Long-Term Intraocular Pressure Control after Trabeculectomy with Ologen Implant in Primary Open Angle Glaucoma

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Abstract
Aim: to evaluate the long-term results of trabeculectomy augmented with Ologen implant in cases with primary open glaucoma (POAG). **Patients and Methods**: a retrospective study including patients with POAG who had undergone trabeculectomy with Ologen implant with at least 2-year follow-up. The charts were reviewed and analyzed for intraocular pressure (IOP), number of anti-glaucomatous drugs (AGD) and any recorded complications. Primary outcome was the IOP reduction. **Results**: The study included18 eyes of 18 patients with POAG with mean age of 56.7±7.4 years (43-68 years) and 24 (66.7%) male. The IOP was statistically reduced from mean of 34.7±5.02 mmHg preoperative to 15.3±3.7mmHg at 24 months postoperative ($p<0.001$). The number of AGD statistically dropped from a mean of 3.1±0.53 preoperative to 1.4±0.9 at 24 months ($p<0.001$). At 24 months; complete success was achieved in 2 eyes (11.1%) and qualified success was recorded in 14 eyes (77.8%). None of the patients developed any vision threatening complications. **Conclusions**: Trabeculectomy augmented with Ologen implant was proved to be safe and effective in long-term IOP control in POAG.
Keywords: Primary open angle glaucoma; Ologen; trabeculectomy.

Introduction
Since trabeculectomy was introduced in 1968; it remained the 'gold standard' for filtration surgery[1]. Nevertheless, the process of wound healing may result in fibrosis of the bleb and thereby obstruction of the drainage fistula with resultant bleb failure[2].

Anti-metabolites were introduced in 1980's to assist trabeculectomy. Fibroblast's proliferation was reduced in the subconjunctival space as well as in the Tenon's capsule. Yet, these agents were proved to result in some hazardous effects as hypotony with maculopathy, thincystic avascular bleb, blebitis, and late onset-endophthalmitis[3].

Other agents as Beta-irradiation[4] and photodynamic therapy[5] as well as gene therapy approach were advocated in order to regulate the process of wound healing[6]. Although promising approaches; they have not proved to be useful for clinical applications.

A biodegradable collagen matrix (Ologen™) is an implant designed to be used with trabeculectomy placed directly over the scleral flap. It regulates the healing process by forcing fibroblasts and myofibroblasts to grow into its pores secreting a loose matrixed- connective tissue[7].

The current study was conducted to evaluate the long-term results of trabeculectomy augmented with Ologen in eyes with primary open angle glaucoma (POAG).

Patients and methods
A retrospective study included patients with POAG who had undergone trabeculectomy with Ologen implant in Mansoura Ophthalmic Center, Faculty of Medicine, Mansoura University. Written informed consent was obtained from all the patients before the operation. The charts were reviewed for demographic characteristics as age, gender and medical history. Basic clinical data was retrieved as pre- and postoperative IOP measured by applanation tonometer, number and type of anti-glaucomatous drugs (AGD), visual acuity measured by Snellen's chart; converted to LogMar for statistical analysis and cup-disc ratio. Reliable visual filed data was available only for small number of cases and was not included in statistical analysis.

Patients were excluded from the study if they had incomplete medical records or follow-up less than 24 months. Patients with other glaucoma diagnoses were also excluded. The primary outcome was the IOP control and the secondary outcome involved the recording of any complications. All the patients had standard subscleral trabeculectomy (SST) with fornix based conjunctival flap. Ologen implant [Version 2-Aeon Astron Europe B.V., the Netherlands. Model 830601, size 6mm (D) x 2mm (H)] was placed at the edge of the trap door after its closure with 2 nylon silk sutures (10\0). All patients received **topical** steroid / antibiotic combination (dexamethasone / tobramycin) eye drops and ointment. The initial frequency of drops was tailored according to the individual cases, in most cases, a frequency of 5 times/day was sufficient. The drops were then tapered according to the patient's response, and continued until the eye appears completely quiet. Short-acting cycloplegic (e.g. cyclopentolate) was used in the early postoperative period. The patients were followed after 1 day, 1 week, 1-, 3-, 6-,12-, 24-months.

Success and Failure rates

Complete success was defined as IOP equal to or less than 18mmHg and equal to or greater than 6mmHg (i.e. 6mmHg≤IOP≤ 18mmHg) without AGD. Qualified success was considered whenever the above criteria were fulfilled with topical AGD. Cases were considered as failed cases whenever topical anti-glaucoma medications were unable to control the IOP for two consecutive visits or whenever another glaucoma surgery was required.

