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Assessment of Suprachoroidal Injection of Triamcinolone Acetonide in Cases of Diabetic Macular Edema

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ABSTRACT

Background: Diabetic retinopathy [DR] remains one of the main causes of visual reduction in the world. The visual reduction in patients with DR is usually due to diabetic macular edema [DME]. Suprachoroidal triamcinolone acetonide injection is a new effective modality used for the management of diabetic macular edema.

The aim of the work: To assess the visual acuity [VA], central macular thickness [CMT] by optical coherence tomography [OCT] and intraocular pressure [IOP] measurement in patients with DME injected with Triamcinolone Acetonide through suprachoroidal space.

Patients and Methods: Forty eyes of 37 patients [18 males and 19 females] with DME were included and followed-up for 6 months to assess VA, CMT and IOP. Patients were included if they were diagnosed as DME.

Results: Baseline measurements were logMAR best corrected visual acuity [VA] which was 0.83 ± 0.09, [OCT] which was 422.42 ± 64.1 µm and [IOP] which was 15.25 ± 1.46 mmHg. Post injection measurements of VA during the four points of the follow-up period showed statistically significant improvement. At one-week post-injection, logMAR VA was 0.82 ± 0.09, at one month follow-up was 0.72 ± 0.09, at three months was 0.68 ± 0.1, at six months, was 0.62 ± 0.1,.. OCT follow-up measurements showed highly significant improvements, which started from the first week post-injection till the end of the follow-up period at six months point. At one week, it measured 391.7 ± 60.6 µm, at one month the measurement was 337.1 ± 54.5 µm, at three months was 302.7 ± 46.5, at six months, was 267.9 ± 40.7.

Conclusion: Injection of TA to the suprachoroidal space in DME, was well tolerated without any serious ocular adverse events and produced significant resolution in CST and significant improvement in BCVA.

Keywords: Diabetic; Macular edema; Triamcinolone acetonide; Suprachoroidal space; Optical coherence tomography.

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* Main subject and any subcategories have been classified according to the research topic.
INTRODUCTION

Diabetic macular edema [DME] is one of the main causes of visual deterioration in patients with diabetes mellitus [DM] [1]. The visual deterioration in patients with diabetic retinopathy [DR] is usually related to diabetic macular edema [DME] [2].

Laser photocoagulation one of the modality for treatment of patients with DME can keep or enhance visual acuity; however, it may lead to a reduction in the field of vision, color vision or contrast sensitivity impairment [3].

It has been shown that the intravitreal injection of steroids can decrease macular edema related to different ocular diseases [4]. Also, due to multiple and repeated injections, compliance with treatment and follow up is usually low with increased risk of ocular or systemic adverse effects [5]. The supra-choroidal space [SCS] provides a new route for drug administration to the posterior segment because it crosses the internal limiting membrane and may theoretically provide higher concentration within the choroid, retinal pigment epithelium [RPE], and ciliary body while decreasing drug levels in the anterior segment, so decreasing the risk of cataract and intraocular pressure [IOP] elevation. However, this flow in restricted and sectionalized by the scleral spur anteriorly and optic nerve posteriorly, so anterior segment component is spared [6].

The SCS is a new modality for intraocular drug administration which can pass the sclera without the risk of IO penetration [7]. SCS drug administration can be done using microneedles, small-gauge needles only 0.7–1.0 mm in length, that are long enough to pierce the sclera and access the SCS [5]. Microneedles have also been developed which allow for injection into the SCS using procedure like that used for intravitreal injections [9].

Triamcinolone acetonide [TAAc] is a synthetic corticosteroid formulated as an injectable suspension and has a 7.5–fold higher in anti-inflamatory potency than cortisone [10]. The clinical efficacy and safety of intravitreal TAAc injections have been evaluated in a number of trials. TAAc increases the levels of tight-junctions in between endothelial cells and thus lessens vessel leakage. It also has an angiostatic action through vascular endothelial growth factor [VEGF] inhibition and therefore may have a useful effect on DME. The dose of TAAc administered by this root is 4 mg/100 μL which was administrated in our study [11].

AIM OF THE WORK

This work aims to assess the visual acuity [VA] and central macular thickness [CMT] by [OCT] in patients with DME injected with Triamcinolone Acetonide through suprachoroidal space.

