POSTERIOR SUBTENON INJECTION OF TRIAMCINALONE ACETONIDE FOR CYSTOID DIABETIC MACULAR EDEMA

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ABSTRACT

Objectives: To assess the efficacy and safety of posterior subtenon triamcinolone acetonide injection for the treatment of diabetic cystoid macular edema.

Methods: This prospective, randomized comparative trial included diabetic patients with cystoid macular edema involving 79 eyes. Forty one eyes were randomly given posterior subtenon triamcinolone acetonide injection while the remaining 38 eyes served as a control group. The eligibility criteria for this study included patients with clinically and angiographically detectable cystoid macular edema during the past six months, glycosylated hemoglobin not more than 8.5% and history of previous laser treatment not earlier than three months. All eyes of posterior subtenon triamcinolone acetonide injection group received 40mg of triamcinalone acetonide through a superotemporal approach in the outpatient clinic. After injection, the visual and anatomical responses were observed at weeks 1, 3, 6, 8, 12, 16, 20 and 24. Intraocular pressure, incidence of reinjection and complications were also noted.

Results: At one week after injection, all injected eyes showed significant visual acuity improvement from baseline measurements ($p<0.001$) and 88% of them showed clinical serous macular edema regression. The most significant improvement in logarithm of the minimum angle of resolution visual acuity was noted at month two post injection. During the next four months a gradual increase in logarithm of the minimum angle of resolution acuity was noted. Comparison between the two groups, showed significant difference of mean logarithm of the minimum angle of resolution acuity at one week after injection and during the subsequent study visits. After injection, recurrence of cystoid macular edema was noted in nine eyes (22%) at a mean time of 5.25±0.71 months. Two eyes (4.9%) developed rise of intraocular pressure (>20mmHg) at the first week post injection and were treated with antiglaucoma drugs for a mean time of 5.5±1.41 months. Another two eyes had localized subconjunctival hemorrhage at the site of injection.

Conclusion: Posterior subtenon triamcinolone acetonide injection of 40mg triamcinolone acetonide through a superotemporal approach appears to be safe and effective for short-term management of diabetic cystoid macular edema.

Key words: Cystoid macular edema, Posterior subtenon injection, Triamcinalone acetonide.

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Introduction

Macular edema is one of the leading causes of vision loss in patients with diabetic retinopathy.[1,2] Cystoid macular edema (CME) occurs by leakage from the perifoveal retinal capillaries. A variety of approaches to the

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treatment of CME have been attempted with a variable degree of success. These options have included topical and oral steroids, nonsteroidal anti-inflammatory agents, and laser photocoagulation treatment.[3] In recent years, intravitreal injection of triamcinalone acetonide (TA) has been reported to improve visual acuity and to reduce the macular thickness in eyes with diffuse macular edema.[4-6] However, the risk of complications such as elevation of intraocular pressure, endophthalmitis, intraocular hemorrhages, and detachment of the retina was reported.[7-9] Posterior subtenon injection of steroids proved to be effective in the treatment of diffuse diabetic macular edema.[10,11] This approach is less invasive than intravitreal injection with a low risk of complications and appears to deliver equivalent therapeutic quantities of TA to the retina.[12-14] Bakri *et al.*,[15] reported improvement of visual acuity of eyes with refractory diabetic macular edema after posterior subtenon triamcinolone acetonide injection (PSTI) of TA. Other researchers reported that eyes with refractory diabetic macular edema subjected to PSTI did not show significant changes of visual acuity from the baseline measurements.[16,17]

The purpose of this study was to assess the efficacy and safety of posterior subtenon triamcinolone acetonide injections for the treatment of diabetic cystoid macular edema.

