ORIGINAL ARTICLE

Efficacy and Safety of Suprachoroidal Triamcinolone Acetonide in Refractory Diabetic Macular Edema in Khyber Teaching Hospital

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Abstract:

Objectives: To evaluate the efficacy and safety of suprachoroidal triamcinolone (SCTA) in patients with refractory diabetic macular edema at Khyber Teaching Hospital, Peshawar.

Methods: This was a quasi-experimental study carried out in the department of ophthalmology at Khyber Teaching Hospital, Peshawar, from 20th March 2023 to 20th March 2024. Data was collected from 101 patients with refractory diabetic macular edema using non-probability consecutive sampling technique. Best corrected visual acuity (BCVA), central macular thickness (CMT), and intraocular pressure (IOP) were assessed at baseline. The same clinical parameters were reassessed and analyzed at 1 week, 1 month and 3 months post SCTA injection. Data was analyzed through SPSS v 26.

Results: The mean age of the patients was 56.861 ± 6.59 years, and the mean duration of symptoms was 20.613 ± 5.41 months. Mean LogMAR BCVA showed statistically significant changes, being 0.792 ± 0.15 at baseline and 0.162 ± 0.07 after treatment ($p < 0.001$). CMT significantly decreased from 478.6 ± 43.3 µm to 312.5 ± 38.9 µm ($p < 0.001$). IOP did not significantly change ($p = 0.09$), and no patient experienced sustained IOP elevation. Efficacy and safety were observed in 84.2% and 87.1% of patients, respectively.

Conclusion: SCTA offer to be a highly effective and well-tolerated treatment option for patients with refractory diabetic macular edema, offering significant visual gain with a good safety profile. *Al-Shifa Journal of Ophthalmology 2025; 21(4): 212-219. Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

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Introduction:

Diabetic retinopathy represents one of the major ocular consequences of diabetes mellitus and is among the primary causes of visual impairment worldwide.[1] Advanced glycation end products (AGEs), key contributors to the pathophysiology of diabetes, are generated through persistent hyperglycemia.[2] Although the exact mechanisms remain not fully understood, diabetic retinopathy is recognized as a multifactorial disease influenced by several interrelated pathways.[2] AGEs, being osmotically active, facilitate fluid accumulation in the macula and are known to compromise the blood–retinal barrier (BRB), a pivotal step in the progression of diabetic macular edema (DME).[3] In addition, AGEs promote the production of pro-inflammatory mediators, such as vascular endothelial growth factor (VEGF), leukocyte adhesion molecules, and

activation of protein kinase C, thereby exacerbating retinal vascular dysfunction.[3] DME is a major contributor to the visual impairment in individuals with diabetes, affecting nearly one-third of this population according to epidemiological studies.[4] Patients with type 2 diabetes are more likely to have the condition than those with type 1 diabetes.[5] According to long-term follow-up studies, people's ten-year incidence of DME is roughly 20% in individuals diagnosed with diabetes before 30 years of age, increasing to nearly 40% in those diagnosed later in life.[6] DME is becoming of increasing importance, reflecting the rising worldwide prevalence of diabetes.

Intravitreal anti-VEGF therapy is the first-line treatment for DME over the past decade, demonstrating better results in improving visual acuity and reducing macular thickness.[7] However, its effectiveness is often compromised, as many cases tend to recur or show a suboptimal response, despite receiving multiple injections and switching between different anti-VEGF agents.[8] This group of patients are said to have refractory DME, typically defined as persistent macular edema despite receiving at least three intravitreal anti-VEGF injections over a minimum period of three to six months. Alternative management options include macular laser photocoagulation and intravitreal corticosteroids, such as triamcinolone acetonide (TCA).[9] Although intravitreal TCA has demonstrated a reduction in macular edema, repeated administration can lead to serious side effects, including cataracts and elevated intraocular pressure (IOP).[9]

Recent advancements have brought the suprachoroidal pathway to attention as an effective alternative of corticosteroid administeration.[10] Suprachoroidal triamcinolone (STCA) permits posterior segment-targeted drug delivery for potentially enhanced safety. The choroid's high vascularity further facilitates drug delivery to the macula while minimizing anterior segment exposure. This approach minimizes the risk of steroid-induced glaucoma and cataract formation associated with intravitreal injections.[11] Previous studies reported significant gains in best-corrected visual acuity (BCVA) and reduction in central subfield thickness (CST) in patients with refractory DME after SCTA. For instance, Jahangir et al. reported a significant decrease in CST and improvement in BCVA at 3 months after injection.[12] Likewise, Akhlaq et al. noted a 95.6% safety profile in patients who were treated with SCTA.[13]

Many patients in Pakistan have been unable to receive treatment due to the restricted availability of bevacizumab, leading to macular edema worsening and vision deteriorating.[14] Considering these challenges, along with the limitations of conventional intravitreal therapy and emerging evidence supporting the safety and efficacy of the suprachoroidal pathway, further exploration is warranted. In the present study, we aimed to evaluate the safety and efficacy of SCTA injection in refractory DME.

