Subconjunctival Administration of Opioid Growth Factor Prolongs Longevity of Glaucoma Filtering Surgery without Tissue Toxicity in Rabbits

Sara C. Roshwalb1, Joseph W. Sassani III2, Patricia J. McLaughlin3 and Ronald P. Wilson1*

1Department of Comparative Medicine, Penn State University College of Medicine, USA
2Department of Ophthalmology and Pathology, Penn State University College of Medicine, USA
3Department of Neural and Behavioral Sciences, Penn State University College of Medicine, USA

Abstract

The aim of this study was to evaluate the use of [Met5] enkephalin, termed opioid growth factor (OGF), as an anti-fibrotic agent in an effort to maximize the time interval before glaucoma-filtering surgical failure. OGF was sterilely prepared in a biocompatible polymer, hydroxymethyl methacrylate (Hydron) and surgically implanted sub-tenon’s capsule at the time of a “full thickness” filtration procedure. Average intra-ocular pressure, surgical bleb height, area, and the degree of hyperemia of the conjunctiva surrounding the surgical site were evaluated daily until surgical failure. OGF-treated rabbits were compared to animals that were treated with phosphate buffered saline, Hydron alone (vehicle control), or mitomycin C. Both OGF and MMC treatments significantly reduced the rate of decay of surgical bleb volume compared to Hydron or PBS. There was no difference in inflammation in the conjunctiva between OGF and the other treatment groups peri-operatively, nor was there evidence of apoptosis or necrosis. OGF has a similar duration of efficacy as MMC and has potential to be used in filtering surgery without the toxic effects of MMC.

ABBREVIATIONS

IOP: Intraocular Pressure; MMC: Mitomycin C; OGF: Opioid Growth Factor; TCFs: Tenon’s Capsule Fibroblasts; NZW: New Zealand White; dpo: Days Post-Operatively; ARVO: Association for Research in Vision and Ophthalmology; BSA: Bovine Serum Albumin; BSS: Balanced Salt Solution; ACD: Anterior Chamber Depth

INTRODUCTION

Glaucoma filtering surgery is the most common surgical non-laser procedure performed in treatment of glaucoma [1]. The procedure creates a fistula to form an alternative drainage pathway forming a structure known as a filtering bleb, providing a reservoir for pooling of aqueous humor beneath the conjunctiva and/or Tenon’s capsule [2]. The bleb is considered the cornerstone of intraocular pressure (IOP) control in glaucoma-filtering surgery, but it is an artificial and unstable tissue structure [1]. This procedure ultimately fails primarily due to subconjunctival wound healing through deposition of fibrous tissue at the filtration site, causing mechanical obstruction of the surgically created outflow tract [1].

Current research efforts are focused on the use of pharmacologic agents as adjunctive therapy to prevent or delay the fibrovascular proliferation process following surgery. Currently, mitomycin C (MMC) is considered the gold-standard of therapy [3]. Because it is applied at the time of surgery, it is difficult to control the concentration being delivered to the local
tissues. Overall, MMC has been associated with a high incidence of complications including hypotony, ciliary body toxicity, endophthalmitis, leaky blebs, and endothelial toxicity [3–7]. Research efforts focus on identifying an adjunctive treatment that has a similar or longer duration of activity than MMC with fewer complications.

Opioid Growth Factor (OGF) is chemically termed [Met\(^{5}\)] enkephalin. OGF is a native, nontoxic, constitutively expressed opioid peptide that delays cell proliferation at the G\(_{0}/G_{1}\) phase [8]. It serves as an inhibitory growth factor targeted to cell proliferation processes as shown in studies on rabbit Tenon's capsule fibroblasts (TCFs), where treatment with exogenous OGF in cell culture results in decreased fibroblast proliferation without toxicity as evidenced by a lack of apoptosis and necrosis [9]. Because TCFs are integral to the outcome of glaucoma-filtering surgery, there is great potential for use of exogenous OGF as an adjunct therapy to prolong surgical success by delaying wound healing if its effect can be prolonged in a time released manner.

In the study, OGF was infused into a biocompatible, non-biodegradable slow-release polymer called hydroxyethyl methacrylate (Hydron) and implanted sub-Tenon's capsule at time of filtering surgery in New Zealand White rabbits and compared to the use of MMC [10–14].

