Original Article

Treatment Outcomes of Suprachoroidal Triamcinolone Injection in Refractory Diabetic Macular Edema

Muhammad Ali Haider[1], Nida Usman[2], Hasnain Muhammad Buksh[3], Aamna Jabran[4]
[1,3,4]Lahore General Hospital, Lahore [2]Rahbar Medical & Dental College, Lahore

ABSTRACT

Purpose: To find out the outcomes of suprachoroidal Triamcinolone injection in refractory diabetic macular edema.

Study Design: Quasi experimental study.

Place and Duration of Study: Al-Ehsan Eye Hospital, Lahore from Jan 2020 to 31st Dec 2020.

Methods: Sixty-five patients with refractory diabetic macular edema were included. Patients underwent complete ocular history and examination. To document baseline macular edema, SD-OCT was done. The recruited patients received 0.1ml of suprachoroidal Triamcinolone injection (40mg/ml) using a 30 gauge syringe. Follow up was performed at one week, one month and third month after injection. At each follow up, best corrected visual acuity, central macular thickness and retinal nerve fiber thickness were documented. Data was analysed using SPSS version 36.0. Comparison of BCVA, central macular thickness and retinal nerve fibre layer thickness (RNFL) before and after injection was analyzed by paired sample t-test with p value of ≤ 0.05 as significant.

Results: Out of 65 patients, 29 (44.62%) were females. Mean age of patients was 54 ± 8.4 years (range 40 to 80 years). Central macular thickness after suprachoroidal Triamcinolone injection changed from 556.2 ± 10.9 to 313.6 ± 7.2 µm. Change in visual acuity was 0.9 ± 0.01 to 0.6 ± 0.02. Pre-treatment and post-treatment visual acuities demonstrated a substantial change after undergoing treatment along with decrease in central macular thickness with p value < 0.001.

Conclusion: Suprachoroidal Triamcinolone injection results in anatomical as well as functional improvement in diabetic patients with refractory macular edema.

Key Words: Diabetes, Macular Edema, Suprachoroidal, Triamcinolone.

How to Cite this Article: Haider MA, Usman N, Bukh HM, Jabran A. Treatment Outcomes of Suprachoroidal Triamcinolone Injection in Refractory Diabetic Macular Edema. Pak J Ophthalmol. 2023, **39 (1):** 28-32.
Doi: 10.36351/pjo.v39i1.1452

Correspondence: Muhammad Ali Haider
Lahore General Hospital, Lahore
Email: alihaider_189@yahoo.com

Received: June 05, 2022
Accepted: December 29, 2022

INTRODUCTION

Diabetic macular edema (DME) is one of the commonest causes of decrease vision in diabetic patients. Treatment of DME has changed markedly over the last few years and laser therapy is no longer the first line of treatment for DME.[1] Currently, anti-vascular endothelial growth factors (anti-VEGF) are used for DME.[2] The three most commonly used anti-VEG Fare Bevacizumab, Ranibizumab and Aflibercept. Despite their widespread use, not every patient achieves the desirable results.[3] The reason could be poor compliance, cost of anti-VEGF and refractory diabetic macular edema, not responding to standard treatment modalities. Other treatment options include; use of intra-vitreal steroids as an alternative for patients who show no or limited response with anti-VEGF.

Intravitreal Triamcinolone has shown promising

results in reducing the macular edema but its use was limited by its undesirable effects; notably rebound macular edema secondary to diminishing effect of the drug which requires multiple injections. Other adverse effects are increase in intraocular pressure and cataract.[5] However, these injections have been used as first line of treatment for DME in pseudophakic eyes with efficacy comparable to Ranibizumab (Diabetic Retinopathy Clinical Research Network, DRCR.net, Protocol I). This study reported elevation in intraocular pressure after the administration of intravitreal Triamcinolone injection.

The effectiveness of the steroids in non-responding edema has led to different ways of delivering steroids to the human eye. Examples are Dexamethasone biodegradable implants (Ozurdex® and Iluvein®). Ozurdex remains in the vitreous cavity for 6 months and rise in intraocular pressure is also associated with this treatment modalities.

To analyse the effectiveness of the steroids without the adverse effects, researchers have developed a novel technique for steroid delivery in the suprachoroidal space. While doing so, researchers have considered the risk versus benefit ratio, the frequency of injections, final systemic, anterior and posterior segment drug concentrations etc.

The safety and efficacy of the steroids by suprachoroidal route has been documented in literature.[9] In this study, we observed and analysed the anatomical (OCT) as well as visual outcomes in diabetic patients with refractory macular edema.

