

ORIGINAL**Efficacy of sub-Tenon's capsule injection of triamcinolone acetonide for refractory diabetic macular edema after vitrectomy**

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Abstract : Purpose : To determine whether or not a sub-Tenon's capsule injection of triamcinolone acetonide (TA) is an effective treatment for refractory diabetic macular edema after vitrectomy. **Methods :** Thirty-nine eyes of 26 patients with diabetic macular edema were injected with 20 mg TA into the sub-Tenon's capsule. The central macular thickness (CMT) measured by an optical coherence tomography (OCT) and visual acuities were compared between pre-treatment and 1, 3 months post-treatment. **Results :** The decrease in the mean CMT between the baseline (435 μm) and 1 month (326 μm) or 3 months (303 μm) time points was statistically significant. Seven eyes (70%) at 1 month and 3 months post-treatment in the vitrectomized eyes or PPV (pars plana vitrectomy) (+) group, 15 eyes (52%) at 1 month, and 19 eyes (66%) at 3 months in the non-vitrectomized eyes or PPV (-) group maintained 20% reduction in CMT from pre-treatment with a single injection of TA. The recurrence of macular edema was observed in 1 eye (14%) in the PPV (+) group, and 3 eyes (16%) in the PPV (-) group. **Conclusion :** The sub-Tenon's capsule injection of TA was effective for refractory diabetic macular edema after vitrectomy. In addition, it was suggested that the treatment of vitrectomized eyes was more effective than that of non-vitrectomized eyes. *J. Med. Invest.* 55 : 279-282, August, 2008

Keywords : *diabetic macular edema, optical coherence tomography, sub-Tenon's capsule injection, triamcinolone acetonide, vitrectomy*

INTRODUCTION

In recent years remarkable progresses have been made in ophthalmology. However, there are still some diseases those are difficult to manage. One of them is diabetic macular edema. Several treatments

for diabetic macular edema have already been reported. The Early Treatment of Diabetic Retinopathy Study (ETDRS) (1) in the U.S.A. reported the efficacy of focal photocoagulation for clinically significant macular edema (CSME). Recently, the efficacies of vitrectomy (2, 3) and intravitreal injection of triamcinolone acetonide (TA) (4-6) for diffuse diabetic macular edema have also been reported. The sub-Tenon's capsule injection of TA (7-9) is easier, and less complicated than its intravitreal injection. In addition, the sub-Tenon's capsule injection of TA with photo-coagulation or

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vitrectomy seems to be more beneficial for diabetic macular edema. However, the efficacy of such treatments has not been established yet.

Wada, *et al.* reported that the sub-Tenon's capsule injection of TA for diffuse diabetic macular edema tended to be more effective in vitrectomized eyes than in non-vitrectomized eyes (8). Therefore, we studied on the efficacy of sub-Tenon's capsule injection of TA for refractory diabetic macular edema after vitrectomy.

MATERIALS AND METHODS

All enrolled patients showed diffuse fluorescein leakage for diabetic retinopathy involving most of the macular area as seen by fluorescein angiography, and their central macular thickness (CMT) was measured to be $> 250 \mu\text{m}$ by an optical coherence tomography (OCT) scan. Thirty-nine eyes of 26 patients were selected, and received a sub-Tenon's capsule injection of 20 mg TA.

We classified 10 vitrectomized eyes as PPV(+) group, and 29 non-vitrectomized eyes as PPV(-) group. The PPV(+) group was followed up for more than 6 months after vitrectomy when they were given TA injection. The range of interval between vitrectomy and the TA injection was from 6 to 48 months (average, 21.1 months). The average follow-up period of the PPV(+) group was 8.4 months, and that of the PPV(-) group was 6.2 months after the initial injection of TA. The mean ages of the PPV(+) and PPV(-) groups were 61.4 ± 7.5 (mean \pm SD) and 63.5 ± 8.2 years, respectively. Material data are shown in Table 1.

No patients had received grid-pattern laser photocoagulation before this treatment. All patients had received pan-photo coagulation. Informed consents were obtained from all patients before treatment.

We selected a dosage of 20 mg TA for this treatment as reported by Okada, *et al.* (10). After topical anesthesia with 4% lidocaine eyedrops, a small

area of the temporal inferior conjunctival fornix was incised to show the bare sclera. Through this incision, TA was injected into the sub-Tenon's capsule with a 25-gauge curved blunt cannula, and the wound was left unsutured. All patients were instructed to instill 0.5% levofloxacin eyedrops five times a day for 2 weeks.

The efficacy of the sub-Tenon's capsule injection of TA was assessed by recording the visual acuity (VA), CMT, clinical findings using slit lamp examination and complications such as high intraocular pressure (IOP).

We defined more than 20% reduction in CMT from pre-treatment to treatment time points as an effective response. In addition, we defined more than 20% increase in CMT according to the shortest period between treatment and pre-treatment time points as recurrence, in effective cases.

These results were analyzed using a one-way or repeated measure analysis of variance (ANOVA). P values less than 0.05 were accepted as significant.