PATIENTS AND METHODS

This prospective study included 40 eyes in patients with evident diabetic macular edema in Faculty of medicine [Damietta] Al Azhar University from March 2020 to December 2020. The study was approved by the Medical Ethics Committee of Al-Azhar University Faculty of Medicine. Calculation of sample size was done using EPI-INFO 2002 software package designed by WHO and centers of disease control and prevention revealed that, at least 38 eyes were required to find a significant difference in visual acuity and central macular thickness at α value of 0.05 and power of study 95%. This calculation was based on results of a previous study [12].

Forty eyes of 37 patients [18 males and 19 females] with [DME] were included and followed-up for 6 months to assess VA, CMT and IOP. Patients were included with diabetic macular edema and patients with evident DME by OCT [Topcon 3D OCT 2000]. Mean patient age was 57.4 years [range 44–67 years].

Inclusion criteria: Written informed consent will be obtained from all patients included in the study after the nature and possible consequences of the procedure have been explained, Patients with diabetic macular edema and patients with evident DME by OCT [Topcon 3D OCT 2000].

Exclusion criteria: Patients who refuse to participate in the study, if there is media opacity interferes with preoperative evaluation [e.g. dense cataract & dense vitreous hemorrhage], macular edema that results from non-diabetic causes [e.g. CRVO, BRVO, Vitro-macular traction, Uveitis or any collagen and vascular disease] and intraoperative complications [choroidal hemorrhage & vitreous hemorrhage].

Surgical procedure: Before the injection, topical
anesthesia was administered at the injection site: either benoxinate or subconjunctival lidocaine 1%. The administration of 2–3 drops of 5% Betadine topically in the lower fornix was performed. The eyelids were scrubbed with cotton-tipped applicators soaked in 5% Betadine. TA vial was drawn up into a sterile syringe using a non-filtered 28 gauge needle. Needles were changed to sterile SCS injection needle, and then air bubbles and excess volume were expelled to 0.1 ml preserved TA. A sterile lid speculum was placed. The patients were asked to look down and the injection site was marked 3.5–4.0 mm posterior to the limbus in the superotemporal quadrant with calipers. Small-gauge needles only 0.7–1.0 mm in length that are long enough to pierce the sclera and access the SCS. This technique was done in several clinical trials. The dose of triamcinolone acetonide administered by this route is 4 mg/100 µL. The eye was rinsed with eye wash or saline.

Follow-up: All patients underwent an ophthalmic examination on days one and seven post injections, to assess injection-related complications such as anterior chamber reaction or IOP rise, etc. Follow-up was performed regularly by determining BCVA, IOP measurement, fundus biomicroscopy and CMT using spectral-domain OCT one week, one month, three months and six months post injection. Anterior segment OCT and UBM were done for some cases immediately after injection and reported that TA located in SCS in these cases. Not done for all cases as this this work aims to assess VA and central macular thickness by [OCT] in patients with [DME] not to assess anatomical site of the injection as this technique of imaging is cost-effective on patients and medical authorities.

Statistical Analysis: All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows [SPSS Inc., Chicago, IL, USA] & MedCalc 13 for windows [MedCalc Softwarebvba, Ostend, Belgium]. Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD [Standard deviation] for parametric and median and range for non-parametric data. All statistical comparisons were two tailed with significance Level of P-value ≤ 0.05 indicates significant, p <0.001 indicates a highly significant difference while, P> 0.05 indicates non-significant difference.

RESULTS

We included forty eyes [20 right eyes and 20 left eyes] of 37 patients, out of them, there were 18 males [48.6%] and 19 females [51.4%]. The mean age of the study patients was 57.4±5.1 years. Baseline [pre-injection] measurements were logMAR visual acuity [VA] which was 0.83±0.09, optical coherence tomography [OCT] which was 422.42 ± 64.1 µm, and intraocular pressure [IOP] which was 15.25 ± 1.46 mmHg measured by applanation tonometer [Table 1]. Post injection measurements of VA during the four points of the follow-up period showed statistically significant improvement. One-week post-injection, logMAR VA was 0.82±0.09, [P = 0.02]; at one-month follow-up was 0.72±0.09, [P < 0.001]; at three months was 0.68±0.1, [P < 0.001]; at six months, was 0.62±0.1, [P < 0.001] [Table 2].

