EFFICACY OF INTRAVITREAL TRIAMCINOLONE ACETONIDE FOR THE TREATMENT OF DIABETIC MACULAR EDEMA

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Abstract
This study aimed to report the clinical outcome of intravitreal injections of triamcinolone acetonide (TA) for the treatment of diabetic macular edema (DME). The study enrolled 20 eyes of 19 patients with persistent diabetic macular edema. Full ocular examination including best corrected visual acuity (BCVA), tonometry, retinal examination with +90D lens and average foveal retinal thickness using an optical coherence tomography (OCT) were monitored before and then weekly for up to four weeks after the injection. All eyes received intravitreal triamcinolone acetinide (IVTA) (4 mg/0.1 ml) under topical anesthesia with Proparacaine 0.5% eye drops.

BCVA at one week improved by two lines or more in six eyes (30%) and in nine eyes (45%) at four weeks. However, no significant improvement in mean BCVA from baseline was observed at one week (p>0.05) and four weeks (p>0.05). Mean retinal thickness (RT) were 411±179µm at baseline, 349±102µm at one week after the injection (p<0.05), and 380±102µm at four weeks (p>0.05), and 380±159µm at four weeks (p>0.05). One week after the injection, significant regression of macular edema was seen. However recurrence occurred at four weeks. No significant complications such as visual loss, endophthalmitis, significant raise in intraocular pressure or systemic complications developed.

In conclusion, no significant changes in BCVA, IOP and RT were observed in the short-term observation after the IVTA. These findings need a larger sample size and a longer term observation to monitor the potential systemic and ocular side effects in Iraqi patients.

Introduction
Diabetic retinopathy (DR) is a major cause of visual loss in patients with diabetes mellitus. Diabetic macular edema (DME), which can occur at any stage of DR, is characterized by increased vascular permeability and deposition of hard exudates at the central retina. Diabetic macular edema is now the principal cause of vision loss in people with diabetes.

According to the results of the early treatment of diabetic retinopathy, DME has usually been treated by focal laser photocoagulation of leaking circumscribed retinal areas. Whereas in eyes with diffuse DME, laser treatment cannot be focused on localized retinal leaking spot since entire macula is involved, therefore grid laser is recommended but has been controversial, since studies proving the efficacy of treatment have not been yet published.

Other studies showed that visual acuity usually does not improve with laser treatment once it's decreased. In view of uncertainties in the treatment of DME, the aim of the present study is to assess the efficacy of IVTA in reducing macular edema, decreasing the central foveal retinal thickness and improving visual acuity.
Patients and Methods

In this study, 20 eyes of 19 patients retrospectively reviewed (12 males, 7 females) with DME treated with IVTA. The patients were followed for four weeks at Basra General Hospital. The decision to treat with IVTA was made with the patients after a complete discussion on its risks, benefits and alternative treatments. If the patient decided to proceed with the therapy, they signed a consent form before administration.

The following protocol was observed: Visual acuity was measured, detailed ocular examination, +90D retinal examination done before treatment and after injection on each follow up visit. Intraocular pressure was measured before and after treatment on each follow up visit. Before injection patients were prescribed topical antibiotic prophylactically, Ciprofloxacin drop 1 day before and 5 days after injection. Oral acetazolamide 250 mg BD before injection and 5 days after injection along with Timolol drop twice a day for 1 month to prevent post injection raise in intraocular pressure(IOP).

The eye was prepared with a topical anesthetic with Proparacaine 0.5% drops before the injection. The eyelid was prepared with a povidone iodine solution. A wire speculum was placed followed by several drops of diluted povidone iodine solution to the conjunctiva at the injection site. An injection of 4 mg of triamcinolone acetonide (0.1 ml) was administered using a 30 G needle at the site of pars plana (3 mm from the limbus). Patients were examined at baseline, at one week, two weeks, and four weeks. Analysis of the retinal anatomic features was performed using an optical coherence tomography (CLO-OCT, OTI; USA). The RT at the fovea of the central 1mm was determined using fast macula scan. Statistical analysis was performed using the Student’s t-test to compare the VA, IOP and the central RT at one, two, and four weeks from baseline.

Results

Twenty eyes of 19 patients (12 males, 7 females) with DME were studied. The ages of the patients ranged from 44 to 74 years with a mean of 59.7±8.0 years. All patients had type II diabetes. There was no history of any other ocular disease except for refractive errors or cataracts. Four patients had panretinal photocoagulation; ten of them had a macular laser treatment with a grid or focal laser. Three patients had sub-Tenon injection of 20 mg triamcinolone acetonide (TA). Nine patients had cataract surgery with intraocular lens implantation, and three patients had pars plana vitrectomy (Table I).

