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EFFECTIVENESS OF SUBTENON BEVACIZUMAB INJECTION ON DIABETIC MACULAR EDEMA AND BEST CORRECTED VISUAL ACUITY TEST

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ABSTRACT

Background: Diabetic macular edema (DME) is a major cause of visual impairment in diabetic patients. Treatment modalities include intravitreal triamcinolone acetonide, pars plana vitrectomy, and antivascular endothelial growth factor (VEGF) therapy. Intravitreal anti-VEGF agents have revolutionized DME treatment, with some studies suggesting better visual acuity compared to posterior sub-Tenon injection (STB). **Aim of the study:** To evaluate the effectiveness of sub-Tenon injections of bevacizumab for the treatment of macular edema. **Patients and Methods:** A non-comparative, prospective interventional case series included 47 patients with diabetic macular edema that was clinically substantial were joined. Monthly macular photocoagulation was carried after following STB injections. history of intraocular surgery, retinal laser photocoagulation, high refractive errors, media opacity, glaucoma, ischemic optic neuropathy, uveitis, retinal vascular occlusion, diseases of the vitreomacular interface, and panretinal photocoagulation were among the exclusion criteria. Version 26 of SPSS was used to compile and analyze the data. **Results:** The experimental analysis included 47 patients, with a mean age of 57.62 years and 61.7%) being males. The mean OCT scores before treatment were 328.34 μm. Only 12.8% had both eyes affected, and there was no significant increase in OCT results after treatment. The McNemar Bowker test was insignificant for the Best Corrected Visual Acuity test. **Conclusion:** The current study concluded that the sub-tenon injection of the Bevacizumab had no role in treatment of DME.

KEYWORDS: Bevacizumab, Macular degeneration, Treatment outcome.

INTRODUCTION

The primary cause of visual impairment in diabetic patients is diabetic macular edema (DME).[1] Focal/grid laser photocoagulation for clinically severe macular edema has been shown to effectively lower the risk of moderate vision loss, according to the Early Treatment of Diabetic Retinopathy Study. Subsequent research revealed that grid laser photocoagulation is not very effective and may worsen eyesight due to subretinal fibrosis and progressive macular scarring.[2] Since macular laser photocoagulation has not yielded satisfactory results, many therapeutic approaches have been assessed, such as intravitreal triamcinolone acetonide (TA), pars plana vitrectomy, and antivascular endothelial growth factor (VEGF) therapy.[3]

Since DME is brought on by numerous, intricate pathological mechanisms, its pathophysiology remains incompletely understood.[4] As a key modulator of the breakdown of the blood-retinal barrier, VEGF plays a crucial role in the development of macular edema and fluid leakage[5], making it a prime candidate for pharmaceutical intervention.[4] Because intravitreal anti-VEGF medicines have shown improvement in vision in several randomized clinical trials, they have completely changed the therapy of DME.[6]

Based on the search results, there is some research comparing the effects of sub-Tenon and intravitreal injections for Diabetic Macular Edema (DME), specifically concerning the drug Bevacizumab. However, the comparisons are generally with other drugs or methods, such as triamcinolone.[7]

Few studies have compared the effects of preservative-free intravitreal Bevacizumab (IVB) and posterior sub-

Tenon Bevacizumab injections for DME, but the results are not consistently clear[6,8], some studies suggest that intravitreal Bevacizumab might achieve better visual acuity compared to posterior sub-Tenon injections of triamcinolone acetonide at 6 months.[8,9] The evaluation of intravitreal Bevacizumab and sub-Tenon triamcinolone acetonide for the management of macular edema due to the occlusion of retinal vein also indicates that intravitreal Bevacizumab may be more effective.[10] Chronic diabetic macular edema was successfully treated with sub-Tenon's bevacizumab injection in a dose of 2.5 mg/0.1 ml, according to a case series.[11] The effects of intravitreal Bevacizumab and posterior subtenon injection of triamcinolone in diffuse diabetic macular oedema are compared, and the results of the former seem to be superior.[9]

AIM OF THE STUDY

To evaluate the effectiveness of sub-Tenon injections of bevacizumab for the treatment of macular edema.

