Triple Subconjunctival Bevacizumab Injection for Early Corneal Recurrent Pterygium: One-Year Follow-Up

Angel Nava-Castañeda,^{1,2} Isabel Ulloa-Orozco,² Lilia Garnica-Hayashi,²
Joaquín Hernández-Ortiz,² María Carmen Jiménez-Martínez,^{1,3} and Yonathan Garfías^{1,3}

Abstract

Purpose: The aim of the study was to evaluate the effect of 3 subconjunctival bevacizumab injections in patients with an early corneal pterygium recurrence.

Methods: This study was a nonrandomized single center trial. Patients with an early corneal pterygium recurrence were selected. All patients received 3 subconjunctival bevacizumab (2.5 mg/0.1 mL) injections (basal, 2 and 4 weeks) in the recurrence area of the pterygium. The corneal and corneal-conjunctival neovascularization areas and the corneal opacification area of each pterygium were determined using digital slit lamp pictures.

Results: Thirty-eight patients were enrolled into the study; all patients were injected within 3 months of the diagnosed pterygium recurrence. Interestingly, the bevacizumab injections had a significant effect ($P < 0.05$) on the reduction of corneal, corneal-conjunctival area of neovascularization determined as pixels and on the corneal opacification area determined as mm² when comparing the basal values, to the values obtained after 15 days, 1 month, 3 months, 6 months, and 12 months after injections.

Conclusions: The vascularized area in all recurrent pterygia and the corneal opacification area with this triple regimen of subconjunctival bevacizumab injections were reduced, which remained until the end of the study. These results suggest that bevacizumab subconjunctival injections could be useful to treat recurrent pterygium.

Introduction

PTERYGIUM IS AN OVERGROWTH of fibrovascular tissue, with a wing-like appearance, from the conjunctiva over the cornea; histologically, the pterygium is composed of epithelium and a highly developed vascular neofunction network consisting of arterioles, venules and a very large number of capillaries found in the connective tissue.¹ Although several theories have been postulated for the pathogenesis of pterygium, including immunological mechanisms, infections, ultraviolet expositions, and oxidative stress imbalance, among others,^{2–6} the precise basis by which this disease is caused still remains under study. However, it has been reported that the density of microvessels in pterygia is significantly higher than that in normal conjunctivas. Moreover, it has been demonstrated that vascular endothelial growth factor (VEGF) is overexpressed in pterygia, which is considered one of the most potent angiogenic factors in this

disease.⁷ Additionally, the VEGF secreted by infiltrating mast cells has an important function in neovascularization of pterygium.⁸ Cumulative evidence has demonstrated that selective VEGF blockade using specific antibodies such as bevacizumab and ranibizumab is able to suppress neovascularization that occurs in pterygium.^{9–13} To prevent pterygium recurrences, conjunctival autograft surgery is generally regarded as the procedure of choice for the treatment of primary and recurrent pterygium, because of its efficacy and long-term safety.^{14–16} Pterygium excision is occasionally combined with some adjunctive measures such as mitomycin-C or β -irradiation. β -irradiation is becoming a less popular procedure because the long-term risk of serious sight-threatening complications.^{17,18} Regardless of the surgical technique or the adjunctive measures, the recurrence rate of pterygium range from 10% to 80%.^{14,19,20}

Other risk factors for recurrence include young age, dark race, and incomplete pterygium removal.¹⁴ It has recently

¹Research Unit and ²Oculoplastics Department, Institute of Ophthalmology Conde de Valenciana Foundation, Colonia Obrera, Mexico City, Mexico.

³Department of Biochemistry, Faculty of Medicine, Universidad Nacional Autónoma de México, Mexico City, Mexico.

been reported that VEGF could be responsible for pterygium recurrence.²¹ Additionally, it has been documented that the expression of VEGFR-2 may have a predictive value in the recurrence of pterygium.²² The aim of this study was to prospectively evaluate the effect of 3 subconjunctival bevacizumab injections in patients with an early corneal pterygium recurrence.

Methods

Study design

This study was a nonrandomized single center trial. The method of ensuring allocation concealment was sequentially numbered. Patients with an early pterygium recurrence between January 2011 and January 2013 were selected and invited to participate in the study. Recurrence was defined as the presence of corneal vessels with concomitant conjunctival hyperemia within the first trimester after primary pterygium removal, and only patients with primary pterygium recurrence were included. In all cases, a conjunctival-autograft surgical technique had been performed as method of pterygium removal. Patients of both sexes older than 18 years were selected. Pregnant women, women seeking to become pregnant, and lactating women were excluded from the study. The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Ethics Committee Board (Registration No. CC-002-2011) and registered at Clinical Trials with the number: NCT02007174. In all cases informed consent was obtained. To obtain an adequate size sample, power analysis was performed to justify the number of patients enrolled in the study. Briefly, a proportion-based analysis using the prevalence of pterygium recurrence of 8%²³ was performed.

