

Immediate intraocular pressure changes following intravitreal injections of triamcinolone, pegaptanib, and bevacizumab

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Abstract

Purpose To assess the intraocular pressure (IOP) changes, within the first 30 min after intravitreal injection of 0.1 ml (4 mg) triamcinolone, 0.09 ml (0.3 mg) pegaptanib, and 0.05 ml (1.25 mg) bevacizumab.

Methods Records of patients who received intravitreal triamcinolone, pegaptanib, and bevacizumab and who had their IOP measured post-injection were reviewed.

Results A total of 212 injections were performed (76 bevacizumab in 63 patients, 42 triamcinolone in 41 patients, 94 pegaptanib in 74 patients). At 10 min, over 87% of eyes receiving each drug had an IOP of less than 35 mmHg. Three of the 42 eyes receiving intravitreal triamcinolone were treated with IOP-lowering drops for pressures of 44, 46, and 60 mmHg. No patients treated with intravitreal bevacizumab or pegaptanib received IOP-lowering drops. The number of eyes in each injection group that had an IOP rise > 10 mmHg within 30 min after injection was 27.6% of eyes receiving bevacizumab, 33.3% of eyes receiving triamcinolone, and 36.2% of eyes receiving pegaptanib. At 10 min, eyes with glaucoma were less likely to have an IOP < 35 mmHg, but this difference became less marked with time.

Conclusion In our series, most patients receiving intravitreal injections did not require IOP-lowering drops after injection, and none required a paracentesis.

Eye (2009) 23, 181–185; doi:10.1038/sj.eye.6702938; published online 10 August 2007

Keywords: eye; bevacizumab; intraocular pressure; intravitreal; pegaptanib; triamcinolone

Introduction

Currently used intravitreal drugs for the treatment of retinal diseases include triamcinolone acetonide (Kenalog-40, Bristol-Myers Squibb, Peapack, NJ, USA), pegaptanib sodium (Macugen, Eyetech-OSI, New York, USA), bevacizumab (Avastin, Genentech, San Francisco, CA, USA), and ranibizumab (Lucentis, Genentech, San Francisco, CA, USA). The most commonly used doses are 0.1 ml (4 mg) of triamcinolone, 0.09 ml (0.3 mg) of pegaptanib, 0.05 ml (1.25 mg) of bevacizumab, and 0.05 ml (0.5 mg) of ranibizumab. Injecting fluid into the eye transiently increases the intraocular pressure (IOP). The current recommendation for performing intravitreal injections advises against performing a paracentesis.¹ However, in patients who suffer from glaucoma or optic nerve damage, there is a concern that a transient high IOP elevation may further damage the ganglion cells in the optic nerve. It is important to know the transient IOP elevations that patients are subjected to after such intravitreal injections for several reasons, such as to assess whether a paracentesis is necessary, whether IOP monitoring is necessary after the procedure, and to reassess, when manufacturing a new drug, the optimum amount of fluid to be injected into the eye. In our practice at the Mayo Clinic, we have routinely performed and recorded IOPs after intravitreal injection, at various time points,

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Received: 4 January 2007
Accepted in revised form: 25 May 2007
Published online: 10 August 2007

starting 5 min after injection, until the IOP decreases to below 30 mmHg.

Methods

Permission was obtained from the Institutional Review Board of the Mayo Clinic to perform this study. Patients who had received intravitreal injections of triamcinolone acetonide, pegaptanib, or bevacizumab, between July 2005 and December 2005, were identified from a computer database. The records were reviewed and the following data were collected: pre-injection IOP, method of measurement, all-post-injection IOPs and their time points, and whether any glaucoma medications were used to lower the IOP.

Results

A total of 212 injections were performed (76 bevacizumab in 63 patients, 42 triamcinolone in 41 patients, 94 pegaptanib in 74 patients). There were 161 unique patients; each patient may have received more than one injection and may have had injections of more than one type of drug. All pre-injection IOPs were performed by Goldmann applanation tonometry, except 5, which were measured with either the pneumotonometer or the Tono-Pen XL (Medtronic Xomed Ophthalmics, Inc., Minneapolis, MN, USA). All post-injection IOP measurements had been measured using the Tono-Pen XL.

