

## Research Article

# Effectiveness of Suprachoroidal Triamcinolone Acetonide at Reducing Central Subfield Thickness in Diabetic Macular Edema, A Descriptive Case Series

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### Abstract

**Background:** Injection of corticosteroids into suprachoroidal space enables therapeutic drug levels to be attained in retina and choroid while minimizing them in anterior chamber. This helps deliver a higher drug concentration in posterior chamber whilst minimizing the potential side effects of conventional intravitreal steroid therapy, like cataract formation and increased intraocular pressure.

**Objectives:** To assess effectiveness of Suprachoroidal Triamcinolone Acetonide (SCTA) injection at reducing central subfield thickness in individuals suffering from diabetic macular edema (DME).

**Methods:** A Descriptive case series study was carried out at Department of Ophthalmology, Lahore General Hospital, Lahore from 1st July 2021 to 31st December 2021. A total of 150 treatment naive patients with DME, age range from 18-70 years and any gender, were selected. We excluded those patients that had history of uveitis, intraocular surgery, cataract, macular ischemia, and ocular hypertension or those with macular edema secondary to any other pathology. They were observed for three months after getting a SCAT injection. They were examined at one week, one month and third month. At the end of three months, the outcome measure was a change in central subfield thickness (CST) from the baseline.

**Results:** The patients in our study had age ranging from 18 to 70 years with a mean of  $51.10 \pm 9.53$  years. Most of the patients 114 (76.0%) had ages between 46 to 70 years. Out of these 150 individuals, 77 (51.33%) were males and 73 (48.67%) were females. Mean pre-injection CST was  $299.76 \pm 13.72 \mu\text{m}$  and after 3 months, it reduced to  $250.49 \pm 17.82 \mu\text{m}$ . Using paired t-test, the difference was found to be statistically significant with a p-value of 0.0001.

**Conclusion:** SCTA results in statistically and clinically significant decrease in DME

**Received:** 02-10-2023 | **1st Revision:** 24-05-2024 | **2nd Revision:** 18-07-2024 | **Accepted:** 26-08-2024

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**Keywords** | diabetic macular edema, suprachoroidal, triamcinolone acetonide.

### Introduction

Diabetes is considered the primary reason of blind-

ness in working age group and diabetic retinopathy (DR) is its most frequent and serious ocular complication.<sup>1</sup> Diabetic macular edema (DME) is the commonest cause of visual deterioration in these individuals and if left unattended, more than half of them can get deprived of around one line of visual acuity (VA) in as little as 2 years.<sup>2</sup> Thus, inflicting considerable burden both on our society and on patients themselves.



#### Production and Hosting by KEMU

<https://doi.org/10.21649/akemu.v30i4.5524>  
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The prevalence of diabetes mellitus in Pakistan is rising and is recently approximated to be around 7.6 to 11%.<sup>3</sup> DME is the commonest cause of central visual loss in these patients and intravitreal anti-VEGF treatment has been the mainstay of its treatment.<sup>4</sup> Some patients do not respond to, and some are not a good candidate for anti-vascular endothelial growth factor (VEGF) therapy. Rising cost can hinder proper compliance. Intra-Vitreous Triamcinolone Acetonide (IVTA) has long been used as a substitute, but it is notorious for its side effects. It is linked with elevated intraocular pressure and faster cataract progression.<sup>5</sup> Thus, suprachoroidal space for injecting steroids is a promising route.

Injection of corticosteroids into suprachoroidal space enables therapeutic drug levels to be attained in retina and choroid while minimizing them in anterior chamber.<sup>6</sup> The scleral spur prevents drug entry into anterior portion and a pressure differential inside the eye keeps the drug posteriorly within suprachoroidal space. This helps deliver a higher drug concentration in posterior chamber whilst minimizing the potential side effects of conventional intravitreal steroid therapy, like cataract formation and increased intraocular pressure.<sup>7</sup> Infectious endophthalmitis secondary to intravitreal injections is a potentially devastating complication.<sup>8</sup> The HULK trial conducted by Wykoff et al. reported that after suprachoroidal injection of triamcinolone acetonide, 89% of patients had a reduction in central subfield thickness to about 50%.<sup>9</sup>

Suprachoroidal route is not only being explored for treating diabetic complications, it has long been proven safe and effective for patients with macular edema secondary to uveitis.<sup>15</sup>

Since the introduction of various treatments for Diabetic Macular Edema, very limited studies have been performed on efficacy of suprachoroidal triamcinolone acetonide injection for the management of DME and they are encouraging enough for us to analyze the local therapeutic response to said treatment.

## Methods

Our study was a descriptive case series, carried out at the Department of ophthalmology, Lahore General Hospital, Lahore from 1st July 2021 to 31st December 2021.

