Effect of intravitreal Triamcinolone (2mg) on diabetic macular oedema in the pseudophakic patient as primary treatment

Mohammed Qasim Al Nuwaini¹, Giyathaldeen T. Neameh¹, Mustafa A. Al Zubaidi Md², Farook M. Albusultan¹
¹Department of Ophthalmology, Faculty of medicine jabber Ibn Hayyen medical university, Najaf, Iraq
²Department of Ophthalmic, Al Sadder teaching hospital, Najaf, Iraq

ABSTRACT

Diabetic macular oedema is still a significant cause of vision drop in the diabetic patient with no definitive regime for treatment. This study was on the result of effects of intravitreal injection of (2mg) triamcinolone on central macular thickness measured by OCT, visual acuity and intraocular pressure in pseudophakic eyes with diabetic macular oedema as a primary treatment line followed in six months. This study is a prospective, interventional case study series. It was on patients who received intravitreal injection of Triamcinolone in a single dose of (2 mg/0.05 ml). Central macular thickness by OCT, visual acuity, and intraocular pressure was measured pre-injection and 1,3,6 months after injection. This study was performed in Iraq, Baghdad, Ibn Al-Haitham Teaching Eye Hospital from October 2014 to July 2015. Results showed 25 eyes received intravitreal injection of Triamcinolone Acetoniod with pre-injection central macular thickness 597.9±98.02 μm, visual acuity 1.096±0.61 Log MAR and intraocular pressure of 16.5±2.53 mmHg. After six months of follow up on central macular thickness 341.6±163.1 μm, visual acuity was 0.63±0.40 Log MAR and IOP was 18.04±5.63mmHg. This study suggests that intravitreal injection of Triamcinolone in a dose 2mg / 0.05ml improves both anatomical and visual outcome in 21 eyes (84%) out of 25 pseudophakic eyes with diabetic macular oedema during first six months after injection and an increase in intraocular pressure in 2 eyes (8%). The intraocular pressure was despite the use of anti-glaucoma medications during this period.

INTRODUCTION

Diabetic Macular Oedema: (DMO), is defined as “the changes of vascular and environment of the retina that lead to increase of retinal thickness at the posterior pole and is considered important cause for vision limitation among diabetic patients” (Rayan et al., 2013). Clinical manifestations are retinal thickness (that may be diffused or focal) with exudates that represent plasma lipoproteins diffused from microaneurysms. The mechanism of diffuse macular oedema from extensive leakage of blood-retinal barrier breakdown that mostly associated with cystoid macular oedema (American academy of ophthalmology, 2013a) confirmation of macular oedema by direct fundus examination by slit
lamp with condensing lens 60,78 and 90 dioptric power or by Fundus fluorescein angiography detecting leakage sites and blocking defects, and Optical coherence tomography (OCT) for macular thickness readings (Sadda et al., 2006). OCT had been considered as the main part in the assessment and followed up for DMO according to the Diabetic Retinopathy Clinical Research Network (DRCR.net) (Diabetic retinopathy clinical research network, 2007). Treatment of DMO-General measures -Good metabolic control as long as the long period of DM, there is a higher risk for progression of retinopathy according to analytical study depends on epidemiological study correlates duration with occurrence and progression of DMO. Also, the poorly controlled DM considered a worsening factor that leads to the increment of DMO. (American academy of ophthalmology, 2013b,c) (American Academy of ophthalmology, basic and clinical course, section 12, Diabetic control and complication trial) - Blood pressure according to United Kingdom Prospective Diabetes Study (UKPDS) the excellent control of hypertension associated with a reduction of retinopathy markedly mainly in type II DM patient (UK Prospective Diabetes Study Group, 1998)-other systemic abnormalities such as nephropathy that assessed by the presence of proteinuria and albuminuria, also the high level of plasma cholesterol increase the exudate formation according to the WESDR and in the ETDRS. Klein even Davis (Klein et al., 1991; Davis et al., 1998)-laser therapy: when the eyes with CSMO get focal green laser photocoagulation there is high possibilities of improvement of vision and reduction risk of vision loss and also macular thickness within 2 years after treatment as compared with controlled group according to The ETDRS, but there is some limitation in visual field function (Focal photocoagulation treatment of diabetic macular edema, 1995) - Medical management of DME Intravitreal therapy by anti VEGF and corticosteroid therapy with or without laser therapy in patients with extensive macular oedema and isolated subfoveal oedema and foveal ischemia with macular oedema, those group of people get benefit from this treatment (Gerstenblith and Rabinowitz, 2012)-Surgery; in the presence of tractional bands with epiretinal membrane and diffuse DMO, Pars plana vitrectomy and detachment of posterior hyaloid may be indicated (Haller et al., 2010). Complications of intravitreal injection of Triamcinolone Acetoniod The increase incidence of cataract and elevation of intraocular pressure after TA have been noted in DRCR. Net as compared with the laser group (13%) of the laser-treated group had undergone cataract surgery within the first two years versus 23% and 51% of TA group 1mg and 4 mg. While, IOP after laser therapy 4% while 16% & 33% in the TA group, respectively.

