The effect of posterior sub-Tenon's capsule triamcinolone acetonide injection to that of pars plana vitrectomy for diabetic macular edema

(糖尿病黄斑浮腫に対する、トリアムシノロンアセトニドテノン嚢下注射と硝子体手術の治療効果の比較)

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先端生命科学　専攻

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The effect of posterior sub-Tenon's capsule triamcinolone acetonide injection to that of pars plana vitrectomy for diabetic macular edema

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Abstract

Purpose: We tried to compare the effectiveness of posterior sub-Tenon's capsule triamcinolone acetonide (STTA) injection to that of pars plana vitrectomy (PPV) for diabetic macular edema (DME).

Patients and methods: We investigated the clinical records of 50 patients (52 eyes) with DME. 26 eyes underwent vitrectomy combined with cataract surgery, while the other 26 underwent STTA (20 mg). We measured the best-corrected visual acuity (BCVA) and central macular thickness (CMT) by optical coherence tomography before and at 1, 3, 6 months after treatment.

Results: There were no significant differences between STTA and PPV group in the BCVA and CMT before or at any time after the treatment. There were significant differences between the before-treatment CMT and after-treatment CMT in both STTA and PPV groups,.

Conclusion: Our results suggest that STTA can improve DME to the same extent of PPV.

Introduction

Diabetic macular edema (DME) is one major cause of visual acuity decrease for diabetic patients suffering diabetic retinopathy (DR).[1] Several treatments, such as grid laser photocoagulation, intravitreal injection of triamcinolone acetonide (IVTA), posterior sub-Tenon's capsule triamcinolone acetonide injection(STTA), pars plana vitrectomy (PPV), subthreshold micropulse diode laser photocoagulation, and intravitreal injection of anti-vascular endothelial growth factor (VEGF) drugs have been done for DME.[2-9] However, which treatment is most effective is still controversial.[1]

There are reports which compare the effectiveness of IVTA to PPV[10], and IVTA to STTA[11], but we couldn't find any reports comparing the effectiveness of PPV to STTA. So, we tried to compare the effectiveness of STTA to PPV for DME eyes.

Patients and methods

We investigated the clinical records of 52 eyes of 50 DME patients who were treated at Chiba University Hospital. Clinical data and features are shown in table1. Twenty-six eyes of 26 patients had undergone 20 mg of STTA alone from January 1, 2010 to December 31, 2010. Among these eyes, 5 eyes were pseudophakic, and 3 eyes underwent STTA twice. In contrast, 26 eyes of 24 patients underwent vitrectomy combined with cataract surgery from January 1, 2009 to December 31, 2010. During the surgery, vitreous and posterior vitreous membrane was removed by using triamcinolone acetonide for the purpose of visualizing the vitreous. Furthermore, some operators combine the internal limiting membrane peeling. Five eyes had already undergone cataract surgery, and underwent vitrectomy only at that time. The other 21 eyes had cataracts, so they underwent the combination of vitrectmy and cataract surgery. The indication of vitrectomy for DME was not specifically determined in our hospital. We chose vitrectomy when the posterior vitreous detachment didn't occur, and patients agreed to that treatment. Also, the indication of STTA for DME was not determined. If the patients wanted conservative treatment, we chose STTA as one option. Previous study reported that there was a tendency that the patients with slightly thick fovea underwent STTA and vitrectimy compared with other treatments.[8]

We explained the procedures of this study to all patients, and obtained informed consent from them. We followed the World Medical Association Declaration of Helsinki, and obtained the approval from the Institutional Review Board of Chiba University Hospital for this study.

We measured the central macular thickness (CMT) using spectral domain-optical coherence tomography (SD-OCT) before and 1, 3, 6 months after the treatment. We also measured the best-corrected visual acuity (BCVA) before and 1, 3, 6 months after the treatment.

We expressed the data by the means ± standard deviations (SDs). We determined the significance by

using Student's t-tests, paired t-tests, chi-square tests, and repeated measured analysis of variance (ANOVA). We evaluated that $P<0.05$ was significant.

Results

Clinical data is shown in Table 1. There were no significant differences in sex, age, numbers of pseudophakic patients, HbA1c , before treatment BCVA, and CMT between PPV and STTA groups. Twenty one eyes underwent pan retinal photocoagulation (PRP) in the PPV group, and 12 eyes that underwent PRP in the STTA group. That made significant difference. In the STTA group, before treatment BCVA was 0.65±0.4 logarithm of the minimum angle of resolution (logMAR) units, and in the PPV group, that was 0.77±0.3 logMAR units (P=0.237; Student's t-test). At 1, 3, and 6 months, the BCVA at the STTA group was 0.60±0.4, 0.59±0.5, and 0.64±0.5, and 0.68±0.4, 0.59±0.4, and 0.59±0.4 respectively at the PPV group (Figure1, 3). There were not significant differences in the BCVA between the two groups before and at any time after treatment (P=0.441, P=0.960, P=0.717 respectively by Student's t-tests, and P=0.5477 by repeated measured ANOVA). In the STTA group, there were no significant differences between the before treatment BCVA and at 1, 3, 6 months after treatment respectively (P=0.226, P=0.340, P=0.775 respectively by paired t-tests). The BCVA in the PPV group, there was no significant difference between the pre-treatment and 1 month after PPV, but there were significant differences between the pre-treatment and 3, 6 months after PPV (P=0.389, P=0.0066, P=0.0169 respectively by paired t-tests).

