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The Effect of Trans-Tenon Triamcinolone Acetonide Injection on Intraocular Pressure in Diffuse Diabetic Macular Edema[*]

Diffüz Diyabetik Maküler Ödemde Trans-Tenon Triamsinolon Asetonid Enjeksiyonu'nun Göziçi Basıncı Üzerine Etkisi

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Objectives: We evaluated the intraocular pressure (IOP) after trans-Tenon retrobulbar injections of triamcinolone acetonide (TTTA) in patients with with diffuse diabetic macular edema.

Patients and Methods: We retrospectively reviewed 30 eyes of 21 consecutive patients (12 females, 9 males; mean age 63.7±6.92 years; range 49 to 77 years) who received a single dose of 20 mg TTTA injection for diffuse diabetic macular edema. Intraocular pressures were evaluated before and one week, one month, and three months after the injection.

Results: Elevation of the IOP occurred only during the first week after TTTA injections. These rises returned to normal values with topical antiglaucoma medications. Improvements in visual acuity were significant at one month and three months.

Conclusion: It was concluded that single-dose 20 mg TTTA injection was a safe and effective treatment in diffuse diabetic macular edema.

Key Words: Diabetic retinopathy/drug therapy; injections; macular edema/drug therapy; triamcinolone acetonide/therapeutic use; visual acuity.

Amaç: Diffüz diyabetik maküler ödemli hastalarda trans-Tenon retrobulber triamsinolon asetonid (TTTA) enjeksiyonu sonrası göziçi basıncı değerlendirildi.

Hastalar ve Yöntemler: Bu retrospektif çalışmada diffüz diyabetik ödem tanısı konan 21 hastanın (12 kadın, 9 erkek; ort. yaş 63.7±6.92; dağılım 49-77) 30 gözüne tek doz 20 mg TTTA enjeksiyonu yapıldı. Göziçi basınçları, enjeksiyon öncesinde ve enjeksiyondan bir hafta, bir ay ve üç ay sonra değerlendirildi.

Bulgular: Enjeksiyon sonrası göziçi basınç artışı sadece birinci haftada meydana geldi. Göziçi basınç artışları, topikal antiglokomatöz tedavi ile normal değerlere döndü. Birinci ve üçüncü ayda görme keskinliğinde gözlenen artış anlamlı bulundu.

Sonuç: Diffüz diyabetik ödemde tek doz 20 mg TTTA enjeksiyonunun güvenli ve etkili bir tedavi olduğu sonucuna varıldı.

Anahtar Sözcükler: Diyabetik retinopati/ilaç tedavisi; enjeksiyon; maküler ödem/ilaç tedavisi; oküler hipertansiyon; triamsinolon asetonid/terapötik kullanım; görme keskinliği.

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Trans-Tenon's retrobulbar injections of triamcinolone acetonide (TTTA) have been shown to be clinically effective in eyes with diffuse diabetic macular edema.[1-3] One of the side effects most often discussed following the injection of triamcinolone is the steroid-induced intraocular pressure (IOP) elevation.[4] The pathogenesis of IOP elevation after trans-Tenon's retrobulbar injections of triamcinolone remains unknown. Clark[4] states the possible mechanism as the corticosteroids entering the trabecular meshwork cells in the anterior chamber of the eye and activating steroid receptors. This activation then leads to changes in the extracellular matrix of trabecular meshwork and accumulation of abnormal extracellular material in the Schlemm's canal, causing outflow resistance to aqueous flow and finally elevated IOP.

Although there are only a limited number of relevant studies, some state a statistically significant IOP increase following trans-Tenon's retrobulbar triamcinolone injection[1,5,6] while others have failed to find such a result.[3,7]

The aim of our study was to determine the significance of the intraocular pressure increase following the injection of TTTA, as it has been stated to have less of a risk of intraocular pressure increase and endophthalmitis compared to currently used intravitreal triamcinolone acetate injection for the treatment of resistant diffuse diabetic macular edema.[1,3,7] In addition, our other aim in this study was to evaluate visual improvement after TTTA injection in diffuse diabetic macular edema.

