Original Article/นิพนธ์ต้นฉบับ

การฉีดยา Bevacizumab เข้าในช่องหน้าตาในผู้ป่วยต้อหินชนิด Neovascular

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาผลของการฉีดยา bevacizumab เข้าในช่องหน้าตาต่อการหดหายของเส้นเลือดงอกใหม่ที่ม่านตาและการควบคุมความดันตาในผู้ป่วยที่เป็นต้อหินชนิด neovascular

ระเบียบวิธีวิจัย: การศึกษาแบบ prospective

วิธีการ: ผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็น neovascular glaucoma ทั้งหมด 20 คน ได้รับการตรวจวัดความดันตา และถ่ายรูปบริเวณม่านตาที่มีเส้นเลือดงอกใหม่ก่อนฉีดยา bevacizumab 0.1 mg/0.04 ml เข้าในช่องหน้าตา ผู้ป่วยได้รับการตรวจติดตามที่ 1, 2 และ 4 สัปดาห์ ผู้ป่วยจะได้รับยาซ้ำอีกครั้งหนึ่งถ้าเส้นเลือดงอกใหม่ยังคงมีอยู่มากกว่า 2/4 ส่วน ที่ 1 สัปดาห์

ผลการวิจัย: เส้นเลือดงอกใหม่บริเวณม่านตาได้หดหายไปบางส่วนภายใน 1 สัปดาห์ และหดหายอย่างมีนัยสำคัญ ($p<0.01$) ที่ระยะเวลา 2 สัปดาห์ สามารถควบคุมความดันตาได้ดีขึ้นในการตรวจติดตามทุกครั้ง โดยเฉพาะในผู้ป่วยที่มีมุมเปิดจำนวน 2 ตา ผู้ป่วยอีก 18 ตามีมุมตาปิดถาวร จำเป็นต้องได้รับการผ่าตัดเพื่อควบคุมความดันตา

สรุป: การฉีดยา bevacizumab เข้าในช่องหน้าตาสามารถทำให้เส้นเลือดงอกใหม่ที่ม่านตาหดหายอย่างมีนัยสำคัญ และช่วยให้ควบคุมความดันตาได้ดีขึ้น ตลอดจนหยุดการเพิ่มขึ้นของมุมตาปิดได้ **จักษุเวชสาร 2553; กรกฎาคม-ธันวาคม 24(2): 95-100.**

กองจักษุกรรม โรงพยาบาลราชวิถี

Original Article/นิพนธ์ต้นฉบับ

Intracameral Bevacizumab in Neovascular Glaucoma

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Abstract

Purpose: To determine the efficacy of intracameral bevacizumab injection in regression of iris neovascularization (NVI) and control of intraocular pressure (IOP) in neovascular glaucoma (NVG).

Design: Prospective, consecutive study

Methods: 20 eyes of 20 patients diagnosed with NVI and NVG were included. All patients had complete eye examination including IOP measurement and anterior segment photography. Bevacizumab (0.1 mg/0.04 ml) was injected intracamerally in each patient. Patients were examined at 1, 2, and 4 weeks post-injection. Each patient had a repeat injection at one week if NVI persisted in at least 2 quadrants.

Results: NVI was regressed partially at one week and significantly at two weeks following intracameral bevacizumab injections. Mean IOP was significantly lowered at 1, 2, and 4 weeks post injection. No signs of corneal endothelial toxicity were observed on slit-lamp examination. IOP of 2 eyes with open angle was controlled with topical medication. Trabeculectomy with mitomycin C was necessary for the other 18 eyes.

Conclusions: The intracameral bevacizumab injection was effective in regression of iris neovascularization. It may help in controlling IOP in eyes with open-angle NVG and impede progression of PAS in those eyes.
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Keywords: Neovascular glaucoma, Iris neovascularization, Bevacizumab

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Introduction

Neovascular glaucoma (NVG) is a devastating secondary glaucoma which frequently results in irreversible severe loss of vision. One of the pathological causes involves retinal hypoxia and ischemia. The mainstay of treatment includes panretinal photocoagulation (PRP)[1-4] to eliminate retinal ischemia and angiogenesis factors such as vascular endothelial growth factor (VEGF), and glaucoma drainage device[1,2] to control intraocular pressure (IOP).

Bevacizumab, a recombinant humanized monoclonal antibody against VEGF approved by the U.S. Food and Drug Administration for treatment of colorectal cancer[5], is widely used off-label in neovascular ocular diseases, for instance age-related macular degeneration (AMD) and other retinal neovascular conditions, as the intravitreal application[2,6]. Recently, the usage of bevacizumab has been extended to glaucomatous disorder including neovascular glaucoma[7-9]. An increasing number of studies reported the effect of intracameral bevacizumab injection in neovascular glaucoma[10-14]. However, few of them[11,12] studied the IOP-lowering effect of bevacizumab. The purpose of this study was to determine the effect of intracameral Bevacizumab injection on regression of iris neovascularization(NVI) and IOP control in NVG.

