

# Efficacy and Safety of Suprachoroidal Administration of Triamcinolone Acetonide in Patients of Refractory Diabetic Macular Edema

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## ABSTRACT

**Background:** To determine the efficacy and safety of suprachoroidal administration of triamcinolone acetonide in patients of refractory diabetic macular edema.

**Study setting:** This study was conducted from September 2020 to April 2021 in the department of Ophthalmology FMU/Allied Hospital Faisalabad.

**Study design** was quasi experimental

**Materials and methods:** sample size was 45, through non probability consecutive sampling. All 45 patients with refractory diabetic macular edema were enrolled and following parameters e.g Best corrected visual acuity (less than 20/40 on Snellen Visual acuity Chart), IOP < 21 mm of Hg, Central macular thickness >300 micrometers, were recorded as baseline at the start of study. Suprachoroidal triamcinolone acetonide injection 0.1 ml given to these 45 patients. Same parameters e.g Best Corrected visual acuity, Intraocular pressure, Central Macular Thickness were measured at each follow-up visit. First follow-up visit was conducted on next day then one week, one month and in third month.

**Results:** In this study, mean of age was  $50.71 \pm 7.05$  years. 23(51.1%) were males and 22(48.9%) were females. Pre-treatment Intra ocular pressure, best corrected visual acuity and macular thickness were  $13.4 \pm 1.9$  mmHg,  $0.72 \pm 0.11$  and  $638.04 \pm 133.9$  micrometers respectively. After one-month Intra ocular pressure, Best corrected visual acuity and Central macular thickness were  $13.71 \pm 2.61$  mmHg,  $0.48 \pm 0.11$  and  $314.11 \pm 53.8$  micrometer and after three months  $13.24 \pm 1.26$  mmHg,  $0.46 \pm 0.12$  and  $306.9 \pm 49.52$  micrometer respectively. Statistical significant difference was found for pre and post Best corrected visual acuity and Central macular thickness (p-value <0.0001). In two (4.4%) patients, intra ocular pressure was raised.

**Practical implication:** This study was highlighted safety and efficacy of suprachoroidal injection of triamcinolone acetonide in cases of refractory diabetic macular edema

**Conclusion:** Suprachoroidal Triamcinolone acetonide injection is proved to be safe and effective treatment modality for the patients of refractory diabetic macular edema as it decreases central macular thickness and improves best corrected visual acuity.

**Keywords:** Diabetic macular edema, Suprachoroidal, Triamcinolone acetonide, Intra ocular pressure, Optical coherence tomography, visual acuity.

## INTRODUCTION

The most important cause of decrease in vision in retinal disorder is macular edema. Most important cause of macular edema in adult patients is diabetes.<sup>1</sup> Prolonged uncontrolled diabetes affects almost every organ of body and every tissue of eye. But the most troublesome complication of diabetic retinopathy is diabetic macular edema.

There are three major reasons of macular edema, 1. Diabetic macular edema 2. macular edema due to retinal vein occlusion 3. macular edema due to Uveitis.<sup>2</sup>

Most important risk factor to develop Diabetic macular edema is prolonged duration of diabetes, that is more than 10 years. According to data, after 10 years 20.5% patients of type 1 diabetes, 13.9% patients with type 2 diabetes taking insulin and 25.4% patient with type 2 diabetes taking oral medicine to control blood sugar level develop diabetic macular edema.<sup>3,4</sup>

Diabetes creates imbalance of various growth factors and cytokines that causes damage to endothelium resulting in capillary leakage that may lead to macular edema. The fluid initially located between Outer Plexiform layer and Inner Nuclear Layer of retina. Later it may involve inner Plexiform and Nerve fiber layer and eventually entire retina is edematous and fovea assumes cystoids appearance that is detected on OCT (Kanski).<sup>5</sup>

There are multiple options to treat macular edema. For the last two decades Argon laser remained the mainstay of treatment. With the passage of time new treatment modalities introduced in which intra-vitreous anti-VEGF injection and intravitreal corticosteroids considered as most effective treatments to treat macular edema. Later on anti-VEGF alone or anti-VEGF in combination with Argon laser and intra-vitreous corticosteroid get

popularity due to better results. Few patients are resistant to conventional treatment, and macular edema does not resolve despite repeated injections of anti-VEGF.<sup>1</sup> This macular edema is called refractory diabetic macular edema. This situation is very challenging for ophthalmologists. In diabetic macular edema, 50% of patients could not get better vision due to persistent diabetic macular edema despite trial of all the available treatments.<sup>7</sup> This edema is called refractory diabetic macular edema. Almost in 32% to 66% of the cases, DME persisted with decreased in vision.<sup>6</sup>

Another treatment modality used for the treatment of diabetic macular edema is triamcinolone acetonide which is a synthetic steroid and injected intra-vitreally, But patients develop complications e.g Glaucoma and Cataract due to repeated administration intra-vitreally.<sup>8</sup>

In this context we need another approach/route of drug administration that is more tolerable, efficacious and safe for the patients. So a recent advancement has been made in drug administration route that is the injection of triamcinolone acetonide in suprachoroidal space. Now this route of drug administration is getting more popular due to its safety, efficacy and affordability.<sup>9</sup> This study is conducted on safety and efficacy of suprachoroidal injection of triamcinolone acetonide in cases of refractory diabetic macular edema.