Methods

Seventy nine diabetic patients (79 eyes) with cystoid macular edema were enrolled in a prospective, randomized comparative trial between February 2005 and November 2007. They were 43 males and 36 females, aged between 50 and 71 years (mean 61.16), with type two diabetes mellitus. All patients were phakic with moderate to severe nonproliferative diabetic retinopathy. Forty one eyes were randomly given PSTI while the remaining 38 eyes served as a control group. In all studied eyes, the best corrected logarithm of the minimum angle of resolution (logMAR) visual acuity was assessed using the Early Treatment Diabetic Retinopathy Study (ETDRS) charts. CME was defined by central thickening with intraretinal cystoid spaces revealed with slit-lamp biomicroscopy using a 78-diopter non-contact lens and by petaloid appearance of fluorescein leakage on fluorescein angiography. The intraocular pressure was measured using Goldman applanation tonometer. Exclusion criteria included eyes with history of CME of more than 6 months, history of grid laser photocoagulation treatment up to three months prior to the injection, pre-existing glaucoma and glycosylated hemoglobin (HbA1c) of more than 8.5%. For the posterior subtenon injection, the patient was placed in a semi setting position and after instillation of 0.4% oxybuprocaine surface anesthesia eye drops the patient was directed to look in the extreme inferonasal field of gaze. One milliliter of a 40 mg/ml of TA was given through the superotemporal forniceal conjunctiva using a 25-gauge needle, 5/8 inch length, on a 3ml syringe. The needle penetrated the conjunctiva and Tenon's capsule with the bevel toward the globe and was advanced toward the macular area, taking care to remain in contact with the globe until the hub was firmly pressed against the conjunctival fornix and then the corticosteroid was slowly injected. After initial examination and/or injection, all eyes were scheduled for follow-up examination at weeks 1, 3, 6, 8, 12, 16, 20, and 24. Patients were evaluated on basis of slit-lamp biomicroscopy, visual acuity, and Intraocular pressure (IOP). In addition, fluorescein angiography was performed before the treatment and after six months (final visit).

The significance of the difference between the pre-treatment and post treatment data was assessed by the two-tailed Student's t test. The data are presented as mean (SD). $P < 0.05$ was considered to be statistically significant.

Results

The mean age of patients (±SD) was 61.16±5.96 years for PSTI group and 59.58±5.19 years for control group, with a range of 50 to 71 years. Patient's characteristics are shown in Table I.

The mean baseline visual acuity was not significantly different between the two groups ($P<0.1$). The change in mean (SD) visual acuity at studied groups during the observational period is illustrated in Table II and Fig. 1.

The difference in mean LogMAR best corrected visual acuity (BCVA) between the injected eyes and those not injected becomes significant after the first week of observation ($p<0.001$). In the next visits the difference in LogMAR acuity continues to increase significantly between the studied groups and reaches its maximum on the second month of observation

Table I. Baseline characteristics of studied patients

Variable	PSTI* group	Control group
Eyes No.	41	38
Mean age	61.16± 5.96	59.58±5.19
Gender (male/female)	23/18	20/18
Right/left	19/22	17/21
Status of DR No. (%)		
Moderate NPDR	16 (39%)	16 (42%)
Severe NPDR	25 (61%)	22 (58%)
Mean HbA1c†	6.85±0.81	6.94±0.77

*PSTI, posterior subtenon injection; DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy.
†HbA1c: glycosylated hemoglobin

Table II. Mean visual acuity (Log MAR) by study visit

Visit time	PSTI* group		Control group		Between two groups
	Mean±SD	P value	Mean±SD	P value	P value
Baseline	1.054± 0.19		1.038±0.16		>0.1
Week 1	0.680±0.13	0.001	1.039±0.16	0.328	<0.001
Week 3	0.588±0.13	0.001	1.044±0.16	0.183	<0.001
Week 6	0.528±0.12	0.001	1.048±0.16	0.097	<0.001
Week 8	0.505±0.13	0.001	1.064±0.16	0.018	<0.001
Week 12	0.612±0.13	0.001	1.069±0.16	0.009	<0.001
Week 16	0.696±0.15	0.001	1.106±0.16	0.001	<0.001
Week 20	0.787±0.19	0.001	1.147±0.17	0.001	<0.001
Week 24	0.916± 0.25	0.001	1.168±0.17	0.001	<0.001

