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Original Article

Outcome of Suprachoroidal Triamcinolone Acetonide in Resistant Diabetic Macular Edema

Muhammad Hannan Jamil[1*], Aneeb Ashraf[1], Asmatullah Khan[1], Bilal Ashraf[2], Muhammad Bilal Afzal[3] and Ferheen Shahbaz[3]

[1]Ophthalmology Department, Ali Fatima Hospital, Lahore, Pakistan
[2]LRBT Eye Hospital, Lahore, Pakistan
[3]Department of Public Health, University of the Punjab, Lahore, Pakistan

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***Corresponding Author:**
Muhammad Hannan Jamil
Ophthalmology Department, Ali Fatima Hospital, Lahore, Pakistan
dr.m.hannan@gmail.com

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ABSTRACT

One of the most frequent cause of central vision deterioration in people with retinopathy due to diabetes is diabetic macular edema. Suprachoroidal injections offer a novel way of delivery for the administration of corticosteroids that may have various benefits. **Objective:** To observe outcome of triamcinolone acetonide given by suprachoroidal route for the treatment of resistant diabetic macular edema. **Methods:** A descriptive case series study which was carried out at Department of Ophthalmology, Layton Rahmatullah Benevolant Trust Hospital Multan Road Lahore from July 14, 2021 till Jan 14, 2022. A total of 60 cases meeting selection criteria was taken after taking approval from hospital ethical committee. All injections were given by a single surgeon to avoid any related bias. 30-gauge 1cc insulin syringe was used in all cases. **Results:** The study included patients aged between 30 and 70 years, and the average age was 52.73 ± 10.99 years. There were 39(65%) male with 21(35%) female cases. The average central subfield thickness before and after one month was 593.62 ± 116.87 µm and 303.55 ± 31.29 µm with statistically significantly less mean central subfield thickness after 1 month, p-value less than 0.001. The mean visual acuity after correction before and after one month was 0.81 ± 0.16 and 0.45 ± 0.03 respectively, with statistically significantly less mean optimally corrected visual acuity after 1 month, p-value less than 0.001. **Conclusions:** It was found that suprachoroidal triamcinolone acetonide is useful in managing the central subfield and optimally corrected visual acuity in resistant diabetic macular edema.

INTRODUCTION

In recent decades, there has been a gradual rise in the prevalence of diabetes, which is expected to reach 430 million by 2030 [1]. Almost all the countries in the world have shown such large increase in DM prevalence. Diabetes causes numerous macrovascular and microvascular complications, which include diabetic retinopathy (DR) [2]. Macular edema is a major consequence of numerous inflammatory and vascular retinal disorders [3]. The risk of developing macular edema in diabetic patients is very high [4]. and the most prevalent reason of central vision deterioration in diabetic retinopathy patients is Diabetes-related macular edema [5, 6]. "Resistant diabetic macular edema is defined as if patient has at least three-monthly treatment of anti-vascular endothelial growth factor injections one month apart and still have central foveal thickness ≥ 300 µm on spectral-domain optical coherence tomography" [7]. VEGF and a number of inflammatory mediators are increased in diabetic macular edema-