PATIENTS AND METHODS

The prospective non-comparative interventional case series involved 47 patients in total between April 2022 and April 2023. Clinically severe diabetic macular edema affected each patient. All patients underwent macular photocoagulation one month following STB injections.

The exclusion criteria included any history of intraocular surgery within the previous eight months, the use of laser photocoagulation for the retina, high refractive errors (>6 diopters of sphere or >3 diopters of cylinder), media opacity affecting visual acuity and optical coherence tomography (OCT) measurements, a history of glaucoma or intraocular pressure greater than 22 mmHg, retinal vascular occlusion, ischemic or inflammatory optic neuropathy, uveitis, disorders of the vitreomacular interface, and the requirement for panretinal photocoagulation. Every individual who satisfied the inclusion criteria had both of their eyes enrolled.

A full ophthalmic examination was conducted, which included a slit lamp and dilated fundus examination, as well as the best corrected visual acuity assessment (BCVA) using a standard Snellen chart (converted to LogMAR). A 3D spectral domain OCT-1000 instrument (software version 3.32.003.04, Topcon Incorporation, Tokyo, Japan) was used to quantify macular thickness. All measurements were made using a 3D Scan 512 × 128 procedure, which covered a 6 × 6 mm2 area centered on the fovea. Pictures that have discontinuity, misalignment, involuntary saccades, blinking artifacts, discontinuity, or a quality factor of less than 45 were not included. Prior and a month after STB injections, measures for BCVA and OCT imaging were obtained.

Every injection was given in the office. In the fornix, one drop of 5% povidone-iodine was injected after one drop of tetracaine. The surgeon did not use a speculum and kept the lids open. The patients were instructed to examine the shoulder on the other side. Using a 27-gauge needle supported by direct view, the sub-tenon's injections were made into the superotemporal fornix (as far posteriorly as could be clearly observed, almost more than 8 mm from limbus). A 2.5 mg dose of bevacizumab in a 0.1 mm volume was used in each injection.

Excel was used to summarize the data, and SPSS version 26 was used for analysis. Two tests were performed to assess the impact of the Avacitin injection intervention. The first was the McNemar Bowker test, which assessed the relationship between the enhancement of vision quality prior to and following treatment, and the second was a paired sample t-test, which assessed the variations in OCT results between pre- and post-treatment.

RESULTS

Of the 47 patients that were part of the experimental study, 29 (61.7%) were male, and their mean age was 57.62 years ± 11.47. The mean OCT scores before treatment was 328.34± 106.86 µm with a minimum score of 138 µm and maximum score was 612 µm. As shown in table (1), the frequency of the affected eyes was presented in which only 6 patients (12.8%) were admitted with both eyes affected. This table showed that there was non-significant increase in OCT results after treatment (p=0.173).

Table 1: Descriptive results of the study population.

Variables		**No.**	**%**	
Gender	Male	29	61.7	
	Female	18	38.3	
Eye Affected	Left	22	46.8	
	Right	19	40.4	
	Both	6	12.8	
Overall improvement	Yes	3	6.4	
	No	43	91.5	
	Deteriorated	1	2.1	
Variable		**Mean**	**Standard Deviation**	**p-value ***
Age		57.62	11.477	--------
OCT before treatment (µm)		328.34	106.862	0.173
OCT after treatment (µm)		356.59	171.160	
**Paired t-test has been used*				

Improvement of the eye and sight quality were evaluated before and after treatment as shown in table (2) using the Best Corrected Visual Acuity (BCVA) test. The McNemar Bowker test was insignificant, which mean that there was no significant association between the two set of results before and after.

Table 2: The Best Corrected Visual Acuity results of the study population.

