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ORIGINAL ARTICLE

To Determine the Efficacy of Suprachoroidal Triamcinolone Injection for the Treatment of Refractory Diabetic Macular Edema

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ABSTRACT

Goal: To determine the safety and effectiveness of suprachoroidal triamcinolone injections (SCT) in refractory diabetic macular edema cases.

Study Design: An Interventional case series.

Place and Duration: In the Ophthalmology department of Allama Iqbal Memorial Teaching Hospital, Sialkot for six-months duration from January 2021 to June 2021

Methods: A total of 40 eyes from patients with type-I or II diabetes who were over the age of 18 years and were included. Inclusion criteria for the study included patients with treatment resistant central Diabetic Macular Edema of at least 320 um or above (as determined by Zeiss Cirrus HD-OCT) and a BCVA of equal to or less than 20/40. The central subfield thickness (CST), BCVA, and intraocular pressure (IOP) were all documented. Patients who had received suprachoroidal triamcinolone (SCTA) were monitored for 3-months and the similar clinical parameters were noted, and the findings were noted.

Results: The results showed that 22 (55%) of the 40 patients were female and 18 (45%) were male. The 0.9± 0.22 was the mean log MAR BCVA and 612.89± 195.58 um was the mean pre-injection CST. In the first and third months, the mean post-injection CST was 308.59± 56.75um and 304.89± 54.29um, respectively. After injection at 1 and 3-months, the mean log MAR BCVA was 00.51± 0.3 and 0.36 ±0.20, correspondingly. At the first and third months, the results for pre- and post-injection CST were statistically significant (p value <0.00001).

Conclusion: The reduction of refractory diabetic macular edema and improvement of macular thickness on OCT can both be accomplished safely and effectively using CST.

Keywords: Central subfield thickness, suprachoroidal triamcinolone, diabetic macular edema.

INTRODUCTION

As a result of hyperglycaemia; rupture of the blood-retinal barrier, fluid from the retinal arteries leaks into the surrounding neuronal retina, resulting in diabetic macular edema (DME)[1-2]. DME is identified when there is increased macula-related retinal thickness. In diabetic patients, DME affecting a central subfield that affects the fovea is a communal reason of loss of vision[3]. In opposite, the vision is not affected by non-center-involving DME. Any stage of diabetic retinopathy can lead to DME[4-5]. Current algorithms for pharmacological intervention in DME identify DME on the involvement basis of non-center involvement and center involvement using simple OCT-based classification. On OCT scans, the central subfield of the retina looks thickened in DME with central involvement. A DME is considered non-center-involved if it doesn't affect the central subfield. For the majority of eyes with central involved macular DME, particularly those with visual impairment, anti-VEGF are currently considered the first line of treatment[6]. Eylea (Leverkusen, Bayer, Germany), Avastin (Genentech Inc., CA, San Francisco, USA) and Lucentis (Novartis, Basel, Switzerland) are common anti-VEGF agents. Although this treatment has been permitted by the FDA but every patient not get benefit from it[7].

Since intravitreal triamcinolone acetonide (IVTA) has long been an alternate treatment for anti-VEGF VEGF, corticosteroids are beneficial options for eyes not suitable for anti-VEGF treatment or have not fully responsiveness to past anti-VEGF treatment or when compliance is a problem[8]. IVTA is very effective for repairing the blood-retinal barrier and treating macular edema, its usage has been hampered by some unfavourable side effects[9]. One is the necessity for additional injections as a result of the IVTA waning effects followed by the recurrence of macular edema. Topical steroids have been demonstrated to be beneficial as first-line therapy in specific clinical conditions. It also causes increased intraocular pressure (IOP) and cataract formation[10]. The Diabetic Retinopathy Clinical Research Network (DRCR.net) Protocol shows that pseudophakic DME reacts to steroids and ranibizumab equally effectively. Patients that received IVTA, however, experienced clinically substantial IOP elevations[11]. As authors discover novel techniques for administering steroids to the eye, interest in steroids has recently surged. The two most notable are Iluvein® and Ozurdex®. The implant of intravitreal dexamethasone Ozurdex (Allergan, Irvine, USA) is intended to stay in the vitreous cavity for 6-months before biodegrading. The steroid is released gradually into the vitreal cavity[12]. The FDA and the majority of European nations have approved it for use in DME patients. Numerous researches have demonstrated that using Ozurdex® is also related with elevated IOP. Other significant obstacles to its use in Pakistan are price and availability[13]. The retina may experience therapeutic concentrations of corticosteroids after being injected into the suprachoroidal region, while these concentrations decline in the anterior part of the eye. This may be effective in treating posterior segment disease while lowering the chance of rapid cataract formation and intraocular pressure increase brought on by injection of intravitreal corticosteroid[14].