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affected eyes [8]. This is one of the major reasons that an effective approach is essential in management of diabetic macular edema to avoid irreversible harm to visual function [9]. Inhibitors of vascular endothelial growth factor and corticosteroids have all proved effective in treating diabetic macular edoema [8]. Dexamethasone intravitreal implant, triamcinolone acetonide, and fluocinolone acetonide intravitreal implant are the three corticosteroids that are currently on the market; nevertheless, the effectiveness of each treatment option varies considerably [8]. Administration of corticosteroids through suprachoroidal injection has provided a new route of delivery which has proved quite advantageous [10]. As a result, there has been an increase in interest in exploring suprachoroidal space for drug administration. This has also been done in order to reduce the adverse effects of intravitreal steroids, despite all this, investigators have weighed the risk-benefit ratio of using the suprachoroidal delivery method for steroids to the posterior portion [5]. Furthermore, due to the reported adverse-effects of corticosteroids such as cataract progression and glaucoma they are still regarded as the second-line of treatment, especially in diabetic macular edema cases refractory to anti-VEGF agents [11]. If a patient with diabetic macular edema does not respond well to repeated injections of intravitreal bevacizumab, the doctor can try alternative anti-VEGFs, corticosteroids, or a macular laser. However, other reasons of macular edema like those of vitreomacular traction may be evaluated via optical coherence tomography, this may suggest surgical treatment. Focal areas of leakage from microaneurysms can be adjunctively identified via fluorescein angiogram, which might be responsive to laser treatment. To date, only a few smaller published uncontrolled studies can provide some insight to compare treatment regimens for refractory diabetic macular edema and no large randomized prospective clinical trials have been done so far [12]. In individuals with residual macular edema, (CSFT >300µm) shifting from bevacizumab to three monthly injections of 0.5 mg ranibizumab has been shown to be beneficial in a 12-month prospective non-randomized trial of 43 patients) [13]. An additional investigation revealed similar outcomes [5]. In order to treat refractory DME, Shoeibi *et al.*, evaluated the effects of combining 2 mg of triamcinolone acetonide with intravitreal bevacizumab. Adding triamcinolone acetonide had no additional benefits, he concluded, despite the fact that intravitreal bevacizumab injections are effective for treating refractory DME [14]. Therefore, the goal of this study was to evaluate how well resistant macular edema in the local population is treated by triamcinolone acetonide given by suprachoroidal route.

METHODS

A descriptive case series study was done at Department of Ophthalmology, Layton Rahmatulla Benevolant Trust Hospital Multan road Lahore after approval from hospital ethical committee. The study duration was 6 months from July 14, 2021 till Jan 14, 2022. We used non-probability consecutive sampling. A total of 60 cases are estimated using mean post injection optimally corrected visual acuity at one month as 0.47 ± 0.3^4 at 95% confidence level and as absolute precision (d) = 0. Inclusion criteria was patients having age 18-70 years, either gender reported as having resistant diabetic macular edema. Exclusion criteria was patients with macular ischemia, diagnosis of retinal vasculopathies besides diabetic retinopathy, glaucoma or ocular hypertension, vitreomacular traction, history of vitreoretinal surgery, intraocular surgery within the last 6 months, focal laser or pan-retinal treatments within the last 3 months. A total of 60 cases meeting selection criteria was collected form department of Ophthalmology, LRBT Multan road Lahore after taking an informed consent from patients. Their demographic details such as name, age, gender and contact details were taken. All injections were given by a single surgeon to avoid any related bias. 30-gauge 1cc insulin syringe was used in all cases. Additional commodities included injectable triamcinolone acetonide (TA) 40mg/ml and 24gauge intravenous branula. Before administering Supra-Choroidal Triamcinolone Acetonide, all patients were dilated, and an indirect ophthalmoscope was used for fundus examination. Only 1000 um of the insulin syringe remained visible at the branula's edge after the needle was removed from it and the branula was cut. The syringe was filled up to 0.1 ml point with Triamcinolone Acetonide. The eye was rinsed using a solution consisting of 10% povidone iodine. 5% of the solution was then applied to the fornices and left there for 30 seconds. An intraocular procedure-like drape was used to cover the eye. A point was marked in the supratemporal quadrant at 3.5mm from the limbus. After labelling, 0.1 ml of a 4 mg triamcinolone acetonide solution was instilled into the suprachoroidal region at a distance of 3.5 mm from the limbus in the aforementioned quadrant. The needle was placed at 90 degree to the sclera and with the bevel pointing backwards. To ensure minimal reflux, the needle was slowly removed, and the injection site was covered with an applicator with a cotton tip. The central artery of retina was immediately examined using indirect ophthalmoscopy, and any drug spillage in the vitreous cavity were noted. A 15-degree phacoemulsification incision knife was used to perform an anterior chamber paracentesis if the central artery of retinal was found to be occluded. One drop of a commonly used antibiotic was administered into the eye after the surgery. Premeasurement and Outcome i.e. central

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subfield thickness on OCT and BCVA on ETDRS chart was measured at one-month post injection as per operational definition. All data were collected by myself on attached Proforma. For data entry and analysis, SPSS version 25.0 was used. Mean ± S.D was calculated for age, duration of disease, before and after central subfield thickness and best corrected visual acuity. Frequency and % was calculated for categorical data like gender. Data were stratified for gender, age, duration of disease and HbA1C (controlled <7 and uncontrolled diabetes ≥ mellitus). The post-stratified paired sample t-test was used, with p-values of 0.05 or below considered notable.