BCVA	Before treatment		After treatment		p-value*
	No.	%	No.	%	
Mild	11	23.4	12	25.5	NS
Moderate	21	44.7	21	44.7	NS
Severe	7	14.9	7	14.9	NS
Very severe	8	17.0	7	14.9	NS
** McNemar Bowker test has been used; NS=not significant*					

DISCUSSION

While intravitreal injection is the most commonly employed technique for administering anti-VEGF in ophthalmology, other approaches have been assessed. Anti-VEGF intravitreal injections have the potential to cause a number of unique side effects, such as endophthalmitis, intraocular inflammation, and lens damage. Adverse outcomes are more likely when injections are required often. Furthermore, a lot of surgeons think that the injections have to be carried out in the operating room. In a small population of patients who are uncomfortable receiving intravitreal injections, STB injection may be a safe substitute for bevacizumab injections, despite the fact that its effect on retinal thickness appears to be less than that of intravitreal injection. Furthermore, larger STB dosages might provide results similar to intravitreal injection.[11,13]

In this study, using of the sub-tenon injection instead of intravitreal injection of studied to evaluate its effectiveness in treatment of DME.

The current study included 47 patients diagnosed with DME; 61.7% were males and the left eye was the most prominent affected side and the overall improvement was detected in only 46.8%. The OCT was measured before and after the sub-tenon injection; before the treatment, the OCT was 328.34±106.862 µm that showed an increase up to 356.59±171.160 µm after the treatment.

Bevacizumab used topically and subconjunctivally has been shown in several studies to be effective in treating corneal neovascularization.[14] According to Kim *et al*.[15], bevacizumab entered the rabbits' anterior chamber following a single 2.5 mg subconjunctival injection. Nomoto *et al*.[13] assessed the pharmacokinetics of bevacizumab in groups of rabbit eyes and found that following sub-tenon bevacizumab injection of 1.25 mg, the greatest concentrations were observed in the iris/ciliary body as, well as, retina/choroid, respectively, at 1418.7 and 295.8 ng/g. They demonstrated that during 8.6 and 8.4 weeks, respectively, the bevacizumab level in both iris/ciliary body and retina/choroid was kept above half-maximum inhibitory concentration. Furthermore, compared to intravitreal injection, they discovered that bevacizumab had a longer half-life in the iris/ciliary body and retina/choroid following sub-tenon injection. They suggested that this might be a byproduct of bevacizumab's scleral depot binding to the scleral matrix, which results in prolonged distribution of the medication into the intraocular tissues. Additionally, Liang *et al.*[16] assessed the efficacy of STB injection in treating nine eyes with myopic CNV. In certain situations, all 9 eyes received repeated injections of 12.5 mg of STB after two weeks. In eight eyes, they documented total absorption of sub-retinal fluid. After intravitreal injection of anti-VEGF drugs, previous investigations have shown a considerable reduction in macular thickness in those with untreated eye.[17,18] Retinal vessels may allow a tiny but potent portion of the medication to enter the systemic circulation and arrive at the retina. This could be taken into account as a different theory explaining the impact of the bevacizumab injection given to the sub-tenon.

The present study showed that the patients under the study had different classification according to the pre-treatment BCVA test and there were no significant difference from post-treatment BCVA test. Previous researches has demonstrated that there is not always a significant correlation between retinal thickness measurements and BCVA, and that more significant factors to consider include the retina's morphologic characteristics, such as the shape of cystoid spaces, the existence of subretinal fluid, and the integrity of the outer layers.[19,20]

There are various restrictions on our investigation. There is a little sample size. There was not much follow-up. The levels of VEGF in the anterior chamber and vitreous were not measured. Furthermore, the study lacks a matched control group and is therefore non-comparative.

CONCLUSION

The current study concluded that the sub-tenon injection of the Bevacizumab had no role in treatment of DME.

Conflict of interest

The authors declared that there is no conflict of interest.

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