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Original Article

Efficacy of Suprachoroidal versus Intravitreal Triamcinolone Acetonide in Refractory Macular Edema; A Quasi-experimental study

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ABSTRACT

Objective: To compare the efficacy of suprachoroidal vs intravitreal triamcinolone acetonide in management of refractory macular edema.

Study Design: Quasi-experimental study

Place and Duration of Study: Ophthalmology Department, Fauji Foundation Hospital, Rawalpindi Pakistan, from Jun to Nov 2022.

Methodology: A total of three hundred and seventy-eight eyes of 189 patients were selected after approval from the Institutional Ethics Review Board. In this study, individuals were divided into two Groups using lottery method: Group-A, received suprachoroidal triamcinolone acetonide and Group-B, received intravitreal triamcinolone acetonide. After intervention, both Groups were followed up at 1 and 3 months. Baseline central macular thickness was noted in each Group. Patients were also observed for complications. Statistical Package for Social Sciences version 23 was utilized for data analysis.

Results: No significant differences were noted between both Groups at baseline Central Macular Thickness (*p*-value =0.29), However, significant difference was noted at 3-month Central Macular Thickness (*p*-value as <0.001). Very few compli-cations were observed in both Groups.

Conclusion: This study revealed that both suprachoroidal and intravitreal routes of administering triamcinolone acetonide were equally effective. Significant reduction in Central Macular Thickness and no increase in Intraocular Pressure along with better tolerance for treatment were seen in suprachoroidal route in our research which indicated its safety.

Keywords: Intravitreal Injections, Macular Edema, Optical Coherence Tomography, Suprachoroidal, Steroids, Triamcinolone Acetonide.

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INTRODUCTION

The macula, which is in center of retina and is adjacent to optic nerve head, is in charge of central vision. Vision loss, distortion, and blurriness are among potential effects of macular conditions. When fluid builds up in macular layers as result of vascular leakage, macular edema (ME) occurs, which causes macula to expand and thicken and impair vision.[1] This is a side effect of number of retinal conditions as well as other illnesses, such as diabetic retinopathy (DR), age-related macular degeneration (AMD), retinal vein occlusion (RVO), and inflammatory conditions.[2,3]

Argon laser photocoagulation, intravitreal injections of Vascular Endothelial Growth Factor (VEGF) inhibitors, or corticosteroids are frequently used in treatment of ME.[4] Ranibizumab, bevacizumab, and aflibercept are examples of anti-VEGF medications that can significantly enhance visual acuity.[5]

Currently, the role of triamcinolone acetonide (TA), either alone or combined with laser, could be considered mainly in refractory DME Best-corrected visual acuity (BCVA) gain ≤5 letters or reduction in Central Macular Thickness (CMT) ≤20% after the loading dose), especially in pseudophakic eyes.[6]

In contrast to intravitreal method, suprachoroidal injections are a unique method for intraocular medi-cation administration with concentrations directed towards posterior part of the eye. The Hulk study has found that repeated Suprachoroidal Triamcinolone Acetonide (SCTA) injections are well tolerated and safe for treating eyes with Diabetic Macular Edema (DME), getting morphological betterment with decreased incidence of side effects.[7] Studies have shown safety of SCTA in ME aggravating uveitis.[8,9] The TANZANITE research found that combination therapy outperforms monotherapy.[10] The importance of the topic and paucity of local data forms the rationale for our study.

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METHODOLOGY

The quasi-experimental study was carried out at the Department of Ophthalmology Fauji Foundation Hospital, Rawalpindi Pakistan, from Jun to Nov 2022, after obtaining approval from the Institutional Ethical Review Committee [Ref No. 608/RC/FFH/RWP].

Inclusion Criteria: Adults of either gender, over the age of 18 years with central macular thickness more than 250 m were included.

Exclusion Criteria: Patients with uncontrolled diabetes, immune deficiencies, or any other conditions requiring administration of systemic corticosteroids were not included. Patients who were monocular, had current infections, suprachoroidal hemorrhages, underwent prior vitreoretinal surgery, or had received intraocular medication in past, recently taken topical ophthalmic steroids and pregnant women were also excluded.

Open Epi calculator was used to calculate the sample size by taking prevalence of macular edema i.e. 43.3%.[1] A total of three hundred and seventy-eight (n=378) eyes were included via non-probability sampling technique after obtaining written informed consent.

