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The Role of Subconjunctival Bevacizumab (Avastin) on recurrence rate of primary Pterygium Surgical Excision.

Amer Jawad Kadhim FRCS Ophthalmology,
Department of Ophthalmology–Baquba Teaching Hospital

Nahid Ibrahim Kadhim AL EZZY M.B. Ch.B
Department of Ophthalmology-Baquba Teaching Hospital

Abstract

Purpose
To evaluate the effect of bevacizumab on recurrence rate of primary pterygium surgical excision.
Methods
This randomized, placebo-controlled clinical trial was conducted on 64 eyes of 64 patients randomized to Group 1 (bevacizumab) and Group 2 (normal saline). Group 1 underwent pterygium excision and received a total of 5mg subconjunctival bevacizumab. Group 2 underwent pterygium excision and received normal salinein the same manner. Recurrence defined as any 1.5mm or more of fibrovascular tissue crossing the limbus.
Results
There was no statistically significant difference between the study groups in terms of demographics, pterygium size, daily sun exposure, preoperative visual acuity, keratometric readings, corneal astigmatism. 3 and 7 patients in each group at the threemonths and sixmonths visits, respectively, had more than 1.5 mm fibrovascular tissue overgrowth on the cornea (P=1.0 and 0.62, respectively). At the three-month visit,3patients in Group 1 versus 3patients in Group 2 (P=1.0), and at the six-month visit 4 patients in Group 1 versus 8 patients in Group 2 (P=0.17) had fibrovascular tissue crossing the limbus.
Conclusion
Bevacizumab had no significant effect on the recurrence rate of pterygium. Although the frequency of fibrovascular tissue crossing the limbus in the bevacizumab group was half that of the normal saline group, the difference failed to reach a statistically significant level.

Keywords: Angiogenesis, Bevacizumab, Pterygium, Pterygium Recurrence.

Introduction

Pterygium is a degenerative fibrovascular proliferation of conjunctival tissue over the cornea. It usually invades the nasal limbus and spreads along the interpalpebral fissure. Pterygium affects 0.3 to 29% of the population worldwide and may necessitate surgical removal. Post-operative recurrence is not uncommon.[1,3] Various adjunctive measures, including medications (mitomycin C, 5-fluorouracil and corticosteroids) and beta irradiation have been used to prevent the recurrence of pterygia[4,6]. However, these methods are associated with side effects, such as punctate epitheliopathy, bacterial superinfection, delayed-onset scleral melting, and elevation of intraocular pressure (IOP). Considering potential complications of these agents, safer adjuvants have been pursued.

The abundant expression of the vascular endothelial growth factor (VEGF) in pterygia suggests that anti-VEGF therapy may induce regression of blood vessels in pterygia or prevent its recurrence after excision.[7] Bevacizumab (Avastin; Genentech Inc., San Francisco, California, USA) a recombinant humanized murine monoclonal immunoglobulin G1 (IgG1), inhibits the VEGF-A isoform, the main stimulant of angiogenesis. This antibody is now widely used as an adjuvant for many neoplasms such as brain, lung, kidney, ovary, and breast cancers.[8,13] Although not FDA approved for intraocular use, it is used extensively for posterior segment vascular diseases and more recently for corneal neovascularization.[14,21]

In several human studies, bevacizumab has been used subconjunctivaly with doses up to 3 times the recommended intravitreal dose without serious systemic or local side effects.[23,24] We do not know how long bevacizumab may exert its effect on the conjunctival tissue, because the pharmacokinetics of subconjunctival bevacizumab has not been elucidated. Because of the abundance of conjunctival vessels, the half-life of subconjunctival bevacizumab seems to be shorter than that of intravitreal administration. The longest reported elimination half-life of bevacizumab after a single intravitreal injection has been 9.8 days.[25]

It has been shown that doubling the dose of intravitreal bevacizumab (from 1.5 mg to 3 mg) extends the pharmacological duration of bevacizumab by 1 half-time (8 to 11 days).[26] Due to the lack of data about the half-life of bevacizumab in the conjunctiva and the pharmacokinetics of intravitreal bevacizumab, we performed this study to evaluate the effect of a 5 mg dose of subconjunctival bevacizumab on the recurrence rate of primary pterygium excision, this was based on the fact that tear levels of VEGF following pterygium excision peak on the fifth postoperative day.[27]

The results of studies on the effect of bevacizumab on recurrence rates have been mixed. Although some studies have shown a beneficial effect from bevacizumab in terms of reducing recurrence,[28,29] the majority did not.[22,30,31] The majority of these studies are limited to case reports or case series. In this randomized placebo-controlled clinical trial we report the results of subconjunctival bevacizumab on the recurrence rate of pterygia following primary excision.

