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Effect of Posterior Subtenon Triamcinolone Acetonide in Refractory Diabetic Macular Edema

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ABSTRACT

Objectives: To see the effect of Posterior Subtenon Triamcinolone Acetonide (PSTT) injection in refractory Diabetic Macular Edema (DME).

Study Design: Quasi-Experimental Study.

Place and Duration of Study: Retina Clinic, Al-Shifa Trust Eye Hospital, Rawalpindi, from Jun to Dec 2018.

Methodology: Patients with Clinically Significant Macular Edema (CSME), with Central Macular Thickness (CMT) >300 microns and those who did not respond to three consecutive Intra-Vitreal Bevacizumab (IVB) injections were included. Posterior Subtenon Triamcinolone Acetonide (PSTT) was administered by a single retina fellow using the same protocol. Each patient's best-corrected visual acuity (BCVA), Intra-ocular pressure (IOP) and Central Macular Thickness (CMT) were evaluated on the day of Posterior Subtenon Triamcinolone Acetonide (PSTT) injection and again at 1, 3 and 6 months.

Results: Out of 52 patients (104 eyes), 16 females and 36 males were present. The mean age was 57.67±9.35 years. Out of 52 right eyes, the mean Central Macular Thickness (CMT) at the first visit was 388.83±172.04 µm, 332.81 ± 144.69 µm after one month, 292.81±147.59µm after six months of Posterior Subtenon Triamcinolone Acetonide (PSTT) Injection. Similarly, for 52 left eyes mean Central Macular Thickness (CMT) at the first visit is 375.79±160.81 µm, 364.52 ± 167.95 µm after one month and 323.37±155.74 µm after six months. Similar results were observed for IOP and BCVA.

Conclusion: Posterior Subtenon Triamcinolone (PSTT) injections are effective in diabetic macular oedema, which does not respond to intravitreal anti-VEGF (IVB) therapy.

Keywords: Central macular thickness, Intraocular pressure, Intravitreal bevacizumab, Posterior subtenon triamcinolone, Refractory diabetic macular edema.

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INTRODUCTION

Diabetic macular oedema (DME) is one of the most common microvascular complications in patients with diabetes, which has a sudden and deteriorating effect on visual acuity (VA), that can finally cause blindness.[1] Diabetic retinopathy destroys blood vessels in the retina, and when it is not treated accordingly, the fluid leaks into the centre of the macula, i.e., fovea.[2] The fovea is the part which is responsible for the sharpest vision. Due to fluid leakage, the macula swells and causes blurring of vision. This condition is called diabetic macular oedema.[3]

Patients with diabetes must have detailed dilated fundal examination yearly.[4] If blurred vision occurs, visual acuity, Optical coherence tomography (OCT),[5] and Fundus Fluorescein Angiography (FFA) is also required.[6] The current management strategy for DME requires early detection and optimal glycemic control to slow the progression of the disease.[7]

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Clinically significant macular oedema (CSME) occurs if there is a thickening of the retina involving the centre of the macula or the area within 500 µm of its centre if there are hard exudates at or within 500 µm of the centre of the macula with thickening of the adjacent retina, or if there is a zone of retinal thickening of one disc diameter area or larger in size, any part of which is within one disc diameter of the centre of the fovea. This definition of CSME generally refers to the threshold level at which laser photocoagulation is carried out. However, it is important to appreciate that most visual loss occurs when macular oedema involves the centre.[8]

Laser photocoagulation is used to treat both DR and DME. In this treatment,[9] focal laser burns or grid laser is used to limit vascular leakage of abnormal blood vessels in the eye in regions of the diffuse breakdown of the blood-retinal barrier. Anti-vascular endothelial growth factor (anti-VEGF) drugs are the drugs which block the development of new blood vessels and limit the leakage from the abnormal blood vessels in the eye. They are delivered through an

injection into the eye. Corticosteroids are also used to treat DME, limiting leakage from the abnormal blood vessels in the eye.[10] They are delivered through an injection into the eye or outside the globe. This study was done to find out the best treatment for refractory diabetic macular oedema, which was not responding to intravitreal Bevacizumab, which had minimum or no side effects and was also cost-effective.

