Diabetic Macular Edema Before and After Intravitreal Triamcinolone Injection

Alireza Ramezani, MD. Homa Tabatabaie, MD. Hamid Ahmadieh, MD.
Ophthalmic Research Center, Shaheed Beheshti Medical University, Tehran, Iran.

Purpose: To compare intravitreal triamcinolone acetonide (IVT) versus natural course in refractory diabetic macular edema.

Methods: In a prospective interventional case series, twenty five eyes with refractory DME which had been allocated to the sham group of a previous clinical trial underwent new examination and optical coherence tomography about 9 months after their first enrollment. Twenty eyes that met the inclusion criteria, visual acuity (VA) < 20/50 and central macular thickness (CMT) > 200 μm, were treated by 4 mg IVT. Evaluations were repeated at 2 and 4 months post-injection to imitate the similar examination intervals after sham injection. Corrected visual acuity and macular thickness changes following IVT were compared to the corresponding changes after sham injection (the natural course).

Results: Visual acuity changes within and between each period were not statistically significant. Visual acuity decreased 0.08 & 0.09 logMAR by 2 months and 0.06 & 0.04 logMAR by 4 months after sham and IVT injections, respectively. The changes of macular thickness after IVT and sham intervention were not meaningful either. However, the difference between thickness changes by 4 months (52±50 μm increase after sham vs. 262±115 μm reduction after IVT) was significant (P=0.014).

Conclusions: Concerning macular thickness, IVT has beneficial effect on refractory diabetic macular edema as opposed to observation. However, considering visual acuity, it does not induce significant difference in comparison to the natural course of the disease.


Key Words: Diabetic macular edema, Intraocular pressure, Intravitreal triamcinolone, Natural course, Macular thickness

Macular edema is the most important manifestation of non-proliferative diabetic retinopathy and a predominant cause of legal blindness in diabetic patients. According to the early treatment of diabetic retinopathy study (ETDRS), the treatment of choice for clinically significant macular edema (CSME) is laser therapy. However, some cases of CSME are refractory to laser therapy and do not have a good prognosis with such treatment.1

Recently, some promising results have been shown in different studies for the treatment of refractory diabetic macular edema with intravitreal triamcinolone acetonide (IVT).2–4 Since diabetic macular edema is a chronic disease and the effect of IVT has been shown to be transient,5–6 the comparison of this therapeutic effect with the natural course of this ailment is necessary. In addition, there are a lot of systemic and ocular factors which influence the natural course and the therapeutic response in these patients.5–9 Therefore, controlling of such confounding elements in research programs seems to be essential.

In clinical trials, there is always a possibility of unequal distribution of various characteristics into the allocated groups and adjusting these many factors is rather difficult. Therefore, a study with two types of intervention on one individual group of cases would be able to overcome this problem. We performed a study by IVT injection on patients with refractory diabetic macular edema who had already been observed for a period of time without any treatment. The purpose was to compare the result of IVT treatment with the natural course of diabetic macular edema in one particular group of patients.

Materials and Methods

In this prospective interventional case series study, all of the patients in the control group of a previous clinical trial who had received sham injection (0.1 cc lidocaine 2%
subconjunctively) for refractory diabetic macular edema were recalled for examination and reassessment of macular thickness by optical coherence tomography (OCT-2, Zeiss, Dublin, CA) about 9 months after the first presentation. An informed consent was obtained from each patient. Both the primary trial and this part of the study were approved by the Review Board/Ethics Committee of the Ophthalmic Research Centre. The results of the primary trial have not been published yet.

The previous study included eyes meeting criteria for CSME based on the ETDRS definition, with an anticipated unfavorable visual outcome after initial or supplemental macular photocoagulation due to one or more of the following findings: 1- macular ischemia, 2- diffuse macular edema, 3- severe hard exudates (HE) accumulation in the fovea, and 4- lack of response to previous laser photocoagulations with the last one being more than 3 months before. The patients were randomly assigned to the treatment (4 mg IVT) and the placebo groups. This primary trial demonstrated a transient improving effect in terms of visual acuity (VA) and central macular thickness (CMT) in IVT-received eyes versus the placebo-received cases. (Article in press)

In the current study, all of the placebo-received patients in the initial part were recalled for a new clinical and tomographic evaluation. IVT injection was planned for all patients except for those who met the following criteria: (1) intraocular surgery after the first intervention; (2) best corrected VA ≥ 20/50; (3) intraocular pressure (IOP) > 21 mmHg and/or taking anti-glaucoma medication at the time of re-examination; (4) lens opacity severe enough to interfere with VA testing and performing OCT; (5) CMT less than 200 µm measured by OCT; (6) being candidate for intraocular surgery; (7) one-eyed patients; and (8) non-compliance.

Injections were done under sterile conditions in the operating room with topical anesthesia and insertion of a lid speculum. Four milligrams (0.1 cc) triamcinolone acetonide (Kenacort) was injected intravitreally with a 27-gauge needle through the superotemporal quadrant. IOP was checked about 10 minutes after injection with a Goldman applanation tonometer and anterior chamber paracentesis was performed if IOP exceeded 30 mmHg.

Examinations were performed at 2 and 4 weeks after IVT injection in an attempt to replicate the follow-up periods after the primary injections in the first part of the study. The data collected from both the new exams and the evaluations after IVT injection (2nd intervention) were recorded to compare with the results following sham injection (1st intervention).

Ophthalmic examinations, both in the previous trial and in the current study, were carried out by two ophthalmologists who were not masked for the treatment received by the patients. However, best corrected VA measurements and OCT were performed by optometrists who were not aware of the protocols of the two studies. Best corrected VA measurements were based on the Snellen chart and were converted to the logarithm of the minimum angle of resolution (logMAR) scale for statistical evaluations.

Statistical analysis: It was performed using paired t and independent sample t tests for evaluating quantitative variables changes within and between the two interventions respectively. P values<0.05 were considered statistically significant.

**Results**

The results are presented in two parts: first, the long-term follow up results comparing the findings of the new exams with the previous data in all of the returned patients before the second intervention. Second, the results of IVT injection in which the findings after the two interventions (IVT vs. sham injection) were compared to each other only in cases who met the criteria for IVT administration.

![Fig. 1](image1.png)  Fig. 1. Mean visual acuity before, 2, 4 and about 8 months after the sham injection.

![Fig. 2](image2.png)  Fig. 2. Mean central macular thickness before, 2, 4 and about 8 months after the sham injection.