Methodology:

Over six months, from September 20, 2023, to March 20, 2024, this quasi-experimental study (one-group pretest–posttest design without a control group) was conducted in the department of ophthalmology at Khyber Teaching Hospital (KTH), Peshawar. The Hospital Ethical Committee approved the study (Reference no. 176/DME/KMC). Written informed consent and detailed history were taken from every patient.

Data was collected from 101 patients with refractory diabetic macular edema using non-probability consecutive sampling technique. Refractory DME was defined as persistent or worsening macular edema (CMT >300 µm) despite having received at least three intravitreal anti-VEGF injections with proper treatment interval (4-6 weeks) for a period of at least 3 months. Patients who had been treated only with a single anti-VEGF agent were eligible for

switching to another molecule before being categorized as refractory to anti-VEGF treatment. The sample size for the study was calculated by using WHO calculator based on assumption of 95% confidence level, 4% margin of error and expected safety rate (95.6%) of STCA from previous published work.[13]

Patients eligible for inclusion were adults between 40 and 70 years of age, any gender, with a documented diagnosis of DM and refractory DME as outlined above, BCVA worse than 6/12 (LogMAR > 0.3), CMT greater than 300 µm, and IOP below 21 mmHg. Patients who had a history of prior intraocular surgery, treatment-naive diabetic macular edema (those who had not received any prior anti-VEGF therapy), poor glycemic control (HbA1c > 8 mmol/mol), or a history of uveitis, ocular hypertension, cataract, or macular ischemia verified by fundus fluorescein angiography were excluded.

On follow-up days, patients visited the eye ward where a short history was obtained (number and type of previous anti-VEGF injections, dates at which previous injections were given, response to the earlier treatments, and control of blood sugar level) as well as any allergies specific to performing the procedure. After history taking, a detailed ocular examination was done. Baseline features, including BCVA measured on the Snellen visual acuity chart (converted to LogMAR), IOP measured using applanation tonometer, and CMT measured by optical coherence tomography with Spectralis (Heidelberg, Germany) equipment were recorded. All results were recorded in a pre-designed proforma.

Under aseptic conditions, TCA (0.1 mL) was injected in suprachoroidal space with a modified technique by a 30-gauge B-Braun syringe into the sclera through a 24 G intravenous cannula and customized sleeve attached to the end of it. The point of injection was 3.5 mm behind the limbus in pseudophakic and 4 mm posterior the limbus in phakic eyes. A needle was then inserted perpendicularly to the plane of sclera. The preparatory preparation for injection was instilling proparacaine hydrochloride 0.5% as topical anaesthetic and povidone-iodine 5% drops for antisepsis. After injection, indirect ophthalmoscopy was performed to exclude CRAO. Anterior chamber paracentesis through the limbus was performed in cases suspected of CRAO or IOP > 40 mmHg. All eyes received a prophylactic drop of moxifloxacin (Vigamox) after injection. Follow-up was done at 1 week, 1 month and 3 months following procedure. The efficacy variable was noted in terms of change in pre- and post-SCTA injection LogMAR BCVA > 0.5; safety was evaluated as a change in IOP from baseline.

All of the data was entered and analyzed through SPSS v26. 0. Numerical variables such as age, duration of complaints and differences in LogMAR BCVA were presented as mean ± SD. Categorical variables, including sex, response to treatment and safety endpoints were described in terms of frequency and percentage. Pre and post-intervention values were compared using paired t-test. Comparisons after stratification by age, gender and symptom duration were made using the chi-square test. P value ≤ 0.05 was considered as a statistically significant.

Results:

Study included over 101 patients with refractory DME. All patients had received at least three anti-VEGF injections in the past. The mean age of the participants was 56.9 ± 6.6 years; range, 40 ‑ 70 years. Summary of the demographic information is presented in Table 1.

