Original Article

Triamcinolone Intravitreal Injection and Intraocular Pressure in Macular Edema Associated with Retinal Vein Occlusion

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Abstract

Purpose: To study the risk factors of increased intraocular pressure (IOP) response to triamcinolone acetonide intravitreal (IVTA) injection in eyes with macular edema associated with retinal vein occlusion.

Methods: Eighty-nine eyes with macular edema associated with retinal vein occlusion first received periocular injection of 40 mg triamcinolone acetonide (TA) and were followed for one month. According to the diversity of IOP after periocular TA (PTA) injection, they were divided into the elevation IOP group (group A, 26 eyes) and the normal IOP group (group B, 63 eyes). They then received 4 mg TA intravitreal injection. IOP measurements were recorded after PTA and IVTA injections, and were followed for six months.

Results: Both PTA and IVTA injections caused a rise in IOP, but it was higher in the IVTA injection (40.45%) than in the PTA injection (29.21%). The mean rise in IOP was more significant in eyes with IVTA injection (28.08 ± 8.24 mmHg) than in eyes with PTA injection (20.87 ± 4.07 mmHg). Patients with an elevation IOP above 6 mmHg after PTA injection had a 73.08% chance of developing a pressure of 24 mmHg or higher, whereas only 12.70% of those with an elevation IOP below 6 mmHg after PTA injection experienced pressure elevation.

Conclusion: IOP response to PTA injection is a good way to judge IOP response to IVTA. If the patient is highly sensitive to corticosteroid, treatments other than IVTA injection are used to avoid the increased risks associated with intravitreal corticosteroid injection. (***Eye Science 2012; 27: 182–187***)

Keywords: triamcinolone acetonide; periocular injection; intravitreal injection; macular edema; intraocular pressure

Periocular and intravitreal triamcinolone acetonide (TA) injections are increasingly popular methods of treating macular edema associated with various retinal diseases, including diabetic retinopathy, retinal venous occlusion, choroidal neovascularization and uveitis[1–4]. Most previous studies showed that TA injections are effective in reducing edema and in improving visual acuity. However, such injections can cause ocular hypertension and glaucoma[5–11]. Both periocular TA (PTA) and intravitreal TA (IVTA) injections cause a rise in intraocular pressure (IOP), but it is higher in the IVTA injection than in the PTA injection[12]. Hence, we propose that the IOP response to PTA injection may be a good way to judge IOP response to IVTA in macular edema associated with retinal vein occlusion.

Patients and methods

This study was performed according to the Declaration of Helsinki of the World Medical Association. The protocol was approved by the Institutional Review Board of Xi'an No.4 Hospital, and informed consent was obtained from the patients.

Eighty-nine eyes in 89 consecutive patients were seen in our outpatient clinic between September 2008 and September 2010. The patients underwent IVTA injections and met the inclusion and exclusion

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criteria for the study. The inclusion criteria included patients undergoing IVTA injection for two diagnoses: branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). The exclusion criteria included a prior diagnosis of glaucoma, history of intraocular surgery, use of IOP-lowering agents, or baseline IOP > 21 mmHg. Clinical data, including age, gender, glaucoma history, diagnosis of retinal disease, and systemic diseases were also recorded.

There were 46 women and 43 men in the group, ranging from 43 to 69 years old. Data on systemic disease was not available for 31 patients (34.83%). Of the remaining 58 patients, 32 patients (35.96%) had hypertension, and 26 patients (29.21%) had hyperlipemia. The majority of patients received the injections for BRVO (61 patients, 68.54%) and CRVO (28 patients, 31.46%). (Table 1)

Table 1 Baseline demographic information

Age (years)	
Range	43–69
Mean	57.48
Gender (patients)	
Male	43(48.31%)
Female	46(51.69%)
Retinal diseases (patients)	
CRVO	28(31.46%)
BRVO	61(68.54%)
Systemic diseases (patients)	
No	31(34.83%)
Hypertension	32(35.96%)
Hyperlipemia	26(29.21%)
IOP elevation after PTA (eyes)	
IOP elevation	26(29.21%)
Normal IOP	63(70.79%)

CRVO = Central retinal vein occlusion; BRVO = Branch retinal vein occlusion. TA = Triamcinolone acetonide; IOP = intraocular pressure; PTA = TA periocular injection.