METHODOLOGY

This quasi-experimental study was done in Retina Clinic, Al-Shifa Trust Eye Hospital, Rawalpindi, from July 2014 to December 2015 for six months (IERB Approval Certificate No. ERC-22/AST-18).

The sample size was calculated with the help of the previous study parameters 11 by using the WHO sample size calculator. The sampling technique for 104 eyes, 52 right eyes and 52 left eyes was non-probability consecutive sampling.

Inclusion Criteria: Patients with Clinically significant macular oedema (CSME), with a Central Macular Thickness (CMT) >300 microns and those who did not respond to three consecutive Intra-Vitreal Bevacizumab (IVB) injections were included.

Exclusion Criteria: Patients having age less than 18 years, history of retinal vein occlusion, retinal artery occlusion, uveitis, epiretinal membrane or any chorioretinal disease other than diabetic retinopathy, previous focal or grid laser treatment, pan-retinal photocoagulation treatment< 3 months before the first IVB treatment, previous Intra-Vitreal Triamcinolone Acetonide (IVTA) or Posterior Sub-tenon Triamcinolone Acetonide injections, suspected glaucoma or a diagnosed case of glaucoma or any kind of ocular surgery, including cataract surgery within the last six months were excluded from the study.

Clinically significant macular oedema (CSME) is refractory to IVB if either Central Macular Thickness (CMT) did not decrease by more than 30 microns after three or more three consecutive IVB injections or Central Macular Thickness (CMT) increased after 1-2 IVB injections.

Every patient that came to the retina clinic was already examined in detail in the screening OPD, in which the optometrist checked vision, and an ophthalmologist did a slit lamp examination. Patients were selected according to the inclusion and exclusion criteria. Any patient having refractory diabetic macular oedema with more than 300 microns not responding to anti-VEGF (3 Injections) was included in the study. Central macular thickness was measured using "Carl Zeiss Meditec Stratus OCT" after taking consent and BCVA & IOP. Each patient was given PSTT (Triamcinolone Acetonide 40mg/1ml) injection under sterile conditions. Patients were prescribed antibiotic eye drops four times daily for five days after the injection.

Follow-ups were done after 1, 3 and 6 months of injection in the retina clinic of the hospital. The optometrist checked the vision, an ophthalmologist checked IOP, and central macular thickness was measured with Carl Zeiss Meditec Stratus OCT on each visit. All the results were noted on a pre-designed structured Proforma. Before enrolling the patients in the study, informed consent was taken from each patient. All the study-related information was collected on a pre-designed proforma.

Statistical Package for Social Sciences (SPSS) version 20.0 was used for the data analysis. Descriptive statistics were presented for gender and eye involved. Mean and standard deviation was calculated for numerical variable, i.e., Age, Visual acuity and central macular thickness at presentation and on follow-ups. Paired sample t-test was used to compare the pre and post-injection best corrected visual acuity, central macular thickness and intraocular pressure. The *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 52 patients (52 right and 52 left eyes) were included in this study. Out of which 16 were females and 36 were males. The mean age was 57.67±9.35 years. Table-I showed that out of 52 right eyes mean central macular thickness at the first visit was 388.83±172.04µm, 332.81±144.69µm after one month, 323.52±144.37µm after three months and 292.81±17.59 µm after six months of PSTT injection which shows significant improvement (*p*-value <0.01).