OCT follow-up measurements showed highly significant improvements, which started from the first
week post-injection till the end of the follow-up period at six months point. At one week, it measured 391.7±60.6µm, [P < 0.001]; at one month, the measurement was 337.1±54.5 µm, [P < 0.001]; at three months was 302.7±46.5, [P < 0.001]; at six months, was 267.9±40.7, [P < 0.001] [Table 3]. IOP showed a transient rise during the follow-up period at one-week [15.7±1.52 mmHg, P-value < 0.001] and one-month points [15.55±1.33 mmHg, P-value = 0.006]. However, at three and six-months point, the IOP nearly returned to baseline and there was no identified significant change from baseline. At three months, the IOP was 15.35±1.38 mmHg, [P = 0.3]; at six months it was 15.3±1.4 mmHg, [P = 0.5] [Table 4].

Table [1] shows the demographics and baseline characteristics of the study patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57.4 ± 5.1</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 [48.6%]</td>
</tr>
<tr>
<td>Female</td>
<td>19 [51.4%]</td>
</tr>
<tr>
<td>Eye</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>20 [50%]</td>
</tr>
<tr>
<td>Left</td>
<td>20 [50%]</td>
</tr>
</tbody>
</table>

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post injection; p3: comparison between baseline values and values at three months’ post injection; P4: comparison between baseline values and values at six months’ post injection.

Table [2] shows the BCVA outcomes during the follow-up period and their comparison to the baseline

<table>
<thead>
<tr>
<th>VA [logMAR]</th>
<th>Result</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA at baseline</td>
<td>0.83 ± 0.09</td>
<td>-----</td>
</tr>
<tr>
<td>VA at 1-week post-injection</td>
<td>0.82 ± 0.09</td>
<td>P1= 0.02*</td>
</tr>
<tr>
<td>VA at 1-month post-injection</td>
<td>0.72 ± 0.09</td>
<td>P2 &lt; 0.001*</td>
</tr>
<tr>
<td>VA at 3 months post-injection</td>
<td>0.68 ± 0.1</td>
<td>P3 &lt; 0.001*</td>
</tr>
<tr>
<td>VA at 6 months post-injection</td>
<td>0.62 ± 0.1</td>
<td>P4 &lt; 0.001*</td>
</tr>
</tbody>
</table>

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post injection; p3: comparison between baseline values and values at three months’ post injection; P4: comparison between baseline values and values at six months’ post injection.

Table [3] shows the OCT outcomes during the follow-up period and their comparison to the baseline

<table>
<thead>
<tr>
<th>OCT [µm]</th>
<th>Result</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCT at baseline</td>
<td>422.42 ± 64.1</td>
<td>-----</td>
</tr>
<tr>
<td>OCT at 1-week post-injection</td>
<td>391.7 ± 60.6</td>
<td>P1 &lt; 0.001*</td>
</tr>
<tr>
<td>OCT at 1-month post-injection</td>
<td>337.1 ± 54.5</td>
<td>P2 &lt; 0.001*</td>
</tr>
<tr>
<td>OCT at 3 months post-injection</td>
<td>302.7 ± 46.5</td>
<td>P3 &lt; 0.001*</td>
</tr>
<tr>
<td>OCT at 6 months post-injection</td>
<td>267.9 ± 40.7</td>
<td>P4 &lt; 0.001*</td>
</tr>
</tbody>
</table>

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post injection; p3: comparison between baseline values and values at three months’ post injection; P4: comparison between baseline values and values at six months’ post injection.

Figure [2] shows OCT changes after injection compared to basal values.

Three months after injection

Six months after injection
The injection of corticosteroid to the suprachoroidal space has the same efficacy to that of intravitreal injection. One difference, however, is that suprachoroidal injection is associated with longer half-life [no washout, more absorption time] and low incidence of IOP rise. Recent studies have approved the safety and efficacy of needle-based suprachoroidal drug injection. In this minimally invasive technique, a microneedle penetrates trans scleral to the appropriate depth during drug delivery.

