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Original Research Article

COMPARING THE EFFICACY OF 4 MG VS 2 MG INTRAVITREAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF DIFFUSE DIABETIC MACULAR EDEMA

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Abstract: *The prospective study was conducted in the Department of Ophthalmology from January 2022 to January 2023 to compare the effectiveness of two doses of TA on DME using central macular thickness (CMT) as the primary criterion. A total of 30 patients were included in the study. Participants were randomly divided into a 4mg TA group (n=16) and a 2 mg TA group(n=16). The injection was given in the eye with higher CMT. Patients were followed up until 6 months after injection. Results showed that regarding mean CMT and change in macular thickness, there was no statistically significant difference between both groups during the whole study period. After 1 month of injection, the ETDRS score in the 4 mg group increased significantly from 37.7±14.1 to 51.3±14.3 (P=0.0012) and from 41.9± 13.3 to 49.4± 13.7 in the 2mg group (P=0.002). Based on the results it can be concluded that the intravitreal 2 mg or 4 mg TA injection had a similar effect on both VA and CMT in patients with DME.*

Keywords: Triamcinolone acetonide, Intravitreal injections, Diabetic macular edema, Macular thickening, Visual acuity

Introduction

Diabetic macular edema (DME) causes visual impairment in subjects with diabetes mellitus. Its pathogenesis is multifactorial and complex. It mainly results from blood retinal barrier (BRB) distortion, leading to fluid accumulation in macular intraretinal layers (Markan et al., 2020). Hyperglycemia is an important risk factor for diabetic retinopathy. It causes an increase in intracellular glucose levels, protein kinase C activation, and oxidative stress. Chronic hyperglycemia results in advanced glycation end products (AGEs), leading to diabetic maculopathy and retinopathy(Li et al., 2019). Although distorted BRB has a central part in the pathogenesis of diabetic macular edema, changed vitreomacular interface significantly contributes to disease progression. Other factors like inflammation, retinal ischemia, altered blood flow, and hypoxia are also associated with DME (Zur et al., 2019).

Different studies have shown that laser photocoagulation therapy is effective for the treating DME (Everett and Paulus, 2021; Jayadev et al., 2023). However, some patients are refractory to photocoagulation; in such cases, intravitreal triamcinolone acetonide (TA) is recommended. Studies have shown that it is significantly lower macular thickness, improving visual activity(Rodríguez et al., 2019). Previous studies have analyzed the impacts of different doses of TA on DME (Abdel-Maboud et al., 2021; Chauhan et al., 2022). However, few studies have been conducted on comparative analysis of various doses of TA. A study reported a correlation between the increase in visual activity and drug dose; however, no correlation was found between dose and intraocular pressure (Cheng et al., 2019). In this study the effect of 2 mg vs. 4 mg intravitreal TA injection has been compared. . This study aims to compare the effectiveness of two doses of TA on DME using central macular thickness (CMT) as the major criterion.

Methodology

The prospective study was conducted in the Department of Ophthalmology from January 2022 to January 2023. The study included patients diagnosed with DME, did not have any signs of epiretinal membrane or vitreomacular traction, and were refractive to laser photocoagulation. Patients with ocular hypertension and glaucoma were excluded. A total of 30 patients were included in the study.

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Participants were randomly divided into a 4mg TA group (n=16) and a 2 mg TA group(n=16). Informed consent of the participants was taken. The ethical board of the hospital approved the study.

CMT in included patients was more than 300µm in one eye, and glycated hemoglobin <9.5%. Baseline data including HbA1C levels, blood pressure, macular mapping by Optical Coherence Tomography, fluorescein angiography, fundus photography, findings of applanation tonometry, lenticular opacity grading, best corrected visual acuity (VA) measured by Early Treatment Diabetic Retinopathy Study (ETDRS) chart and the number of photocoagulation sessions was recorded a month before injection. The patients were prescribed topical dexamethasone 0.1% for the month. If the increase in IOP did not exceed 15mmHg, the patient was included in the study. Macular mapping and best corrected visual acuity were again measured. 2 or 4mg TA was injected. 200 mg IV ofloxacin was given as prophylactic treatment. A 2 or 4 mg dose was assigned randomly, and only the surgeon was aware of the dose administered. The injection was given in the eye with higher CMT. Patients were followed up until 6 months after injection. IOP and CMT were measured at every follow-up visit. Fundus photography was done after 6 months. ETDRS score was measured at 1, 3, and 6 months. The primary endpoint was analyzing the change in CMT at 1, 3, and 6 months of injection. The normal value of retinal thickness is less than 206 µm. The difference between initial and final thickness was standardized changes in macular thickness (SCMT). A more than 50% decrease in CMT was considered a responder's eye. CMT increase ≥25% in the initial responder eye was considered recurrence of DME. Secondary outcomes were cataract progression and change in IOP and ETDRS scores.

Data was analyzed by SPPS version 23.0. Results were expressed as mean and standard deviation. Student t-test was used to compare results between groups, and the Wilcoxon test was used for comparison within the group. Life table analysis was used for analyzing recurrence. P <0.05 was considered statistically significant.

Results

The age of the participants was 64.3± 13 years. 15 subjects had insulin-dependent, and 15 had non-insulin-dependent diabetes mellitus. There was no baseline difference between the groups regarding the extent of macular capillary closure, VA, and CMT. Before injection, mean systolic blood pressure was 144.2± 18.2 mm Hg, mean diastolic blood pressure was 76.5± 8.9 mm Hg, and mean HbA1c was 7.6 ±1.1%. 2 patients were lost to follow up, 1 in 2mg TA group developed intravitreal hemorrhage because of posterior vitreous detachment, and the other in 4 mg TA group had central venous occlusion requiring laser follow up after 3 months of follow up.

