results were noted:

- Flat AC and hypotony occurred in four cases (26.6%) in early postoperative period. In two of them, one 10/0 nylon stitch was applied for closure of the scleral flap. In the two other cases, loose conjunctival closure was done with only two 10/0 nylon stitches.
- Two cases (13.3%) needed supplemental medications to lower IOP. Tight closure of the scleral flap was done by two 10/0 nylon stitches. Ocular massage and frequent topical steroids were needed for few weeks postoperatively.
- Five cases (33.3%) showed very stable postoperative AC with Na hyaluronate injection at the end of the surgery, one loose 10/0 nylon stitch for closure of the scleral flap but with tight closure of the conjunctiva with three 10/0 nylon stitches.
- Bleb morphology was monitored by frequent photography, vascularity of the bleb was more intense in the first two weeks after the operation, and gradually faded in the following weeks under frequent topical dexamethasone eye drops to be nearly the same vascularity as the neighboring conjunctiva after four months. (Figure 2 a,b,c).
- The success rate was: 13 cases (86.6%) with full success and two cases (13.4%) with qualified success.

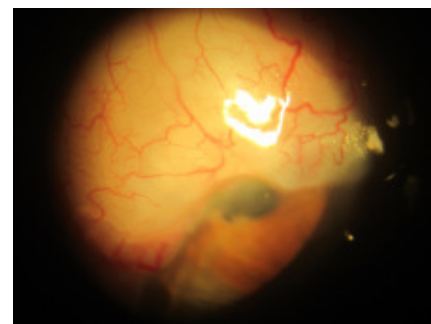
Figure 2:



(a)Bleb at 2 weeks postop



(b)Bleb at 6 weeks postop



(c)Bleb at 4 months postop

SST for PCG:Regarding the five cases of SST with CM for PCG the following was noted:

- One case(20%) showed flat AC and hypotonyin the early postoperative period ;one very loose 10/0 nylon stitch was appliedfor closure of scleral flap.
- One case (20%) showed failure.

- One case (20%) needed supplemental medications to lower IOP. The last two cases had more risk factor as they were recurrent PCG after previous SST.
- The success rate was : one case (20%) full success, two cases (40%) with satisfactory success, one (20%) case with poor success and one case (20%) with failure for which glaucoma drainage implant was done.

Figure 3 shows successful SST in PCG with a superior bleb

Figure 3



Figure 4 shows successful SST in PCG with temporally located bleb

Figure 4



Phaco-trabeculectomies

Regarding the fifteen cases of phacotrabeculectomies with CM, the following was noted:

- Four cases (26.6%) showed flat AC and hypotony in early postoperative period due to loose closure of the conjunctiva with two 10/0 nylon stitches.
- Four cases (26.6%) needed supplemental medications to lower IOP. In these cases, tight closure of the scleral flap with two 10/0 nylon stitches were

used and concurrently deep AC in first week) .Ocular massage and frequent topical steroids (dexamethasone were needed few weeks postoperatively.

- Two cases (13.4%) resulted in failure due to the presence of more risk factor which was previous SST.
- Five cases (33.3%) showed very stable postoperative AC with Na hyaluronate injection at the end of the surgery, one loose 10/0 nylon stitch for closure of the scleral flap but with tight closure of the conjunctiva with 3 10/0 nylon stitches.
- Tortuous vascularized bleb was frequently noted four weeks after phacotrabeculectomy with cork screw vessels (figure 5) ; which improved after three months with more intensive topical steroids and ocular massage (Figure 6).
- The success rate was: nine cases (60%) with full success, four cases (26.6%) with qualified success and two cases (13.4%) with failure for which glaucoma drainage implant was done.

Figure 5

Tortuous vascularized bleb 4 weeks after phacotrabeculectomy

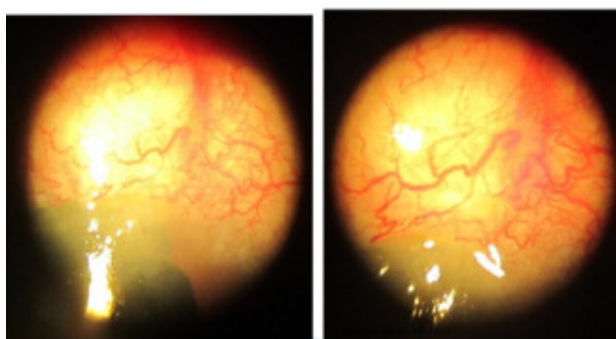
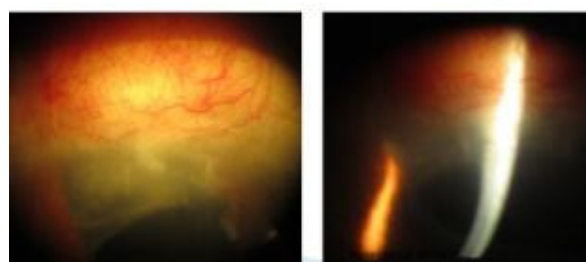