A total of 150 patients were selected via non-probability,

consecutive sampling. Sample size was determined using 95% confidence level, a 5% margin of error and an estimated triamcinolone effectiveness of 89.0%.<sup>9</sup>

The study began after clearance from the hospital ethical review board. Each participant gave written informed consent before participating. If treatment was to be performed on both eyes, readings from the first injected eye were chosen and utilized. The participating surgeon was in charge of deciding whether the procedure was needed or not. Patients selected had an age range of 18-70 years with either type 1 or 2 diabetes. All of them had a central foveal thickness of 275 microns or more on SD-OCT and BCVA equal to or less than 20/40. None of them had ever received any former treatment. Those having macular edema due to any other pathology, history of previous intraocular surgery/ injection, cataract, uveitis, ocular hypertension, macular ischemia or an intra ocular pressure of more than 21 mmHg were excluded. Additionally, those who had previous intravitreal triamcinolone acetonide injections were also omitted;

During initial evaluation, Snellen best-corrected visual acuity (BCVA) was recorded. Afterwards, every participant had a thorough ocular examination which included assessment of anterior/posterior segment and IOP measurement via applanation. Central foveal thickness was recorded using an SD-OCT. These individuals were monitored for three months after SCAT injection. Follow up appointments were set at one week, one month and three months. Subsequently, IOP and CST were recorded at every visit for final evaluation. Variation in CST at the end of three months, compared to initial thickness, was the primary outcome measure. Efficacy was labeled as good if central subfield thickness returns to the normal range i.e.  $\leq 250$   $\mu$ m. BCVA was not taken as an outcome measure due to inconsistency in recording. Study data was recorded on a pre-decided proforma and interpreted using SPSS version 23. Mean and SD were estimated for age and CST at baseline and 3 months. Frequency and percentages were calculated for qualitative variables e.g., gender and efficacy.

Effect modifiers like age and gender were assessed. Paired t-test was utilized and P value  $\leq 0.05$  was considered significant.

Before injection, all patients had their pupils dilated, and an indirect ophthalmoscope was available to check

the fundus afterwards. Needle was withdrawn from a 24-gauge IV cannula and a 30-gauge 1cc insulin syringe (BD) was inserted in it. The cannula was cut so that its margin only revealed 1000µm of the insulin syringe. 0.1 ml TA was aspirated in the syringe and chosen eye was draped using aseptic measures. Injection location was imprinted 3.5-4 mm from the limbus, in suprotemporal quadrant. The needle was introduced perpendicular to sclera, into the suprachoroidal space and 4mg (0.1ml) triamcinolone acetonide was injected. To ensure minimum reflux, the needle was gently retracted, and a cotton-tipped bud was placed at the location of injection.

Indirect ophthalmoscope was used to establish permeability of central retinal artery and to record any inadvertent drug leakage into vitreous cavity. At the end, a prophylactic drop of antibiotic was placed in the fornix.

## Results

The patients in our study had age ranging from 18 to 75 years with a mean of  $51.10 \pm 9.53$  years. Most of the patients 114 (76.0%) had ages between 46 to 70 years. Out of these 150 individuals, 77 (51.33%) were males and 73 (48.67%) were females. Mean baseline central foveal thickness was  $299.76 \pm 13.72\mu\text{m}$  and after 3 months, it was  $250.49 \pm 17.82\mu\text{m}$ . On the other hand, mean Log MAR BCVA pre and post injection was recorded as  $0.5 \pm 0.22$  and  $0.4 \pm 0.30$  respectively. The difference between CST calculated before and after injection was found to be statistically significant with a p-value of 0.0001, calculated via paired t-test.

**Table 1:** Stratification of efficacy with respect to age and gender

Variable	Efficacy		P-value
	Yes	No	
18-45 years	25 (69.44%)	11 (30.56%)	0.093
46-70 years	94 (82.46%)	20 (17.54%)	
Male	64 (51.33%)	13 (48.67%)	0.239
Female	55 (75.34%)	18 (24.66%)	

In current study, SCTA injection was found effective at reducing CST in 119 (79.33%) patients. Males and recipients aged 46-70 responded better than their counterparts. During the brief followup, only 4 patients experienced a transient rise in IOP that did not require any medication. Table 1 displays the stratification of effectiveness across age and gender, while Table 2 depicts the pre and post-injection CST amongst them.