The mean change in macular thickness after TA injection and mean CMT before and after TA injection is summarized in Table I. In the 4 mg TA group, mean CMT decreased from 564.6± 119.1 µm preoperatively to 275.1 ± 79.9 µm after 1 month of injection (P = .0004) and to 271.5±128.6 µm after 3 months(P <.0007). In the 2 mg TA group, mean CMT decreased from 522.8 ±148.6 µm to 267.4±83.6 µm after 1 month (P = .0004) and to 289.9 ±111.5 µm after 3 months of injection (P=.0005). Regarding mean CMT and change in macular thickness, there was no statistically significant difference between both groups during the whole study period. After 1 month of injection, 4 (26.6%) patients in the 2 mg group and 3 (20%) patients in the 4 mg group had normal CMT (<206 µm). After 3 months of injection, 5 (33.3%) patients in the 2 mg group and 6 (40%) in the 4 mg group had normal CMT. 1 patient in each group did not respond to injection. After 6 months, DME recurred in the majority of patients in both groups, though 1 of 15 eyes in each group still had normal CMT. The mean ETDRS score, change in it before injection and during the study period, and Snellen VA in both groups is summarized in Table II. After 1 month of injection, the ETDRS score in the 4 mg group increased significantly from 37.7±14.1 to 51.3±14.3 (P=.0012) and from 41.9± 13.3 to 49.4± 13.7 in the 2mg group (P=.002).

IOP increased to more than 24mmHg in 4 patients in the 4 mg group, and in 7 patients in the 2 mg group, topical dorzolamide or brimonidine was used for it. There was no significant difference between groups regarding mean cortical cataract grade. No complications were reported in any group.

Table I Comparison of CMT and SCMT between study groups

	4 mg TA group	**2 mg TA group**	**P value**
Before injection			
CMT (µm)	564.6±119.1	522.8 ±148.6	.39
1 month after the injection			
CMT (µm)	275.1 ± 79.9	267.4±83.6	.31
SCMT (%)	73.1± 21.7	67.9 ±26.6	.49
3 months after the injection			
CMT (µm)	271.5±128.6	289.9 ±111.5	.28

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SCMT (%)	72.2 ±26.57	62.5 ±33.3	.66
6 months after the injection			
CMT (µm)	458.7 ±156.3	384.6 ±188.9	.42
SCMT (%)	27.8 ±34.4	35.2 ±40.1	.81
The duration between injection and DME recurrence (week)	21	17	.11
standardized changes in macular thickness (SCMT), visual acuity (VA), central macular thickness (CMT), Diabetic macular edema (DME)			

Table II Comparison of VA between study groups.

	4 mg TA group	2 mg TA group	P value
Before injection			
VA	20/160	20/160	
ETDRS score	37.7±14.1	41.9± 13.3	.42
1 month after the injection			
VA	20/100	20/80	
ETDRS score	51.3±14.3	49.4± 13.7	
Change in ETDRS score	12.3± 11.5	7.3± 7.5	.87
3 months after the injection			
VA	20/100	20/160	
ETDRS score	53.3 ±11.8	48.9± 13.2	
Change in ETDRS score	10.8 ±13.6	7.5± 7.5	.34
6 months after the injection			
VA	20/160	20/125	
ETDRS score	42.7± 18.5	47.1 ±12.6	
Change in ETDRS score	5.6± 7.5	5.4± 7.5	.61

Discussion

Intravitreal 4 mg TA injection has been shown to treat DME (Gao et al., 2021). In this study, the effect of 4 mg TA on DME was compared with 4 mg TA. Results showed that CMT was significantly decreased with both doses. The difference between groups regarding the change in thickness was not statistically significant. This may be because our study had 80% theoretical power for detecting a 175µm difference in central macular thickness.

However, the clinically reported difference in CMT was not significant. VA was also significantly improved in both groups after 1, 3, and 6 months of the injection. The increase in visual activity was in line with the findings of previous studies (Kusumowidagdo et al., 2019). However, unlike the results of the study conducted by Carreira et al., TA did not have any dose-dependent effect on VA (Carreira et al., 2022). In this study effects of 13, 5, and 2 mg TA injections were studied; 2 or 5 mg did not have any significant impact on DME, likely due to the small sample size. 13 mg TA has a significantly more significant impact than 2mg, which suggested dose-dependent effect. In the current study, the only intergroup difference was the duration between injection and DME relapse. It occurred later in the 4 mg group compared to the 2 mg, but the difference was statistically insignificant. A study conducted by Anwar et al. reported a correlation between the dose and duration of action of TA (Anwar et al., 2022). As triamcinolone acetonide is a depository corticosteroid, the dose affects the duration of effect rather than its magnitude. In the current study, there was no significant association between injected dose and time or rate of increase in IOP. This finding was in line with the results of previous studies (Allmendinger et al., 2021; Maeda et al., 2019). In our study, there was no inter-group difference regarding lens opacification, which may be due to the short follow up time for assessing cataracts. In the current study, two adverse effects, including central retinal vein occlusion and vitreous hemorrhage, were reported, which were not likely to be associated with the dose. A major issue in dose studies is the reproducibility of the dose; it depends upon the preparation technique. A study by Tariq et al. showed that filtration modifies the final availability of TA dose. This should be considered in any dose study (Tariq et al., 2022). There are a few limitations of our study. It was conducted on a smaller sample and the follow up duration was short. A larger, more extensive study is recommended for more elaboration.

Conclusion

Intravitreal 2 mg or 4 mg TA injection had a similar effect on both VA and CMT in patients with DME.

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There was also no difference in side effects like increased IOP.

Conflict of interest

The authors declared absence of conflict of interest.

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