Statistical analysis

Data was analyzed by SPSS version 16 (Chicago, SPSS Inc, 2008). Normality of data was tested with Shapiro-wilk test. Qualitative data were described by number and percent. Quantitative data were described in mean± standard deviation (parametric) and median with range (non-parametric). Paired t-test was used to compare between to continuous variables. Repeated measure Anova test was used to compare between the results along the follow-up. Results were considered significant when P value was≤ 0.05.

Results

The study included18 eyes of 18 patients with POAG with mean age of 56.7± 7.4 years (43-68 years) and 24 (66.7%) males. All the patients completed 24 months follow up with mean 29.4± 4.1 months (24-36 months). Almost all included the patients had moderate to severe glaucomatous damage based on visual field and optic disc parameters. The IOP was statistically reduced from mean of 34.7± 5.02mmHg preoperative to 15.3±3.7mmHg at 24 months postoperative ($p<0.001$) with mean percentage of 56% IOP reduction rate. **Figure 1** illustrates the scatter-gram plot for the pretreatment versus post-treatment IOP at 24 months.

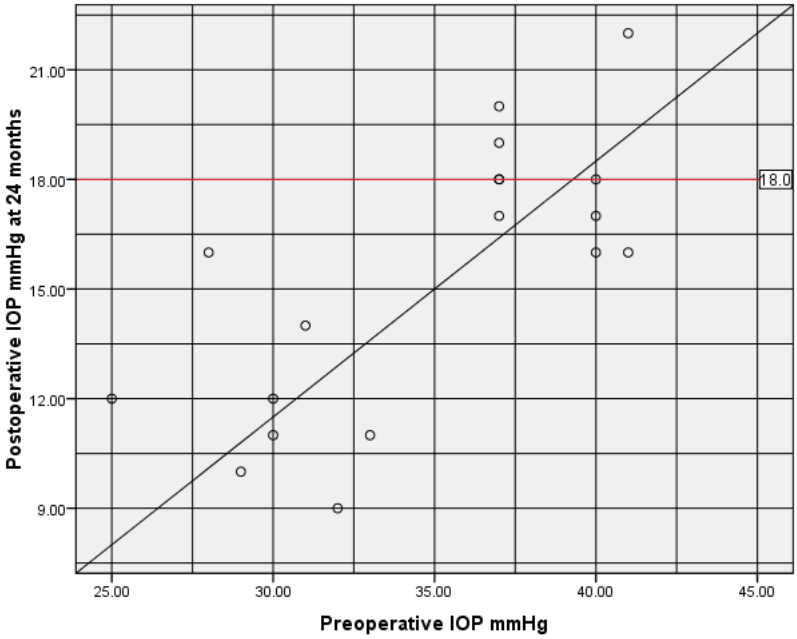

Figure 1: Scatter gram plot for preoperative IOP (X axis) and IOP at 24 months (Y axis). All the points below the red horizontal line represent eyes with IOP ≤18 mmHg the cut point for success.

The curve displayed in **Figure 2** represents the mean IOP in all patients over the follow-up time. There was significant reduction in the IOP at 1st day (11.05±1.1 mmHg) after treatment followed by rise at the 3rd month (17.7±2.8 mmHg). This was followed by reduction of the IOP till the end of the follow-up.

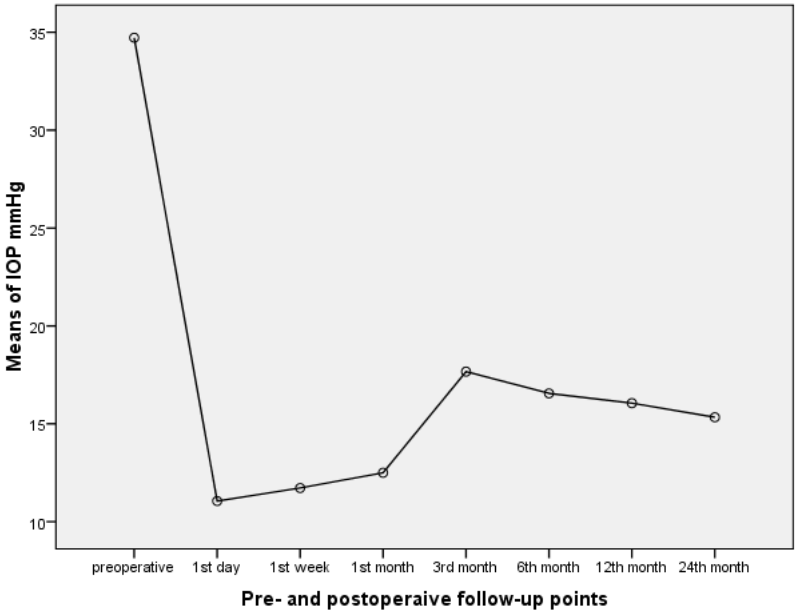

Figure 2: Means of intraocular pressure (IOP) of the included eyes at preoperative and at different points along the follow-up period.