**MATERIALS AND METHODS**

**Animals**

A total of 32 New Zealand White (NZW) (*Oryctolagus cuniculus*) rabbits, 15 females and 13 males, weighing 2-4 kg (~16 weeks) were used in this study. Twenty-eight rabbits were used for survival analysis of the glaucoma filtering surgery, while four were euthanized at 5 days post-operatively (dpo) for assessment of perioperative inflammation and fibrosis. The animals were wild-type NZW rabbit offspring from wild-type NZW female rabbits purchased from Millbrook Labs (Amherst, MA) and male breeder NZW rabbits of a genetically-engineered NZW strain purchased from Robinson Services (Mocksville, NC).

Experimental animals were individually housed with a 12:12-h light/dark cycle, ambient temperature 19 ± 3°C, relative humidity between 30-70% and *ad libitum* food and water. The housing and care of the animals were in accordance with the Guide for the Care and Use of Laboratory Animals [16]. All procedures were approved by the Penn State College of Medicine Institutional Animal Care and Use Committee and animal experiments were conducted in accordance with the Association for Research in Vision and Ophthalmology (ARVO) standards.

**Chemicals and Agents**

Pharmaceutical grade sucralfate powder, mitomycin C powder from *Streptomyces caespitosus* (MMC), [Met\(^{5}\)] enkephalin acetate salt powder (OGF), Hydron (poly-2-hydroxyethyl methacrylate) powder, and bovine serum albumin (BSA) - Fraction V were obtained from Sigma-Aldrich (St. Louis, MO). Intra-operatively, pharmaceutical grade sterile balanced salt solution (BSS; Alcon, Fort Worth, TX) was used to irrigate after MMC treatment.

**Hydron pellet preparation**

Pellets were made of a slow-release polymer 12% Hydron (poly (2-hydroxyethyl methacrylate; Sigma, St. Louis, MO) containing sucralfate, with or without 0.05 mg OGF dissolved in 1% BSA. Pellet preparation was adapted from a previously described protocol by Kenyon *et al.* [11]. All equipment and buffers were sterilized, and pellets were aseptically prepared in a biosafety cabinet. The pellets of approximately 0.4 x 0.4 x 0.2 mm size (Figure 1) were stored in sterile Eppendorf tubes.

**Experimental design and filtering surgery**

Baseline IOP levels were measured in both eyes prior to surgery using a tonometer (Tono-Pen®XL applanation tonometer, Medtronic Solan, Jacksonvile, FL); the ocular surface was anesthetized with sterile parracaine hydrochloride 0.5% ophthalmic solution (Akron, Lake Forest, IL).

The rabbits were sedated with 35 mg/kg ketamine hydrochloride (Ketathesia™, Butler Schein Animal Health, Dublin, OH) and 5 mg/kg xylazine hydrochloride (AnaSed®, Akorn, Decatur, IL) intramuscularly, intubated and maintained on 1-2% isoflurane anesthesia (Isothesia™, Butler Schein Animal Health, Dublin, OH).

A “full thickness” filtration procedure using a limbal based flap of the conjunctiva and Tenon’s capsule was performed as described by Scheie on the left eye of 32 total NZW rabbits by the same surgeon [17]. The right eye served as individual controls. A 3 mm wide sclerotomy was made using a fine tip Accu-Temp high-temperature cautery pen (Beaver-Visitec Inf1, Waltham, MA) followed by peripheral iridectomy. Rabbits received either 0.1 ml sterile 0.15 M PBS injected subconjunctivally, 2 Hydron vehicle-control pellets or Hydron pellets infused with OGF placed subconjunctivally intra-operatively, or 0.1 ml MMC (4 mg/ml) applied to the filtration site intra-operatively for 5 minutes followed by copious irrigation with 15 mL sterile BSS (Alcon, Fort Worth, TX). The conjunctiva was reapprised with 9-0 Vicryl suture (Ethicon, Mexico). A tight seal was confirmed by a negative Seidel test. Rabbits were randomly assigned to 4 treatment groups in including PBS control (n=6), Hydron (n=6), OGF+Hydron (n=8), and MMC (n=8).

![Figure 1](image-url)
Post-operative care included daily application of antibiotic ointment (Neomycin, Polymyxin B sulfates, Bacitracin zinc ophthalmic ointment USP; Bausch&Lomb, Tampa, FL) in the surgical eye and buprenorphine hydrochloride (Buprenex®, Reckitt Benckiser Pharmaceuticals, Richmond VA) 0.02 mg/kg subcutaneously twice daily for 3 days post-surgery.