PATIENTS AND METHODS

This study is a prospective, interventional case series study, hospital-based, performed in Ibn Al Haitham teaching eye hospital in Iraq, Baghdad. The patients referred from retina and vitrectomy clinic in the hospital during the period from October 2014 to January 2015, and follow up of patients continue to July 2015. All the studied patients were informed verbally about the aim of the study, the intervention (the drug that was used, the route of administration, and the side effects) and the ways of investigation before being enrolled with their verbal consent insured. Inclusion criteria: adult patients male/female, type II diabetes mellitus, diabetic macular oedema with central macular thickness more than 300 μm by OCT, Pseudophakic eyes. Exclusion criteria Previously treated eyes with laser photocoagulation, intravitreal anti-VEGF or intravitreal steroid patient with proliferative diabetic retinopathy patient with ischemic changes in fluorescein angiography patients with a previous history of glaucoma family history of glaucoma, IOP more than 20 mm Hg, cup /disc ratio more than 0.3 or patients on anti-glaucoma medications. Anatomical changes that lead to macular oedema (vitreomacular traction, epiretinal membrane) and patients with uncontrolled diabetes mellitus (HbA1c more than 8) or patients with uncontrolled hypertension (systolic blood pressure more than 150 mmHg).

Data collection

The identifying data were age, sex, examination date, centre macular thickness by OCT, visual acuity by Snellen chart (and documented number of lines seen by this chart), intraocular pressure by air puff, optic disc cup to disc ratio (C/D ratio), and recording of any other possible complications.

All patients received intravitreal injection of Triamcinolone in a single dose of (2 mg /0.1ml) as a primary treatment for diabetic macular oedema, assessments of each patient in four follow up visit as following: Visit 0; this was before intravitreal injection with Triamcinolone Acetoniod, Measuring of visual acuity (best corrected) by Snellen chart, IOP by air puff, slit lamp examination of anterior and posterior segment with use of 90 Dioptric power lens were done for each patient. Central macular thickness by OCT and fundus fluorescein angiography was performed to determine the baseline of macular oedema and exclude ischemic diabetic retinopathy, proliferative diabetic retinopathy, and
Table 1: Distribution of the Study Sample by their Demographic Data

| Demographic       | Rating and intervals | Frequency | Percent |
|-------------------|----------------------|-----------|---------|
| Ages/years        | 41-50                | 5         | 20      |
|                   | 51-60                | 11        | 44      |
|                   | 61-70                | 7         | 25      |
|                   | 71 and more          | 2         | 5       |
| Sex               | male                 | 15        | 60      |
|                   | female               | 10        | 40      |
| Affected eye      | OD                   | 16        | 64      |
|                   | OS                   | 9         | 36      |