Injection information

All patients received 3 subconjunctival bevacizumab (2.5 mg/0.1 mL) injections (basal, 2 and 4 weeks), in the recurrence area of the pterygium. Neovascularization and corneal opacification evaluations were performed at basal time before the first bevacizumab injection; then, neovascularization and corneal opacification evaluations were performed 15 days after the first bevacizumab injection, which coincided with the second bevacizumab injection; afterward, the neovascularization and corneal opacification evaluations were done 1 month after the first bevacizumab injection, which overlapped with the last bevacizumab injection; thereafter, the follow-up period continued 3, 6, and 12 months after the first bevacizumab injection. Only one surgeon (I.U.O.) applied the bevacizumab injections and all the patients received each injection at the slit lamp using an eye lid speculum as follows: the eye was anesthetized using 0.5% tetracaine hydrochloride (Ponti-Ofteno; Laboratorios Sophia, Jalisco, México) eye drops, then a 2.5 mg/0.1 mL bevacizumab (Avastin®; F-Hoffman-La Roche, Basel, Switzerland) dose was subconjunctivally injected adjacent to the abnormal growing vessels at the limbus. Following the bevacizumab injection, each patient was treated with topical eye drops of 0.3% tobramycin and 0.1% dexamethasone (Trazidex; Laboratorios Sophia) and 0.5% carboxymethylcellulose lubricating eye drops (Refresh Tears; Allergan, Irving, CA) 4 times daily; corticosteroids and antibiotic eye drops were tapered and discontinued after 3

months. To reduce bevacizumab cost, we used a vial of 100 mg Avastin to prepare ~fifty 2.5 mg/0.1 mL individual doses. To prevent microbial contamination, we used the approach proposed by Gonzalez et al.,²⁴ to aseptically prepare a batch of syringes containing the aforementioned bevacizumab dose. These syringes were properly stored and were available when needed.^{9–13}

Data collection

All data were prospectively obtained. The collected data included demographic characteristics, clinical inspection findings prior to and after bevacizumab injections and clinical photographs. Photographs were taken prior to each bevacizumab injection, and then, they were taken at the second week and fourth weeks visits prior to bevacizumab injection. After accomplishment of the 3-bevacizumab injections regimen, all patients were followed up and photographed through 1 year as mentioned above.

Outcome measures

The main outcome measurements in this study were the changes in the neovascularization area measured in pixels and the corneal opacification measured in mm². The vessel area was assessed using the methodology previously described¹² with slight modifications. In each recurrent pterygium we performed 3 area measurements: The first measurement included only the vessels area in the corneal surface (Fig. 1), the second measurement included both conjunctival and corneal vessels area (corneal-conjunctival area of neovascularization) (Fig. 2), and a third measure was made over the area of corneal opacification (Fig. 3). Briefly, digital slit lamp pictures were taken by a canon EOS 20D digital camera (Canon, Inc., Tokyo, Japan) mounted on a BX900 Haag-Streit slit lamp (Haag-Streit AG, Koeniz, Switzerland). All images were taken at the same magnification and the patients were asked to fixate at the same

FIG. 1. Slit lamp photograph of a representative patient before the subconjunctival bevacizumab injections. The marked zone with the *black line* was considered as the corneal neovascularized area and was converted into pixels for further analyses. It can be observed that the marked zone covers only the corneal neovascularized area.

FIG. 2. Slit lamp photograph of a representative patient before the subconjunctival bevacizumab injections. The marked zone with the *black line* was considered as the corneo-conjunctival neovascularized area and was converted into pixels for further analyses. It can be observed that the marked zone covers only the corneo-conjunctival neovascularized area.

target. The digital images were captured with a resolution of at least 2544×1696 pixels. The OIS WinStation Slit Lamp software (Ophthalmic Imaging Systems, Sacramento, CA) was used to archive the images. Digital slit lamp pictures were analyzed using Photoshop CS4 (Adobe Systems, Inc., Berkeley, CA). The same graphical editing procedure was used for all images. Corneal and conjunctival blood vessels were enhanced using the channel mixer and filter functions of the program. The first measurement (corneal neovascularization) was achieved by outlining the limbus and the area of corneal neovascularization on the baseline images,