Figure 1 shows the mean IOPs for the eyes receiving the three drugs at different time points. IOP

measurements were discontinued when the IOP was less than 30 mmHg. All eyes had a pre-injection IOP of less than 35 mmHg. It can be seen that three eyes that received intravitreal triamcinolone had prolonged IOP rises of over 35 mmHg, which had to be monitored. The highest IOP recorded was an IOP of 60 mmHg, 10 min after receiving intravitreal triamcinolone. The patient was treated with brimonidine tartrate 0.15% (Alphagan P, Allergan, Irvine, CA, USA) eye drops, which lowered the IOP to 31 mmHg, 30 min after the drops, and to 21 mmHg, 60 min after the drops. Overall, 3 of the 42 eyes receiving intravitreal triamcinolone were treated with IOP-lowering drops (timolol maleate 0.5%, and/or brimonidine 0.15%) for pressures of 44, 46, and 60 mmHg. No patients treated with intravitreal bevacizumab or pegaptanib received IOP-lowering drops.

Table 1 shows the proportion of eyes for each drug injection that had a post-injection pressure of less than or equal to 35 mmHg. At 10 min, over 87% of eyes receiving each drug had an IOP of less than 35 mmHg. There was no statistically significant difference at 10 min between the mean IOPs of each drug ($P > 0.05$). At 15 min, over 83% of eyes receiving each drug had an IOP of less than 35 mmHg. Over 90% of eyes in all groups maintained an IOP of less than 35 at all time points measured; there was no statistically significant difference between the mean IOPs of each drug ($P > 0.05$) at all time points.

Table 2 shows the number of eyes in each injection group that had an IOP rise of greater than 10 mmHg at any time point during the follow-up. This was 27.6% of eyes receiving bevacizumab, 33.3% of eyes receiving

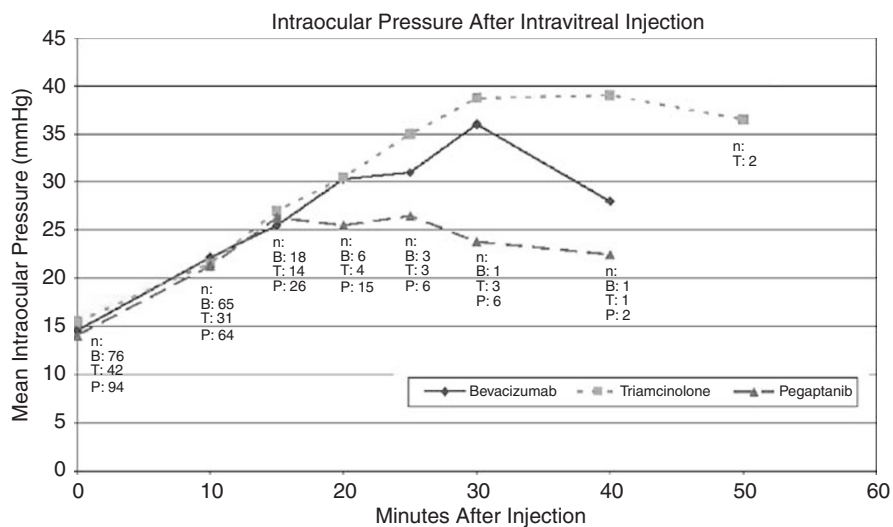


Figure 1 Graph to show mean IOP variations after intravitreal injections of bevacizumab, triamcinolone, and pegaptanib with time. B = bevacizumab, T = triamcinolone, P = pegaptanib. The numbers in the graph show the number of patients who received each drug and received an IOP measurement at that time point.

Table 1 Proportion of eyes receiving an intravitreal injection of bevacizumab, triamcinolone, and pegaptanib that had a post-injection pressure of less than or equal to 35 mmHg

Number of eyes with intraocular pressure <35 mmHg after injection	Intravitreal drug			P-values		
	Bevacizumab N (%)	Triamcinolone N (%)	Pegaptanib N (%)	Bevacizumab vs triamcinolone	Bevacizumab vs pegaptanib	Triamcinolone vs pegaptanib
10 min	61 (93.4)	27 (87.1)	59 (92.2)	0.6	0.7	0.8
15 min	15 (83.3)	13 (92.9)	25 (96.2)			
20 min	5 (83.3)	3 (75.0)	15 (100.0)			
All time points after injection	71 (93.4)	38 (90.5)	88 (93.7)	0.7	0.9	0.6