The goal of this study was to determine the safety and effectiveness of suprachoroidal triamcinolone injections (SCT) in refractory diabetic macular edema cases.

METHODS

This Interventional case series was held in the Ophthalmology department Allama Iqbal Memorial Teaching Hospital, Sialkot for six-months duration from January 2021 to June 2021. The hospital's ethics committee approved this study. All participants gave their informed consent. 40 patients in total were enrolled in the study and selected by convenient sampling technique. Inclusion criteria for the study included patients with treatment resistant central Diabetic Macular Edema of at least 320 um or above (as determined by Zeiss Cirrus HD-OCT) and a BCVA of equal to or less than 20/40. Patients with macular ischemia (confirmed by fluorescein fundus angiography), cataracts, ocular hypertension, uveitis, IOP > 21 mmHg, macular edema attributable to any other cause and prior intraocular surgical procedure were omitted from the study. Patients who had had an intravitreal or periocular dose of triamcinolone acetonide during the preceding six

months, as well as prior anti-VEGF medication within the previous ninety days, were also not included.

Treatment resistance was definite as DME not responding to 3 injections anti-VEGF (of any type) given after one month duration. BCVA and/or central subfield thickness (CST) by spectral domain optical coherence tomography were used to determine non-response (Zeiss Cirrus HD-OCT). DME is considered to be refractory if, one month afterwards the 3rd injection of anti-VEGF, no improvement in BCVA of more than five letters or CST did not drop by 50 m or 10% from baseline. At the beginning of the study, every participant got a thorough ophthalmologic assessment that comprised measuring their IOP (with Goldmann applanation tonometer) and evaluation of their anterior and posterior segments. The patients were followed-up for one-week, one-month, and three-months following injection. At every subsequent visit, IOP, CST and BCVA were noted for use in the final analysis of data. Changes in CST and BCVA from the beginning to the end of the 3-month period were the main efficacy outcomes. SPSS 20.0 was used to analyse the data. We conducted significance tests for normal and skewed continuous data using the paired t-test and the Wilcoxon signed-rank test, correspondingly. A p-value of less than 0.05 was regarded as statistically significant.

In this analysis; 40 eyes from 40 participants were studied. We measured intraocular pressure (IOP), BCVA and CST. The patients were re-examined on 1 and 3 months after receiving SCTA, the similar clinical parameters were once again documented for data analysis. With the use of a 30 G, 1 cc insulin syringe, SCTA injection was given. Prior to SCTA, all patients had their pupils dilated, and an indirect ophthalmoscopy was done to evaluate the fundus after the injection. Only the 1000 um insulin syringe was visible from the branula edge after the needle was taken out and trimmed. The syringe was filled with TA to the 0.1 ml mark. A 10% solution of povidone iodine was used to paint the eye, then 5% of it wasinstilled into the eye's fornices and left for thirty seconds in the fornices. Similar to other intraocular procedure, the eye was draped in the same way. The area was marked 3.5 mm from the limbal area in the supratemporal quadrant. A bevel was posteriorly pointing at 3.5mm distance from the limbal area in the mentioned quadrant, and triamcinolone acetonide at dosage of 4 mg (0.1 ml) was given into the suprachoroidal space after marking. The needle was positioned at the sclera perpendicularly during this procedure. To ensure minimum reflux, the needle was carefully removed, and a cotton-tipped applicator was placed to the injection site. After that, an indirect ophthalmoscopy was done to check the central retinal artery patency and to look for any signs of drug infiltration into the vitreal cavity. If the occlusion of central retinal artery was noted, the paracentesis of anterior chamber was done using a phacoemulsification -incision knife. Instillation of one drop of antibiotic was done into the eye following injection.

RESULTS

The study included a total of 40 eyes from 40 participants. The results showed that 22 (54.54%) of the 40 patients were women and 18 (45.45%) were men. The patients' mean age was 51.07 ± 15.59. There had been 6 previous injections on average. A total of 11 injections were given in maximum with four being the minimum. The mean CST value prior to injection was 612.89± 195.58 um.