Post-operative assessment

The same individual evaluated the rabbits daily and was masked to the treatment groups. Observations and measurements included IOP, length, width, and height of the surgical bleb, severity of hyperemia of the conjunctiva surrounding the bleb, intraocular inflammation or hemorrhage, anterior chamber depth (ACD), and Seidel test for leakage from the bleb or surgical incision. IOP measurements were taken in triplicate with a tonometer, after applying proparacaine hydrochloride 0.5%. The area and height of the bleb were measured with straight tipped Castroviejo calipers (Strong Vision Technology, Jackson, MI), with accuracy to 0.5 mm. Conjunctival hyperemia was graded subjectively based on a 3 point scale previously described (Figure 2) [18–22]. The presence of intraocular inflammation and ACD were subjectively graded using a hand-held slit lamp (Zeiss Osram 64222, Jena, Germany). Any bleb leakage was noted as a positive Seidel test.

To be included in the study, the rabbit’s average IOP in the surgical eye had to be 12.5% lower than the average IOP of their corresponding control eye within 48 hr post-surgery. This significantly decreased IOP in the surgical eye indicated an effective surgery and negated expected normal individual IOP variations between the eyes of the same rabbit. If this difference in IOP levels was not noted within 48 hrs, the rabbit was not included in the study.

Failure of the filtering surgery, and hence the endpoint for this study, was based on the absence of a discernable bleb (height = 0 mm) with concurrent normalization of average IOP of the surgical eye compared to the control. Rabbits were humanely euthanized with sodium pentobarbital (Pentasol®, Virbac, Ft. Worth, TX) intravenously after sedation with ketamine and xylazine, and both eyes enucleated for histological study. One rabbit from each treatment group was euthanized 5 days post-surgery.

Histology

Enucleated eyes were fixed in Bouin’s solution. The surgical area and corresponding area on the contralateral control eye were trimmed, sectioned, and processed for paraffin embedding. Sections (6 µm) were stained with hematoxylin and eosin and Masson’s Trichrome stains. Macrophages and heterophils were manually counted in three non-adjacent high power (200x) fields at the filtration site in the conjunctiva and sclera to assess for inflammation. Native lymphocytes in the conjunctiva and inflammatory cells indicating foreign body reaction (i.e. multinucleated giant cells) were excluded from inflammatory cell counts. To evaluate fibrosis in the conjunctiva and sclera, images of sections stained with Masson’s Trichrome stain were analyzed microscopically using ImagePro® Plus (Media Cybertenics, Warrendale, PA).

Statistical analyses

Survival curves were evaluated by log-rank test for statistical significance using GraphPad Prism 6 (La Jolla, CA). Average time to failure was calculated with standard error of the mean. Average bleb volume per treatment group was calculated based on daily observations of bleb length, width, and height.

The rate of decay of the surgical bleb volume was assessed using a survival decay model with repeated measures to account for multiple measures for the same subject. The basic model fits a traditional exponential decay curve capturing the relationship between bleb volume and decay that is curvilinear relative to time, which was transformed to a linear model using the natural logarithm of the volume. In this form, bleb decay was estimated as the slope of the simple regression line. The analysis was performed using SAS PROC Mixed (SAS Institute Inc., Cary, NC), a modeling procedure accounting for random effects within subjects coding binary variables for categorical values to account for the experimental groups. T-tests were used to compare statistical analysis between the different groups.

Hyperemia scores were evaluated by calculating the mode of the scores in each treatment group until the hyperemia resolved. A Kruskal-Wallis test of the mean day for each hyperemia score per group was calculated using SAS.

Inflammatory cell counts were analyzed by paired t-tests within a group and by analysis of variance across groups. Post-hoc analyses were conducted using Newman-Keuls tests. Average inflammatory cell counts between the different treatment groups

---

**Figure 2** Representative pictures illustrating the hyperemia scoring system. Visual evaluation of the hyperemia of the conjunctiva surrounding the filtration site was graded on a scale of 1, 2, or 3. A hyperemia score of 1 (A) is similar to un-operated control eyes with minimally injected blood vessels, a score of 2 (B) is moderately hyperemic, and a score of 3 (C) is severely hyperemic.
comparing the sclera and conjunctiva separately were evaluated at 5 days post-surgery by unpaired t-tests with Welch’s correction for unequal variance.