Figure 6

Improved vascularization after 3 months with more topical steroids and ocular massage



Discussion and Conclusion

CM is a successful adjunct to glaucoma surgeries. Intra operative and postoperative precautions should be taken to maintain proper aqueous drainage, functioning blebs, and better degree of success; thus, reaching target IOP and stable visual field changes.

Operative precautions to ensure filtration entail mainly loose closure of the scleral flap by two 10/0 nylon stitches. This should be supported by avoiding leakage through tight closure of the fornix based conjunctiva flap by two peripheral and one middle continuous 10/0 nylon stitches buried at the limbus. Na hyaluronate injection in AC at the end of the surgery promote a stable AC in the early few days following the operation. Closure of the scleral flap by one loose 10/0 nylon stitch can be done but with more experience regarding the degree of looseness at the end of the learning curve of the use of CM.

Postoperative precautions include frequent ocular massage in the first few weeks, more frequent topical steroids for up to three months. Additional IOP lowering medication may be needed with some cases not achieving the planned target IOP.

Full success (IOP < 17 mm Hg without medications) was found more with cases which had slightly shallow AC in the 1st week postoperatively with raised bleb. This would promote filtration and smooth incorporation of the CM into the bleb. Proper filtration necessitates loose scleral flap closure with tight conjunctival closure.

Qualified success (IOP < 21 mm Hg with IOP lowering medication) was encountered with cases in which there was tight closure of scleral flap, very deep AC in day-1 postoperative. Ocular massage and frequent steroids were needed few weeks postoperatively up to three months.

Failure (IOP > 21 mm Hg not responding to medications) occurred in the presence of one or more additional risk factors mainly previous SST, trauma, ocular surface disease, dark race, etc. These cases were candidates for glaucoma drainage implants later.

The relative disadvantages of CM are that filtration adjustment needs experience with the implant as well as possible infection and shallow AC (as any SST complication).

The most peculiar finding which had to be managed vigorously was the foreign body like reaction and encapsulation around the CM as manifested by cork-screw vessels; which occurred few weeks postoperatively leading to failure. The latter happened in phacotrabeculectomies mainly due to the severe postoperative inflammation.

It can be also explained by the indolent episcleral fibrosis that produces a dense coat around an extrascleral foreign body such as a scleral buckle.⁽⁹⁾

In a research work by Rosentreter in 2012 to study the reaction of the subconjunctival tissue and the histopathologic findings in explanted Ologen Implant,

Ologen matrices and scar tissue were explanted in revision surgery in case of failed trabeculectomies or after glaucoma drainage device surgery. Histological sections were studied by hematoxylin-eosin (HE) staining. Further immunohistochemical stainings were performed for α -smooth muscle actin (α -SMA), fibronectin (FN), collagen III (COL3) and CD68.9. In case of failed trabeculectomies, HE staining of the explanted Ologen revealed an invasion of fibroblasts into the implant. The implants were enclosed by a collagenous pseudocapsule and surrounded by a loose connective tissue. α -SMA staining showed an accumulation of myofibroblasts predominantly in the ologen implant, whereas COL3 was mainly detected at the border area of the implant and the pseudo capsule around the implant. Immune histochemistry for FN showed an intensive staining inside the implant and at the pseudocapsule.⁽¹⁰⁾

Based on the last study by Rosentreter and the close follow up of my cases, CM should be "floating" within the bleb to minimize the previously mentioned foreign body reaction which manifest by cork screw vessels as in figure 6. These tortuous vessels are more encountered with phacotrabeculectomies in which postoperative reaction are more intense than SST. This explains also the need for prolonged topical steroids to inhibit inflammation and ocular massage to break any possible fibrous threads or pseudo capsule around the implant to promote aqueous filtration.

This study focuses mainly on the operative and postoperative precautions with CM in glaucoma surgeries. These tips are important in the learning curve of using this product. Studies on OlogenTM focused on the final IOP results only. Modification of some steps in glaucoma surgery and special postoperative care are essential for the success of CM to smoothly reach the target IOP. Longer follow up period and larger number of cases are needed to consolidate the conclusion.

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