Similar to our study [HULK Trial; N = 20] found the basis of safety and efficacy of SCTA for DME in treatment. The difference in our study and HULK trial was that did not combine the first injection of SCTA with Aflibercept. The mean pre-treatment CST in HULK trial was 473 um whereas in our study it was 422.42 ± 64.10 um. At six months, mean CST in HULK reduced to 369 um whereas in our study, mean CST at six month follow up was 267.90 ± 40.70 um.

In agreement with the study of Ameen Marashi and Benjamin J. [study of 50 eyes of 36 patients. Approximately 42% of eyes required an injection within 8 weeks; the mean CMT was 456 μm at baseline and decreased to 309 μm within 6 weeks but the CMT increased to 384 μm in 8 weeks and decreased again to 330 μm after the second injection. On average, BCVA improved from 0.8 to 0.5 at 16 weeks in these eyes. Approximately 58% of eyes required only one injection during 16 weeks; the mean CMT was 421 μm at baseline and decreased to 339 μm within 6 weeks, but the CMT increased to 384 μm at 16 weeks while in our study showed highly significant improvements which started from the first week post-injection till the end of the follow-up period at six months point. At 1 week, it measured 391.7 ± 60.6 μm; at 6 months, was 267.9 ± 40.7 μm, On average, BCVA improved from 0.6 to 0.4 at 16 weeks in these eyes this goes with our study which showed statistically significant improvement. At 1 week post-injection, logMAR VA was 0.82 ± 0.09.; at 6 months, was 0.62 ± 0.1.

Injecting triamcinolone into the suprachoroidal space may reduce the risk of IOP elevation because drug delivery is directed to the choroid and the retina and is restricted from the trabecular meshwork achieving better improvement in BCVA and reduction of macular edema compared with intravitreal steroid injection.

Also the study of Isaac DL et al. showed that regarding IOP in the group of eyes treated with triamcinolone, no statistical difference was found between the initial visit and the 4-week [p = 0.08] and the 24-week visits [p = 0.25]. However, a statistically significant difference regarding week 12 [p = 0.01] was determined.

Among the eyes treated with triamcinolone, IOP in three eyes [27.3%] increased to more than 21 mmHg, and for this reason, they were treated with antiglaucoma drugs. While our study showed that a transient rise during the follow-up period at one week [15.7 ± 1.52 mmHg, P-value < 0.001] and one month points [15.55 ± 1.33 mmHg, P-value = 0.006]. However, at three and six months point, the IOP nearly returned to the baseline and there was no identified significant change from the baseline. At three months the IOP was 15.35 ± 1.38 mmHg; at six months it was 15.3 ± 1.4 mmHg.

The most common side effects were local hyperemia or subconjunctival hemorrhage at the site of injection which were self-limited. In our study no patient experienced IOP elevation, the progression of cataract, suprachoroidal and vitreous hemorrhage, choroidal or retinal detachment or endophthalmitis during the period of follow up.

<table>
<thead>
<tr>
<th>IOP [mmHg]</th>
<th>Result</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP at baseline [mmHg]</td>
<td>15.25 ±1.46</td>
<td>-----</td>
</tr>
<tr>
<td>IOP at 1-week post-injection</td>
<td>15.7 ± 1.52</td>
<td>P1&lt;0.001*</td>
</tr>
<tr>
<td>IOP at 1-month post-injection</td>
<td>15.55 ± 1.33</td>
<td>P2&lt;0.001*</td>
</tr>
<tr>
<td>IOP at 3 months post-injection</td>
<td>15.35 ± 1.38</td>
<td>P3&lt;0.3</td>
</tr>
<tr>
<td>IOP at 6 months post-injection</td>
<td>15.3 ± 1.4</td>
<td>P4=0.5</td>
</tr>
</tbody>
</table>

P1: comparison between baseline values and values at one week; P2: comparison between baseline values and values at one-month post-injection; P3: comparison between baseline values and values at three months' post injection; P4: comparison between baseline values and values at six months' post injection.
Conclusion: Injection of TA to the suprachoroidal space in DME, was well tolerated without any serious ocular adverse events and produced significant resolution in CST and significant improvement in BCVA. Future studies on larger sample size and longer duration, possibly with a different regimen will need to be conducted to establish the safety and efficacy of this technique.

Financial and Non-financial Relationships and Activities of Interest

None

REFERENCES