Table 2 The number of eyes in each injection group that had an IOP rise of greater than 10 mmHg at any time point during the follow-up

Rise in intraocular pressure at any time point measured	Intravitreal drug			
	Bevacizumab, N (%)	Triamcinolone, N (%)	Pegaptanib, N (%)	Total, N
≤ 10 mmHg	55 (72.4)	28 (66.7)	60 (63.8)	143
> 10 mmHg	21 (27.6)	14 (33.3)	34 (36.2)	69
Total number of injections, N	76	42	N = 94	212

P-values: bevacizumab vs pgaptanib: 0.382; bevacizumab vs triamcinolone: 0.505; pegaptanib vs triamcinolone: 0.970.

Table 3 The proportion of eyes for each drug injection that had a post-injection pressure ≤35 mmHg, depending on whether there was a history of glaucoma

Number of eyes with intraocular pressure <35 mmHg after injection	History of glaucoma	Bevacizumab, N (%)	P-value	Triamcinolone, N (%)	P-value	Pegaptanib, N (%)	P-value	All injections, N (%)	P-value
10 min	Yes	5 (62.5)	0.0048	7 (77.8)	0.56	9 (81.8)	0.20	21 (75)	0.002
	No	56 (98.25)		20 (90.9)		50 (94.3)		126 (95.5)	
15 min	Yes	8 (80)	1.00	5 (83.3)	0.43	9 (90)	0.38	22 (84.6)	0.16
	No	7 (87.5)		8 (100)		16 (100)		31 (96.9)	
20 min	Yes	3 (100)	1.00	1 (50)	1.00	9 (100)		13 (92.9)	1.00
	No	2 (66.7)		2 (100)		6 (100)		10 (90.9)	
All time points after injection	Yes	43 (84.3)	0.0497	10 (83.3)	0.56	21 (87.5)	0.17	43 (84.3)	0.01
	No	154 (95.6)		28 (93.3)		67 (95.7)		154 (95.7)	

triamcinolone, and 36.2% of eyes receiving pegaptanib. There was no statistically significant difference in the number of eyes with an IOP rise of greater than 10 mmHg between the three drugs ($P > 0.05$).

Table 3 shows the proportion of eyes for each drug injection that had a post-injection pressure of less than or equal to 35 mmHg, depending on whether there was a history of glaucoma. A history of glaucoma was based on whether the patient had a clinical diagnosis or was taking glaucoma drops.

Owing to the overlap of patients receiving more than one injection and injection type, generalized estimating equation models were used when calculating P -values to

account for the potential correlation among the eyes from the same patient.

A Kaplan–Meier plot (Figure 2) shows the cumulative probability with time that the IOP attained 30 mmHg or less. Figure 3 is a Kaplan–Meier plot showing the cumulative probability with time that the IOP attained 30 mmHg or less, in patients with glaucoma vs no glaucoma.

Discussion

There is individual variation in IOP elevation after the injection of the same amount of drug. This variation is