Periocular TA (PTA) injection was performed in the outpatient clinic. After topical instillation of 0.4% oxybuprocaine, 1.0 ml (40 mg) of TA (Erba CO. Italy). mixed with 0.2 ml of 2% xylocaine was injected via a 25-gauge needle through the inferior lid margin into the periocular space.

The intravitreal injection was done under sterile conditions in the operating room. Povidone-iodine was applied before the injections. Paracentesis was performed into the anterior chamber under the operating microscope, and some aqueous fluid was aspirated by using a 26-gauge needle to decrease the volume of the eye A portion. 0.1 ml of TA (4 mg) was injected slowly via a 27-gauge needle through the inferior pars plana 4 mm posterior to the limbus. Topical antibiotic was used in all of the patients for 3 days.

In 89 eyes of 89 patients, they first received the periocular injection of 40 mg TA (40 mg/1.0 ml suspension) and were followed for one month. According to the diversity of IOP after the periocular TA injection, we designated these patients as the elevation IOP group (group A, 26 eyes) and the normal IOP group (group B, 63 eyes). They then received 4 mg of TA intravitreal injection (0.1 ml of 40 mg/1.0 ml suspension) and were followed for 6 months.

IOP measurements with a noncontact tonometer plus central corneal thickness measurements[13] before injection, two and four weeks after PTA injection, and at monthly intervals after IVTA injection for 6 months were recorded. The monthly IOP records were obtained within ±7 days of the specific visit. Patients who did not have IOP records for more than two consecutive visits were excluded.

We defined cases with post-periocular/IVTA injection IOP elevation as eyes exhibiting an IOP rise of more than 6 mmHg higher than the pre-injection IOP at least one visit during the post-injection follow-up period[13], Central corneal thickness measurements or Goldmann applanation tonometry were performed if we determined the use of anti-glaucoma medications when IOP elevation was more than 24 mmHg[14].

Statistical analysis for descriptive statistics was performed using SPSS statistical software (version 11.5; SPSS, Chicago, IL). The data obtained were analyzed with frequency and descriptive statistics. Univariate analyses to determine the association between baseline demographics and IOP in the different groups were performed using One-way ANOVA, χ^2 test, and the Fisher's exact test, as appropriate. The critical value of significance was set at $P < 0.05$ for all tests.

Results

Both periocular TA and intravitreal TA injections

caused a rise in intraocular pressure, which was higher in the IVTA-injected eyes (36 eyes, 40.45%) than in the PTA-injected eyes (26 eyes, 29.21%), although no significant difference was found between them ($P = 0.116$). The mean rise in IOP was significantly greater in eyes with IVTA injection (28.08 ± 8.24 mmHg) than in those with PTA injection (20.87 ± 4.07 mmHg). The rise in IOP started approximately 2 weeks after PTA injection. The duration of TA induced IOP elevation was about 3 months after IVTA injection (Tables 2,3).

Table 2 Clinical data of cases with IOP elevation after TA intravitreal injection

	Group A (26 eyes)	Group B (63 eyes)	*P*
IOP elevation (eyes)	23(88.46%)	13(20.63%)	0.000
> 24~30	8	5	0.923
> 30~35	5	2	0.549
> 35~40	3	1	1.000
> 40	3	0	
Age (yrs)			
> 55	11	6	
≤ 55	12	7	
Gender (patients)			
Male	10	7	
Female	13	6	
Retinal diseases (patients)			
CRVO	8	5	
BRVO	15	8	

Group A = The elevation IOP after TA periocular injection; Group B = The normal IOP after TA periocular injection; TA = Triamcinolone acetonide; IOP = intraocular pressure; yrs = years; CRVO = Central retinal vein occlusion; BRVO = Branch retinal vein occlusion.