PATIENTS AND METHODS

This was a retrospective, nonrandomized, interventional case series of 30 eyes of 21 diabetic patients (12 females (57.1%), 9 males (42.9%); mean age 63.71±6.92 years; range 49 to 77 years) diagnosed with refractory diffuse diabetic macular edema according to ETDRS (The Early Treatment Diabetic Retinopathy Study) criteria. After a detailed explanation of the risks and benefits of the injection and obtaining informed consent, all patients underwent complete ophthalmologic examination including best-corrected Snellen visual acuity, anterior segment and fundus examination and IOP measurements by Goldman applanation tonometer. Inclusion criteria were patients with type II diabetes and refractory diffuse diabetic macular edema three months after at least two sessions of macular laser photocoagulation with visual acuity loss, and leakage shown by fluorescein angiography (Imagenet 2000, Topcon TRC50IX, Topcon Corp, Japan). All eyes had open anterior chamber angles. Hypertensive patients were included only if they showed satisfactory blood pressure control (systolic blood pressure <150 mmHg, diastolic blood pressure <90 mmHg).

Exclusion criteria were intraocular surgery within three months and any other laser administration within one month, monocularity, history of deep vitrectomy, glaucoma, or ocular hypertension, significant media opacity and a history of corticosteroid-responsive IOP rise.

For the trans-Tenon's retrobulbar injection of triamcinolone acetonide, the patient's eye was anesthetized with topical proparacaine 0.5%. After the conjunctiva and Tenon's capsule were incised in the inferotemporal quadrant, a 25-gauge curved, blunt cannula approximately 2.1 cm in length (#HS-2764, Handaya Co, Ltd, Tokyo, Japan) was inserted into the retrobulbar space, followed by the injection of 20 mg of triamcinolone acetonide.[5]

Intraocular pressure and visual acuity (VA) were evaluated before the injection (baseline) and at the first week, first and third months after the injection.

The IOP and VA levels showed a normal distribution (according to Kolmogorov-Smirnov normality test). We therefore used 'Repeated-Measures Two Way ANOVA' to compare values between two measurement periods. A p value of less than or equal to 0.05 was considered to be statistically significant. The analyses were performed with the SPSS 15.0 demo software (SPSS inc, Chicago, IL).

RESULTS

There was no statistically significant difference for age and gender distribution of the patients.

Table 1. IOP and visual acuity were shown before the injection (baseline) and at 1st week, 1st and 3rd months after the injection.

	Baseline MD±SD	1 week MD±SD	1 month MD±SD	3 month MD±SD	F	*p*
IOP (mmHg)	15.30±2.55	16.57±2.80	15.97±1.65	15.40±1.81	3.351	0.034*
VA (logMAR)	0.78±0.22	0.79±0.23	0.73±0.24	0.72±0.25	5.013	0.007*

*: Statistically significant; MD: Mean deviation; SD: Standard deviation, IOP: Intraocular pressure, VA: Visual acuity.

All patients had nonproliferative diabetic retinopathy (NPDR).

The mean baseline IOP was 15.30±2.55 mmHg; and it was 16.57±2.8 mmHg, 15.97±1.65 mmHg, and 15.43±1.81 mmHg, one week, one month, and three months after the injection, respectively. There was a statistically significant difference ($p<0.05$) between the measurement periods for IOP and this was due to the statistically significant difference ($p<0.05$) between the baseline and week 1. There was no difference between the IOP measurements at baseline and other periods ($p>0.05$; Table 1).

The mean VA was 0.78±0.22 logMAR, and one week, one month, and three months after injection, it was 0.79±0.23, 0.73±0.24, and 0.72±0.25 logMAR, respectively. There was a significant difference for the change in visual acuity between measurement periods ($p<0.05$) and this was due to the statistically significant difference between baseline and first month and third month ($p<0.05$). There was no significant difference between the visual acuity at baseline and at first week ($p>0.05$; Table 1).

DISCUSSION

Previous studies have reported that the main side effect of intravitreal triamcinolone acetonide injection (IVTA) is the elevation of the IOP.[8-10] On the other hand, studies have shown that the side effects of trans-Tenon's triamcinolone acetonide injection (TTTA) such as IOP elevation and endophthalmitis are less than IVTA.[1,3,7] There are conflicting reports about IOP elevation after TTTA injections. In some of these studies, a statistically significant IOP increase after trans-Tenon's retrobulbar triamcinolone injection have already been reported.[1,5,6] We also found a statistically significant increase at week 1 following TTTA injection but the increase after one and three months was not statistically significant.