RESULTS AND DISCUSSION

Surgical bleb survival

All of the PBS controls, 83.3% of vehicle controls, 62.5% of the MMC, and 75% of OGF treated rabbits respectively had successful surgeries as dictated by a 12.5% decrease in IOP of the surgical eye within 48 hours following surgery. Time to surgical failure was defined as the time point when a flat surgical bleb existed concurrently with normalized average IOP for 2 consecutive days. The PBS and Hydron control groups reached surgical failure at 29 ± 7.8 (mean days post-surgery ± standard error) and 21.2 ± 2.5 days, respectively. OGF + Hydron treated rabbits reached failure at 36 ± 16.5 days, while the MMC treated rabbits reached failure at 66.8 ±22.8 days. There was no significant difference in survival times between the treatment groups by log rank test as it was affected by outliers which creates large standard errors of the mean. If bleb height decay is considered independently of IOP, the time to failure for PBS and Hydron treatment groups were 12.2 ± 1.3 and 11.8 ± 1.2 days, respectively. By contrast, OGF + Hydron treated animals failed at 33.5 ± 17 days, and MMC treated animals developed flat surgical blebs by 52 ± 25.2 days. When considering this single criterion, the latency to failure of the trabeculectomy for the OGF + Hydron (p = <0.0001) and MMC (p = 0.0002) treated animals was significantly greater than animals treated with PBS or Hydron.

The rate of decay of the bleb volume over time was analyzed for a more accurate representation of response to treatment. This analysis takes into account the change in height and area of the surgical bleb. The decay of bleb volume was modeled for each of the groups (Figure 3A) and the slopes of the lines for the log of volume over time were compared (Figure 3B). The most

![Figure 3](image-url)

**Figure 3** Survival analysis model of bleb volume within the first 21 days to accurately demonstrate the rate of change in response to treatment without influence of outliers. A. Regression model of bleb volume for all treatment groups within the first 21 days after surgery. B. Linear regression model of bleb volume decay, with rate of decay depicted as a slope. The flatter the slope indicates the longest survival time.
dramatic changes in bleb volume were noted in the first 14 days after surgery, followed by minimal change thereafter. Analyzing the data of the first 21 days following surgery eliminated the influence of outliers and reflected the true change in individual animals within the treatment groups. According to this model, the more negative the slope, the faster the rate of decay of bleb volume. Over the 21 days following surgery, the rate of decay for PBS (-0.3324, \( p = 0.0003 \)) and Hydron (-0.3374, \( p = 0.0007 \)) was significantly greater than OGF + Hydron treated animals (Figure 3B). Similarly, when compared to the MMC treatment, the rate of decay for PBS (\( p = 0.0033 \)) and Hydron (\( p = 0.0050 \)) controls were significantly faster. In contrast, the rate of decay of OGF + Hydron treated animals (\( p = 0.2919 \)) was not statistically different from MMC treatment. Even accounting for outliers in the analysis until failure, the results are the same where the OGF + Hydron (slope -0.0517, \( p = 0.0154 \)) and MMC (slope -0.0402, \( p = 0.005 \)) groups have slower rates of decay than the PBS (slope -0.104, \( p = <0.0001 \)) and Hydron (slope -0.338, \( p = <0.0001 \)) control groups. Interestingly, when outliers are accounted for, there are significant differences between all treatment groups, where OGF + Hydron has a slower rate of decay than the PBS and Hydron treated rabbits, and only slightly faster the MMC group.

**Hyperemia scores**

The conjunctiva overlying the filtration site and comprising the surgical bleb was avascular after surgery. Occasionally Hydron pellets were grossly visible under the conjunctiva in the area of the bleb and no gross inflammation was observed. The duration for hyperemia to resolve after surgery was evaluated to assess reaction of the conjunctiva surrounding the surgical site to surgery and treatment. Across all treatment groups, the conjunctiva was moderately hyperemic (score = 2) at 24 hours.

![Figure 4](image)

**Figure 4** Conjunctival hyperemia after surgery. The graph shows the trend in mode of hyperemia scores over time of hyperemia scores for each treatment group during the first 10 days following surgery when hyperemia was observed *in situ*.