Table 1. Characteristics of participants with refractory DME (n=101)

Parameter	Mean ± SD or Frequency (%)
Age (years)	56.86 ± 6.59
Duration of complaints (months)	20.61 ± 5.41
Gender	N(%)
Male	57 (56.4%)
Female	44 (43.6%)

Patients experienced substantial improvements in visual acuity after suprachoroidal injection. Mean LogMAR BCVA at baseline was 0.792 ± 0.15, which improved to 0.162 ± 0.07 after treatment ($p < 0.001$), showing a mean improvement of 0.641 ± 0.13 LogMAR units. Similarly, CMT significantly decreased from 478.6 ± 43.3 µm to 312.5 ± 38.9 µm ($p < 0.001$). There was no statistically significant difference in IOP ($p = 0.09$) (Figure 1).

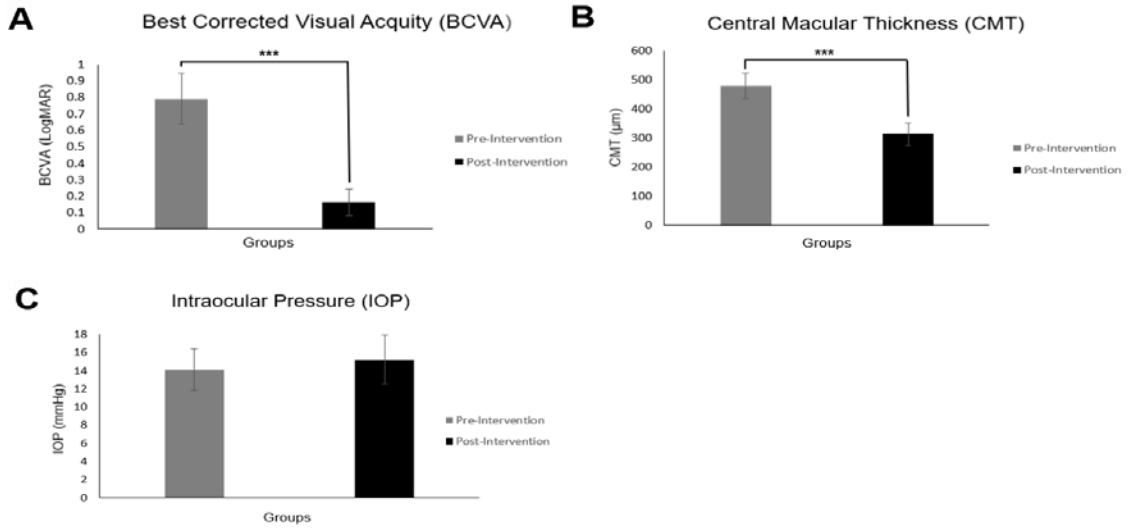

Figure 1. Bar graphs of clinical parameters after suprachoroidal triamcinolone administration in patients with refractory diabetic macular edema (n=101 at each time point). (A) LogMAR best corrected visual acuity (BCVA), (B) central macular thickness (CMT), and (C) intraocular pressure (IOP). The standard deviation is represented as error bars.***$p < 0.001$, suggesting significant improvement in BCVA and CMT after treatment.

Treatment efficacy was observed in 84.2% (n = 85) of patients, while safety (absence of adverse ocular events) was observed in 87.1% (n = 88). Patients between the ages of 40 and 55 experienced significantly greater efficacy (95.3%) than patients between the ages of 56 and 70 (75.9%) ($p = 0.008$). Efficacy outcomes were comparable across different genders and disease durations. Likewise, safety parameters showed no significant variation across age, gender, or complaint duration (Table 2 and Table 3).

Table 2. Efficacy and Safety Outcomes

Outcome	Frequency (n)	Percentage (%)
Efficacy	85	84.2
Safety	88	87.1

Table 3. Stratified Analysis of Efficacy and Safety

Variable	Sub-group	Efficacy (%)	p-value	Safety (%)	p-value
Age (years)	40–55	95.3	0.008	86	0.780
	56–70	75.9		87.9	
Gender	Male	80.7	0.279	87.7	0.840
	Female	88.6		86.4	
Duration of Complaints (months)	≤20	87.3	0.349	89.1	0.520
	>20	80.4		84.8	

Discussion:

In this study, SCTA resulted in significant enhancement of BCVA and decrease of CMT without a statistically significant reduction on IOP among patients with refractory DME. 84% of patients achieved treatment efficacy, and 87.1% had a favourable safety profile. There was a strikingly better benefit among the 40- to 55-year-old patients.