Materials and Methods

Twenty patients diagnosed with NVI and NVG who came to the glaucoma clinic, Rajavithi Hospital from July 2008 to March 2009 were enrolled. Ophthalmic assessment including visual acuity, IOP, anterior segment photography, the extent of NVI on slit-lamp examination, the extent of peripheral anterior synechiae (PAS) on gonioscopy and fundus examination were recorded along with number of anti-glaucoma medications in all visits. NVI and PAS were graded in 4 quadrants, each for 3 clock hours. The informed consents regarding risks, benefits, and off-label use of bevacizumab were obtained from all patients.

Intracameral bevacizumab injection was performed at slit lamp using a standardized technique. Tetracaine 0.5% and povidone-iodine drops were instilled before injection. A wire lid-speculum was inserted into palpebral fissure. 1 mg/0.04ml of bevacizumab was injected into the anterior chamber through a temporal paracenthesis with a 30-gauge needle. Topical antibiotic eye drops were prescribed four times per day for a week. The follow-up visits were scheduled at 1, 2 and 4 weeks. The injection was repeated in eyes with persistent NVI at 1 week.

Results

Of 20 eyes from 20 patients, 10 were men and 10 were women. The mean age was 57.45 years (range 40-71). 12 from 20 eyes (60%) had had proliferative diabetic retinopathy (PDR) while 8 (40%) had had central retinal vein occlusion (CRVO) as the etiology of NVG.

At presentation, the mean IOP was 38.1 $\pm$ 10.2 mm Hg, mean NVI was 3.5 quadrants, and mean PAS was 3.2 quadrants. After bevacizumab injection, NVI regressed in size, however still persisted in same quadrants at the first week in all patients. A second bevacizumab injection was performed. The mean NVI was significantly decreased at 2 and 4 weeks ($p < 0.01$). The mean IOP was significantly lowered at 1 week ($p = 0.01$), 2 weeks ($p < 0.01$), and 4 weeks ($p < 0.01$) compared to pre-injection. The mean PAS was 3.4 quadrants, 3.6 quadrants, and 3.6 quadrants at 1, 2, and 4 weeks respectively. Mean LogMAR visual acuity was improved significantly ($p < 0.01$) from 1.31 pre-injection to 0.89 at 4 weeks post injection.

There was a significant correlation between IOP and NVI at one week post injection (p = 0.02), but no correlation at two or four weeks post injection (p = 0.07)

No adverse side effect of intracameral bevacizumab was observed in this study.

Discussion

Intravitreal bevacizumab was widely used off-label as first-line treatment for exudative AMD by early 2006[2-6] and extended for NVG at approximately same period[7-9]. Recently, the use of intracameral bevacizumab for treatment of NVG has increasingly been reported[10-14] after its safety profile had been indicated[15,16]. The advantages of this approach of bevacizumab over the intravitreal administration include its simplicity, ease, and less aggressive approach.

Studies[11,12] have showed dramatic regression of NVI within two days to three weeks after intracameral bevacizumab injection. In our study, partial regression of NVI was noted at the first week in all cases. There was statistically significant regression of NVI at the second week. Complete regression of NVI was observed in 18 of 20 (90%) eyes at the fourth week post injection.

Table 1 Demographic and clinical data of our patients

Age/Sex	Etiology	At presentation			At 2 weeks			At 4 weeks		
		IOP	NVI	PAS	IOP	NVI	PAS	IOP	NVI	PAS
65/F	PDR	46	4	4	30	2	4	32	0	4
71/F	PDR	32	4	3	30	1	4	45	0	4
42/F	CRVO	53	4	4	40	2	4	40	0	4
66/M	CRVO	40	4	4	28	1	4	50	0	4
65/M	CRVO	24	4	0	12	2	1	15	1	1
52/M	CRVO	40	4	3	38	1	3	28	1	3
62/F	PDR	30	3	2	28	1	3	26	0	3
60/M	PDR	35	4	3	28	0	3	26	0	3
53/M	CRVO	54	4	4	46	1	4	30	0	4
56/F	PDR	50	2	4	30	0	4	26	0	4
40/F	CRVO	14	2	0	18	0	1	18	0	1
48/F	PDR	52	3	4	26	0	4	28	0	4
54/M	PDR	44	3	4	22	1	4	23	0	4
53/M	CRVO	38	3	3	22	1	4	24	0	4
63/F	PDR	36	4	4	22	1	4	25	0	4
57/M	PDR	42	4	3	26	2	4	24	0	4
64/F	PDR	34	4	4	21	0	4	28	0	4
55/M	PDR	28	3	4	22	1	4	24	0	4
57/M	PDR	38	4	3	24	2	4	24	0	4
66/F	CRVO	32	4	4	22	1	4	22	0	4

IOP indicates intraocular pressure; NVI, iris neovascularization; PAS, peripheral anterior synechiae; PDR, proliferative diabetic retinopathy; CRVO, central retinal vein occlusion.