RESULTS

Central Macular Thickness (CMT)

The mean CMTs before TA injection, at 1 and 3 months post-treatment were $435 \pm 112 \mu\text{m}$ (mean \pm SD), $326 \pm 102 \mu\text{m}$, and $303 \pm 94 \mu\text{m}$, respectively. The decrease in the mean CMTs between the pre-treatment and post-treatment of 1 month or 3 months was statistically significant ($p < 0.0001$, paired t-test). The mean CMTs of the PPV(+) group at pre-treatment, 1 and 3 months were $463 \pm 142 \mu\text{m}$, $287 \pm 80 \mu\text{m}$, and $264 \pm 93 \mu\text{m}$, respectively. The mean CMTs of the PPV(-) group at pre-treatment, 1 and 3 months were $429 \pm 134 \mu\text{m}$, $329 \pm 101 \mu\text{m}$, and $300 \pm 97 \mu\text{m}$, respectively. The difference in the mean CMTs between the PPV(+) and PPV(-) group was statistically significant ($p = 0.041$, repeated-measure ANOVA, Fig. 1).

Table 1. Clinical characteristics of the PPV(+) group and the PPV(-) group

Group	PPV(+)	PPV(-)
Number of the cases	10 eyes	29 eyes
Sex(Male/Female)	8 eyes/2 eyes	24 eyes/5 eyes
Mean age	61.4 ± 7.5 years	63.5 ± 8.2 years
Average follow-up period	8.4 months	6.2 months

PPV(+) group, eyes which pars-plana vitrectomy was performed

PPV(-) group, eyes which pars-plana vitrectomy was not performed

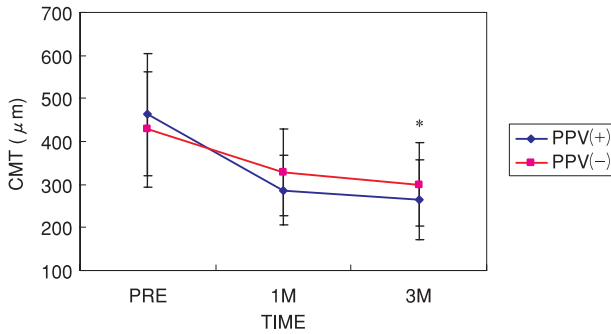


Figure 1. Central macular thickness. PPV(+) group showed a significantly greater reduction of CMT than those PPV(-) group at 3 months after TA treatment[* $P=0.041$, repeated-measure analysis of variance(ANOVA)].
PPV(+) : eyes with vitrectomy PPV(-) : eyes without vitrectomy

The efficacy and the rate of recurrence

The numbers of effectively treated cases were 7 eyes (70%) at 1 month and 3 months post-treatment in the PPV(+) group, and 15 eyes (52%) at 1 month and 19 eyes (66%) at 3 months in the PPV(-) group. The numbers of recurrent cases were 1 eye (14%) in the 7 effective cases of the PPV(+) group, and 3 eyes (16%) in the 19 effectively treated cases of the PPV(-) group.

The PPV(+) and PPV(-) group did not show any significant differences in efficacy and rate of recurrence.

Visual Acuity and Complications

After the TA injection, the log MAR (minimal angle of resolution) visual acuity significantly improved from the pre-treatment value at all follow-up periods. The mean visual acuity improved from 0.86 ± 0.42 (mean \pm SD) at pre-treatment to 0.76 ± 0.40 at 1 month and 0.70 ± 0.41 at 3 months post-treatment. However, the PPV(+) and PPV(-) groups did not show any significant difference in visual acuity.

No cases with an IOP elevation exceeding 21 mmHg after TA injection were seen in all 39 eyes. The progression of cataract, ptosis, and other injection-related complications were not observed, either.

DISCUSSION

Improving the macular edema that is the most common cause of visual impairments in diabetic retinopathy is one of the major concerns in ophthalmic researches. The efficacy of vitrectomy for dia-

betic macular edema has been assessed, and reported as the prevailing treatment for this condition. However, the efficacy of vitrectomy has not been fully established yet, and we have experienced some cases with refractory macular edema after vitrectomy. We expected that the sub-Tenon's capsule injection of TA would be effective for refractory diabetic macular edema.

In the PPV(+) group, the mean CMTs at 1 month and 3 months post-treatment were significantly smaller than those obtained at pre-treatment. This demonstrates that TA injection could be used as a short-term treatment even if diabetic macular edema persists after vitrectomy.

In addition, the mean CMTs after the sub-Tenon's capsule injection of TA, in the PPV(+) group, was significantly smaller than that in the PPV(-) group. We suppose the following reasons :

- 1) The retrobulbar TA in the PPV(+) group reaches to the retina more effectively than that in the PPV(-) group.
- 2) We did not randomly choose patients to perform or not to perform PPV before TA injection. The PPV(+) group consisted of more severe cases than the PPV(-) group. In severe cases in which the sub-Tenon's capsule injection of TA worked effectively, we considered that their macula were more atrophic and thinner than in the normal group.

The efficacy and the rate of recurrence at 1 month and 3 months post-treatment were almost the same. The efficacy of TA at 1 month post-treatment was as good as that reported by previous report (8), and the effects lasted for 3 months. It seems that we should study longer-term results to investigate the recurrence which is another major problem of TA injection. Although the improvement of visual acuity was slight in our study, we got a good impression on the patient's subjective improvement because of the improvement of macular edema.

Our results not only indicate that the sub-Tenon's capsule injection of TA is an effective treatment for refractory diabetic macular edema after vitrectomy, but also show that vitrectomized eyes were more effectively responding to TA than non-vitrectomized eyes.

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