Table-I: Descriptive Statistics of central macular thick-ness in both eyes (µM) (n=52)

Central Macular Thickness	Right Eye (n=52)	Left Eye (n=52)
First Visit	388.83±172.04	375.79±160.81
Six Months	292.81±147.59	323.37±155.74
p-value	<0.01	<0.01

Similarly, for 52 left eyes mean central macular thickness CMT at the first visit is 375.79±160.81µm, 364.52 ± 167.95µm after one, 338.33±159.92µm after three months, 323.37±155.74µm after six months of PSTT injection which again shows significant improvement (*p*-value <0.01) (Table-II).

Table-II: Paired sample t-test showing correlation of pre & post injection central macular thickness (μM) (n=52)

Central macular Thickness	Right Eyes (n=52)	Left Eyes (n=52)
First Visit	388.83±172.04 (120 - 781)	375.79±160.81 (113 - 748)
One Month	332.81±144.69 (110 - 722)	364.52±167.95 (100 - 690)
Three Months	323.52±144.37 (110 - 669)	338.33±159.92 (100 - 670)
Six Months	292.81±147.59 (100 - 640)	323.37±155.74 (100 - 650)

Table-III showed that out of 52 right eyes mean central intraocular pressure at the first visit was 19.40± 3.79 mm of Hg, 17.79±3.81 mm of Hg after one month, 16.37±4.23 mm of Hg after three months and 14.69±4.03 mm of Hg after six months of PSTT injection which shows significant improvement (*p*-value <0.01).

Table-III: Descriptive statistics of intra-ocular presuure in both eyes (mm of Hg) (n=52)

Intra ocular Pressure	Right Eyes (n=52)	Left Eyes (n=52)
First Visit (mm of Hg)	19.40±.79 (8 - 30)	19.67±3.25 (12 - 30)
One Month (mm of Hg)	17.79±3.81 (7 - 28)	18.29±3.98 (10 - 30)
Three Months (mm of Hg)	16.37±4.23 (7 - 28)	16.42±3.59 (10 - 24)
Six Months (mm of Hg)	14.69±4.03 (6 - 26)	14.75±3.70 (10 - 26)

Similarly, for 52 left eyes mean intraocular pressure at the first visit is 19.67±3.25 mm of Hg, 18.29±3.98 mm of Hg after one month, 16.42 ± 3.59 mm of Hg after three months, 14.75±3.70 mm of Hg after six months of PSTT injection which again shows signifi-cant improvement (*p*-value <0.01) (Table-IV).

Table-IV: Pre & Post pstt injection intra-ocular presuure (mm Hg) and pre and post pstt injection best corrected visual acuity (Logmar) (n=52)

Intra-Ocular Presuure	Right Eye (n=52)	Left Eye (n=52)
First Visit (mm of Hg)	19.40±3.79	19.67±3.25
Six Months (mm of Hg)	14.69±4.03	14.75±3.70
p-value	<0.01	<0.01
Best Corrected Visual Acuity	**Right Eye (n=52)**	**Left Eye (n=52)**
First Visit	0.21±0.22	0.27±0.23
Six Months	0.45±0.32	0.55±0.33
p-value	<0.01	<0.01

Out of 52 right eyes, BCVA at the first visit was 0.21±0.22, 0.29±0.26 after one month, 0.37±0.27 after three months and 0.45±0.32 after six months of PSTT injection which shows significant improvement (*p*-value <0.01). Similarly, for 52 left eyes, BCVA at the first visit was 0.27±0.23, 0.37±0.30 after one month, 0.46±0.31 after three months, 0.55±0.33 after six months of PSTT injection, which again shows signifi-cant improvement (*p*-value <0.01) (Table-V).