FIG. 3. Slit lamp photograph of a representative patient before the subconjunctival bevacizumab injections. The marked zone with the *white line* was considered as the corneal opacification area and was measured as proposed by VanRoekel.²⁵ It can be observed that the marked zone encompasses the corneal opacification in front of the neovascularized corneal area.

the size of the neovascularized area was then measured in terms of pixels as described in a previous publication. For the second measurement (corneo-conjunctival vascularization), we included the total neovascularization area of the recurrent pterygium that included both corneal and conjunctival area of neovascularization. The size of the neovascularized area was then measured in terms of pixels as described in a previous publication.²⁵ The third measurement encompassed the corneal opacification area in front of the neovascularized area of recurrent pterygium and its area determined in mm^2 was calculated using the method proposed by VanRoekel et al.²⁵

Statistical analysis

Statistical analyses were performed using the SPSS version 18 (Chicago, IL). The demographic variables were analyzed using descriptive statistics. To determine differences among neovascularization area during the different time points in the period of the study, we performed repeated measures analysis and comparison was performed using 1-way ANOVA test with Dunn's correction; meanwhile, paired Student's *t* tests were performed to analyze the effect of bevacizumab on corneal opacification; in all cases $P < 0.05$ was taken as statistically significant.

Results

Thirty-eight patients were enrolled into the study. The median age at presentation was 47 years (range 27–67 years). Twenty-four patients were women and 14 patients were men. All recurrent pterygia were situated in the nasal region, 20 pterygia were found in the right eye, while 18 were located in the left eye. All patients were injected within 3 months of the diagnosed pterygium recurrence (range 20 days–2.5 months).

The measurements of the corneal vascularization determined in pixels were as follows: $148.1 \times 10^3 \pm 11.5 \times 10^3$ at the basal time point; $128.1 \times 10^3 \pm 10.7 \times 10^3$ at 15 days postinjection (PI); $116.9 \times 10^3 \pm 4.8 \times 10^3$ at 1st month PI; $102.9 \times 10^3 \pm 13.9 \times 10^3$ at the 3rd month PI; $96.8 \times 10^3 \pm 13.5 \times 10^3$ at the 6th month PI; and $91.1 \times 10^3 \pm 18.9 \times 10^3$ at the 12th month PI (Fig. 4).

The preinjection values in corneal-conjunctival area measured in pixels were as follows: $186 \times 10^3 \pm 20.8 \times 10^3$ at the basal time point; $163.1 \times 10^3 \pm 24.5 \times 10^3$ at 15 days PI; $156.1 \times 10^3 \pm 26.7 \times 10^3$ at 1st month PI; $135.8 \times 10^3 \pm 21 \times 10^3$ at the 3rd month PI; $129.3 \times 10^3 \pm 18.3 \times 10^3$ at the 6th month PI; and $131.5 \times 10^3 \pm 27.9 \times 10^3$ at the 12th month PI (Fig. 5).

To support the hypothesis that decreased vascularity does correlate with decreased progression of the disease, we measured the opacified area in only those patients who presented clinically significant corneal opacification. Only 10, out of all the patients included in this study presented a clinically significant corneal opacification. In all the cases, a reduction in corneal opacification area was seen as soon as the neovascularization started to show regression. To calculate whether these reductions on the opacification area were statistically significant paired Student's *t*-tests were performed.

The measurements of the corneal opacification determined in mm^2 as previously described²⁵ were as follows:

FIG. 4. Effect of the bevacizumab injections on the corneal neovascularization area on recurrent pterygia. Corneal neovascularization evaluation was performed at basal time before the first bevacizumab injection. Then, corneal neovascularization evaluation was performed 15 days after the first bevacizumab injection, which coincided with the second bevacizumab injection. Afterward, the corneal neovascularization evaluation time was done 1 month after the first bevacizumab injection, which overlapped with the last bevacizumab injection. Thereafter, the follow-up period continued 3, 6, and 12 months after the first bevacizumab injection. * $P < 0.05$; *** $P < 0.001$.

FIG. 5. Effect of the bevacizumab injections on the corneo-conjunctival neovascularization area on recurrent pterygia. Neovascularization evaluation was performed at basal time before the first bevacizumab injection. Then, neovascularization evaluation was performed 15 days after the first bevacizumab injection, which coincided with the second bevacizumab injection. Afterward, the neovascularization evaluation time was done 1 month after the first bevacizumab injection, which overlapped with the last bevacizumab injection. Thereafter, the follow-up period continued 3, 6, and 12 months after the first bevacizumab injection. * $P < 0.05$; *** $P < 0.001$.