Methods

This randomized, placebo-controlled clinical trial was done in Baquba teaching hospital.Indications for pterygium surgery included decreased visual acuity due to involvement of the visual axis or induced astigmatism, discomfort and irritation unresponsive to lubricants, cosmetic concerns, or more than 3 mm extension of the pterygium over the cornea.

Patients with glaucoma, regurgitation from the lacrimal puncta (indicating nasolacrimal duct obstruction), diabetes mellitus, pregnancy, lactation, ocular surface disorders or infections, autoimmune diseases, and previous ocular surgery were excluded from the study.

We recorded all participants' demographic data, average duration of daily sun exposure, best corrected visual acuity (BCVA), manifest refraction and keratometry, IOP, detailed slit lamp examination including horizontal length of the pterygium in mm, and fundus examinations. The following conditions were regarded as risk factors for recurrence: inflamed pterygium, occupations with considerable solar exposure, recurrent pterygium in the fellow eye.

Patients were randomized to 2 groups, in group 1 (bevacizumab group) underwent pterygium excision and received a total of 5 mg subconjunctival bevacizumab (5 mg/0.2 ml on the day of surgery). Patients in group 2 also had pterygium excisionbut received 0.2 ml normal saline at the end of surgery.

All procedures were performed by one surgeon (me). Postoperatively, patients were examined at day 1, week 1, and months 1, 3, and 6. In postoperative visits, the following factors were evaluated: horizontal dimension of the corneal epithelial defect in mm, conjunctival status (retraction, melting, or infection), refraction, keratometry, IOP, and recurrence (defined as more than 1.5 mm of fibrovascular tissue overgrowth on the cornea and any fibrovascular tissue crossing the limbus).[32]

Surgical Technique

To accomplish anesthesia, after instilling topical anesthetic eye drops, subconjunctival lidocaine was injected under the area of the pterygium. The pterygium was excised from its conjunctival side, and the corneal component was peeled off. After excision of the pterygium, a pedunculated conjunctiva devoid of Tenon's capsule was created from the adjacentconjunctiva and was cover the bare sclera and sutured with 8-0 Virgin silk sutures. At the end of the surgery, 0.2 ml bevacizumab (5 mg) or normal saline was injected in the inferior fornix depending on randomization. Postoperatively, a topical antibiotic and steroid four times a dayand artificial tears four times day were initiated and tapered over the course of four weeks. All sutures were removed at the one week visit.

Results

A total of 64 eyes of 64 patients were enrolled including 32 eyes in each group. All patients completed the postoperative visits. There was no statistically significant difference between the study groups in terms of demographic data, operated eye, horizontal size of the pterygium, duration of daily sun exposure, preoperative BCVA, keratometric readings, corneal astigmatism, and IOP (Table 1).

Table 1, Demographics and ocular characteristics of the study patients.

	Group 1.	Group 2.	Significance
Number	32	32	
Sex (female/male)	15/17.	16/16.	0.76
Eye (right /left)	10/22.	16/16	0.34
Age (years).	41.9 ± 12.2.	45.12 ± 12.	22 0.55
Sun exposure per day (hours).	5.67± 4.57	5.68 ± 5.07.	0.98
Horizontal pterygium size (mm).	2.89 ± 1.22.	3.02± 1.23.	0.87
Preoperative BCVA	0.10 ± 0.28.	0.16 ± 0.30.	0.52
Preoperative keratometry	44.56 ± 1.98	44.46 ± 2.02.	0.76
Preoperative corneal astigmatism.	2.38 ± 2.30.	1.89 ± 1.86.	0.42
Preoperative spherical equivalent.	0.56 ± 0.82.	0.78 ± 1.75.	0.65
Preoperative IOP (mmhg).	13.65 ± 2.65.	14.24 ± 1.32	0.12

Regarding recurrence risk factors, there was also no significant difference between the study group (Table 2).

Table 2, Prevalence of risk factors for recurrence of pterygium in groups 1&2.