Before treatment, CMT was 569.2±167 μm in the STTA group and 534.4±157 μm in the PPV group. At 1, 3, 6months after the treatment, CMT was 356.1±116 μm, 326.7±111.7 μm, 377.4±137.6 μm, in the STTA group, and 386.8±175 μm, 354.2±101.7 μm, 354.2±156.4 μm in the PPV group (Figure 2, 4). There were not significant differences of CMT between the STTA and PPV groups before and at any time after the PPV (P=0.444, P=0.460, P=0.469, P=0.273 respectively by Student's t-tests and P=0.2053 by repeated measured ANOVA). In both STTA and PPV groups, CMT made significant differences between before treatment group and 1, 3, 6 months after treatment groups. (STTA; P<0.0001, P<0.0001, P=0.0001 respectively by paired t-tests, PPV; P=0.0013, P<0.0001, P<0.0001 respectively by paired t-tests).

Three eyes in the STTA group increased intraocular pressure (IOP) temporarily, and underwent eye drop treatment. One eye in the PPV group also increased IOP, another eye had wound infection but that was not endophthalmitis.

Discussion

IVTA was reported to significantly reducing the CMT in DME eyes, and that there was no

significant difference in CMT between IVTA and PPV group 3 months after the treatment. [10]That report coincided with our results. Also, DME recurred 6 months after IVTA in that report[10], while in our study, 3 eyes recurred DME 3 to 6 months after STTA and retreated with STTA. PPV group remained resolved after treatment. [10] Those results suggest that repeated treatment of IVTA or STTA for refractory DME is considerable 3 to 6 months after first treatment.

IVTA is reportedly more effective than STTA for DME within 3 months, but the benefit is not distinct after that period.[11]So, our results suggest that although DME sometimes recurs, STTA is effective to the same extent of IVTA and PPV during the short period.

When we performed PPV for DME, we always combined cataract surgery, so there is a possibility that the cataract removal took part in improving BCVA of PPV group. Those facts indicate that we should carefully interpret the results and compare the BCVA between STTA and PPV groups.

In this study, there was no significant progress of cataract after STTA. There is a possibility that both the cataract and improvement of CMT are not relevant to BCVA improvement at 3 or 6 months after STTA.

It is said that VEGF is main cause of DME.[12] Hyperglycemia, inflammation, and ischemia increase VEGF in retinal cells, and the permeability of retina is up regulated.[11][13] Also, hyperglycemia causes inflammation which increases vascular permeability .[14] Those facts suggest that IVTA[7][15] and STTA[2][16] restrain inflammation and decrease retinal VEGF expression. [17]-[19]

Main complications of IVTA are IOP elevation, endophthalmitis, and cataracts. IVTA recorded higher level of IOP elevation than STTA.[20]Among TA treated eyes, endophthalmitis occurred in 7 (0.12%) of 5,665 eyes treated with IVTA, and 7 (0.026%) of 26,819 eyes treated with PPV.[21] On the contrast, endophthalmitis occurred only 1 (0.008%) of 12,344 eyes after STTA treatment.[21] Recent study reports that the percentage of endophthalmitis after intravitreal injection of anti-VEGF drugs was 0.025% [22], but anti VEGF drugs are usually injected to vitreous repeatedly for DME [4][5][6][9], so the risk of endophthalmitis increases after treatment. The RESOLVE and RESTORE studies reported that the rate of endophthalmitis was 1.4% at 1 year.[4]

Hoerauf et al reported complications of PPV for DME. Among 50 patients, 10 patients had iatrogenic tears intraoperatively, 42 phakic eyes developed cataracts within 6 months, 1 patient had vitreous hemorrhage after surgery and underwent second vitrectomy with silicone oil tamponadea, 3 eyes had retinal detachment and underwent second vitrectomy.[23]

Those facts suggest that STTA has a significantly lower risk than intravitreal injection of anti-VEGF drugs, IVTA, and PPV for DME treatment.

Our study has a limitation because it was a retrospective study, the follow up period was short, the group was small. Big scale randomized studies are needed to compare the effectiveness of each treatment for DME.

Conclusion

Both STTA and PPV significantly reduced CMT in patients with DME, and there were no significant differences in BCVA and CMT between the two groups. Also, STTA had less complications than PPV, so our results suggest that STTA can be an alternative treatment of PPV for DME.

Disclosure

The authors report no conflicts of interest in this work.