$2.1 \pm 1.2 \text{ mm}^2$ at the basal time point; $1.6 \pm 0.94 \text{ mm}^2$ at 15 days PI; $1.4 \pm 0.8 \text{ mm}^2$ at 1st month PI; $1.1 \pm 0.7 \text{ mm}^2$ at the 3rd month PI; $1.0 \pm 0.6 \text{ mm}^2$ the 6th month PI; and $0.9 \pm 0.6 \text{ mm}^2$ at the 12th month PI. The changes in the opacification area are shown in Fig. 6, the analyses of the results indicate that there was a reduction of the opacification area in all patients, throughout the time of the study.

Interestingly, the bevacizumab effects on the reduction of corneal and corneal-conjunctival neovascularization and on the reduction of corneal opacification were observed as early as 15 days after the first injection, and these effects persisted at the end of the study. These changes can be corroborated in the clinical photographs of a representative patient observed in the Fig. 7. Interestingly, the basal values (pre-injection values) were in all cases significantly ($P < 0.05$) greater than all the PI values.

There were no systemic or local complications associated to the subconjunctival administration of bevacizumab. All patients reported a subjective improvement in conjunctival hyperemia starting at day 1 PI. No patients had undergone surgery during the study period and 22 patients ended the study.

Discussion

Our findings suggest that a three 2.5 mg/0.1 mL subconjunctival bevacizumab dose regimen can diminish the corneal and conjunctival neovascularization growth and the corneal opacification process in corneal recurrent pterygia.

Although a number of strategies have been used to prevent recurrence of pterygium after excision, recurrent pterygium is still the most common undesirable treatment sequel. The rate of recurrences differs depending on the method of pterygium excision and the method of dealing with the defect created. Since conjunctival autograft procedure has shown the best results in reducing pterygium recurrence, it is the surgical technique most performed in our institution for surgical pterygium treatment. Nevertheless, a pterygium recurrence rate between 2% and 39% has been reported when using this procedure.²⁶ The recurrence rate greatly varies not only among different surgical procedures, but also between different groups performing the same procedure, which is also affected by surgeon skills and dexterity. Additionally, demographic and ethnic differences can influence in the final outcome. There is a worldwide distribution of pterygia, but ultraviolet light exposure and warm and dry climates have been attributed as a major cause of pterygia. Patients with augmented UV exposure such as those living close to the equator have an increased risk of pterygia formation; consequently, the common factor appears to be the latitude, since pterygia primarily occur within the peri-equatorial "pterygium belt," which is located within latitudes 37° north and south of the equator.³ Mexico is a country situated within this "pterygium belt." Pterygium prevalence in our institution is 18% and the recurrence rate when using conjunctival autograft technique is 10.5%. The outcome of pterygium can be classified into 4 grades: grade 1, the conjunctiva has a normal appearance with no signs of recurrence; grade 2, only fine episcleral vessels are present at the surgical site without any fibrous tissue; grade 3, fibrovascular tissue is present in the excised area, reaching to the limbus but not invading the cornea (conjunctival recurrence); and grade 4,

FIG. 6. Effect of the bevacizumab injections on the corneal opacification area on recurrent pterygia. The corneal opacification was exclusively performed on those patients who clinically exhibited corneal opacification. Corneal opacification evaluation was performed at basal time before the first bevacizumab injection. Then, corneal opacification evaluation was performed 15 days after the first bevacizumab injection, which coincided to the second bevacizumab injection. Afterward, the corneal opacification evaluation time was done 1 month after the first bevacizumab injection, which overlapped with the last bevacizumab injection. Thereafter, the follow-up period continued 3, 6, and 12 months after the first bevacizumab injection. * $P < 0.05$; *** $P < 0.001$.

true corneal recurrence with fibrovascular tissue covering the excision area and invading the cornea.¹² Because the development of true corneal recurrence is often more troublesome, in which it tends to have a more exuberant fibrovascular growth response and causes more surgical difficulty than the primary pterygium, several intraoperative and postoperative adjunctive treatment modalities, such as mytomicin C, topical and subconjunctival corticosteroids, 5-fluorouracil in addition to β -irradiation, have been variably recommended to either prevent the recurrence or inhibit the progression of recurrence.^{26–28} However, these adjuvant therapies are not free of ocular morbidity and the side effects could be serious.