*PSTI: posterior subtenon injection group

(t=14, p<0.001). At the end of observation (month 6) the mean LogMAR acuity increases at PSTI eyes to 0.916± 0.25 and at control eyes to 1.168±0.17, the observed difference is statistically significant (P<0.001). Separate within-group analysis showed significant reduction in mean LogMAR acuity from baseline in the PSTI group throughout the study period visits. In the control group, a significant increase in mean LogMAR acuity from baseline was noted from the 2nd month till the 6th month of the observational period (table 2). Clinical examination after one week of PSTI revealed a decrease in macular edema and disappearance of cyst-like spaces in 88% of injected eyes. After three weeks the cyst-like spaces disappeared in all injected eyes. Recurrence of CME was noted in nine eyes (22%) of PSTI group at a mean time of 5.25±0.71 month. These eyes underwent reinjection and were observed for two months. The mean LogMAR acuity for this group was 1.275±0.15 and after two months of reinjection it decreases to 0.82±0.10. The difference was statistically significant (p<0.001). Figure 1 illustrates the changes in fluorescien angiography (FA) images of a representative patient in the PSTI group.

Baseline image (A) shows fluorescien dye leakage in the foveal area with accumulation of the dye in the cystic spaces around the foveola. At six months after injection (B) a mild reduction in fluorescein dye accumulation is noted.

Two eyes (4.9%) of PSTI group developed a significant rise in IOP from the baseline (mean 35mmHg) at the first week post-injection. Antiglaucoma drugs were used to lower IOP of these two eyes for a mean time of 5.5 months. Figure 3 show insignificant rise of mean IOP (14.38± 1.72 to15.45± 5.37, P>0.05) at the first week post-injection in PSTI group. The difference between the two groups at this time point and subsequent time points was not statistically significant. Another two (4.9%) had localized subconjunctival hemorrhage at the site of injection. During the study observation period we did not notice change in lens status or cataract progression.

Discussion

This study demonstrates that PSTI has a beneficial effect in reducing diabetic CME. On clinical examination and after the first week of PSTI, 88% of the injected eyes show decrease in macular edema

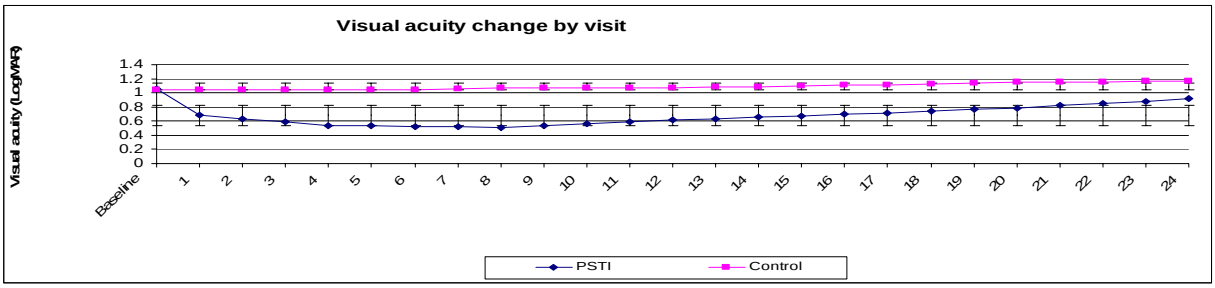

Fig. 1. Dynamics of mean visual acuity in the PSTI and control eyes throughout the study period

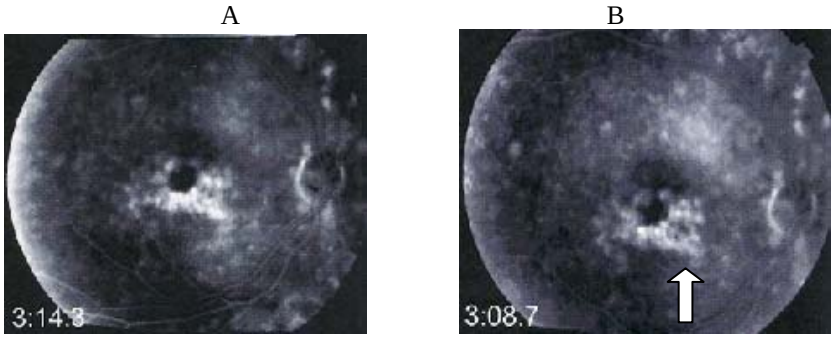

Fig. 2. Fluorescein angiogram of right eye, before injection (A) the LogMAR acuity 1.0 and 6 months after injection the LogMAR acuity 0.9. There is a mild reduction of dye leakage after 6 months of injection (arrow)

