Intravitreal ranibizumab as adjuvant treatment for neovascular glaucoma

Ranibizumabe intravítreo como tratamento adjuvante para glaucoma neovascular

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ABSTRACT

The purpose of this study was to describe a prospective case series of 5 eyes treated with intravitreal ranibizumab injection for neovascular glaucoma (NVG). Five patients with clinically uncontrolled NVG secondary to proliferative diabetic retinopathy (4 patients) and central retinal vein occlusion (1 patient), non-responsive to maximal tolerable medication and panretinal photocoagulation, received intravitreal ranibizumab injection (0.5 mg). Patients were seen at 1st, 3rd and 7th day after the ranibizumab injection and when it was necessary. Success was defined as intraocular pressure (IOP) <d" 21mmHg, with or without medication. Those with persistent IOP > 21, despite maximal tolerable medication, underwent trabeculectomy with 0.5mg/ml mitomycin C (MMC) for 1 minute. Failure was defined as IOP > 21 mmHg, phthisis bulbi, loss of light perception or additional glaucoma surgery. The primary outcome was 6-month IOP control. Mean IOP before the ranibizumab injection was 37 mmHg (7 mmHg SD). Two out of five eyes underwent only ranibizumab injection, having an IOP control after the procedure. Three patients were submitted to trabeculectomy with MMC on the 7th day after the injection. At 6-month follow-up, the mean IOP was 12mmHg (3 mmHg SD). All eyes showed regression of rubeosis iridis and IOP control. Visual acuity improved in 2 eyes worsened in 1 eye, and remained stable in 2 eyes. These data suggest that intravitreal ranibizumab injection may be a useful tool in the treatment of NVG.

Keywords: *Neovascular, glaucoma/drug therapy; Chemotherapy, adjuvante; Intraocular pressure; Intravitreal injections; Antibodies, monoclonal/therapeutic use; Case reports*

RESUMO

O objetivo deste estudo foi descrever uma série de casos prospectivos de 5 olhos tratados com ranibizumabe intravítreo para glaucoma neovascular (GNV). Cinco pacientes com GNV refratário, secundário a retinopatia diabética proliferativa (4 pacientes) e oclusão de veia central da retina (1 paciente), não responsivos a terapia medicamentosa máxima tolerada e panfotocoagulação da retina, receberam ranibizumabe intravítreo (0,5 mg). Os pacientes foram vistos no 1º, 3º e 7º dia após a aplicação e conforme necessário. O sucesso foi definido como pressão intraocular (PIO) d"21 mmHg, com ou sem uso de medicação antiglaucomatosa. Aqueles com PIO > 21 mmHg, apesar da medicação máxima tolerada, foram submetidos à trabeculectomia com mitomicina C (MMC) 0,5mg/mL por 1 minuto. Falência foi definida como PIO > 21 mmHg, phthisis bulbi, perda da percepção de luz ou necessidade de cirurgia antiglaucomatosa adicional. O resultado primário avaliado foi o controle da PIO após 6 meses do procedimento. A PIO média antes da injeção era de 37 mmHg (DP=7 mmHg). Dois pacientes foram submetidos somente a injeção intravítrea de ranibizumabe, obtendo controle da PIO após o procedimento. Três pacientes foram submetidos à trabeculectomia com MMC no 7º dia após a injeção. Após 6 meses de seguimento, a PIO média era de 12 mmHg (DP=3 mmHg). Todos os olhos mostraram regressão da rubeosis iriana e controle da PIO. A acuidade visual melhorou em 2 olhos, piorou em 1 olho e permaneceu estável em 2 olhos. Estas informações sugerem que a injeção intravítrea de ranibizumabe pode ser uma ferramenta útil no tratamento do GNV.

Descritores: Glaucoma neovascular/quimioterapia; Quimioterapia adjuvante; Pressão intraocular; Injeções intravítreas; Anticorpos monoclonais/uso terapêutico; Relatos de casos

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Introduction

Neovascular glaucoma (NVG) is a severe form of glaucoma characterized by rubeosis iridis and intraocular pressure (IOP) elevation. Hypoxic disease of the retina such as diabetic retinopathy and occlusion of major retinal vessels account for more than one half of this glaucoma**.** Once retinal hypoxia is established the natural history of neovascular glaucoma can be divided in four stages: prerubeosis stage, preglaucoma stage, open-angle glaucoma stage, and angle-closure glaucoma stage.[1]