Table 2: Distribution of the Study Sample according to the Pre-Injection Measures

| Measures           | Rating      | Frequency | Percent |
|--------------------|-------------|-----------|---------|
| Central Macular    | 299 >       | 0         | 0       |
| Thickness          | 300-450     | 2         | 8       |
|                    | 451-600     | 10        | 40      |
|                    | 601<        | 13        | 52      |
| Visual Acuity Pre-injection | Less Than 6/60 | 7 | 28 |
| 6/60               | 6           | 2         | 24      |
| 6/36               | 6           | 2         | 20      |
| 6/24               | 4           | 1         | 16      |
| 6/18               | 1           | 1         | 4       |
| 6/12               | 1           | 1         | 4       |
| 6/9                | 1           | 1         | 4       |
| IOP Pre-injection  | 10-15       | 7         | 28      |
|                    | 16*21       | 18        | 72      |
|                    | 22-27       | 0         | 0       |
|                    | 27<         | 0         | 0       |

Table 3: Distribution of the study sample according to their measures

| Measures           | Rating      | Frequency | Percent |
|--------------------|-------------|-----------|---------|
| Central Macular    | 299 >       | 10        | 40      |
| Thickness          | 300-450     | 6         | 24      |
|                    | 451-600     | 5         | 20      |
|                    | 601<        | 4         | 16      |
| Visual Acuity Post-Injection | Less Than 6/60 | 2 | 8 |
| 6/60               | 5           | 2         | 20      |
| 6/36               | 2           | 8         |         |
| 6/24               | 6           | 2         | 24      |
| 6/18               | 3           | 1         | 12      |
| 6/12               | 4           | 1         | 16      |
| 6/9                | 3           | 1         | 12      |
| IOP Post Injection | 10-15       | 5         | 20      |
| One month          | 16*21       | 11        | 44      |
|                    | 22-27       | 7         | 28      |
|                    | 27<         | 2         | 8       |
Table 4: Distribution of the Study Sample according to their Visual after Three Months of Injection

| Measures           | Rating    | Frequency | Percent |
|--------------------|-----------|-----------|---------|
| Central Macular    | 299-13    | 13        | 52      |
| Thickness          | 300-450   | 4         | 16      |
|                    | 451-600   | 5         | 20      |
|                    | 601<      | 3         | 12      |
| Visual Acuity      | 6/60      | 6         | 24      |
| Pre-injection      | 6/36      | 3         | 12      |
| Three Month        | 6/24      | 5         | 20      |
|                    | 6/18      | 3         | 12      |
|                    | 6/12      | 5         | 20      |
|                    | 6/9p      | 3         | 12      |
| IOP Pre-injection  | 10-15     | 4         | 16      |
| Three month        | 16*21     | 19        | 76      |
|                    | 22-27     | 0         | 0       |
|                    | 27<       | 2         | 8       |

Table 5: Distribution of the Study Sample according to their Measures after Six Months of Injection

| Measures           | Rating    | Frequency | Percent |
|--------------------|-----------|-----------|---------|
| Central Macular    | 299-13    | 13        | 52      |
| Thickness          | 300-450   | 5         | 20      |
|                    | 451-600   | 4         | 16      |
|                    | 601<      | 3         | 12      |
| Visual Acuity      | Less Than 6/60 | 1   | 4 |
| Post-Injection     | 6/60      | 6         | 24      |
| Six Month          | 6/36      | 2         | 8       |
|                    | 6/24      | 4         | 16      |
|                    | 6/18      | 3         | 12      |
|                    | 6/12      | 6         | 24      |
|                    | 6/9p      | 3         | 12      |
| IOP Post Injection | 10-15     | 7         | 28      |
| 6 month            | 16*21     | 16        | 64      |
|                    | 22-27     | 0         | 0       |
|                    | 27<       | 2         | 8       |

Table 6: Mean and standard deviation (SD) of central macular thickness, visual acuity and intraocular pressure pre-injection, one month, three month and six month after injection of triamcinolone