![Figure 5](image)

**Figure 5** Histologic sections of the filtration site in the intermediate post-operative period. Tissue sections were collected at 5 days after surgery to assess peri-operative inflammation. Displayed is inflammation at the surgical site of PBS control (A), Hydron control (B), OGF + Hydron (C), and MMC (D). Low power field, hematoxylin and eosin stain. Bar = 500 µm in A, C, and D. Bar = 200 µm in B.
following surgery (Figure 4). Severe hyperemia (score = 3) was not observed until 48–72 hours following surgery and varied by treatment and individual animal, although MMC treated rabbits had a severe score sooner and for longer duration than the other groups. It was noted that half of the rabbits in the OGF + Hydron group only developed moderate hyperemia following surgery. The earliest day for hyperemia to resolve (score = 1) was 7 days for PBS, and 8 days for the remaining groups (Figure 4). The Kruskal–Wallis test compared the average day in each treatment group when severe, moderate, or no hyperemia was observed in the conjunctiva. There was no statistical significance between the groups.

**Histology**

Ocular tissue was assessed at 5 days following surgery to assess inflammation and fibrosis during the post-operative period. Eye tissues from rabbits collected at failure were considered incomparable as the time of collection varied widely individually. Regardless of time of collection, Hydron pellets were not observed in histology sections.

Tissue surrounding the filtration site did not have major differences in the type of inflammation present between the treatment groups at 5 days post-surgery (Figure 5). Typically, macrophages and heterophils were the predominant cell type present in the conjunctiva and sclera, with smaller numbers of lymphocytes. A unique histologic finding in MMC-treated rabbits was severe tissue edema within the conjunctiva (Figure 5D). There was no evidence of overt infection, necrosis, or apoptosis in tissue sections of any treatment groups.

Inflammatory cell counts revealed that the conjunctiva had more inflammatory cells present than in the sclera. While there were higher cell counts in the conjunctiva, no statistical significance comparing the conjunctiva or sclera existed between any of the treatment groups at 5 days based on paired t-test ($p = 0.098$) (Figure 6).

The amount of fibrosis in tissue sections around the surgical site was quantified in the conjunctiva and sclera at 5 days following surgery. In the sclera, the PBS control (13.06%) and OGF + Hydron (14.92%) groups had higher amounts of fibrosis present compared to the other two groups (Hydron, 5.31%; MMC, 8.99%). In the conjunctiva, the Hydron control (24.36%) and OGF + Hydron group (26.29%) had higher amounts of fibrosis compared to the PBS (16.23%) and MMC (13.56%) groups. There were too few data entries available to perform statistical analysis.

**CONCLUSIONS**

Filtration surgery is employed when medical management of glaucoma no longer is effective in lowering IOP levels to safe levels but usually fails secondary to progressive fibrosis. MMC has been used to reduce scarring and enhance the long-term success of this procedure, but it has a nonspecific mechanism of action and is often associated with adverse side effects [23]. Finding a tolerable, biocompatible adjunctive treatment to be employed at the time of surgery to prolong the surgical success through wound modulation is a highly active area of biomedical research. The present study found that the use of OGF in a biocompatible, slow-release polymer had similar survival longevity as MMC without tissue toxicity.

The surgical bleb is the visible component of filtration procedure and is functionally considered the major contributor to success, failure, and complications after surgery [12,4,25]. A focused method of describing the bleb was used in this study including the bleb height, area, and general hyperemia of the conjunctiva at the bleb edge. To prevent inter-observer variability, a single observer evaluated each filtering bleb on a daily basis.

Bleb height is considered a hallmark characteristic of surgical success in filtration surgery but doesn’t account for changes in bleb area which has also been used as an indirect measure of rate of healing [23,26]. To account for the variability of both parameters, the bleb volume was used to assess the rate of decay to evaluate subtle changes in bleb morphology as a result of different treatments. The survival model of bleb volume noted that the pattern of decay fits a statistical regression model to evaluate rate of change. The general linear model with repeated measures analysis that was performed accounted for random effects within individual animals, which is more accurate with limited numbers of subjected. These factors are not accounted for by log rank tests that are commonly used to evaluate glaucoma-filtering studies. This study determined that both OGF + Hydron and MMC treated rabbits have statistically significant longer bleb survival with slower rates of decay compared to the PBS and Hydron control groups. As OGF has similar bleb survival duration as MMC, this shows that OGF has good potential for being used as adjunctive therapy during filtration surgery.