Table-V: Descriptive Statistics of Best Corrected Visual Acuity (Bcva) in both eyes (Logmar) (n=52)

Best Corrected Visual Acuity	Right Eyes (n=52)	Left Eyes (n=52)
First Visit	0.21±0.22 (0.01 - 1)	0.27±0.23 (0.01 - 1)
One Month	0.29±0.26 (0.01 - 1)	0.37 ± 0.31 (0.01 - 1)
Three Months	0.37±0.27 (0.01 - 1)	0.47±0.31 (0.01 - 1)
Six Months	0.45±0.32 (0.01 - 1)	0.55±0.33 (0.01 - 1)

DISCUSSION

Diabetic macular oedema is one of the common causes of visual impairment in diabetic retinopathy, and those patients who do not respond to treatment are considered refractory cases. Studies have shown that intravitreal injection of steroids is effective in the treatment of refractory cases.[12,13]

We conducted the study to see the effect of Posterior Subtenon Triamcinolone Injection (PSTT) on Central Macular Thickness (CMT), Best Corrected Visual Acuity (VA) and Intraocular Pressure (IOP). Our results are comparable with the previous studies, and there was an overall improvement in all three areas at the end of 6 months.

Ibraheem *et al.*[11] did a similar study at Layton Rahmatulla Benevolent Trust, Lahore, Pakistan, from October 2014 to March 2015, which included the eyes of patients with refractory macular oedema treated with PSTT. Comparisons of central macular thickness at various follow-ups showed a significant difference from the baseline to the last follow-up (*p*<0.001). Moreover, 14% of subjects showed consistent improvement in central macular thickness. This study showed similar results to our study.

Kim *et al.*[14] in their prospective interventional comparative study, showed that a Sub-Tenon Injection of Triamcinolone reduced the incidence of cystoids macular oedema after cataract surgery in patients with diabetes. In addition, it reduced the central macular

thickness and improved visual acuity in the short term. Although the results of this study were similar to our study, we did not include any patients with a history of previous surgeries or inflammation.

In another such study, Tatsumi *et a.,*[15] compared the efficacy of Posterior Subtenon Triamcinolone Acetonide (PSTT) to Intravitreal Triamcinolone Acetonide (IVTA) injections after cataract surgery for treatment of DME. The results showed that both the treatment options showed similar results, but the complication of raised intraocular pressure was more when the steroid was administered intravitreally than when it was given via the Posterior Subtenon route.

Ozdek *et al.*[16] compared the clinical outcomes of PSTT and IVT injections to treat DME. Both Posterior subtenon triamcinolone acetonide (PSTT) and intravitreal triamcinolone acetonide (IVT) injections caused a significant improvement in visual acuity and a decrease in central foveal thickness, especially in the short term. The effect was more pronounced in the IVT group; however, PSTT injection also seemed to be a safe and effective technique for the treatment of DME.

In another study by Srilatha *et al.*[17] intravitreal anti-VEGF and PSTT in managing diabetic macular oedema with an adjunct to laser treatment. The results showed that both have some efficacy in reducing the central macular thickness, but the percentage decrease in CMT was more in IVB + Laser group as compared to PSTT + Laser group. In our study, we took only those patients who were not responding to IVB and did not include Laser as a treatment option.

Arain *et al.*[18] in his study, evaluated the efficacy of the IVB + IVT combination for treating refractory diabetic macular oedema. The results showed that a combination of steroids and anti-VEGF worked well for diabetic macular oedema that did not respond to other treatment modes. In our study, we also used steroids but not in combination with other drugs. Furthermore, the drug administration route was diffe-rent, i.e., we administered steroids via the Posterior Subtenon route.

Our study has various strengths and limitations side by side. There were various treatment options for refractory diabetic macular oedema, but we must choose one with maximum efficacy and minimum side effects. Although future studies are required to confirm whether PSTT injections are safer compared to other treatment options like IVTA or Intravitreal Steroid implant but till now, studies show that PSTT has fewer side effects compared to other treatment modalities mentioned above.

CONCLUSION

Posterior subtenon Triamcinolone (PSTT) injection should be used in cases of diabetic macular oedema which do not respond to intravitreal anti-VEGF (IVB) therapy.

Conflict of Interest: None.

Authors' Contribution

MKH:, RS:, ZKOK:, AAG: Direct Contribution, NJ:, MUS: Intellectual Contribution.

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