The number of AGD statistically dropped from a mean of 3.1±0.53 preoperative to 1.4±0.9 at 24 months ($p<0.001$). There was statistically insignificant difference in the mean LogMAR visual acuity from baseline 0.86±0.2 to 0.88±0.2 at 24 months ($p= 0.269$). At 12 months; only 3 eyes (16.7%) showed complete degradation of the implant while the rest showed only partial degradation. At 24 months all the cases showed complete degradation.

At 24 months; complete success was achieved in 2 eyes (11.1%) and qualified success was recorded in 14 eyes (77.8%) with 89% total success rate. The IOP in two eyes (11.1%) remained higher than the cut point of success despite the use of maximal tolerated topical AGD however the patients refused further surgeries. None of the cases developed any intraoperative complications related to the implant itself. Hypotony with shallow anterior chamber was recorded in 3 eyes (16.7%), subconjunctival hemorrhage in 2 eyes (11.1%) hyphema in 2 eyes (11.1%), conjunctival slipped suture in 1eye (5.6%), corneal edema in 1 eye (5.6%) and progression of preexisting cataract in 3 eyes (16.7%). None of the cases developed encapsulated bleb.

Discussion

Ologen is a bioengineered biodegradable collagen matrix proposed as a potential alternative method for controlling the wound healing process following filtering surgery. Instead of inhibiting fibroblast proliferation, Ologen guides the fibroblasts to grow randomly in its porous structure resulting in random alignment of the collagen fibers with loose connective tissue matrix that could reduce scar formation and wound contraction effectively. This function is achieved without the complications of anti-fibrotic agents[7].

The current study was a retrospective study involved 18 eyes of 18 patients with POAG who had undergone trabeculectomy augmented with Ologen implant for at least 24-month. The primary outcome measure was the IOP control at 24 months with the recording of any adverse complications as a secondary outcome.

In our study the postoperative IOP showed early rise in the third month than other scheduled visits. This increase in the IOP may be related to the reservoir effect of the implant which acts as a valve that absorbs the aqueous humor and presses over the scleral flap providing physical resistance against over-filtration. With our surgical protocol, using 2 reasonable fitting sutures of the scleral flap, early rise was accepted. This resistance was expected to decrease progressively as the implant degrades.

Senthil et al.,[8] compared trabeculectomy augmented with Ologen to mitomycin-C (MMC) in Indian eyes and reported significant difference in IOP between the 2 groups at 1st and 6th month postoperative being higher in the Ologen group than MMC group.

In the current study; there was significant reduction in postoperative IOP; with 56% reduction in IOP at 24-months follow-up. This was consistent with the results reported by Chen and Hsu[9] who achieved 58.3% reduction in mean IOP after 9 months follow-up in 59 eyes that had undergone trabeculectomy with Ologen implantation.

In the current study total success was achieved in 89% of the eyes by the 24th month postoperative. Higher success rates were reported by Senthil et al.,[8] in which complete success was achieved in 100% of the eyes at 6 months. This difference might be related to our longer follow up period. Moreover, the difference may be related to the stringent definition of success applied in our study (18 mmHg) instead of 21mmHg used in other studies. We chose this cut point as almost all the cases included were considered moderate degree of severity whom required lower IOP levels for proper control.

In the present study; there were no intraoperative complications related to the Ologen implant itself. No allergy was detected, no translocation of the implant or erosion of the overlying conjunctiva. Moreover, the postoperative complications were transient. This was in consistent with

the results published by Nilforushan et al.,[10] used Ologen as adjuvant for trabeculectomy in a non-randomized study in cases with OAG. None of our patients encountered encapsulated bleb. Papaconstantinou et al.,[11] encountered less encapsulated blebs in the Ologen than in traditional SST group. In contrast to that; Min et al.,[12] reported 9 cases (30%) with encapsulated bleb that required only digital massage in 8 of them and needling in 1 case.

Limitations of this study include the small number of operated eyes, short duration of follow-up, and the lack of another group of trabeculectomy with a widely accepted anti-fibrotic agent like MMC. So our suggestion is to conduct a randomized case- control study with larger number of eyes and longer duration of follow-up, which can reveal more about the safety and the efficacy of Ologen.

Conclusion

Ologen implant was proved to be a safe and effective method in augmentation of trabeculectomy in eyes with POAG.

Financial disclosure:
The author declares no financial interest in any of the materials used in the study.

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