## METHODOLOGY

Before starting study a written permission was taken from Ethical Review committee of university Hospital. This Quasi experimental study was conducted in department of ophthalmology FMU/AHF from Sep 2020 to April 2021. A written informed consent was taken from every patient before including him or her in study.

Sample size of 45 patients was calculated by taking mean postoperative best corrected visual acuity (BCVA)  $0.45 \pm 0.27$ , 9, confidence level 95% and absolute precision (d) 0.09. Non probability consecutive sampling method was used.

Inclusion criteria for the patient to include in study was defined as patients having type II diabetes, age between 30 to 60 years, both males and females, refractory diabetic macular edema, BCVA < 6/12 and CMT > 300  $\mu$ m, IOP < 21 mm of Hg and HbA1c less than 8 mmol/mol. These patients were included in study from outpatient department of Allied Hospital Faisalabad through non probability consultant sampling. Exclusion criteria was also defined as following categories of patients were not included in study e.g Prior any intraocular surgery H/O periocular, subtenon or intravitreal injections of Triamcinolone acetonide over past 6 months, macular edema other than diabetes e.g Central retinal vein occlusion Age related macular degeneration, Macula dystrophy and Uveitis and HbA1c more than 8mmol/mol

Refractory Diabetic macular edema is defined as DMO that is non responsive to conventional treatment for last 6 months. Patient were called on specific days in eye ward for brief history about their previous treatment, control of blood sugar level and allergy to any drug used during procedure. After history, complete ocular examination was performed. These baseline parameters, BCVA on snellen visual acuity chart, IOP on applanation tonometer and dilated fundus examination with binocular slit lamp using 78 D lens and OCT Macula on spectral domain optovue OCT were noted and documented on predesigned Performa.

Before administering suprachoroidal injection Pupils of patients were dilated and topical Anesthesia with proparacaine hydrochloride 0.5% (Alcaine) and one drop of 10% povidone (pyodine) for complete asepsis of conjunctivitis Sac were instilled. A 30 gauge 1 cc B- Braun syringe and 24 G Intravenous branula were taken. Needle was withdrawn out from branula and sleeve was cut in such a way that B- Braun syringe was barred, Triamcinolone Aceoinide injection was filled in 1cc syringe up to 0.1 mark.

Under complete aseptic condition in eye operation theatre at 3.5 mm distance from limbus measured with caliper, 0.1 ml solution of TCA was injected in suprachoroidal space at marked place in such a way that direction of needle is perpendicular to sclera. After injection, Needle was withdrawn and aseptic Q tip was pressed over place of injection, one drop of moxifloxacin eye drop named vigamox was instilled in conjunctival sac after injection. After injection indirect ophthalmoscopy was performed to rule out intravitreal infusion of injection and CRAO. If there is suspicion of CRAO and IOP is more than 40mm of Hg the anterior chamber paracentesis was done through limbus using 1cc master syringe

Patients were sent to home after injection and called for follow up after one week, one month & 3 months. At every visit BCVA, CMT, IOP, were noted. Efficacy was measured in terms of reduction in CMT & Increase in BCVA and safety is measured in term of change with IOP from baseline. Data was analyzed by using SPSS V-16. Along with descriptive statistics, paired t-test for normally distribute data and Wilcoxon signed rank test for skewed numerical data was used. For checking the normal distribution Shapiro Wilk test was applied. P-value  $\leq 0.05$  was set as significant.

**RESULTS**

Forty five eyes of 45 patients of refractory diabetic macular edema were enrolled and undergone for Supra-Choroidal Triamcinolone Acetonide (SCTA) injection.

Minimum age of the patients was 32 years and maximum age was 60 years. Almost equal number of male and females suffers from refractory DME. Table 1 demonstrates the demographics and baseline characteristics of the patients.

Intraocular pressure and central subfield thickness after 1 and 3 months of SCTA were  $13.71 \pm 2.61$  mmHg and  $13.24 \pm 1.26$  mmHg respectively. There is no statistical significant difference between baseline and 1 and 3<sup>rd</sup> month post injection with p-values 0.41 and

0.58 respectively. Mean BCVA after 1 and 3 months of treatment were  $0.48 \pm 0.11$  and  $0.46 \pm 0.12$  with p-values < 0.0001 which shows statistical significant difference baseline and post treatment BCVA.