Table-1: shows the demographic features of the patients

Characteristics	No
Males	18(45%)
Females	22(55%)
Mean Age	51.07 ± 15.59
Mean Pre-injection CST value	612.89± 195.58
Mean Pre-injection Log MAR BCVA	0.9± 0.22
Mean Pre-injection IOP	13.50 ± 4.32 mmHg

In the first and third months, the mean post-injection CST was 308.59± 56.75 and 304.89± 54.29 um, respectively. With a p-value of less than 0.00001, there was a statistically significant difference between pre-injection and CST one month after injection. The 0.9± 0.22 was the mean log MAR BCVA and 612.89± 195.58 um was the mean pre-injection CST. Prior to the injection, the mean IOP was 13.50 ± 4.32 mmHg.

Table-2: shows the mean CST values at one and three-months

Mean CST		P-value
At one-month	308.59± 56.75um	<0.00001
At three-months	304.89± 54.29um	
Mean log MAR BCVA		
At one-month	0.51± 0.3	<0.00001
At three-months	0.36 ±0.20	
Mean IOP		
At one-month	14.95 ± 3.18 mmHg	<0.00001
At three-months	14.02± 2.29 mmHg	

After injection at 1 and 3-months, the mean log MAR BCVA was 0.51± 0.3 and 0.36 ±0.20, correspondingly. At the first and third months, the results for pre- and post-injection CST were statistically significant (p value <0.00001). One month after the injection, the intraocular pressure was 14.95 ± 3.18 mmHg, and three months later, it was 14.02± 2.29 mmHg.

Figure-1: shows the marked reduction in central subfiled thickness at one month(Pre and Post SCTA injection)

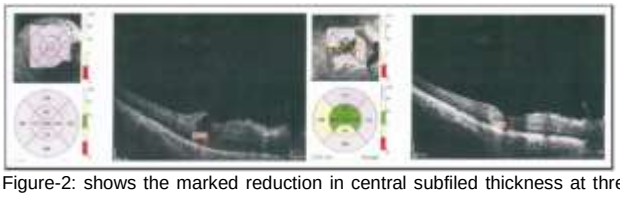

Figure-2: shows the marked reduction in central subfiled thickness at three month(Pre and Post SCTA injection)

In comparison to baseline, BCVA at 3 months was similarly statistically significant (p-value less than0.05). When assessed separately, there was no change in the IOP before and after the injection (at 1 and 3 months). At one month, the p-value was 0.131, and at three months, it was 0.711. During the brief study time, we experienced no complications or unwanted sequel.

DISCUSSION

Despite being extremely operative in the diabetic macular edema (DME) treatment, intravitreal anti-VEGF medications do not completely eradicate the edema in all individuals, indicating that processes other than VEGF are involved in the aetiology[15]. According to various analysis, each patient needs an average of nine to eleven anti-VEGF injections in the first year and up to seventeen over the course of five years for DME resolution. Treatment of naïve and refractory DME with Ozurdex has excellent results[16]. However, using it also caused a noticeable rise in intraocular pressure (IOP). In recent years, the efficacy of IVTA in the treatment of DME has become thoroughly established. However, numerous investigations have demonstrated the high incidence of cataract development and gradually raises intraocular pressure[17]. This is particularly factual when chronic DME is controlled by a series of repeated injections. Similar to intravitreal injection, the corticosteroids delivery into the suprachoroidal space produces a beneficial effect. However, suprachoroidal delivery has

a longer half-life and is less frequently linked with increased intraocular pressure[18]. Compared to the intravitreal method, the drug's anterior chamber concentration is quite low. In order to assess the effectiveness and safety of SCTA for DME in formerly untreated and treated eyes, the HULK study; N=20 was completed recently. In the previously treated group in the HULK research, the average number of injections given were 21.6 as opposed to 7.4 in our study[19]. The HULK study and our analysis differ in a numerous way. Patients who have never been treated before are excluded. Additionally, the initial SCTA injection was not combined with Aflibercept[20].

In our study, the mean pre-treatment central subfield thickness was 612.89± 195.58um, while the mean pre-treatment CST in the HULK treatment group was 473 um. The mean CST after three months in our study was 304.89± 54.29um, but the CST mean in HULK study dropped to 368 um after six months. In this analysis, the central subfield thickness attained at the end of the study was lower than the HULK study, and our study baseline CST was greater than the HULK study. We did not re-administer suprachoroidal Triamcinolone to any patient in this study, in contrast to the HULK research where it was repeated as necessary.