	Group 1.	Group 2.	P value
Inflamed pterygium	5	6	1
Sun exposure	8	8	1
Recurrent pterygium in fellow eye	0	3	0.48
Arcus senilis	4	5	1
Age < 30 years	8	7	1
No risk factor	13	14	2

As shown in (Table 3) the recurrence rate of pterygium, changes in keratometry, corneal astigmatism, and spherical equivalent in both groups revealed no statistically significant difference. Although no statistically significant difference was seen between groups for recurrence at all postoperative visits, the number of patients who had fibrovascular tissue crossing the limbus in group 2 was twice that of group 1 (7 versus 3 at three months and 8 versus 4 at six months).

Table 3, Recurrence rate of pterygium

	Preoperative.			Month 1			Month 3			Month 6		
	G1	G2	Sig.	G1	G2	Sig.	G1	G2	Sig.	G1	G2	Sig.
Recurrence (any fibrovascular growth on cornea)	-	-	-	1	2	0.55	3	7	0.13	4	8	0.17
Recurrence (> 1.5 mm fibro) vascular Overgrowth on the cornea).	-	-	-	-	-	-	3	3	1	4	4	0.62
Keratometry (Mean SD).	44.2	44.3	0.74	44.9	44.7	0.69	45.1	44.2	0.02	44.6	44.1	0.29
Spherical equivalent.	0.53	0.74	0.63	0.09	0.26	0.65	0.12	0.19	0.83	0.05	0.25	0.55
Corneal astigmatism.	2.25	1.75	0.41	1.20	1.25	0.80	1.28	1.30	0.94	1.62	1.40	0.63

Recurrence of pterygium and changes in keratometry, spherical equivalent and corneal astigmatism over the postoperative course in groups 1 and 2, no necrosis, ischemia, infection in the surgical bed area, or conjunctival retraction and melting developed.

Although baseline IOP was similar in both groups, patients in group 1 experienced a statistically significant rise at week one postoperatively (P=0.007). IOP returned to baseline levels in later visits with no intervention (Fig 1).