<table>
<thead>
<tr>
<th>Characteristic</th>
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<tbody>
<tr>
<td>Male</td>
<td>12</td>
</tr>
<tr>
<td>Female</td>
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<tr>
<td>Age(years), Mean±SD</td>
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<td>Panretinal photocoagulation</td>
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<tr>
<td>Macula focal/grid treatment</td>
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<tr>
<td>Posterior subtenon triamcinolone injection</td>
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<tr>
<td>Pars plana vitrectomy</td>
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<tr>
<td>Lens status</td>
<td>No.</td>
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<tr>
<td>Phakic</td>
<td>11</td>
</tr>
<tr>
<td>Pseudophakic</td>
<td>9</td>
</tr>
<tr>
<td>Baseline retinal thickness, Mean±SD (µm)</td>
<td>411±170</td>
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</tbody>
</table>
The BCVA at one week improved by two lines or more in six eyes (30%) (Figure 1).

![Figure 1: Best Corrected Visual Acuity (BCVA) results after 1 week of treatment. Six eyes (30%) improved by 2 lines or more, one eye (5%) decreased by 2 lines or more. There's no significant improvement between mean BCVA and baseline (p>0.05, paired t-test).](image)

And the BCVA at four weeks improved in nine eyes (45%) (Figure 2). No significant improvement in the mean BCVA from baseline was observed at one week (p>0.05), or four weeks (p>0.05).

![Figure 2: Best Corrected Visual Acuity (BCVA) results after 4 weeks of treatment. Nine eyes (45%) improved by 2 lines or more, 3 eyes (15%) decreased by 2 lines or more.](image)

There's no significant improvement between mean BCVA and baseline (p>0.05, paired t-test). Mean RT was 411±170µm at baseline, 349±102µm at one week, 365±149µm at two weeks, 380±159µm at four weeks (Figure 3).
The central RT significantly decreased from baseline at 1 week (p<0.05). However, it did not significantly decrease at 2 weeks (p>0.05), and 4 weeks (p>0.05). The central RT significantly decreased from baseline at one week (p<0.05). However, no significant decrease was recognized at two weeks (p>0.05), and four weeks (p>0.05). During the follow up of the patients in this study, no significant complications such as severe inflammation, increased IOP (Figure 4), severe visual loss, endophthalmitis, or systemic complications was observed.

Discussion
DME has been characterized by inflammation, including intravitreous induction of proinflammatory cytokines, intraretinal expression of proinflammatory caspases and mediators. Many clinical investigators have found that intravitreal injection of TA may reduce macular edema. The use of corticosteroids to treat DME follows from the observation that the increase in retinal capillary permeability that results in DME may be caused by a breakdown of blood retinal barriers mediated in part by VEGF (Vascular Endothelial Growth Factor). Antonetti and his colleagues demonstrated that VEGF may regulate vascular permeability by increasing the phosphorylation of tight junction proteins such as occludens and zonula occludens. Corticosteroids with anti-inflammatory properties inhibit the expression of VEGF gene. In previous studies, patients experienced a rapid and dramatic resolution of macular edema and improvement in visual acuity after treatment with IVTA. The typical dose of triamcinolone acetonide used to treat DME is 4mg/0.1ml, and I conformed to this dose in the present study.
There was a marked reduction in macular edema soon after injection at one week. However, recurrence of macular edema occurred within four weeks. Mean retinal thickness was reduced at one week after the injection (p<0.05). However, there was no significant improvement in the mean BCVA. It is possible that visual acuity may not improve with the same time course as thickness of the macula. It depends on macular on macular function improvement and it may have time lag. Previous studies reveal some serious complications of IVTA such as significant raise in IOP, progression of cataract and even endophthalmitis. These complications was not observed probably because of the strict sterilization and disinfection preoperatively and operatively and the prophylactic use of antibiotics and IOP lowering agents.

Maia, et al. reported that combination therapy of intravitreal TA and laser photocoagulation decreased DME. Martidis and his colleagues reported results using IVTA injection in 16 eyes with macular edema due to diabetic retinopathy. All the 16 eyes had persistent macular edema after laser photocoagulation. Optical coherence tomography in these patients demonstrated that the mean thickness of the central macula decreased from 540µm before injection to 242µm after injection (the normal average thickness of the central macula is 175µm). Visual acuity was improved by 2.4 and 1.3 lines (from the baseline value).

The above results was not observed on the present study, therefore I think the combination of laser photocoagulation with TA may improve BCVA and decrease RT more than laser photocoagulation alone or TA alone for the treatment of DME.

In summary the treatment with triamcinolone acetonide alone for DME is effective in the short-term; however it is not effective in the long-term.

References