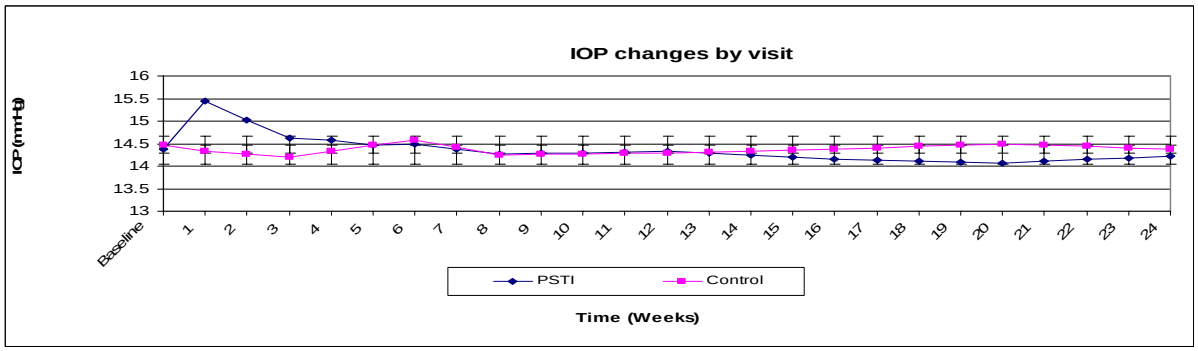

Fig. 3. Mean intraocular pressure in the PSTI and control eyes throughout the study period.

with loss of cyst-like foveal formations. At the same time a significant increase in mean visual acuity from the baseline measurement was noted. Between groups, analysis reveals a statistically significant difference in mean logMAR visual acuity from the first week of observation. At the end of the second month of observation the difference reached a plateau-like maximum. During the next four months a gradual decrease in visual acuity of PSTI group was noted and this could be related to steroid effect withdrawal. Accordingly, at week 24 (end of observation), the difference in LogMAR acuity between the two groups diminished, but it was still significant ($p<0.001$). The recovered positive functional and anatomical responses after PSTI were obtained by other researchers in the treatment of diffuse diabetic macular edema.[18,19] Recurrence of CME was noted in 22% of injected cases at a mean time of 5.25±0.71. Reinjection of these eyes was associated with significant improvement in visual acuity for the next two months.

Nussenblat[20] reported that in cases of CME there was no significant relationship between the estimation of visual acuity and the amount of fluorescein staining in the posterior pole. In agreement with that report we noticed in our series that the changes in fluorescein angiography were mild but functionally the vision was much better.

Cellini *et al.*[21] used the inferior-temporal approach technique to inject the steroid. In our study we found it easier to do the injection through a superior-temporal approach as Young *et al*[13] performed, but without having to create a surgical opening in the conjunctiva to access the subtenon. This technique

prevents reflux of TA after infusion, simplifies the procedure that it could be performed in outpatient clinics and improves patient's compliance with this therapy.

Marco[17] reported a significant rise in IOP from the baseline measurements in eyes with diffuse diabetic macular edema after four weeks of PSTI. In our study, a significant rise in IOP from the baseline was noted in two eyes after the first week of PSTI. These eyes were treated with antiglaucoma drugs for a short time period (5.5 month).

Other possible complications of posterior subtenon corticosteroid injection include ptosis, cataract formation, inadvertent globe perforation.[15]

Conclusion

PSTI of 40mg TA through a superotemporal approach appears to be safe and effective for short-term management of diabetic CME.

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