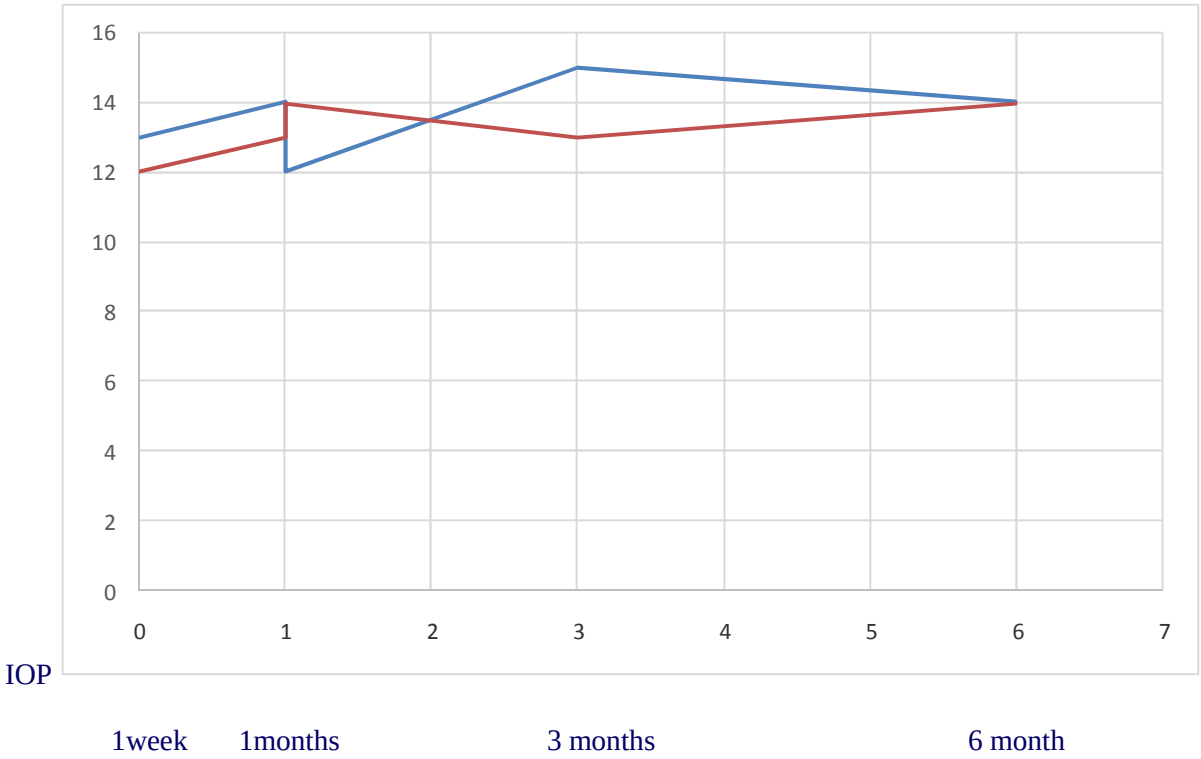

Fig.1, Mean intraocular pressure at baseline and various postoperative intervals in group 1red line (bevacizumab) and group 2 blue line (Normal saline).

Discussion

The current study was designed to evaluate the safety of bevacizumab and its effect on recurrence rate of pterygia when used as an adjunct to primary excision, Statistically, no beneficial effect was observed from 5 mg subconjunctival bevacizumab on preventing the recurrence of pterygium. This is compatible with some other studies reporting no beneficial effect from bevacizumab administration on prevention of pterygium recurrence.[28,29,31,33]

In our study, all patients were followed for at least 6 months. Recurrence was defined as any fibrovascular growth of conjunctival tissue extending more than 1.5 mm across the limbus. The recurrence rate in both groups was similar and no serious ocular side effect was observed.

Fallah et al[28] evaluated the effect of topical bevacizumab in 54 patients undergoing pterygium surgery using the bare sclera technique with mitomycin C who had been diagnosed with impending recurrent pterygium. Of the 54 patients, 26 received topical bevacizumab eye drops (5mg/ml) twice daily and betamethasone 4 times daily for one week, and betamethasone alone was administered to the remainder of the patients, who were followed for 3-6 months, however the interval to invasion of fibrovascular tissue over the cornea was significantly longer in the bevacizumab group. They concluded that topical bevacizumab together with betamethasone drops can cause a delay in progression, especially when administered earlier than 30 days following pterygium excision. In our patients, the rate of fibrovascular tissue crossing the limbus in group 1 was half of that of group 2 at months 3 and 6, which seems to be clinically important although not statistically significant.

In a study, pterygia were excised using the bare sclera technique and 33 patients received 1.25 mg subconjunctival bevacizumab and another 33 subjects had distilled water administered to them as the control group intraoperatively. The control group experienced higher recurrence rate (defined as any fibrovascular growth crossing the limbus and extending over the cornea) as compared to the bevacizumab group; however, this difference was not statistically significant.[34]The difference in the recurrence rate between our study and theirs may be due to both recurrence definition criteria and surgical technique. The reported recurrence rate after bare sclera technique has been around 40%.[35,36]

In contrast to the above mentioned studies, four others have reported success for treatment of pterygium recurrence with administration of topical bevacizumab.[37,40] Wu et al administered topical bevacizumab (25mg/ml, 4 times a day for 3 weeks) to a patient with an impending recurrent pterygium and noted prominent regression of vessels after treatment.[37]Leippi et al. stated that the use of bevacizumab eye drops prevents the recurrence of pterygium.[38]. Fallah et al administered intralesional injections of bevacizumab (2.5mg/0.1 ml) to 17 patients with pterygia (14 subjects with primary and 3 with recurrent lesions).[39] The size of vascularized cornea showed a statistically significant decrease at the end of the 3-month follow-up period. Although a statistically significant decrease in pterygium size (4%) was also observed, it did not seem to be clinically important.

In the present study, bevacizumab appeared to be associated with no local side- effects when administered via subconjunctival injection, but no significant beneficial effect on recurrence rate was observed. However, in the third month, three patients in group 1 versus seven patients in group 2 (P=0.13) and at 6 months 4 patients in group 1 versus 8 patients in group 2 (P=0.17) had fibrovascular tissue crossing the limbus, which seems to be clinically significant. The lack of a detectable intergroup difference may be due to small sample size. Furthermore, the subconjunctivaly delivered dose might have been insufficient to inhibit a continuously generated pool of VEGF by the pterygia. Moreover, the presence of abundant conjunctival vessels increases the rate of systemic drug absorption, reducing the amount of locally available drug. Hence, using bevacizumab topically for several weeks may have a beneficial effect. Better results are likely to be achieved if long-term topical forms of bevacizumab or more injections and consequently a higher local concentration are used. However, Bahar et al reported five patients with recurrent pterygium who received 2.5mg/ml subconjunctival bevacizumab twice without any regression during a three-month follow-up period.[31]
Potential side-effects of topical and subconjunctival anti-VEGF agents are still being evaluated. In a prospective study by Kim et al topical bevacizumab (12.5 mg/ml) was used twice day for three months in seven patients with corneal vascularization.[21] It was found that while corneal blood vessels regressed in