RESULTS

The average age of patients was 52.73 ± 10.99 years with minimum and maximum 30 and 70 years. There were 24(40%) cases who were 30-50 years old and 36(60%) case were 51-70 years old. There were 39(65%) males and 21(35%) females. The mean duration of 5.12 ± 1.40 years, with minim 4 and 10 years. There were 46(76.7%) case who had duration of disease since ≤ 5 years and 14(23.3%) cases had duration since > 5 years. A total of 38(63.3%) patients had controlled and 22(36.7%) patients had uncontrolled diabetes. The mean central subfield thickness before and after one month was 593.62 ± 116.87 µm and 303.55 ± 31.29 µm with statistically significantly less mean central subfield thickness after 1 month, p-value < 0.001. (Table 1).

Table 1: Central subfield thickness (pre and after 1 month)

Central subfield thickness		
	Pre	**At 1 month**
Mean ± SD	593.62 ± 116.87	303.55 ± 31.29
Range	392.00	99.00
Minimum	407.00	251.00
Maximum	799.00	350.00

t-test = 18.962, p-value < 0.001

The average optimally corrected visual acuity before and after one month was 0.81 ± 0.16 and 0.45 ± 0.03 respectively, with statistically significantly less mean best corrected visual acuity after 1 month, p-value less than 0.001 (Table - 2).

Table 2: Best corrected visual acuity (pre and after 1 month)

Best corrected visual acuity		
	Pre	**At 1 month**
Mean ± SD	0.81 ± 0.16	0.45 ± 0.03
Range	0.51	0.10
Minimum	0.58	0.40
Maximum	1.09	0.50

t-test = 16.22, p-value < 0.001

When data were clustered for age, gender, duration and HbA1c, mean central subfield thickness and optimally corrected visual acuity after one month was statistically reduced in each stratum, p-value < 0.001 (Table 3 to 6).

Table 3: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to age groups (years)

Age groups (years)	Central subfield thickness	Mean ± SD	t-test	p-value
30-50	Pre	599.42 ± 131.38	10.768	<0.001**
	1 month	308.54 ± 32.39		
51-70	Pre	589.75 ± 107.91	15.753	<0.001**
	1 month	300.22 ± 30.54		
Best corrected visual acuity				
30-50	Pre	0.79 ± 0.16	9.471	<0.001**
	1 month	0.46 ± 0.03		
51-70	Pre	0.82 ± 0.16	13.211	<0.001**
	1 month	0.45 ± 0.03		

**Highly Significant

Table 4: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to gender

Gender	Central subfield thickness	Mean ± SD	t-test	p-value
Male	Pre	585.13 ± 105.38	16.717	<0.001**
	At 1 month	304.38 ± 29.70		
Female	Pre	609.38 ± 137.10	9.951	<0.001**
	At 1 month	302.00 ± 34.77		
Best corrected visual acuity				
Male	Pre	0.80 ± 0.16	12.605	<0.001**
	At 1 month	0.45 ± 0.03		
Female	Pre	0.82 ± 0.16	10.075	<0.001**
	At 1 month	0.45 ± 0.03		

**Highly Significant

Table 5: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to duration (years)

Duration (years)	Central subfield thickness	Mean ± SD	t-test	p-value
≤ equal 5 years	Pre	599.63 ± 116.06	17.152	<0.001**
	At 1 month	301.17 ± 31.27		
>5 years	Pre	573.86 ± 121.74	8.173	<0.001**
	At 1 month	311.36 ± 31.21		
Duration (years)	**Best corrected visual acuity**	**Mean ± SD**	**t-test**	**p-value**
≤ equal 5 years	Pre	0.81 ± 0.15	14.794	<0.001**
	At 1 month	0.45 ± 0.03		
>5 years	Pre	0.81 ± 0.18	6.785	<0.001**
	At 1 month	0.45 ± 0.03		