There was minimum increase in EDTA letters was 4 and maximum was 16 after treatment. After SCTA injection mean EDTRS letters and mean CST is shown in figure 1 and 2 respectively. There is also statistical significant difference between baseline and 1 and 3<sup>rd</sup> month after SCTA injection with each p-value < 0.0001 separately.

Out of 45 patients, after SCTA injection IOP was increased in only 2 patients (4.44%). In one patient IOP increased from 18 to 23mm Hg and in other patient it arises from 18 to 24 mm Hg at one month. The glaucoma treatment was given to both of the patients and decreases the IOP up to 16 and 17 mmHg respectively.

Table 1: Demographics & Baseline characteristics (n = 45)

Table 1: Age and gender of included patients

Characteristics	Variables	Frequency
Age	Mean $\pm$ SD	50.71 $\pm$ 7.05 years
Gender	Male	3 (51.1%)
	Female	22 (48.9%)

Table 2: details of outcome variables of study

Characteristics	Variables	Values
Number of previous injections	Mean $\pm$ SD	7.22 $\pm$ 1.85
Duration of refractory DME	Mean $\pm$ SD	9.22 $\pm$ 2.4 months
Baseline IOP	Mean $\pm$ SD	13.4 $\pm$ 1.9 mmHg
Baseline EDTRS letters	Mean $\pm$ SD	49.33 $\pm$ 5.7
Baseline BCVA	Mean $\pm$ SD	0.72 $\pm$ 0.11
Baseline CST	Mean $\pm$ SD	638.04 $\pm$ 133.93 $\mu$ m

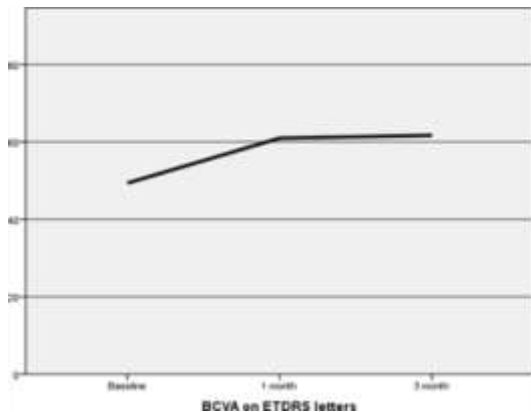


Figure 1(A): Baseline, one month after SCTA injection, and three months later BCVA on EDTRS letters

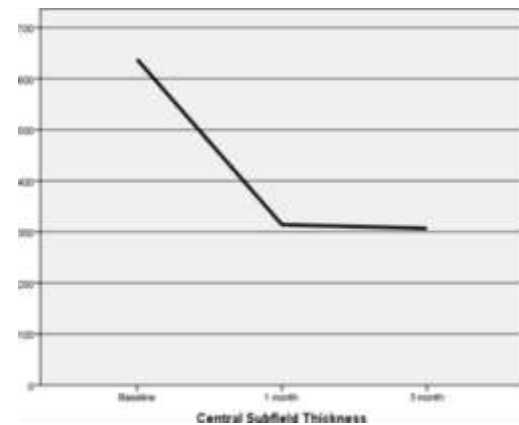


Figure 2 (B): Baseline, 1 month and 3 months later SCTA injections & central subfield thickness (CST) on EDTRS letters

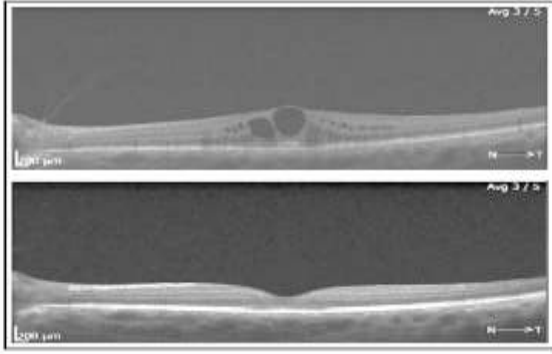


Figure 3 (A): SD-OCTs before and after SCTA injections reveal a notable decrease in CST.