seven of ten treated eyes, 6 eyes developed epithelial defects during the second month of treatment. In one patient, the epitheliopathy progressed to stromal thinning resulting in a descemetocele. Another report described a 75-year-old man with a history of an idiopathic corneal melting who was treated with topical bevacizumab (25 mg/ml, four times a day for one month), which caused marked regression of the blood vessels. He also used it for six weeks after corneal transplant surgery. The patient was found to develop recurrent stromal melting in the donor necessitating repeat corneal transplantation and a Gunderson flap.[41]

An intravitreal injection of anti-VEGF agents causes a predictable and probablyvolumerelated rise in IOP, although there are reports of persistent IOP elevation.[42,43] In volume-related IOP elevation, a very rapid decrease in IOP over a short period occurs. Persistent IOP elevation ranging from 8 to 35 mmHg in magnitude has been observed in patients who received intravitreal anti-VEGF injcetions.[42,43] Possible mechanisms contributing to sustained IOP elevation following intravitreal injection are inflammation, drug-induced trabeculitis, uveitis, endophthalmitis, and undetectable low-grade inflammation.[44,45] It is also possible that anti-VEGF agents may cause IOP elevation by decreasing the physiological function of the trabecular meshwork.[43] Since the mode of injection was a subconjunctival in our study and because intraocular inflammation was not detected in any patient, the possible mechanism seems to be trabeculitis or a decrease in physiologic trabecular meshwork function.

In our study, there were no statistically significant difference in patient's demographic data, and subconjunctival bevacizumab had no beneficial effect on the recurrence rate of pterygium. The relatively short follow-up could be limitations of the study. However, the commonly reported mean recurrence time after pterygium excision is 3-6 months.[46,47]Conducting a prospective, randomized clinical trial strengthens the credibility of the results. In addition, the absence of any difference between groups for the evaluated outcome measures (except IOP on the seventh day) is a convincing argument that normal saline does not affect the result.

In summary, this study revealed that subconjunctival bevacizumab injections had no statistically but a probably clinically significant effect on the recurrence rate of pterygia. The efficacy of topical bevacizumab after intraoperative injection or more postoperative subconjuctival injections combined with topical treatment targeting other growth factors involved in pterygium pathogenesis need to be investigated.

References

1. Hirst LW. The treatment of pterygium. SurvOphthalmol. 2003;48:145–180. [PubMed]
2. Moran DJ, Hollows FC. Pterygium and ultraviolet radiation: a positive correlation. Br J Ophthalmol. 1984;68:343–346. [PMC free article] [PubMed]
3. Taylor HR, West S, Munoz B, Rosenthal FS, Bressler SB, Bressler NM. The long-term effects of visible light on the eye. Arch Ophthalmol. 1992;110:99–104. [PubMed]
4. Ang LP, Chua JL, Tan DT. Current concepts and techniques in pterygium treatment. CurrOpinOphthalmol. 2007;18:308–313. [PubMed]
5. Frucht-Pery J, Raiskup F, Ilsar M, Landau D, Orucov F, Solomon A. Conjunctival autografting combined with low-dose mitomycin C for prevention of primary pterygium recurrence. Am J Ophthalmol. 2006;141:1044–1050. [PubMed]
6. Bekibele CO, Baiyeroju AM, Olusanya BA, Ashaye AO, Oluleye TS. Pterygium treatment using 5-FU as adjuvant treatment compared to conjunctiva autograft. Eye (Lond) 2008;22:31–34. [PubMed]
7. Marcovich AL, Morad Y, Sandbank J, Huszar M, Rosner M, Pollack A, et al. Angiogenesis in pterygium: morphometric and immunohistochemical study. Curr Eye Res. 2002;25:17–22. [PubMed]
8. Nowosielski M, Recheis W, Goebel G, Güler O, Tinkhauser G, Kostron H, et al. ADC histograms predict response to anti-angiogenic therapy in patients with recurrent high-grade glioma. Neuroradiology. 2011;53:291–302. [PMC free article] [PubMed]
9. BarrenaMedel NI, Herzog TJ, Wright JD, Lewin SN. Neoadjuvant bevacizumab in a granulosa cell tumor of the ovary: a case report. Anticancer Res. 2010;30:4767–4768. [PubMed]
10. Di Lorenzo G1, Buonerba C, Biglietto M, Scognamiglio F, Chiurazzi B, Riccardi F, et al. The therapy of kidney cancer with biomolecular drugs. Cancer Treat Rev. 2010;36(Suppl 3):S16. [PubMed]
11. Stinchcombe TE, Socinski MA. Maintenance therapy in advanced non-small cell lung cancer: current status and future implications. J Thorac Oncol. 2011;6:174–182. [PubMed]