The HULK study observed an average rise of 7 letters from baseline after 3 months of follow-up, whereas our analysis revealed an average increase of 11 letters from baseline. This was most likely caused by the fact that our study baseline BCVA was lower than that of the HULK study. In the HULK study, the mean IOP was 14.2 mmHg initially and 14.8 mmHg at six-month. Two cases of increased intraocular pressure needing topical glaucoma therapy were reported in the HULK research. Whereas we had no such instance, HULK reported a case of triamcinolone accidentally leaking intravitreally. Despite minor variations in patient selection and follow-up, SCTA efficacy and safety were generally relatively similar between the two studies[21]. The central subfield's thickness was permanently decreased and BCVA was improved in the José-Vieira R study on treatment of non-infectious posterior uveitis using SCTA[22]. There have been successful outcomes from other trials, like Jahangir T et al, that evaluated the efficiency and safety of SCTA[23]. Triamcinolone has also been administered via the suprachoroidal route in cases of macular edema caused by posterior uveitis and retinal vascular occlusion (RVO)[24].

The Yousef MS et al research compared the effectiveness of SCTA and intravitreal Aflibercept in treating macular edema caused by retinal vascular occlusion[25]. The better visual outcomes with fewer injections and consequent persistent edema reduction were considered positive results. A local investigation by Haroon et al exhibited good visual outcomes[26]. The fundamental benefit of suprachoroidal space for drug distribution is that it causes less concurrent exposure to anterior segment structures and more distribution in the posterior chamber resulting in high fractions to the choroid, retinal pigment epithelium and retina[27]. Triamcinolone's anterior side effects, like as cataract formation and high intraocular pressure, are lessened as a result. Similar research like the HULK, DOGWOOD, and TANZANITE investigations have shown this[28].

The study's limitations include the limited sample size, a smaller number of follow-ups and absence of a control group. However, other than diabetic macular edema, this new drug administration route seems to be efficient and safe. However, cautious and restricted use is advised in selected cases. Before this injection procedure is widely used, it is essential that the surgeon feels confident using it.

CONCLUSION

After one Triamcinolone acetonide (TA) injection; both morphological and functional improvement occurred. Refractory diabetic macular edema can be reduced and macular thickness can be improved with SCT.