**Highly Significant

Table 6: Comparison of Central subfield thickness (pre and after 1 month) and Best corrected visual acuity (pre and after 1 month) with respect to HbA1c

HbA1c	Central subfield thickness	Mean ± SD	t-test	p-value
Controlled	Pre	598.84 ± 115.84	15.153	<0.001**
	At 1 month	305.84 ± 33.35		
Uncontrolled	Pre	584.59 ± 120.82	11.150	<0.001**
	At 1 month	299.59 ± 27.66		

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HbA1c	Best corrected visual acuity	Mean ± SD	t-test	p-value
Controlled	Pre	0.80 ± 0.16	11.596	<0.001**
	At 1 month	0.45 ± 0.03		
Uncontrolled	Pre	0.83 ± 0.15	12.027	<0.001**
	At 1 month	0.45 ± 0.03		

**Highly Significant

DISCUSSION

Several researches have looked into various techniques to treating diabetic macular edema (DME), a disorder that affects the retina in diabetics. Ahmadieh *et al.*, investigated the long-term outcomes of intravitreal bevacizumab, with or without triamcinolone, for refractory DME [14]. Al Rashaed and Arevalo explored the potential of combination therapy for DME, taking into account the utilization of multiple therapeutic modalities to successfully address the condition [15]. Patel *et al.*, investigated suprachoroidal drug administration using hollow microneedles, proposing a novel method for delivering drugs to the back of the eye [16]. We investigated diabetic macular edema (DME) as one of the primary reasons contributing to patients' deteriorating vision who have diabetes mellitus (DM). Diabetic macular edema (DME) is commonly associated with visual impairment in persons with diabetic retinopathy (DR). Laser photocoagulation is one way for treating people with DME. It can retain or increase visual acuity but can potentially reduce contrast sensitivity, color vision, and range of vision. The suprachoroidal region has attracted interest as a possible route for ocular medication administration. Emami-Naeini and Yiu examined different medical and surgical applications for the suprachoroidal area, emphasizing its potential for drug delivery to the posterior portion of the eye [17]. Specific investigations looked into the efficacy of suprachoroidal medication administration in the treatment of DME. Jahangir *et al.*, investigated the effect of suprachoroidal triamcinolone injection on refractory DME, whereas Yousef *et al.*, investigated the use of triamcinolone acetonide injection in cases of DME [18, 19]. Rai *et al.*, went on to highlight the suprachoroidal channel as a new medication delivery route to the back of the eye, highlighting its potential benefits for treating disorders such as DME [20]. The intravitreal injection of steroids has been demonstrated to reduce macular edema caused by various eye disorders. Lastly, Seiler *et al.*, conducted an ex-vivo study to investigate the effect and distribution of contrast medium after injection into the anterior suprachoroidal space. This work shed light on the anatomical characteristics of this drug delivery method [21]. In summary, several studies have been conducted to investigate the possibility of intravitreal and suprachoroidal medication administration for the treatment of DME. While some research looked at the long-term effects of certain treatments, others focused on the suprachoroidal space's potential as a unique drug delivery channel. The findings emphasize the importance of more research to completely comprehend the efficacy and safety of these therapy approaches for diabetic macular edema. Diabetic macular edema (DME) is one of the major causes of failing eyesight in people with diabetes mellitus (DM). Diabetic macular edema (DME) is commonly associated with visual impairment in persons with diabetic retinopathy (DR). Laser photocoagulation is one way for treating people with DME. It can retain or increase visual acuity but can potentially reduce contrast sensitivity, color vision, and range of vision. Steroid injections intravitreally have been shown to alleviate macular edema caused by a variety of eye conditions.

CONCLUSIONS

It is concluded that suprachoroidal triamcinolone acetonide in resistant diabetic macular edema is useful to manage the central subfield and best corrected visual acuity. Hence it can be used to improve patient's visual conditions and to improve their quality of life.

Authors Contribution

Conceptualization: MHJ, AA
Methodology: AK
Formal Analysis: BA, MBA
Writing-review and editing: MHJ, AA, AK, BA, MBA, FS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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