12. Fojo T, Wilkerson J. Bevacizumab and breast cancer: the E2100 outlier. Lancet Oncol. 2010;11:1117–1119. [PubMed]
13. Lai A, Tran A, Nghiemphu PL, Pope WB, Solis OE, Selch M, et al. Phase II study of bevacizumab plus temozolomide during and after radiation therapy for patients with newly diagnosed glioblastoma multiforme. J Clin Oncol. 2011;29:142–148. [PMC free article] [PubMed]
14. Waisbourd M, Goldstein M, Loewenstein A. Treatment of diabetic retinopathy with anti-VEGF drugs. Acta Ophthalmol. 2011;89:203–207. [PubMed]
15. Figueroa MS, Contreras I, Noval S, Arruabarrena C. Results of bevacizumab as the primary treatment for retinal vein occlusions. Br J Ophthalmol. 2010;94:1052–1056. [PubMed]
16. Schouten JS, La Heij EC, Webers CA, Lundqvist IJ, Hendrikse F. A systematic review on the effect of bevacizumab in exudative age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 2009;247:1–11. [PubMed]
17. Krebs I, Lie S, Stolba U, Zeiler F, Felke S, Binder S. Efficacy of intravitreal bevacizumab (Avastin) therapy for early and advanced neovascular age-related macular degeneration. Acta Ophthalmol. 2009;87:611–617. [PubMed]
18. Gharbiya M, Allievi F, Conflitti S, Esposito M, Scavella V, Moramarco A, et al. Intravitreal bevacizumab for treatment of myopic choroidal neovascularization: the second year of a prospective study. Clin Ter. 2010;161:e87–93. [PubMed]
19. Lee JY, Chae JB, Yang SJ, Yoon YH, Kim JG. Effects of intravitreal bevacizumab and laser in retinopathy of prematurity therapy on the development of peripheral retinal vessels. Graefes Arch Clin Exp Ophthalmol. 2010;248:1257–1262. [PubMed]
20. Habot-Wilner Z, Barequet IS, Ivanir Y, Moisseiev J, Rosner M. The inhibitory effect of different concentrations of topical bevacizumab on corneal neovascularization. Acta Ophthalmol. 2010;88:862–867. [PubMed]
21. Kim SW, Ha BJ, Kim EK, Tchah H, Kim TI. The effect of topical bevacizumab on corneal neovascularization. Ophthalmology. 2008;115:e33–38. [PubMed]
22. Lekhanont K, Patarakittam T, Thongphiew P, Suwan-Apichon O, Hanutsaha P. Randomized controlled trial of subconjunctival bevacizumab injection in impending recurrent pterygium: a pilot study. Cornea. 2012;31:155–161. [PubMed]
23. Enkvetchakul O, Thanathanee O, Rangsin R, Lekhanont K, Suwan-Apichon O. A randomized controlled trial of intralesional bevacizumab injection on primary pterygium: preliminary results. Cornea. 2011;30:1213–1218. [PubMed]
24. Krohne TU, Eter N, Holz FG, Meyer CH. Intraocular pharmacokinetics of bevacizumab after a single intravitreal injection in humans. Am J Ophthalmol. 2008;146:508–512. [PubMed]
25. Meyer CH, Krohne TU, Holz FG. Intraocular pharmacokinetics after a single intravitreal injection of 1.5 mg versus 3.0 mg of bevacizumab in humans. Retina. 2011;31:1877–1884. [PubMed]
26. Lee JK, Song YS, Shin JS, Kwon YS, Shin MS, Kim JC. The change of cytokines in tear and blood after different pterygium operation. Cytokine. 2010;49:148–154. [PubMed]
27. Fallah MR, Khosravi K, Hashemian MN, Beheshtnezhad AH, Rajabi MT, Gohari M. Efficacy of topical bevacizumab for inhibiting growth of impending recurrent pterygium. Curr Eye Res. 2010;35:17–22. [PubMed]
28. Teng CC, Patel NN, Jacobson L. Effect of subconjunctival bevacizumab on primary pterygium. Cornea. 2009;28:468–470. [PubMed]
29. Shahin MM, Elbendary AM, Elwan MM. Intraoperative subconjunctival bevacizumab as an adjunctive treatment in primary pterygium: a preliminary report. Ophthalmic Surg Lasers Imaging. 2012;43:459–466. [PubMed]
30. Bahar I, Kaiserman I, McAllum P, Rootman D, Slomovic A. Subconjunctival bevacizumab injection for corneal neovascularization in recurrent pterygium. Curr Eye Res. 2008;33:23–28. [PubMed]
31. Young AL, Tam PM, Leung GY, Cheng LL, Lam PT, Lam DS. Prospective study on the safety and efficacy of combined conjunctival rotational autograft with intraoperative 0.02% mitomycin C in primary pterygium excision. Cornea. 2009;28:166–169. [PubMed]
32. Mandalos A1, Tsakpinis D, Karayannopoulou G, Tsinopoulos I, Karkavelas G, Chalvatzis N, et al. The effect of subconjunctival ranibizumab on primary pterygium: a pilot study. Cornea. 2010;29:1373–1379. [PubMed]
33. Shenasi A, Mousavi F, Shoa-Ahari S, Rahimi-Ardabili B, Fouladi RF. Subconjunctival bevacizumab immediately after excision of primary pterygium: the first clinical trial. Cornea. 2011;30:1219–1222. [PubMed]