In the study groups, 23 patients (88.46%) in group A, 13 patients (20.63%) in group B experienced IOP elevation ($P = 0.000$). IOP elevation occurred immediately and up to 2 weeks after IVTA injection. The most elevated IOP happened at 1-2 months in both groups. In patients with an elevated IOP above 6 mmHg after PTA injection had a 73.08% (19 eyes) chance of developing a pressure of 24 mmHg or higher (group A), whereas only 12.70% (8 eyes) of those with an elevated IOP below 6 mmHg after PTA injection experienced pressure elevation (group B). A maximal IOP reading value higher than 30 mmHg was detected in 11 patients in group A and in 3 patients in group B. A maximal IOP reading value higher than 35 mmHg was measured in 6 patients in group A and in 1 patient in group B. A maximal IOP reading value higher than 40 mmHg was measured in 3 patients (3%) in group A and in no patients in group B (Table 2).

Table 3 Intraocular pressure elevation before and after triamcinolone acetonide periocular and intravitreal injection

	Mean IOP ± SD (mmHg)	
	Group A(23 eyes)	Group B(13 eyes)
Before injection	14.08 ± 2.59	15.38 ± 2.02
2 w after PTA	20.87 ± 4.07	16.77 ± 2.05
4 w after PTA	19.43 ± 1.44	18.00 ± 1.53
1 m after IVTA	24.83 ± 5.23	23.69 ± 2.29
2 m after IVTA	28.08 ± 8.24	26.46 ± 4.70
3 m after IVTA	24.82 ± 5.83	22.15 ± 3.41
4 m after IVTA	19.39 ± 4.31	19.00 ± 2.04
5 m after IVTA	17.43 ± 2.87	17.85 ± 2.15
6 m after IVTA	16.78 ± 2.00	17.08 ± 1.61

IOP = intraocular pressure; SD = standard deviation; w = week; m = months; PTA= periocular triamcinolone acetonide injection; IVTA = intravitreal triamcinolone acetonide injection.

Regarding the reason for IVTA injection, the rise in IOP was significantly greater in patients with CRVO (13/28 eyes, 46.43%) than in those with BRVO (23/61 eyes, 37.70%). The IOP was significantly elevated in the "young" patients (≤ 55 years) with RVO (19/40 patients, 47.50%) than in the "old" patients (> 55 years) with RVO (17/49 patients, 36.69%). However, there were no significant differences in IOP between the young and the old patients. ($P > 0.05$, Table 2) Young males (≤ 55 years) with CRVO had a high risk of refractory IOP after IVTA injections (Table 4).

Of the 36 patients who experienced pressure elevation, 27 patients (75.00%; IOP>24 mmHg) were taking anti-glaucoma medications at the time of IOP elevation, and 9 patients (25.00%; IOP≤24 mmHg) were not. Elevated IOP was controllable in most cases with a mean of 1–2 anti-glaucoma medication. Nine patients required the addition of anti-glaucoma medication; 3 patients needed systemic anti-glaucoma medication and argon laser trabeculoplasty (Table 4).