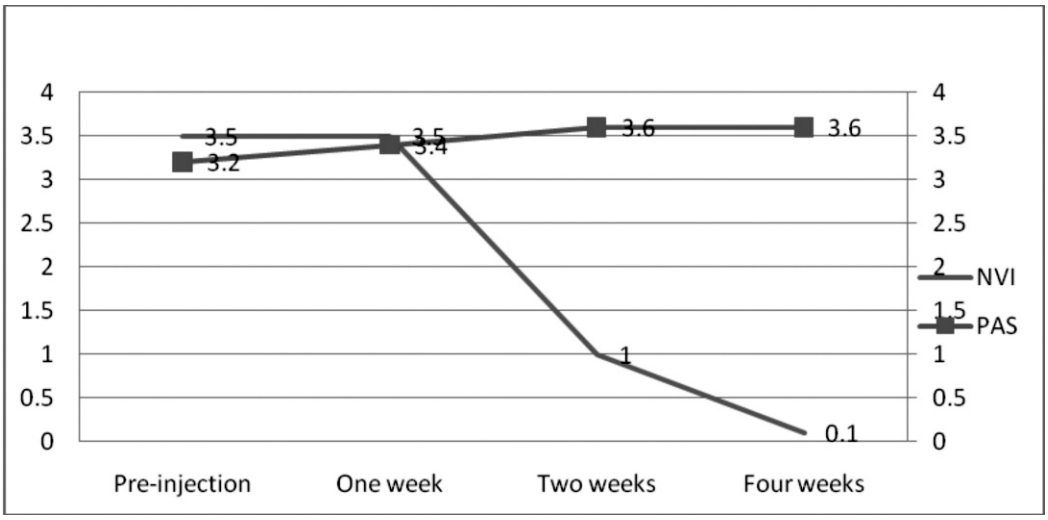

Figure 1 *Mean NVI vs Mean PAS*

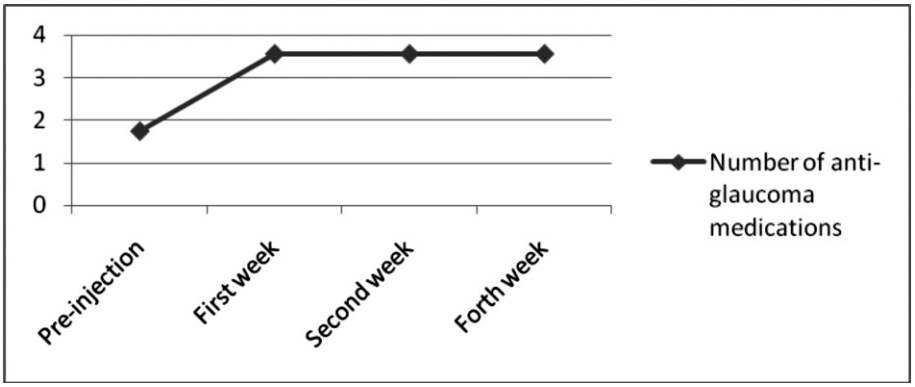

Figure 2 *Mean number of anti-glaucoma medications*

Chalam and colleagues[11] have reported that after intracameral bevacizumab injection IOP was controlled in eight of nine eyes with maximum medical therapy. We found significant IOP reduction in all eyes after the first week post injection. IOP was controlled in 2 of 20 eyes with topical anti-glaucoma medication at four weeks after injection even though the mean number of medication was not decreased. These two eyes had open angle at presentation. It is suggested that bevacizumab may preserve trabecular function in OAG stage of NVG consistent with the report of Duch and colleaques[12] which reported one case of IOP control in open-angle NVG without pre-existing glaucoma after intracameral bevacizumab injection. On the contrary the bevacizumab can cause sustained elevation of intraocular pressure by toxicity or inflammation from the medication itself.[17]

The other 18 cases underwent trabeculectomy with mitomycin C afterwards. There were no major complications.

Conclusion

Intracameral bevacizumab may be an adjunctive treatment for NVG. The mainstay of treatment remains PRP and glaucoma drainage device for IOP control. It is suggested that bevacizumab may control IOP in eyes with open-angle NVG and impede progression of PAS in those eyes.

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