Panretinal photocoagulation has been shown to significantly reduce or eliminate anterior neovascularization and may reverse IOP elevation in the open-angle glaucoma stage. When the IOP begins to rise, medical therapy is required to control the pressure during the open-angle glaucoma stage. The mainstays of the therapy at this stage are drugs that reduce aqueous production such as carbonic anhydrase inhibitors, topical beta-blockers and alpha agonists. Although surgical intervention is often necessary, trabeculectomy alone and other shunt-tube drainage procedures for NVG are challenging because new vessels tend to recur, bleed easily, are always associated with postoperative inflammation and have higher rate of failure to control IOP.[2] Recent case series have demonstrated a role for bevacizumab in reducing rubeosis iridis and as an adjunct treatment for NVG.[2-4]

Intravitreal ranibizumab is the standard of care for the treatment of exudative macular degeneration. This pharmacologic agent, which selectively inhibits vascular endothelial growth factor (VEGF), might be an important adjunctive therapy in the management of NVG by causing rapid and consistent regression of neovascularization in the anterior segment.

The purpose of this study is to describe a prospective case series of five eyes treated with intravitreal ranibizumab injection for NVG.

Cases report

A total of 5 patients with clinically uncontrolled NVG, secondary to proliferative diabetic retinopathy (PDR) (4 patients) and central retinal vein occlusion (CRVO) (1 patient), non-responsive to maximal tolerable medication and panretinal photocoagulation, received intravitreal ranibizumab (0.5 mg) injection via the pars plana and if necessary were scheduled for trabeculectomy, at University of Campinas - Brazil. Ethics committee approval was obtained and all participants gave informed consent.

Table 1

Clinical data of cases of intravitreal ranibizumab injection as adjuvant treatment for neovascular glaucoma

Patient number	1	2	3	4	5
Age (years)	50	42	57	56	61
Diagnosis	PDR	PDR	CRVO	PDR	PDR
Pre-injection IOP (mmHg)	48	32	28	40	38
Pre-injection BCVA	HM	20/200	HM	HM	CF
Trabeculectomy	Yes	No	Yes	Yes	No
6-month IOP (mmHg)	13	15	9	16	10
6-month BCVA	CF	CF	HM	HM	20/400
6-month number of antiglaucoma medications	0	2	0	1	1

IOP – intraocular pressure; BCVA – best corrected visual acuity; CF – count fingers at 1 meter; HM – hand movements; PDR – proliferative diabetic retinopathy; CRVO – central retinal vein occlusion

We excluded patients with cloudy media, previous surgery on the superior conjunctiva, history of uveitis, infectious retinopathy, retinal detachment, hemoglobinopathy, trauma or previous vitreoretinal surgery.

After discussing treatment options and obtaining informed consent, a single injection of intravitreal ranibizumab (0.5 mg) was administered (Figure 1). Patients were seen on 1st, 3rd and 7th day after the ranibizumab injection and when it was necessary. Success was defined as IOP ≥ 21mmHg with or without medication. Those with persistent IOP > 21, despite maximal tolerable medication, underwent trabeculectomy with 0.5mg/ml mitomycin C (MMC) for one minute. Failure was defined as IOP > 21 mmHg, phthisis bulbi, loss of light perception or additional glaucoma surgery. The primary outcome was 6-month IOP control.

All patients were on the open-angle glaucoma stage. Mean IOP before the injection was 37 mmHg (7 mmHg SD). Two of them underwent only intravitreal ranibizumab injection, having an IOP control after the procedure with 2 anti-glaucoma medications. Three patients were submitted to trabeculectomy with MMC on the 7th day after the injection. At 6-month follow-up, the mean IOP was 12mmHg (3 mmHg SD). Other outcome