Discussion

One aim of this study was to analyze the increased

Table 4 Clinical data of cases with refractory IOP after IVTA injections

Age(yrs)	Gender	Retinal diseases	Post–IVTA peak IOP (mm Hg)	No. of glaucoma drugs	Further treatment	Final IOP(mm Hg)
48	M	CRVO	43	5	ALT	17
46	M	CRVO	45	5	ALT	15
43	M	CRVO	47	5	ALT	13

IOP = intraocular pressure; IVTA = intravitreal triamcinolone acetonide; yrs = years; M = male; CRVO = central retinal vein occlusion; Trab = trabeculectomy; ALT = argon laser trabeculoplasty.

risk for elevated IOP in IVTA injection compared with characteristics of changes in IOP following PTA injection. Some studies of Western populations reported that the risk for elevated IOP increased if there was a higher baseline IOP in patients[15–17]. In our study, we could not identify a correlation between initial pressure and the occurrence of an elevated IOP, but we identified a strong correlation between those patients with an elevated IOP above 6 mmHg after PTA injection and the occurrence of an IOP 24 mmHg or greater during follow-up in the Chinese population. An IOP rise of more than 6 mmHg may be a more appropriate definition because the normal diurnal IOP variation of 3 to 6 mmHg is taken into consideration[18,19].

The rise in IOP started approximately 2 weeks after PTA injection. The duration of TA-induced IOP elevation was about 3 months after IVTA injection. Some eyes included in the investigation showed ophthalmoscopically visible TA crystals in the vitreous for as long as the increase in IOP lasted. This suggests that when the TA crystals have resolved, IOP may return to its baseline level, and thus the TA-induced increase in IOP is reversible. The mechanism of corticosteroid-induced IOP elevation increased aqueous outflow resistance through structural changes in the trabecular meshwork, reduced endothelial phagocytosis, and increased extracellular matrix deposition[21].

In our study, patients with a history of CRVO were more likely to develop a pressure of 24 mmHg or greater than patients with a history of BRVO. Many investigators described the association of CRVO with primary open-angle glaucoma (POAG) or ocular hypertension(OHT). The prevalence of POAG in patients with CRVO reported in the literature varies from 6% to 69%[22;23], whereas there were no similar associations between branch retinal vein occlusion and glaucoma/OHT shown in the literature[24]. In our study, we did not compare CRVO with other diseases, such as diabetic retinopathy, choroidal neovascularization, and uveitis. Thus, we did not conclude that CRVO had a major risk for IOP elevation after IVTA injection.

The effect of age on IVTA-induced IOP elevation is controversial. Some studies reported that young age was a significant factor contributing to TA-induced increase in IOP[25,26]. However, others did not find age a significant risk factor of IOP elevation after IVTA injection[27–29]. In our study, we did not identify that patients younger than 55 years had a larger magnitude of IOP elevation than patients older than 55 years did. However, we found that male patients younger than 55 years had a high risk of developing refractory IOP elevation after IVTA injection. This age-dependent response may arise from differences in the extracellular matrix constitution of the aqueous outflow pathway in patients of different ages, which can lead to variable responses to steroid application, as demonstrated by a histopathologic study of anterior segment changes in a rabbit model of steroid-induced glaucoma[30].

Gender has been inconsistently identified as a risk factor for IOP elevation[31,32]. We could not identify that males had a higher risk of IOP elevation compared with females after a single IVTA injection.

Some studies reported that noncontact tonometer by appropriate correction for corneal thickness can be used as reliably as Goldmann applanation tonometry in following up glaucomatous patients[33]. In our study, the IOP was measured by noncontact tonometer + central corneal thickness measurements instead of a Goldmann tonometer. Goldmann applanation tonometry was performed if we determined the use of anti-glaucoma medications at the time of IOP elevation more than 24 mmHg. We found that the data

from the Goldmann applanation tonometry were the same as the date from the noncontact tonometer by appropriate correction for corneal thickness.

Based on our findings, patients with macular edema associated with CRVO should be monitored more carefully after IVTA injection because they may have a higher chance of postoperative IOP elevation. IOP response to PTA injection is an effective way to judge IOP response to intravitreal injection TA. In many patients, an adequate IOP change response from PTA injection may be seen. If he/she is highly sensitive to corticosteroid, treatments other than IVTA injection can be prescribed to avoid the increased risks associated with intravitreal corticosteroid injection.

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