**Table 2:** Pre and Post-injection CST across age groups and gender

Variable	Pre injection CST Mean(SD)	p-value	Post-injection CST Mean(SD)	p-value
18-45 years	297.03(14.99)	0.292	253.06(17.37)	0.438
46-70 years	300.09(13.28)		249.68(17.96)	
Male	301.97(13.22)	0.478	249.01(15.39)	0.047
Female	296.60(13.79)		252.05(20.06)	

## Discussion

The supra-choroidal space is being utilized as a relatively novel approach for minimizing the chances of intraocular infiltration of drug while still bypassing sclera.<sup>10</sup> It is now possible to inject into the suprachoroidal space using microneedles, following the same protocol as intravitreal injections.<sup>11</sup> Triamcinolone acetonide [TA] is a corticosteroid analogue with more compelling anti-inflammatory activity than cortisone.<sup>12</sup> Multiple trials have shown its potential with relatively fewer side effects. It augments the endothelial cell junctions, thus regulating vascular permeability. It is beneficial for DME as it inhibits vascular endothelial growth factor [VEGF] and prevents angiogenesis.<sup>13</sup>

Our research has a greater number of patients than other local studies and it concerns treatment naive patients of DME. All prior studies have been conducted on refractory DME. The SCTA injection was found to be effective in 119 (79.33%) patients out of 150. Similarly, HULK Trial [N = 20], conducted in 2018, established the foundation of safety and effectiveness of SCTA for macular edema secondary to diabetes. Our study did not supplement the first SCTA injection with Aflibercept, like HULK trial did. The mean pre-treatment CST in HULK was 473 µm, while our study compiled it to be  $299.76 \pm 13.72\mu\text{m}$ . After 6 months, mean CST in HULK dropped down to 369 µm while ours reduced to  $250.49 \pm 17.82\mu\text{m}$  at 3 months follow up.<sup>9</sup>

Injecting triamcinolone acetonide in suprachoroidal space is a relatively novel way of treating multiple retinal vascular diseases. The TANZANITE study compared efficacy of intravitreal Aflibercept with and without SCTA, in individuals with macular edema post retinal venous occlusion. The outcomes demonstrated persistent edema reduction with better visual results, utilizing fewer injections in the SCTA and Aflibercept combi-

nation arm due to addition of SCTA.<sup>14</sup> Similarly, another study (DOGWOOD) came up with favorable outcomes in terms of success at persistent reduction of edema and enhanced BCVA, with the use of SCTA, for non-infectious posterior uveitis. 69% of their 22 enrolled subjects had reduced CST while 65% experienced improved vision at two months follow up.<sup>15,16</sup> In our study 79.33% individuals exhibited a decline in CST. Afterwards, the PEACHTREE Phase III trial assessed efficacy and safety of SCTA in terms of IOP and cataract formation.<sup>17</sup> Other than a brief augmentation of IOP in four of our subjects, lasting side effects were not observed.

In a local study, conducted on 22 patients with refractory DME, mean CST prior to SCTA was  $615.5 \pm 200.28$   $\mu\text{m}$ , while BCVA was  $0.9 \pm 0.20$ . Mean CST at three months was  $301.66 \pm 55.82$   $\mu\text{m}$  with BCVA of  $0.40 \pm 0.22$ . Before and after results for both BCVA and CST were statistically significant.<sup>18</sup>

In another local study on resistant DME, out of 24 patients, mean CST before SCTA was  $636.5 \pm 200.11$   $\mu\text{m}$  with BCVA  $0.8 \pm 0.24$  on ETDRS chart. Mean CST at three months after injection was  $302.66 \pm 66.93$   $\mu\text{m}$ , while BCVA  $0.45 \pm 0.27$  on ETDRS chart. Again, the results were statistically significant for change in CST and BCVA.<sup>19</sup> However, our study didn't take pre and post injection BCVA as an outcome variable, due to inconsistent data. The therapeutic impact of corticosteroid therapy delivered to suprachoroidal space is comparable to intravitreal treatment. Nevertheless, suprachoroidal route has less chances of IOP spike and a longer half-life. In addition, it is associated with much less anterior chamber concentrations compared to the intravitreal delivery.<sup>20</sup>

One of the limitations of our study was that significant improvements in visual acuity were not observed and the patients were not followed enough to recognize rebound edema. Despite these shortcomings, we have demonstrated the efficacy of a single dose of SCTA injection at treating DME in terms of CST. In the future, we need to conduct bigger and longer studies to strengthen the evidence in favor of suprachoroidal triamcinolone.

## Conclusion

Our study concludes that SCTA injection is clinically and statistically effective at reducing central subfield thickness in treatment naive patients with DME, with no

adverse consequences. Further studies assessing BCVA, with longer follow-up can potentiate the observation at hand.

**Ethical Approval:** The Institutional Review Board, Post Graduate Medical Institute, Lahore, Ameer Ud Din Medical College/ Lahore General Hospital, approved this study vide letter No. RefNo. 109/07.

**Conflict of Interest:** The authors declare no conflict of interest.

**Funding Source:** None

**Authors' Contribution:**

**MA:** Conception & design, analysis & interpretation of data, drafting of article, critical revision for important intellectual content, final approval

**AC:** Conception & design, critical revision for important intellectual content, final approval

**TG:** Critical revision for important intellectual content, final approval

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