To account for the functional success of the filtering surgery, study endpoint was determined as a flat bleb with concurrent normalization of average IOP values. IOP measurements are a common way to gauge the success of the procedure as IOP levels in the surgical eye should be lower than that of the control eye [27–29]. While variations in IOPs are a normal occurrence, the IOP of the surgical eye was always compared to that of the contralateral control eye by the same individual.
The duration of surgical success in OGF-treated eyes following filtration surgery is comparable to MMC treatment but without evidence of tissue toxicity. While MMC had the most inflammatory cells present in the conjunctiva, there was no statistical significance in inflammatory cell counts in between the different treatment groups around the filtration sites peri-operatively at 5 dpo when an inflammatory reaction should be at its peak. This was supported by histology where the type and degree of inflammation did not differ between groups. Another indirect measure of inflammation is hyperemia of the conjunctiva. OGF + Hydron treated eyes retained an overall moderate hyperemia score throughout the course of the initial healing period while rabbits in the control PBS and Hydron groups had severe hyperemia scores in the first few days post-operatively. Additionally, the MMC group developed severe hyperemia sooner post-operatively and for longer duration than that of all the other groups. Based on inflammatory cells counts being comparable to other controls, moderate hyperemia scores, and lack of histologic evidence of necrosis or apoptosis, OGF is a biocompatible peptide that doesn't result in tissue toxicity.

The mechanism of action of OGF ultimately inhibits fibroblast proliferation thereby modulating wound healing by delaying the development of fibrosis and scarring. Inhibition of fibroblast proliferation with OGF treatment has previously been demonstrated in cell culture [9]. Quantification of fibrosis around the filtration site in the conjunctiva found only slightly higher levels in the OGF + Hydron and Hydro control groups compared to the other groups. The minute differences could be accounted for by small group numbers, individualized tissue reactions, differences in tissue manipulation during surgery, or altered release of OGF from the Hydron pellet. Studies have shown that maximum subconjunctival fibroblast proliferation occurs on the third to fifth day after surgery [7]. Collecting tissues at 5 dpo may have hindered efforts to demonstrate inhibition of fibroblast proliferation as this might occur earlier in time. Interestingly, histology at 5 dpo demonstrated large numbers of fibroblasts present in the tissue around the filtration site in all treatment groups, even OGF treated rabbits. It is likely that OGF prevented the proliferation of fibroblasts at the surgical site surrounding the pellets, but did not prevent release of several tissue factors that stimulate TCF proliferation at other locations whereby fibroblasts then migrated to the surgical site [7]. This demonstrates that wound healing is a complex process and inhibiting fibroblast proliferation at the surgical site is only one factor that can help delay tissue healing.

There were several limitations inherent to this study. The sample size was small and the exclusion criteria limited the sample size even further, thus creating large standard errors of the means. The rabbits were of different sexes due to availability and did not have glaucoma. In humans, the goal of surgical therapy is to see a reduction of IOP levels to within a normal range, whereas this study evaluated the time for normalization of an initially decreased IOP to return to normal range.

Other limitations include the lack of in vitro studies to determine the concentration of OGF present in the Hydron pellet or the rate of drug release from the pellet to determine the potential expected efficacy. The concentration was chosen based on previous cell culture studies that had the best inhibitive effects on Tenon's capsule fibroblasts [9]. The pellets were not sterilized because of the unknown effects heat would have on the stability and bioavailability of the OGF, so aseptic technique was used instead. Despite this, there was no evidence of infection clinically or on histologic sections.

Glucoma-filtering procedures and wound modulation are a major focus of research efforts to reduce the incidence of blindness in people with this disease. Rabbits are a common animal model for such studies, and are considered a very aggressive model of filtration surgery because rabbits are notorious for TCF proliferation [6,30,31]. They often represent the worse-case scenario in people and any fibrotic response seen in rabbits should be more pronounced and prolonged than in humans [6]. Any effect OGF might display in the rabbit model of filtration surgery should have a considerably longer term effect in preventing or delaying fibroblast proliferation in humans. Despite the exaggerated response common in rabbits, these results show that OGF has similar survival times as MMC and is well tolerated by tissue without displaying toxicity. Based on these results, OGF might be a viable option as an adjunct therapy to prolong surgical success at time of trabeculectomy surgery in humans.

ACKNOWLEDGEMENTS

The authors would like to thank the technicians Ellen Mullady and Gretchen Snively in the Department of Comparative Medicine diagnostic laboratory for their assistance with histology. Dr. Timothy K. Cooper was gracious in providing professional assessment of the some of the histology. The authors would also like to thank Dr. Alan Roshwalb for his assistance with the statistical analysis.

Funding acknowledgements

This research investigation was supported by Department of Comparative Medicine endowment funds.

REFERENCES

7. Grewal DS, Jain R, Kumar H, Grewal SP. Evaluation of subconjunctival...


