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Intraocular pressure changes following intravitreal anti-VEGF injections in AMD patients

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ABSTRACT

Background: It has been demonstrated that vascular endothelial growth factor (VEGF) plays a role in the development of age-related macular degeneration (AMD) as well as other eye disorders linked to choroidal neovascularisation (CNV). The present study was assessed intraocular pressure changes following intravitreal anti-VEGF injections in AMD patients.

Materials & Methods: 45 wet age-related macular degeneration(AMD)patients of both genders were divided into 3groups of15 each. Group I patients received bevacizumab(1.25mg/0.05ml), group II patients received ranibizumab(0.5 mg/0.05 ml)and group III patients received both bevacizumab (1.25 mg/0.05 ml), and ranibizumab (0.5 mg/ 0.05 ml). Parameters such as prevalence of intraocular pressure elevations and mean interval between injections (days) were recorded.

Results: There were15 patients and 30 eyes in all groups. The mean age was 68.4years,70.2 years and 74.2 years and pre-existing glaucoma was seen in 4,3and1 patient in group I,II and III respectively. The difference was significant ($P<0.05$). In pre-existing glaucoma, IOP elevations was seen in 3, in group I in 2, in group II in 2 and in group III in 0 patients. The mean interval between injections was 65.2 days, 87.5 days, 54.2 days and 50.4 days respectively. The difference was significant ($P< 0.05$).

Conclusion: The occurrence of sustained elevated IOP in patients receiving intravitreal anti-VEGF injections is considerable. Moreover, these data indicate that patients with pre-existing glaucoma who are treated with either bevacizumab or ranibizumab may have an increased risk of further IOP elevation.

Keywords: Age-related macular degeneration, Bevacizumab, ranibizumab.

1. INTRODUCTION

It has been demonstrated that vascular endothelial growth factor (VEGF) plays a role in the development of age-related macular degeneration (AMD) as well as other eye disorders linked to choroidal neovascularisation (CNV). Inhibition of VEGF, in particular with ranibizumab and bevacizumab has proven to be an effective treatment for these conditions.[1]

Anti-VEGF agents have revolutionized the treatment of wet AMD, diabetic retinopathy, retinal vein occlusions, and other retinal pathology.[2] A common intravitreal injection volume is 0.05 mL, and serial injections are often needed over months or years. In addition, anti-VEGF therapy is widely used to manage neovascular glaucoma.[3]Bevacizumab is a humanised monoclonal IgG antibody that works by inhibiting VEGF, whereas ranibizumab is a Fab fragment (IgG1) of a humanised

monoclonal antibody. The US Food and Drug Administration (FDA) has tested and approved ranibizumab for use in AMD. Bevacizumab, initially approved by the FDA for colorectal cancer treatment, is also widely used off-label for AMD.[4]

Concerning local adverse event (AE) safety profiles, ranibizumab and bevacizumab are both deemed safe, though there is a lack of randomized, prospective trials involving intravitreal bevacizumab.[5] There have been recent publications of case reports detailing prolonged increases in IOP following intravitreal bevacizumab and ranibizumab.[6]The present study was assessed intraocular pressure changes following intravitreal anti-VEGF injections in AMD patients.

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2. MATERIALS&METHODS

The study was carried out on 45 wet age-related macular degeneration (AMD) patients of both genders. All gave their written consent to participate in the study Consent to participate in the study.
Data such as name, age, gender etc. was recorded. Patients were divided into 3 groups of 15 each. Group I patients received bevacizumab (1.25 mg/0.05 ml), group II patients received ranibizumab (0.5 mg/ 0.05 ml)and group III patients received both bevacizumab (1.25 mg/0.05 ml), and ranibizumab (0.5 mg/ 0.05 ml). All patients had a pre injection and post injection ultrasound biomicroscopy (UBM) scan. Parameters such as prevalence of intraocular pressure elevations and mean interval between injections (days) were recorded. Results thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

3. RESULTS

Table I Demographic data

Parameters	GroupI	GroupII	GroupIII	P value
Noofeyes	30	30	30	1
Age(mean)	68.4	70.2	74.2	0.05
pre-existing glaucoma	7	3	1	0.05

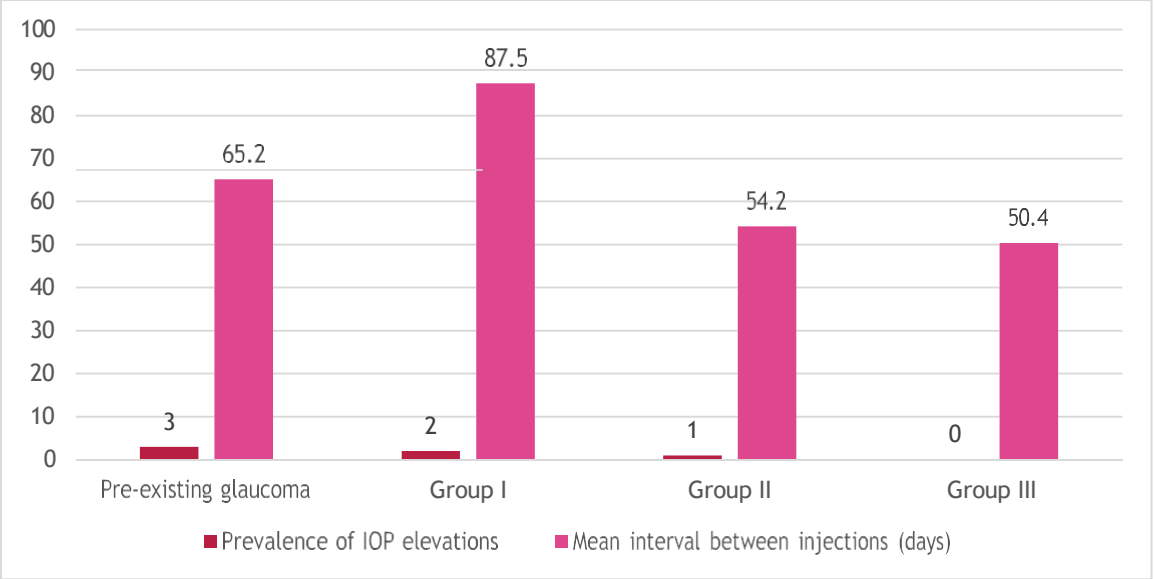
Table I shows that there were 15 patients and 30 eyes in all groups. The mean age was 68.4 years, 70.2 years and 74.2 years and pre-existing glaucoma was seen in 4, 3 and 1 patient in group I, II and III respectively. The difference was significant (P< 0.05).