REFERENCES

1. Jahangir T, Riaz S, Amjad A. Evaluation of the Effect of Suprachoroidal Triamcinolone Injection on Refractory Diabetic Macular Edema. Pakistan Journal of Ophthalmology. 2021 May 5;37(3).
2. Chawan-Saad J, Wu M, Wu A, Wu L. Corticosteroids for diabetic macular edema. Taiwan Journal of Ophthalmology. 2019 Oct;9(4):233.
3. Kim EJ, Lin WV, Rodriguez SM, Chen A, Loya A, Weng CY. Treatment of diabetic macular edema. Current diabetes reports. 2019 Sep;19(9):1-0.
4. Price KW, Albini TA, Yeh S. Suprachoroidal Injection of Triamcinolone—Review of a Novel Treatment for Macular Edema Caused by Noninfectious Uveitis. US ophthalmic review. 2020;13(2):76.
5. Emami-Naeini P, Yiu G. Medical and surgical applications for the suprachoroidal space. International ophthalmology clinics. 2019;59(1):195.
6. Le NT, Kroeger ZA, Lin WV, Khanani AM, Weng CY. Novel Treatments for Diabetic Macular Edema and Proliferative Diabetic Retinopathy. Current Diabetes Reports. 2021 Oct;21(10):1-1.
7. Esmaili DD, Boyer DS. Recent advances in understanding and managing retinal vein occlusions. F1000Research. 2018;7.
8. Szymanska M, Mahmood D, Yap TE, Cordeiro MF. Recent advancements in the medical treatment of diabetic retinal disease. International Journal of Molecular Sciences. 2021 Aug 31;22(17):9441.
9. Riccardo S, Chiara G, Eleonora C, Enrico B, Giuseppe Q, Francesco B. Emerging therapies in the management of macular edema: a review. F1000Research. 2019;8.
10. Grzybowski A, Markeviciute A, Zemaitiene R. Treatment of macular edema in vascular retinal diseases: a 2021 update. Journal of Clinical Medicine. 2021 Nov 15;10(22):5300.
11. Kang-Mieler JJ, Rudeen KM, Liu W, Mieler WF. Advances in ocular drug delivery systems. Eye. 2020 Aug;34(8):1371-9.
12. Yiu G, Welch RJ, Wang Y, Wang Z, Wang PW, Haskova Z. Spectral-domain OCT predictors of visual outcomes after ranibizumab treatment for macular edema resulting from retinal vein occlusion. Ophthalmology Retina. 2020 Jan 1;4(1):67-76.
13. Mansour SE, Browning DJ, Wong K, Flynn Jr HW, Bhavsar AR. The evolving treatment of diabetic retinopathy. Clinical Ophthalmology (Auckland, NZ). 2020;14:653.
14. Taylor SC, Montana C, Shah M, Apte RS, Sinha A, Agarwal D. 28 Diabetic Macular Edema. Retina: Medical & Surgical Management. 2021 Nov 30:308.
15. Taylor SC, Montana C, Shah M, SApte R. Diabetic Macular Edema. Retina: Medical & Surgical Management. 2018 May 31:309.
16. Thomas AS, Lin P. Local treatment of infectious and noninfectious intermediate, posterior, and panuveitis: current concepts and emerging therapeutics. Current opinion in ophthalmology. 2020 May 1;31(3):174-84.
17. Teper SJ. Update on the management of uveitic macular edema. Journal of Clinical Medicine. 2021 Sep 14;10(18):4133.
18. Patil MA, Kompella UB. Noninvasive monitoring of suprachoroidal, subretinal, and intravitreal implants using confocal scanning laser ophthalmoscope (cSLO) and optical coherence tomography (OCT). International Journal of Pharmaceutics. 2021 Sep 5;606:120887.
19. HULK MV, Cavalleri M, Lattanzio R, Bandello F. The current role of steroids in diabetic macular edema. Expert Review of Ophthalmology. 2020 Jan 2;15(1):11-26.
20. Chawan-Saad J, Wu M, Wu A, Wu L. Corticosteroids for diabetic macular edema. Taiwan Journal of Ophthalmology. 2019 Oct;9(4):233.
21. Attique U, Mahsood YJ, Jan S. COMPARISON OF INTRAVITREAL BEVACIZUMAB AND TRIAMCINOLONE ACETONIDE WITH INTRAVITREAL BEVACIZUMAB ALONE IN MACULAR EDEMA SECONDARY TO CENTRAL RETINAL VEIN OCCLUSION. Khyber Medical University Journal. 2021 Mar 31;13(1):15-9.
22. José-Vieira R, Ferreira A, Menéres P, Sousa-Pinto B, Figueira L. Efficacy and safety of intravitreal and periocular injection of corticosteroids in non-infectious uveitis: a systematic review. Survey of Ophthalmology. 2021 Dec 9.
23. Jahangir T, Riaz S, Amjad A. Evaluation of the Effect of Suprachoroidal Triamcinolone Injection on Refractory Diabetic Macular Edema. Pakistan Journal of Ophthalmology. 2021 May 5;37(3).
24. Saidkasimova S. Suprachoroidal Drug Delivery. InSuprachoroidal Space Interventions 2021 (pp. 117-139). Springer, Cham.
25. Yousef MS, Abd Elhafez YA, Farag MH. Assessment of suprachoroidal injection of triamcinolone acetonide in cases of diabetic macular edema. International Journal of Medical Arts. 2021 Apr 1;3(2):1384-9.
26. Tayyab H, Ahmed CN, Sadiq MA. Efficacy and safety of suprachoroidal triamcinolone acetonide in cases of resistant diabetic macular edema. Pakistan Journal of Medical Sciences. 2020 Jan;36(2):42.
27. Criado JM, Pérez-Maqueda LA, Koga N. Sample controlled thermal analysis (SCTA) as a promising tool for kinetic characterization of solid-state reaction and controlled material synthesis. InThermal Physics and Thermal Analysis 2017 (pp. 11-43). Springer, Cham.
28. Wykoff CC, Khurana RN, Lampen SIR, Noronha G, Brown DM, HULK Study Group, et al. Suprachoroidal Triamcinolone Acetonide for Diabetic Macular Edema: The HULK Trial. Ophthalmol Retina, 2018; 2 (8): 874-877. Doi: 10.1016/j.oret.2018.03.008