METHODS

This study was conducted at Al-Ehsan Eye Hospital, Lahore, from January 2020 to December 2020. Study design was Quasi experimental study and sample size of 65 patients was estimated by using 5% level of significance, 90% power of test with expected mean value before therapy 1.0 and after therapy as 0.7.[12]

Sampling techniques was non-probability convenient sampling. The study was approved by ethical committee of the hospital. After informed consent, patients diagnosed with refractory diabetic macular edema were included. Patients with macular edema due to any other cause, raised intraocular pressure, cataract, uveitis and macular ischemia on fundus fluorescence angiography (FFA) were excluded from the study.

Macular edema that did not decrease by 50 ųm or 10% from baseline or if BVCA did not improve by 5 letters one month after the third anti-VEGF injection was defined as refractory.

Patients were examined for best-corrected visual acuity (BCVA), slit lamp anterior segment and posterior segment examination and IOP were recorded in all patients. To document baseline macular edema, SD-OCT was done.

Patients meeting the inclusion criteria received suprachoroidal Triamcinolone. Triamcinolone acetonide (TA) 40 mg/ml was injected using a 30 gauge commercially available syringe. Dilated fundus examination was carried out before and after the injection. Injection was filled upto the 0.1 ml mark. 10% povidone solution was used to paint the patient's eye followed by draping like any other intraocular surgery. In supra temporal quadrant a 3.5mm mark was made from limbus with calliper and 0.1 ml of injection was injected in the suprachoroidal space. After injecting the drug, needle was slowly withdrawn. A drop of topical antibiotic was than instilled in the eye.

After the injections as per standard protocol, indirect ophthalmoscopy was done. This was performed to check the central artery or if the drug has entered the vitreous cavity. Follow up was performed at one week, one month and third month after injection. At each follow up, complete ocular examination was carried out with special emphasis on visual acuity, central macular thickness and ocular examination were documented.

Data was analysed using SPSS version 36.0. Quantitative variables like age was presented as mean ± standard deviation. Qualitative variables like gender was presented as frequency and percentages. Comparison of BCVA, central macular thickness and retinal nerve fibre layer thickness (RNFL) before and after injection was analyzed by paired sample t-test with p value of ≤ 0.05 as significant.

RESULTS

Out of 65 patients, 29 (44.62%) patients were females while 36 (55.38%) were males. Mean age was 54 ± 8.4 years with maximum of 80 and minimum of 40 years. Central macular thickness after suprachoroidal Triamcinolone changed from 556.2 ± 10.9 to 313.6 ± 7.2 um mean while change in visual acuity was 0.9 ±

Table 1: *Paired sample t- test.*

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Post-treatment macular thickness – Pre-treatment macular thickness	-242.54	78.27	9.71	-261.93	-223.15	-24.98	64	.000
Post-treatment visual acuity – Pre-treatment visual acuity	-.33	.1649	.021	-.3655	-.2838	-15.87	64	.000

0.01 to 0.6 ± 0.02. Paired sample t- test showed that there was significant difference in pre and post-treatment central macular thickness and visual acuity (Table 1).

DISCUSSION

Diabetic macular edema warrants a long term approach with serial periodic follow ups. Currently, Anti-VEGF therapy is considered the mainstay of treatment for diabetic macular edema. The two major drawbacks of this treatment are cost and multiple number of injections. In a single patient, the median number of injections during the first year of treatment is 9 – 11 and the number increases to 17 injections over 5 years of treatment.[1] Cost of ranibizumab is £4,191 according to restore trial for 0.17 quality adjusted life year and for 15 years may mount to £24,028. Although, this cost is lower in third world countries but taking into account the socioeconomic status, the cost is still a significant factor in treatment compliance. Other treatment modalities include steroid implants, which are effective in treating refractory macular edema but there is associated risk of increased intraocular pressure.[11,12] Similarly, intravitreal injection of Triamcinolone has shown promising results but adverse effects include cataract and elevation of intraocular pressure.[13]

Triamcinolone injection into suprachoroidal space is a new technique in retinal diseases. Animal model studies have shown that suprachoroidal Triamcinolone injection attains considerable concentration of drug in the posterior segment with very low drug concentration in the anterior chamber compared to intravitreal Triamcinolone injection.[1] The safety and efficacy of suprachoroidal Triamcinolone in macular edema patients secondary to diabetes has been evident by the HULK trial.[1,1] Our study included patients who received treatment for DME but failed to response. The other difference was use of Aflibercept with the first injection of suprachoroidal Triamcinolone in HULK trial and six months follow up of the patients. In HULK trial, the central macular thickness in the treated group was 473 um while in our study it was 556.2 ± 10.9 um. In HULK trial, the central macular thickness improved from 473 um to 369 um at 6 months. In this study, it was 556.2 ± 10.9 to 313.6 ± 7.2 um at 3 months. Our study has shown greater improvement in central macular thickness than HULK trial. HULK trial repeated the injection while in our study we did not repeat the injection. In HULK trial, 2 patients had elevation of intraocular pressure while in our study none of the patients reported with raised IOP.