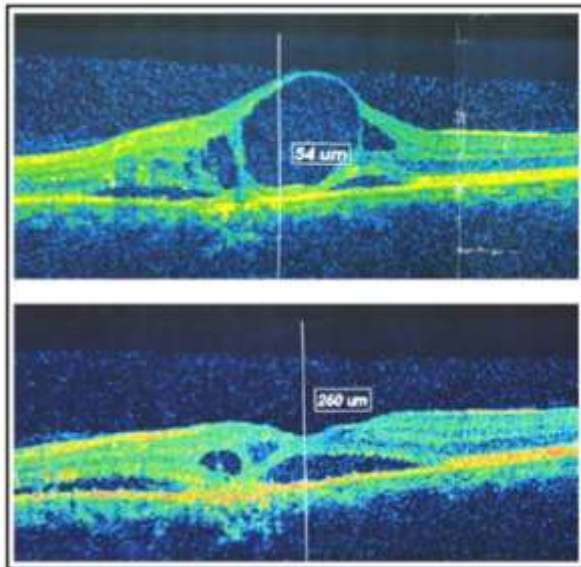


Figure 3 (B): SD-OCTs before and after SCTA injections reveal a notable decrease in CST

**DISCUSSION**

Diabetic macular edema is main cause of visual loss in diabetic patients. There are multiple options to treat DMO. Macular grid laser was initially treatment of choice to treat DMO. In 2010 macular grid laser was replaced by intravitreal anti VEGF injection. With the passage of time it was observed that 50% of DMO does not respond even after repeated injections of Anti VEGF.<sup>10</sup> So, researchers tried to experience other drugs and new routes of administration. Ozurdex, dexamethasone implants got popularity but could not be used routinely due to its adverse effect that is raised IOP. Intravitreal Triamcinolone acetonide also had some serious complications that is cataract & glaucoma.<sup>11,12</sup>

Suprachoroidal Triamcinolone Acetonide is comparatively new technique & new route of administration that is presumed to be having less adverse effect.<sup>13</sup> As in suprachoroidal injection, drug is in direct contact with choroidal vessel and retina, there are minimal chances of drug spill over to anterior chamber resulting in less chances of developing post injection glaucoma & cataract.<sup>14,15</sup> Different animal studies have proved the efficacy Suprachoroidal triamcinolone acetonide and saved anterior chamber from adverse effect of above mentioned drug.<sup>16</sup> The Hulk Trial was conducted by the Wykoff on the effectiveness of suprachoroidal triamcinolone acetonide in patients of DME (both previously treated and treatment naïve). In the refractory DME group, mean number of previously injections was 21.6, pre treatment CST was 473µm, pre IOP was 13.8mmHg and pre BCVA was 67.2 letters. After the follow up of 6

months of SCTA injection, CST was 302.66 µm and IOP was 14.2 mm Hg. BCVA was increased by seven letters on ETDRS chart. Two patients required glaucoma control as their IOP was rises.<sup>17</sup> In our study we take only previously treated DME patients who did not achieve sufficient macular edema control. Pre treatment values for IOP, BCVA and CST in our study were 13.4 mmHg, 49.33 letters and 638.04 µm. We follow the patients for only 3 months after SCTA injection. After 3 months of follow up IOP was 13.24 mmHg, BCVA was 61.7 letters and CST was 306.9 µm. IOP was increased in 2 patients in our study. The difference between the two studies might be due to sample size and follow up period difference. At the end both studies found SCTA injection effective as well as safe.

Another study conducted by Haroon Tayyab et al. on effectiveness of SCTA injection in resistant DME patients. Their pre treatment IOP, BCVA and CST were 13.37 mmHg, 0.8 and 636.5 µm.<sup>9</sup> Post 1 month IOP, BCVA and CST were 13.95mmHg, 0.47 and 304.54 µm and post 3 months were 13.45mmHg, 0.45 and 302.66 µm which are almost similar to the results of our study. The results of their study showed mean increase of 12 letters on ETDRS while our study showed mean increase of 16 letters. In only 1 patient, IOP was rise from 18 to 24 mmHg in their study. In our study, IOP was rise in two patients from 18 to 23 mmHg and 24 mmHg. Overall results of both studies favor the SCTA injection for treatment of refractory DME.

Lampen carried out their study on the anatomic changes after SCTA injection and they also found SCTA injections safe for the patients of DME.<sup>18</sup> Goldstein and DOGWOOD study used SCTA injection for treatment of non infectious uveitis and found SCTA injection efficacious for uveitis.<sup>13, 16</sup>

**CONCLUSIONS**

Suprachoroidal triamcinolone acetonide injection is effective and safe for treatment of patients suffering from refractory diabetic macular edema. It improves the visual acuity and central field thickness with no side effects after 3 months of treatment. The results of our study recommends the early switching to SCTA injection for patients non responsive to anti VEGF therapy.

**Limitation of the study:** There is no control or comparative group in this study so comparative studies should be performed. Suprachoroidal Triamcinolone Acetonide injection trials also be performed for treatment of other causes of macular edema patients.

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