| Duration | Pre-injection | One month | Three month | Six month |
|----------|---------------|-----------|-------------|-----------|
|          | Mean | SD   | Mean | SD   | Mean | SD   | Mean | SD   |
| µm Central Macular Thickness | 597.9 | 98.02 | 387.4 | 159.5 | 348.4 | 165.2 | 341.6 | 163.1 |
| Visual Acuity Logmar Iop | 1.096 | 0.612 | 0.70 | 0.475 | 0.60 | 0.291 | 0.63 | 0.409 |
| Iop      | 16.58 | 2.53 | 19.62 | 5.03 | 18.75 | 6.20 | 19.04 | 6.83 |
Irven Gass Syndrome. Blood test for glycosylated haemoglobin and measurement of blood pressure performed to exclude uncontrolled DM and hypertension visit 1; this was after one month from the date of receiving intravitreal injection of Triamcinolone Acetonide. Visit 2; this visit after three months from date of receiving intravitreal injection of Triamcinolone Acetonide. Visit3; this visit after six months from date of receiving intravitreal injection of Triamcinolone Acetonide. In each follow-up visit measuring of best-corrected visual acuity by Snellen chart, intraocular pressure by air puff, slit lamp examination for anterior and posterior segment by using 90 D lens and measuring of central macular thickness by OCT was performed in these visits. Patients had a measuring of blood pressure in those visits. Also, in the second and third visit patients had a blood test for glycosylated haemoglobin. The technique of intravitreal injection of Triamcinolone Acetonide (Kanski and Bowling, 2011) The intravitreal infusion was given in operating room with adequate illumination, and the procedure and its risk were explained to the patient and appropriate consent obtained. The topical anaesthetic agent was instilled (Propracaine hydrochloride 0. 5%). Standard aseptic technique was used. A 27 –gauge needle was used to inject 0. 05 ml of Triamcinolone Acetonid at 3. 5 mm posterior to the limbus ( pars plana). Antibiotic drops (Ciprofloxacin) were instilled immediately after the injection and continued four times daily for seven days. The patients were instructed that he could return to regular activity after 24 hours and warned to seek advice urgently if they experience any deterioration in their vision or symptoms of inflammation.

RESULTS AND DISCUSSION

This study was conducted on 29 eyes of 26 patients, four patients were excluded due to uncontrolled DM in follow up visits and one other patient exclude from the study due to developing proliferative diabetic retinopathy in follow up visits, the investigation continues on 25 eyes of 21 patients with age range 42 to 75 years. The Table 1 shows that (44%) of the study sample are (51-60) years old age. Besides, (60 %) of the study sample are male, and (64%) for the right patient’s eye as affected one.

The Table 2 shows that (52%) of the patients’ central macular thickness was (more than 601). Also, (28%) of the patients, have visual acuity less than 6/60 on Snellen chart and (72%) of the patients their intraocular pressure equal to (16-21) mmHg.

After One Month of Injection, This Table 3 shows that (40%) of the patients’ central macular thickness 299 µm and less. Besides, (24%) of the patients had visual acuity of 6/24 by Snellen chart. Moreover (44 %) of the patients their intraocular pressure equal to (16-21 mm HG).

This Table 4 shows that (52%) of the patients’ central macular thickness 299 µm and less. In addition (24%) of the patients are able to see only one visual line on Snellen chart (6/60). Moreover (6%) of the patients their intraocular pressure equal to (16-21mHg).

Table 5 shows that (52%) of the patients’ central macular thickness 299 µm and less. In addition (24%) of the patients are able to see only one (6/60) and five (6/12) visual line. Moreover (64%) of the patients their intraocular pressure equal to (16-21) and 2 patients (8%) had IOP more than 27 mmHg with treatment.

Table 6 shows that to facilitate statics calculation of visual acuity we converted the results of visual acuity measured by Snellen chart to Log MAR values.

Based on the paired t-test results, there was a hugely significant difference between the central macular thickness measures pre and after one, three and six months of injection at p-value less than 0. 01.

There was a significant difference between the visual acuity measures pre and after one, three and six months of injection at p-value less than 0. 01. And there was a substantial difference between the intraocular pressure pre and after one month of dose at p-value less than 0. 01. At the same time, there was a non-significant difference between the intraocular pressure pre and after, three and six months of injection. This study showed a significant increase in IOP after one month of injection at p-value less than 0. 01. While there was a non-significant increase in IOP after three and six months of injection at p-value less than 0. 05. In this study we use a dose of (2mg / 0. 05 ml ) of Triamcinolone Acetoniod as an intravitreal injection by comparison with other studies that use a dose of (4mg/0. 5ml ) of Triamcinolone Acetoniod as an intravitreal injection for the treatment of diabetic macular oedema the finding was that:

1-Central macular thickness, in Audren (Audren...
et al., 2006a; Edema, 2009) study that measuring Central Macular Thickness in 17 treated eyes before intravitreal injection of 4 mg Triamcinolone Acetonid and after 1,3 and 6 months found Central Macular Thickness

less than 299 μm in 82. 4% of patients after one month, Central Macular Thickness

less than 299 μm in 76. 5% of patients after three months and Central Macular Thickness

less than 299 μm in 47. 1% of patients after six months.