Previous studies have reported that IOP elevation is observed in 31-52% of patients who undergo IVTA injections and 2-15% of patients who undergo TTTA injections.[2,3,8,11,12] There are many possible side effects of TTTA injections including retrobulbar hemorrhage, ptosis, orbital fat prolapse and cataract progression as well as increased IOP.[13-15] None of the side effects associated with TTTA injection in previous studies were observed in any of our patients except IOP elevation.

Trans-Tenon's retrobulbar injections of triamcinolone acetonide is a medical treatment for diffuse diabetic macular edema just like IVTA or protein kinase C inhibitors and a sustained release intravitreal corticosteroid implant.[16] Although there are limited studies on the IOP increase following TTTA injection for diffuse diabetic edema, Hirooka et al.[5] have recently found a statistically significant IOP increase in 49 patients, 10 with diabetic macular edema, following a 20 mg TTTA injection. Hirooka et al. stated that the IOP increase was especially statistically significant in the diabetic macular edema group and that eight of the 49 patients had IOP increases of 6 mmHg or more. Patients with an increase of 6 mmHg or more were considered 'steroid responders'. Most of the increases were between first and fourth weeks. All our patients were being followed-up with a diagnosis of diffuse diabetic edema and only four of the 30 eyes (13.3%) had an IOP increase of 5 mmHg or more following 20 mg single-dose TTTA injection, all in the first week.

Ohguro et al.[17] reported no IOP increase in any of the six eyes of six patients with dif-

fuse diabetic macular edema following TTTA. Similarly, Wada et al.[3] administered TTTA into 39 eyes of 30 patients with diabetic persistent edema and only one patient's IOP increased over 21 mmHg. We only had two patients whose IOP increased over 21 mmHg and the pressure dropped below 21 mmHg in both patients rapidly with antiglaucoma medication.

Cardillo et al.[7] administered 4 mg IVTA to one eye and 40 mm TTTA to the other eye of 12 patients with bilateral diffuse diabetic edema. The intraocular pressure did not show any significant difference between the two forms of triamcinolone acetonide delivery at any follow-up visit, and no eyes had an IOP>25 mmHg after the procedure. We used a single dose of 20 mg TTTA and we did not measure an IOP over 25 mmHg in any patient.

Koga et al.[2] administered 40 mg TTTA to 20 vitrectomized eyes with diffuse diabetic edema. In three (15%) of the 20 treated eyes, IOP elevation was found between one week and two months after the TTTA injection. We excluded vitrectomized eyes from our study and the dose was 20 mg.

Entezari et al.[18] reported no statistically significant increase in VA four months after posterior subtenon triamcinolone acetonide injection. Bakri and Kaiser[1] reported the rate of improvement in VA of 3-lines or more following TTTA injection as 14.%, 17%, 19% and 21% at 1st, 3rd, 6th and 12th months respectively. The same study reported the rate of improvement in VA of at least 1-line as 50%, 44%, 57% and 36% at 1st, 3rd, 6th and 12th months respectively. There was no difference following TTTA in 46%, 49%, 26% and 29% of the patients at 1st, 3rd, 6th and 12th months respectively and a decrease of at least 1-line was present in 4%, 7%, 17% and 36% at the same periods respectively with 1% of the patients suffering a 3-line VA loss. In our study, there was one patient with increased vision and one with decreased vision of 1-line (3.3%) at first week. There was an increase of 2-lines in one patient (3.3%) and 1-line in eight patients (26.6%) at first month. At month 3, there was an increase of 1-line in seven patients (23.3%), 2-lines in three patients (10%) and a decrease of 1-line in one patient (3.3%).

In conclusion, although IOP increase following TTTA injection in the treatment of diffuse diabetic macular edema is important in the first few weeks, this increase is transient and not a significant problem. The study also showed a significant increase in the VA one and three months after the TTTA injection, attesting to its efficacy.

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