Table II. Assessment of parameters.

Parameters	Pre-existing glaucoma	Group I	Group II	Group III	P value
Prevalence of IOP elevations	3	2	1	0	0.87
Mean interval between injections (days)	65.2	87.5	54.2	50.4	0.05

Table II, graph I shows that in pre-existing glaucoma, IOP elevations was seen in 3, in group I in 2, in group II in 2 and in group III in 0 patients. The mean interval between injections was 65.2 days, 87.5 days, 54.2 days and 50.4 days respectively. The difference was significant (P< 0.05).

Graph I Assessment of parameters.


100
90
80
70
60
50
40
30
20
10
0
65.2
87.5
54.2
50.4
3
2
1
0
Pre-existing glaucoma
Group I
Group II
Group III
Prevalence of IOP elevations
Mean interval between injections (days)

4. DISCUSSION

A patient with a diagnosis of primary open-angle glaucoma undergoes an anti–vascular endothelial growth factor (VEGF) intravitreal injection for concomitant wet age-related macular degeneration (AMD).[7] After injection, the patient experiences the acute onset of eye pain with a decline in vision. The intraocular pressure (IOP) is noted to be 45 mm Hg. The symptoms rapidly resolve without intervention.[8] The present study was assessed intraocular pressure changes following intravitreal anti-VEGF injections in AMD patients.

We found that there were 15 patients and 30 eyes in all groups. The mean age was 68.4 years, 70.2 years and 74.2 years and pre-existing glaucoma was seen in 4, 3 and 1 patient in group I, II and III respectively. Good et al[9] reported the rate of intraocular pressure (IOP) elevation associated with repeated intravitreal injections of antivascular endothelial growth factor (VEGF) agents and to determine if a pre-existing diagnosis of glaucoma is a risk factor for this phenomenon. The charts of 215 eyes undergoing intravitreal injection with anti-VEGF agents for wet age-related macular degeneration (AMD) were retrospectively examined with respect to frequency of injections, number of injections and changes in IOP. Of the 215 eyes receiving injections with bevacizumab and/or ranibizumab, 6% (n-13) had sustained IOP elevation requiring medical or laser interventions. Of the eyes receiving only bevacizumab, 9.9% (10/101) had sustained elevated IOP, while 3.1% (3/96) of eyes receiving only ranibizumab experienced increases (p-0.049). Patients with pre-existing glaucoma experienced higher rates of elevated IOP when compared with patients without pre-existing glaucoma (33% vs 3.1% respectively; $p<0.05$). The glaucoma subgroup had a lower median number of injections (6; interquartile range 5e10) compared with the non-glaucoma group (9.5; interquartile range 6-13.7; p-0.031).

We found that in pre-existing glaucoma, IOP elevations was seen in 3, in group I in 2, in group II in 2 and in group III in 0 patients. The mean interval between injections was 65.2 days, 87.5 days, 54.2 days and 50.4 days respectively. Kahook et al[10] published a case series of 6 eyes injected with bevacizumab that developed sustained elevations in IOP, while fellow eyes remained at baseline IOP. The IOP elevations reported by the case series appeared temporally related to injections. In the past decade, many more studies have examined the relationship between intravitreal injections and IOP elevation.

de Vries et al[11] reported that the mean difference in IOP after anti-VEGF injection (rise above pre-injection) was 23.41 mm Hg immediately after injection, 2.51 mm Hg at 30 minutes, −0.63 one day after injection, and back to baseline by 1 week. For some patients, the acute IOP elevation does persist for at least several hours, and so it might make sense to define 3 categories of postinjection IOP rise, in particular to capture these sensitive eyes: early (or acute) is a rise in IOP within minutes, intermediate is a rise lasting hour, and late is a chronic elevation over months.Cui et al[12] identified 17,113 non- glaucomatous eyes receiving intravitreal injection. Their group demonstrated that eyes receiving more injections (14 or more injections at 2 y follow-up and 20 or more injections at 3 years follow-up) had higher odds of initiating IOP-lowering therapy or having a new diagnosis of glaucoma (defined by inclusion of a glaucoma diagnosis in medical claims data). 1.6% of all included eyes initiated IOP-lowering therapy within 2 years follow-up, and there was no difference in age, sex, or history of diabetes or hypertension between the group requiring IOP-lowering therapy and the group that did not.The shortcoming of the study is small sample size.

5. CONCLUSION

Authors found that the occurrence of sustained elevated IOP in patients receiving intravitreal anti-VEGF injections is considerable. Moreover, these data indicate that patients with pre-existing glaucoma who are treated with either bevacizumab or ranibizumab may have an increased risk of further IOP elevation.

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