So the sustained effect of intravitreal TA (2 mg) on Central Macular Thickness, in this study after six months was 52% and in Francois Audren that used (4 mg) dose was 47. 1%.

Both Hauser and Audren (Hauser et al., 2008; Audren et al., 2006b)

Showed that the use of the higher 4-mg dose of intravitreal Triamcinolone did not have enough advantages over lower 1- or 2-mg treatment.

However, (Lamds et al., 2007) Published a comparison between 4 and 8mg dose of intravitreal Triamcinolone and showed that the higher dose had a more sustained effect on both visual acuity and central macular thickness. Norlaili (Norlaili et al., 2011) study 20 eyes of 20 patients received intravitreal injection of Triamcinolone in a single dose of 4 mg / 0. 1ml as a primary treatment and visual acuity was measured preoperatively. At postoperative 1 month and three months using Snellen visual acuity chart, the result was that preoperatively there were 3 eyes (15%) visual acuity 6/18, 10 eyes (50%) with visual acuity 6/24- 6/36 and 7 eyes (35%) had visual acuity of 6/60 or less. On third postoperative month follow up visit there were six eyes (30%) with visual acuity 6/18 or better, nine eyes (45%) with visual acuity 6/24- 6/36 and 5 eyes (25%) had visual acuity 6/60 or less. In Norlaili (Norlaili et al., 2011) study only (30%) of eyes had visual acuity 6/18 and better after three months while in this study we had (44%) of eyes with visual acuity 6/18 or better after three months and (48%) after six months. In Norlaili (Norlaili et al., 2011) (25%) had visual acuity 6/60 or less after three months of injection while in this study only (24%) of eyes had visual acuity of 6/60 or less after three months and six months. Visual outcome in this study after three months was better than visual outcome in Norlaili (Norlaili et al., 2011). This outcome may be due to selection of involving pseudophakic patients alone in this study, while in Norlaili al study, there was a risk of developing cataract after intravitreal steroid injection that reduces visual outcome. Intraocular pressure, in this study of intravitreal triamcinolone injection there, was a significant increase in IOP after one month (36%) had IOP of 22 mmHg or more nine eyes seven eyes (28%) controlled by medication, only 2 eyes (8%) had IOP more than 27 mmHg, these two eyes uncontrolled by medication and IOP in three months visit and six months visit was more than 27 mmHg. In Khalid study (Khalmehmood et al., 2010), secondary glaucoma developed in 18 (36%) which was successfully treated with topical medication in all patients, so Khalid study is similar to this study result in evaluating IOP increase after injection. Other complications, in this study, no eye developed other postoperative complication, while in Khalid (Norlaili et al., 2011) one eye (2%) developed postoperative endophthalmitis. Until recently laser photocoagulation was the mainstay of treatment for diabetic macular oedema and following substantial clinical study intravitreal anti-VEGF has been adopted as a critical element of management of diabetic maculopathy (Kanski and Bowling, 2016) Current studies indicated that using of intravitreal anti-VEGF is better than intravitreal Triamcinolone as primary treatment of diabetic macular oedema (Kanski and Bowling, 2016).

CONCLUSION

Macular oedema in diabetic patients is a significant factor of visual impairment. In this study, intravitreal Triamcinolone was used as a primary treatment for diabetic macular oedema. This study suggests that intravitreal injection of Triamcinolone in a dose 2mg / 0. 1ml improve both anatomical and visual outcome in a pseudophakic patient with diabetic macular oedema during first six months after injection with the risk of increase IOP. Future studies on larger sample size and longer duration of follow up might provide more reliable results.

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Conflict of interest

Nil

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