Recently, there have been several studies conducted to evaluate the effect of local therapy of bevacizumab in both primary and recurrent pterygium.^{9,13,29–36}

Bevacizumab has been used at various doses, at variable times, and by different routes of administration. Ideal dose and treatments regimen should be important factors for the effects of bevacizumab on pterygium treatment. The effects of anti-VEGF agents are often transient owing to the short half-life of the drug, and treatment often needs to be repeated, therefore, how to achieve a minimal effective dose and a maximum safe dose turned out to be the key and difficult problem.³⁷

Our study evaluated the effect of multiple subconjunctival bevacizumab injections in patients with an early true or corneal pterygium recurrence. As multiple injections are often required for a sustained effect in age-related macular degeneration, we decided to apply a triple dose regimen.^{38,39}

Anti-VEGF therapy in recurrent pterygium may be more effective, especially when the treatment started before neovascularization is well established.⁴⁰ Lekhanont et al., investigated the efficacy and safety of subconjunctival bevacizumab injection for the treatment of impending recurrent pterygium. A prospective, randomized, single-masked controlled trial was conducted in 80 patients. A single subconjunctival bevacizumab injection seemed to only partially and transiently decrease conjunctival vascularization in a dose-dependent manner and the recurrence rate was not affected by this treatment.³⁷ Fallah et al. investigated the use of topical bevacizumab alone or in combination with betamethasone in patients with impending recurrent pterygium, in his study patients in both groups failed and pterygia eventually recurred. However, the mean progression of fibrovascular tissue was reduced in the bevacizumab group.²⁹ A different observation was reported by Wu et al., in a case of impending recurrent pterygium that regressed following administration of topical bevacizumab for 3 weeks.³⁴ More recently, Bayar et al. has suggested that repeated injections of bevacizumab may help to prevent the high recurrence rate of residual impending pterygium, due to its adjuvant role in decreasing lesion size, especially in the first year after surgery.⁴¹ All of these authors have employed the subconjunctival bevacizumab injections in impending or conjunctival pterygium recurrence to stop its development to a corneal or true pterygium recurrence. Just a few authors have employed this anti-VEGF therapy in true pterygium recurrence, defined as the presence of corneal vessels and/or fibrous tissue. Bahar et al., in a small case of 5 patients with established recurrent pterygium, corneal neovascularization did not regress after the application of 2 subconjunctival bevacizumab injections.⁹ Hurmeric et al., included patients with pterygium recurrence defined as the presence of corneal vessels, to which they compared single vs. multiple injections of 0.5 mg/0.05 mL subconjunctival

FIG. 7. Representative slit lamp photographs of a patient who significantly improved in the clinical neovascularization and corneal opacification after the 3 subconjunctival injections. (A) Preinjection photograph; (B) 15 days after the first injection; (C) 1 month after the first injection; (D) 3 months after the first injection; (E) 6 months after the first injection; (F) 1 year after the first injection. Note that bevacizumab treatment induced reduction on neovascularization and on corneal opacification processes.

ranibizumab. They reported that conjunctival hyperemia is reduced after treatment, finding no advantages when using the multiple injections schedule.¹²

In this study, we decided to initiate the anti-VEGF therapy as soon as abnormal neovascularization vessels were recognized over the corneal surface and in a 3-month period after pterygium excision. We selected this 3-month period because during this time, patients could participate more in constant ophthalmic consultation, and any surgery complications such as pterygium recurrence could be hastily detected and immediate action taken. Likewise, the anti-VEGF agents are more effective in regressing new blood vessels that are in a growth phase as opposed to more mature vessels; hence, the early recognition of neovascularization vessels and rapid injection of these agents are crucial. In accordance to Lekhanont et al., we included patients with high recurrence risk: large and vascularized preoperative pterygia and surgery performed by trainees.³⁷ They described a recurrence developing in ~2.5 months after excision, when regrowth of fibrovascular tissue had already occurred. They have pointed out that this event might be the cause of the lack of the effect of the anti-VEGF therapy on controlling the recurrence rate.³⁷ In our study, new vessels regrowth were seen in 1 patient as soon as 20 days after surgery, finding most of the recurrences in 1.5 months period after surgery.

Although it has been described that the use of topical steroids does not have any protective effect on pterygium treatment,^{13,29,37} the possible synergistic effects of topical steroids for 3 months in combination with the triple 2.5 mg/0.1 mL bevacizumab regimen on reducing vascularized area of recurrent pterygium cannot be ruled out. A randomized controlled trial will be useful to clarify this question.