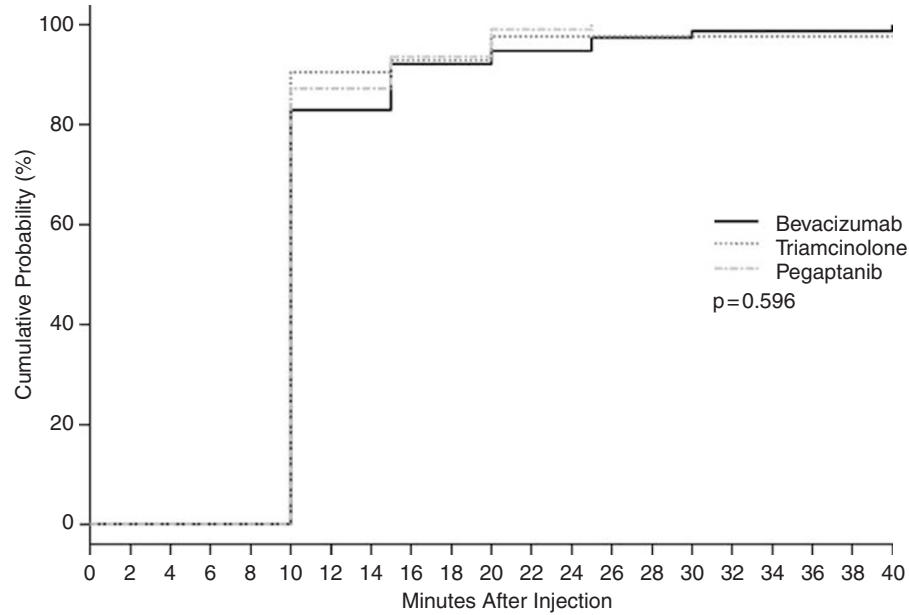


Figure 2 Kaplan–Meier survival plot showing the cumulative probability with time that the IOP attained 30 mmHg or less.

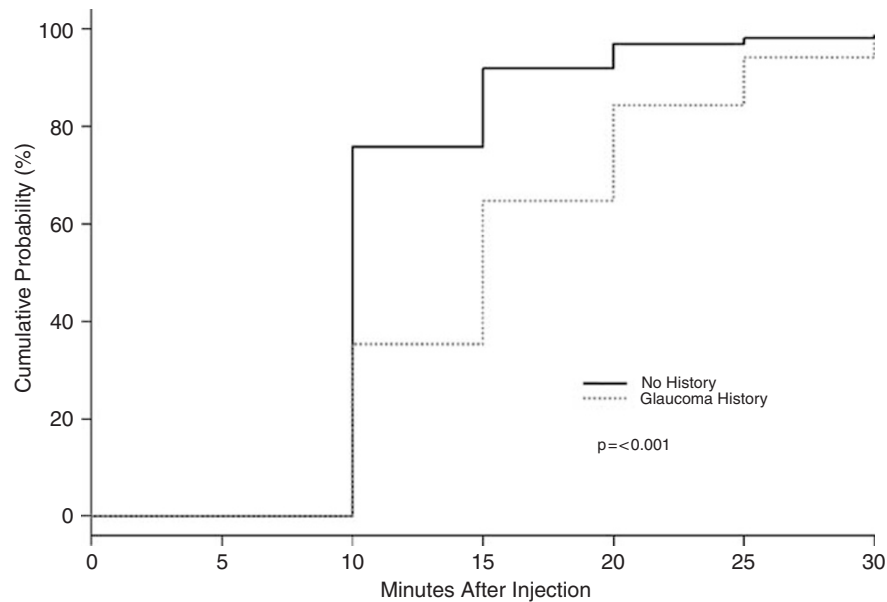


Figure 3 Kaplan–Meier survival plot showing the cumulative probability with time that the IOP attained 30 mmHg or less in patients with glaucoma vs no glaucoma.

due to relative inaccuracy of dosing exactly the intended amount in a clinical setting. In addition, scleral rigidity differs between patients. Another source of variation is whether there is reflux from the injection site after the needle is withdrawn.² Larger needles may allow more reflux from the injection site, and therefore a lower immediate IOP. We use 31-gauge needles to inject bevacizumab, 27-gauge needles for triamcinolone, and the prepackaged 27-gauge needles for pegaptanib.³ In

our series, anterior chamber paracentesis was not necessary after the intravitreal injections. A review of IOPs in 122 eyes, after intravitreal pegaptanib injection,⁴ showed that only 13% had an IOP greater than 30 mmHg, 30 min after injection. No eyes required a paracentesis in that series. However, the authors did not measure the IOP fluctuation within the 30 min period. Another study describes the IOP fluctuations in 38 eyes after intravitreal triamcinolone⁴, but the authors did not separate patients

into groups depending on whether they had glaucoma. Our results show that at 10 min, across all injection types, eyes with glaucoma were less likely ($P < 0.05$) to have an IOP lower than 35 mmHg. This difference became less significant with time (Figure 3).

Knowledge of the IOP fluctuations after intravitreal injection allows ophthalmologists to make a clinical judgment regarding whether a patient with glaucomatous optic nerve damage may benefit from an anterior chamber paracentesis to avoid the damage associated with repeated episodes of high IOP.

None of the authors have any proprietary interest in any of the products mentioned in this paper.

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