In another study, 9 patients were injected with suprachoroidal Triamcinolone with no adverse effects and with improvement in macular edema, which was consistent with our results.[1]

Role of suprachoroidal Triamcinolone is not limited to DME alone. For the treatment of vein occlusion, TANZANITE study compared suprachoroidal Triamcinolone to injection Aflibercept.[1] Results of the study showed reduction in edema with visual acuity improvement where combined injections were given.[1] Likewise, DOGWOOD trial used suprachoroidal Triamcinolone for non-infectious posterior uveitis with improvement in edema and BCVA.[1,2] The safety and efficiency of suprachoroidal therapy was also documented in PEACHTREE Phase III trial.[21]

Preclinical data has shown that suprachoroidal route has achieved considerable concentration of the drug in the retina, choroid and retinal pigment epithelium with very little concentration in the anterior segment of the eye. This observation alleviates the potential adverse effects of intravitreal route as shown in our study and in HULK trial.[12]

There were limitations of this study, which include small sample size, short follow up and no control group.

CONCLUSION

Suprachoroidal Triamcinolone injection is effective in anatomical as well as functional improvement in diabetic patients with refractory macular edema.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval

The study was approved by the Institutional review board/Ethical review board (**EC Ref No: 045/20).**

REFERENCES

1. **Blinder KJ, Dugel PU, Chen S, Jumper JM, Walt JG, Hollander DA, et al.** Anti-VEGF treatment of diabetic macular edema in clinical practice: effectiveness and patterns of use (ECHO Study Report 1) Clin Ophthalmol. 2017; **11:** 393–401. doi:10.2147/OPTH.S128509.
2. **Schmidt-Erfurth U, Garcia-Arumi J, Bandello F, Berg K, Chakravarthy U, Gerendas BS, et al.** Guidelines for the Management of Diabetic Macular Edema by the European Society of Retina Specialists (EURETINA) Ophthalmologica. 2017; **237 (4):** 185–222. Doi: 10.1159/00045⅛.
3. **He Y, Ren XJ, Hu BJ, Lam WC, Li XR.** A meta-analysis of the effect of a dexamethasone intravitreal implant versus intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema. BMC Ophthalmol. 2018; **18 (1):** 121. Doi:10.1186/s12886-018-0779-1.
4. **Ghoraba HH, Leila M, Elgouhary SM, Elgemai EEM, Abdelfattah HM, Ghoraba HH, et al.** Safety of high-dose intravitreal Triamcinolone acetonide as low-cost alternative to anti-vascular endothelial growth factor agents in lower-middle-income countries. Clin Ophthalmol. 2018; **12:** 2383–2391. Doi:10.2147/OPTH.S185274.
5. **Villegas VM, Schwartz SG.** Current and Future Pharmacologic Therapies for Diabetic Retinopathy. Curr Pharm Des. 2018; **24 (41):** 4903–4910. Doi: 10.2174/1381612825666190130140717.
6. **Bressler SB, Odia I, Glassman AR, Danis RP, Grover S, Hampton GR, et al.** Changes in diabetic retinopathy severity when treating diabetic macular edema with ranibizumab:DRCR.NET Protocol I 5-Year Report. Retina, 2018; **38 (10):** 1896–1904. Doi: 10.1097/IAE.0000000000002302.
7. **Elman MJ, Aiello LP, Beck RW, Bressler NM, Bressler SB, Edwards AR, et al.** Diabetic Retinopathy Clinical Research Network, Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. Ophthalmology, 2010; **117 (6):** 1064-1077.e35. Doi: 10.1016/j.ophtha.2010.02.031.
8. **Urbancic M, Gardasevic Topcic I.** Dexamethasone implant in the management of diabetic macular edema from clinician's perspective. Clin Ophthalmol. 2019; **13:** 829–840. Doi:10.2147/OPTH.S206769.
9. **Habot-Wilner Z, Noronha G, Wykoff CC.** Suprachoroidally injected pharmacological agents for the treatment of chorio-retinal diseases: a targeted approach. Acta Ophthalmol. 2019; **97 (5):** 460–472. Doi: 10.1111/aos.14042.
10. **Elman MJ, Ayala A, Bressler NM, Browning D, Flaxel CJ, Glassman AR, et al.** Diabetic Retinopathy Clinical Research Network. Intravitreal Ranibizumab for diabetic macular edema with prompt versus deferred laser treatment: 5-year randomized trial results. Ophthalmology, 2015; **122 (2):** 375–381. Doi: 10.1016/j.ophtha.2014.08.047.
11. **Mello Filho P, Andrade G, Maia A, Maia M, Biccas Neto L, Muralha Neto A, et al.** Effectiveness and Safety of Intravitreal Dexamethasone Implant (Ozurdex) in Patients with Diabetic Macular Edema: A Real-World Experience. Ophthalmologica. 2019; **241 (1):** 9–16. Doi: 10.1159/000492132.
12. **Nagpal M, Mehrotra N, Juneja R, Jain H.** Dexamethasone implant (0.7mg) in Indian patients with macular edema: Real-life scenario. Taiwan J Ophthalmol. 2018; **8 (3):** 141–148. Doi: 10.4103/tjo.tjo_62_17.
13. **Ghoraba HH, Leila M, Elgouhary SM, Elgemai EEM, Abdelfattah HM, Ghoraba HH, et al.** Safety of high dose intravitreal Triamcinolone acetonide as low-cost alternative to anti-vascular endothelial growth factor agents in lower-middle-income countries. Clin Ophthalmol. 2018; **12:** 2383–2391. Doi: 10.2147/OPTH.S185274.
14. **Willoughby AS, Vuong VS, Cunefare D, Farsiu S, Noronha G, Danis RP, et al.** Choroidal Changes After Suprachoroidal Injection of Triamcinolone Acetonide in Eyes With Macular Edema Secondary to Retinal Vein Occlusion. Am J Ophthalmol. 2018; **186:** 144–151. Doi: 10.1016/j.ajo.2017.11.020.
15. **Lampen SIR, Khurana RN, Noronha G, Brown DM, Wykoff CC.** Suprachoroidal Space Alterations Following Delivery of Triamcinolone Acetonide: Post-Hoc Analysis of the Phase 1/2 HULK Study of Patients With Diabetic Macular Edema. Ophthalmic Surg Lasers Imaging Retina, 2018; **49 (9):** 692-697. Doi: 10.3928/23258160-20180831-07.