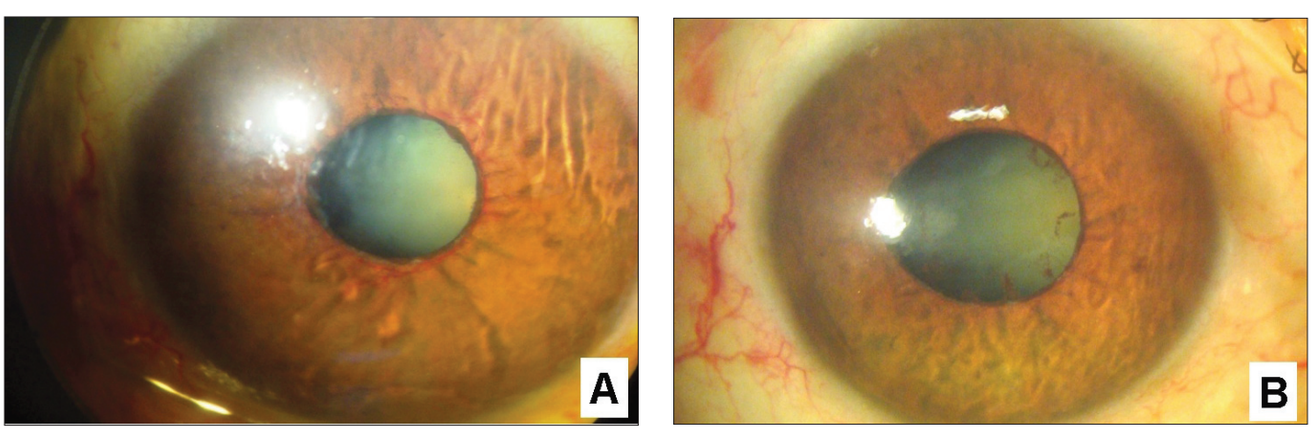

Figure 1: (A) Right eye of a 56-year-old male with neovascular glaucoma secondary to proliferative diabetic retinopathy; (B) Three-day follow-up of the same eye after intravitreal ranibizumab injection; note the rubeosis iridis regression

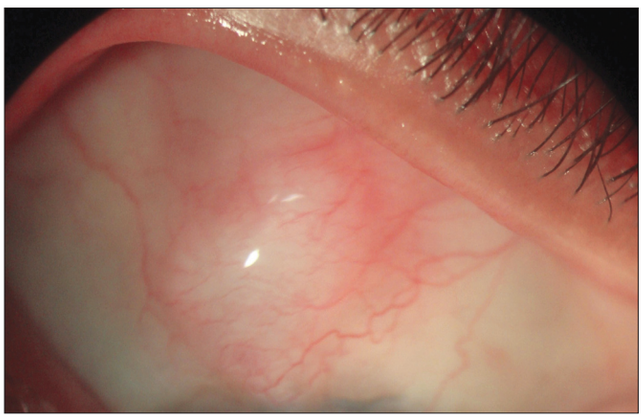

Figure 2: Right eye of a 56-year-old male with neovascular glaucoma secondary to proliferative diabetic retinopathy, submitted to intravitreal Ranibizumab and trabeculectomy with 0.5% C mitomycin; note the partially encapsulated bleb with good IOP control under one antiglaucoma medication (6-month follow up)

measures included 6-month best correct visual acuity (BCVA) and anti-glaucoma medications to control IOP at 6-month follow up (Table 1). All eyes showed regression of rubeosis iridis and IOP control. Visual acuity improved in two eyes, worsened in one eye, and remained stable in two eyes. There were no treatment-related adverse effects.

Discussion

This article describes a consecutive case series of 5 eyes (5 patients) with NVG. Two patients underwent only intravitreal ranibizumab injection and obtained IOP control after the procedure under anti-glaucoma medications. Beutel et al. evaluated the long-term effects of intraocular bevacizumab injections as adjuvant treatment in patients with neovascular glaucoma and hypothesized that bevacizumab may be beneficial as adjuvant treatment because of its anti-angiogenic properties, its ability to induce new vessels regression and to prevent progression of angular obstruction.[2,3]

Three patients underwent trabeculectomy with mitomycin C on the 7th day after the intravitreal ranibizumab injection, with successful IOP control, two eyes without antiglaucoma medication and one under one antiglaucoma medication at 6-month follow up (Figure 2). There are reports that intravitreal bevacizumab injection may be an effective adjunct to trabeculectomy in NVG.[5] Although there was no improvement in visual acuity due to patients' severe disease, the IOP reduction was achieved with treatment, which traditionally does not occur with standard filtering procedures without anti-VEGF. Trabeculectomy for NVG eyes has been described as a challenging treatment with a poor surgical success rate.[1]

We are unaware of previous reports using ranibizumab as an adjuvant treatment in patients with neovascular glaucoma. This antibody fragment inhibits all forms of biologically active VEGF and its use is specifically intraocular, with known local and systemic safety but we should concern about the cost of therapy and the benefit to the patient.

These data suggest that ranibizumab may also be a useful tool in the treatment of this devastating disease. Randomized clinical trials are necessary to confirm the importance of this adjuvant therapy for the treatment of NVG.

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