The interpretation of the areas of neovascularization in pterygium recurrence has been difficult to evaluate. To get more objective values of neovascularization area, a numeric pixel scale was used as previously described with slight modifications. Hurmeric et al., only assessed the corneal blood vessel area, but in the present study we assessed both the corneal and conjunctival blood vessel area.^{12,25} In this study, we have found that the reduction in new vessels after anti-VEGF injection occurred in the whole pterygium recurrence area: conjunctival and corneal areas. We think that the changes found in corneal neovascularization area provide more clinically relevant information as that is the area of most concern. Furthermore, when the whole pterygium recurrence area is evaluated, it is difficult to demarcate and distinguish the actual neovascularization pterygium recurrence extension in conjunctival area as it can be confounded with an area of hyperemia or inflammation not concerned with the true conjunctival recurrence. Besides, we were able to measure the evolution of corneal opacification due to corneal edema existing in some patients. Corneal neovascularization often causes tissue scarring, lipid deposition, and corneal edema.⁴² Changes in corneal opacification area were evaluated through the study period, and we could corroborate corneal opacification reduction in conjunction with corneal neovascularization decrease. This finding supports that the decreased vascularity does correlate with decreased progression of the disease showing clinical stabilization of the disease.

As mentioned, no suitable anti-VEGF posology for pterygium treatment in time and dose has been collectively chosen. In this study, we decided to apply a three 2.5 mg/0.1

mL bevacizumab dose regimen. Hurmeric et al., assessed the effect of a single versus multiple subconjunctival ranibizumab injection in patients with an early pterygium recurrence. They concluded with respect to corneal blood vessels after ranibizumab treatment that some patients in both groups had a decrease in vessel area over time, with the effect being greater in the multiple injection groups. Similar to Hurmeric et al., who have used ranibizumab, we found comparable findings with the other anti-VEGF agent, bevacizumab. We only included 1 group who received multiple doses of subconjunctival bevacizumab. As shown in our results, the reduction in neovascularization area, measured in a pixel scale, was seen after the first injection, this was corroborated by patient satisfaction (not measured in this study), and the neovascularization reduction was slightly improved after the next 2-bevacizumab injections. After 1-year follow-up, all the patients remained stable. We found a little increase of neovascularization scale at the end of the study, which we think could be mostly attributed to environmental/working factors and the absence of a particular eye drops treatment. Nevertheless, this neovascularization grade was inferior to preoperative values and was still statistically different. The strength of our study is based on its long follow-up period, the use of an objective numeric scale for neovascularization, and corneal opacification grading, which allows a more robust statistical analysis and a relatively high sample of patients. Unexpectedly, 14 patients did not show up for the final 1-year evaluation. Nine of the 14 patients who abandoned the study were contacted by telephone call and declined ophthalmologic consultation because they referred themselves as been satisfied with the treatment.

As previously exposed, no effective treatment is available for treating pterygium recurrence. Based on the literature reports, it seems that the use of subconjunctival bevacizumab for pterygium recurrence treatment has a favorable side effect profile and it appears to be a better first-line option than a sub-conjunctival injection of corticosteroid or a vasoconstrictor agent. As mentioned by Hurmeric et al., patients must be warned that the effect may be mild and the fluctuations in hyperemia will be expected.¹² Also, better results will be obtained when employing a multiple injections treatment.¹² Fortunately, the bevacizumab dose cost is affordable for most patients, and this will allow performing a multiple treatment schedule in most cases.

Based on the results of our study, we can recommend a three 2.5 mg/0.1 mL subconjunctival bevacizumab dose regimen, which is safe, with no systemic or local complications, and we must highlight that an early application of this anti-VEGF treatment will result in better a corneal-conjunctival neovascularization vessels regression associated to a reduction in corneal opacification; thus, the detection of early areas of neovascularization in pterygium recurrence cases is crucial. The use of bevacizumab for pterygium treatment is still evolving, so future studies are needed to confirm the present results, add new indications, dosing and frequency of anti-VEGF agents for the treatment of this ocular surface disease.

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Author Disclosure Statement

All the authors declare that there are no competing interests.

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Address correspondence to:

Dr. Yonathan Garfias

Department of Biochemistry

Faculty of Medicine

Universidad Nacional Autónoma de México

Mexico City 04510

Mexico

E-mail: yogarfias@institutodeoftalmologia.org