16. **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.
17. **Goldstein DA, Do D, Noronha G, Kissner JM, Srivastava SK, Nguyen QD.** Suprachoroidal Corticosteroid Administration: A Novel Route for Local Treatment of Noninfectious Uveitis. Transl Vis Sci Technol. 2016; **5 (6):** 14. Doi: 10.1167/tvst.5.6.14.
18. **Campochiaro PA, Wykoff CC, Brown DM, Boyer DS, Barakat M, Taraborelli D, et al.** Tanzanite Study Group. Suprachoroidal Triamcinolone Acetonide for Retinal Vein Occlusion: Results of the Tanzanite Study. Ophthalmol Retina, 2018; **2 (4):** 320-328. Doi: 10.1016/j.oret.2017.07.013.
19. **Behar-Cohen F.** Recent advances in slow and sustained drug release for retina drug delivery. Expert Opin Drug Deliv. 2019; **16 (7):** 679–686. Doi:10.1080/17425247.2019.1618829.
20. **Shatz W, Aaronson J, Yohe S, Kelley RF, Kalia YN.** Strategies for modifying drug residence time and ocular bioavailability to decrease treatment frequency for back of the eye diseases. Expert Opin Drug Deliv. 2019; **16 (1):** 43–57. Doi: 10.1080/17425247.2019.1553953.
21. **Yeh S, Khurana RN, Shah M, Henry CR, Wang RC, Kissner JM, et al.** PEACHTREE Study Investigators. Efficacy and Safety of Suprachoroidal CLS-TA for Macular Edema Secondary to Noninfectious Uveitis: Phase 3 Randomized Trial. Ophthalmology, 2020; **127 (7):** 948-955. Doi: 10.1016/j.ophtha.2020.01.006.

Authors' Designation and Contribution

Muhammad Ali Haider; Assistant Professor: *Concepts, Design, Literature search, Data acquisition, Manuscript preparation, Manuscript editing.*

Nida Usman; Senior Registrar: *Data acquisition, Statistical analysis, Manuscript editing, Manuscript review.*

Hasnain Muhammad Buksh; Senior Registrar: *Statistical analysis, Manuscript editing, Manuscript review.*

Aamna Jabran; Senior Registrar: *Statistical analysis, Manuscript editing, Manuscript review.*