The findings suggest that SCTA is a safe and effective option for the management of DME refractory to anti-VEGF treatment, providing significant anatomical and functional improvement in terms of BCVA gain and CMT decrease. The lack of sustained IOP rise further supports the safety profile of suprachoroidal delivery; it may reduce the typical steroid-related burden associated with intravitreal deployment. All included patients had received at least three previous anti-VEGF injections and also were considered a truly refractory population, which differentiates this study and emphasizes SCTA as an option for second-line therapy when there is failed first-line treatment with anti-VEGF.

The findings of the present study show statistically significant increase in BCVA, confirming and expanding those reported in literature.[15] The average change in LogMAR BCVA indicates significant improvement in vision, which means better functional vision for the patients. Tayyab et al. in anti-VEGF-resistant cases, demonstrated a 41.25% increase in BCVA at 1 month and a 43.75% increment by the third month-follow-up.[16] Yaraghi et al reported similar results, demonstrating the SCTA's ability to improve visual loss in treatment-resistant DME.[17] Likewise, another study also showed patients treated with SCTA delivered by microneedle had a substantial increase in BCVA, reinforcing the effectiveness of such targeted deliveries.[18]

CMT represents the thickness of the foveal retina, where clear and detailed central vision is generated.[19] In DME, continuing vascular leakage causes fluid accumulation in the macula with CMT enlargement. Increased CMT is a characteristic of active macular edema, and highly associated with decreased visual function.[19] Moreover, a marked decrease in CMT was seen in our study, suggestive of increased macular edema resolution. This reduction of retinal swelling is thought to result from the anti-inflammatory and anti-vascular permeability effects of corticosteroids, which may modulate gene expression and VEGF production, along with other inflammatory mediators, administered through suprachoroidal injection.[20] Notably, such large CMT decrease observed in the reported study demonstrates resistance to anti-VEGF therapy which suggests that the combination of anti-inflammatory and anti-

permeability mechanism of corticosteroids may be beneficial when VEGF inhibition alone proves insufficient. Our results are in accordance with those of Yaraghi et al. and Jahangir et al who observed decrease in CST with SCTA.[12,17] A similar treatment effect was reported in one study that even demonstrated a marked reduction of CMT following SCTA.[21] However, However, in contrast to our work, which had a three-month follow-up, their study followed patients up to 12 months, allowing for evaluation of longer-term outcomes. These studies collectively corroborate the structural efficacy of SCTA in reducing retinal thickness.

The absence of a significant elevation in IOP following injection indicates that the suprachoroidal route may limit spread of corticosteroid to the anterior chamber and therefore decrease post-steroid ocular hypertension, a common side effect associated with intravitreal steroid. The rise in IOP following intravitreal triamcinolone has been demonstrated by Saric et al.,[22] and Batioglu et al.,[23] however, there were no significant differences found in our study. Yaraghi et al revealed that there was only a mild, non-threatening IOP increment after SCTA, verifying the fact that the suprachoroidal route could reduce anterior segment drug exposure and its side effects.[17] A series of Abdelshafy Tabl et al., study on refractory DME patients (due to ERM) also reported statistically significant decrease in IOP at 1 month following injection.[24] In contrast, Ateeq et al. reported a statistically significant elevation of the IOP at 1 and 3 months.[25] However, both studies concurred that no clinically relevant IOP elevation was observed at six months, indicating that the effect of IOP following SCTA could be short acting.

Our study also adds more evidence to support the use of SCTA as a treatment option for refractory DME patients. The remarkable anatomic and functional improvements, together with a low side-effect profile, suggests SCTA as a potential alternative therapy when anti-VEGF agents or other established therapies are ineffective. The present study also provides detailed characterization of prior anti-VEGF treatment history, clarifying the refractory nature of the cohort. This study is one of the few studies which stratifies results according to age, gender and symptoms duration that brings new insights and better comprehension of responses specific to each individual. The validity of the findings is increased by the utilization of both functional (BCVA) and anatomical (CMT) metrics. Nevertheless, this study has limitations. The single-arm nature and short duration of follow-up of the study restricts its applicability. In addition, the absence of a control group prevents direct comparison with alternative therapy modalities. The long-term safety, especially the recurrence of IOP and macular edema has not been studied. To confirm these findings and establish sustainability over the long term, longer follow-up periods are necessary, as well as more randomized controlled trials.

Conclusions:

In conclusion, this study provided an in-depth evaluation of SCTA as a method to treat refractory DME. The treatment had a favorable safety profile and led to a robust improvement in patients' BCVA. This indicates it as a promising therapeutic approach for the disease.

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