	PPV	STTA	P-values
Age, mean ± SD (years)	62.65 ± 1.55	61.92±2.27	P=0.793
Sex, no. (%)			
Men	12 (46)	16(73)	P=0.404
Women	14 (54)	6 (27)	
Type of diabetes,no (%)			
Type Ⅰ	0 (0)	1 (5)	P>0.999
Type Ⅱ	26 (100)	21(95)	
Hemoglobin A1c, mean ± SD (%)	6.52 ± 0.19	6.7 ± 1.0	P=0.311
Treatment of diabetes			
Medication	8 (31)	14(82)	P=0.161
Insulin	18 (69)	3 (18)	P<0.0001
Diabetic nephropathy, no (%)	13 (50)	10 (56)	P=0.577
Pseudophakic eyes	5	5	P>0.999
BCVA, mean ± SD (logMAR)	0.77±0.31	0.57±0.43	P=0.237
CMT, mean ± SD (μ m)	534±157	551±167	P=0.444

Table.1 Clinical data and features

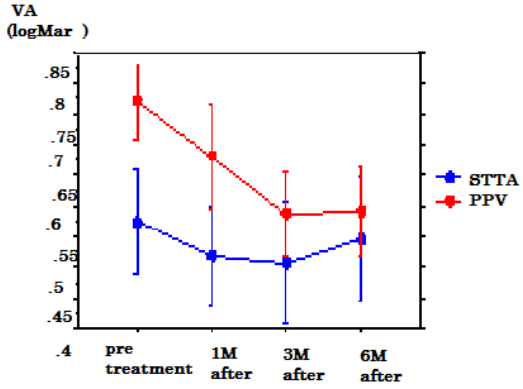

Fig.1 Change of VA

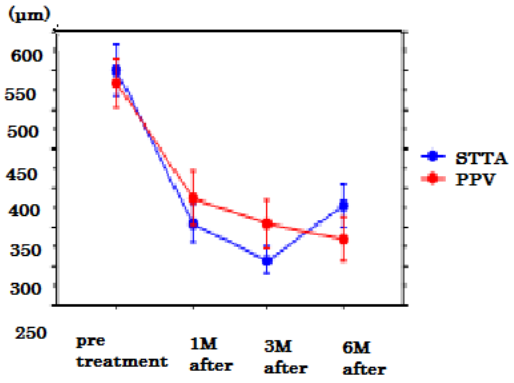

Fig.2 Change of CMT

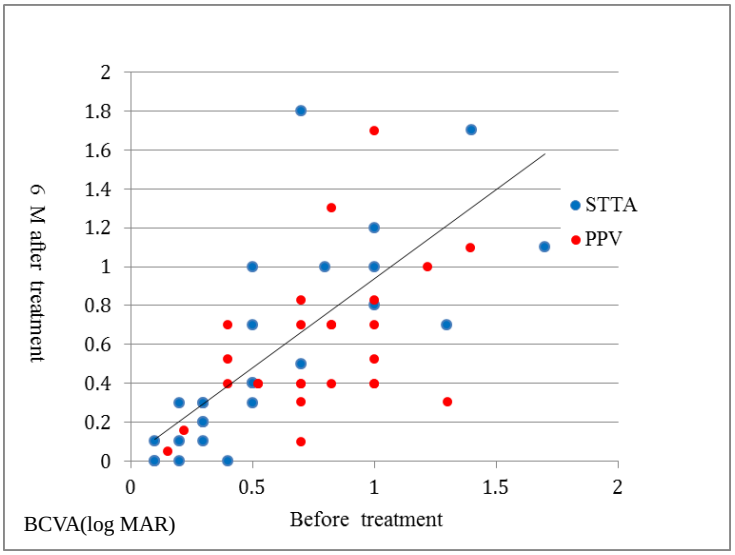

Fig.3

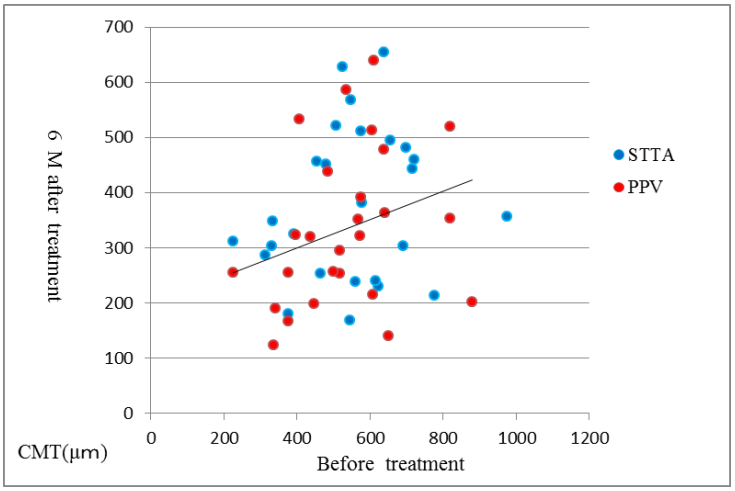

Fig.4

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