34. Youngson RM. Recurrence of pterygium after excision. Br J Ophthalmol. 1972;56:120–125. [PMC free article] [PubMed]
35. Alpay A, Ugurbas SH, Erdogan B. Comparing techniques for pterygium surgery. Clin Ophthalmol. 2009;3:69–74. [PMC free article] [PubMed]
36. Wu PC, Kuo HK, Tai MH, Shin SJ. Topical bevacizumab eyedrops for limbal-conjunctival neovascularization in impending recurrent pterygium. Cornea. 2009;28:103–104. [PubMed]
37. Leippi S, Grehn F, Geerling G. Antiangiogenic therapy for pterygium recurrence. Ophthalmologe. 2009;106:413–419. [PubMed]
38. FallahTafti MR, Khosravifard K, Mohammadpour M, Hashemian MN, Kiarudi MY. Efficacy of intralesional bevacizumab injection in decreasing pterygium size. Cornea. 2011;30:127–129. [PubMed]
39. Mansour AM. Treatment of inflamed pterygia or residual pterygial bed. Br J Ophthalmol. 2009;93:864–865. [PubMed]
40. Galor A, Yoo SH. Corneal melt while using topical bevacizumab eye drops. Ophthalmic Surg Lasers Imaging. 2010:1–3. [PubMed]
41. Bakri SJ, McCannel CA, Edwards AO, Moshfeghi DM. Persisent ocular hypertension following intravitreal ranibizumab. Graefes Arch Clin Exp Ophthalmol. 2008;246:955–958. [PubMed]
42. Adelman RA, Zheng Q, Mayer HR. Persistent ocular hypertension following intravitreal bevacizumab and ranibizumab injections. J OculPharmacolTher. 2010;26:105–110. [PubMed]
43. Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY, et al. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med. 2006;355:1419–31. [PubMed]
44. Brown DM, Kaiser PK, Michels M, Soubrane G, Heier JS, Kim RY, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med. 2006;355:1432–1444. [PubMed]
45. Panda A, Das GK, Tuli SW, Kumar A. Randomized trial of intraoperative mitomycin C in surgery for pterygium. Am J Ophthalmol. 1998;125:59–63. [PubMed]
46. Ivekovic R, Mandic Z, Saric D, Sonicki Z. Comparative study of pterygium surgery. Ophthalmologica. 2001;215:394–397. [PubMed]
47. Sodhi PK, Verma L, Pandey RM, Ratan S. Comparison between the role of intraoperative mitomycin C and doxorubicin in preventing the recurrence of primary pterygium. Ophthalmic Res. 2005;37:1–6. [PubMed]

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