The total three hundred and seventy-eight (n=378) eyes were divided into two Groups using lottery method. Intravitreal Triamcinolone Acetonide (IVTA) Group (Group-A) got a single dose of 4 mg/0.1 ml injected, as did Suprachoroidal Triamcinolone Acetonide (SCTA) Group (Group-B) Group (Figure). To evaluate changes in central macular thickness (CMT) and Intraocular Pressure (IOP) from baseline measurements, individuals were monitored at 1 and 3-months following injection.

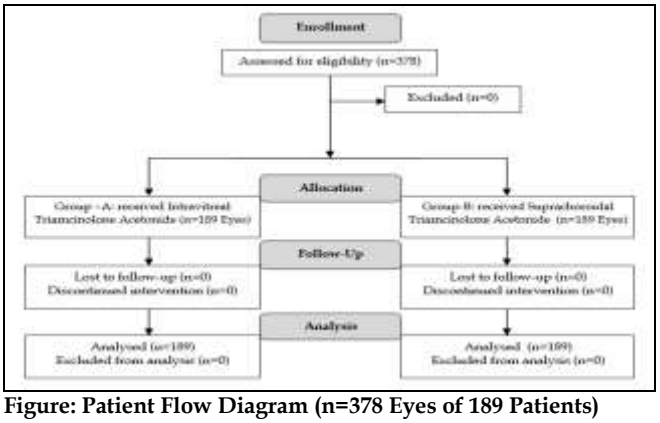

Figure: Patient Flow Diagram (n=378 Eyes of 189 Patients)

All patients had full history-taking and thorough ocular examination (visual acuity, IOP, CMT) one week prior to therapy. Before examination, every individual had their pupils enlarged with tropicamide 1% eye drops. Slit-lamp examination was performed on JAPAN-made TOPCON IEC60601-1 slit light. The TOPCON applanation tonometer was used to measure IOP."OPTOPOL REVO 80," OCT was used to measure CMT, which was then analyzed statistically.

The same surgeon carried out the procedures in the operation room under completely sterile settings. Surgical preparations for both techniques were same: topical anesthetic eye drop were instilled into conjunctival sac, 10% periocular povidone-iodine was applied to skin, or 5% povidone-iodine was applied to conjunctiva after placing sterile speculum and eye draping. We used 4 mg/0.1 ml of TA for the non-filtering sedimentation procedure employed to purify the TA suspension.

Suprachoroidal injection was done using a custom-made needle preparation. To expose only 1 mm of the 27-gauge needle to enter the supra-choroidal space; we used the silicon tube with a sterile 22-gauge blue IV cannula to use it as a guard for the 27-gauge needle; after cutting the silicon tube from its base, we inserted the 27-gauge needle inside; then, we cut the silicon tube by Westcott scissor to expose only 1 mm of the 27-gauge needle bevel using a sterile caliper to measure the desired length. Surgeon aspirated 0.1 ml of triamcinolone suspension into a sterile 27-gauge syringe and then inserted the custom 27-gauge suprachoroidal needle we had prepared. Paracentesis was created; then, suprachoroidal injection was done 3.5 mm posterior to the limbus in the inferotemporal quadrant. The surgeon aspirated 0.1 ml of triamcinolone suspension into sterile syringe before inserting specialist suprachoroidal 27-gauge needle. Three point five mm posterior to limbus, in the supratemporal quadrant, a suprachoroidal injection was then administered.

After paracentesis, an intravitreal injection was administered using a standard 27-gauge needle (1 ml of insulin syringe and 27 g needle) at 3.5 mm posterior to the limbus.

Patients were maintained under close supervision in the eye OPD for 30 minutes in case there was an increase in pain or IOP. Then a puff-tonometer was used to measure IOP. Following the surgery, patients were given instructions for follow-up appointments two days, one week, and one and three months later. One and three months after the injection, for each Group, all patients had their CMT and IOP evaluated.

Statistical Package for Social Sciences (SPSS) version 23 was used for statistical analysis. Quantitative variables were reported in terms of Mean+SD and frequency and percentage was calculated for qualitative variables. Independent t-test was applied to compare the values between two Groups and paired t-test was applied to compare values within the Group. The *p*-value <0.05 was considered significant.

RESULTS

A total of three hundred and seventy-eight (n=378) eyes were included and divided into two Groups. The mean age in Group-A was 62.00±7.42 years and in Group-B was 60.12±8.71 years. No statistically significant difference was seen between two Groups in respect of age, gender, etiology and side of eye as *p*-value was >0.05 as shown in Table-I. Considerable reduction in CMT from baseline at 3 months was observed between both Groups, as shown in Table-II. Similarly, no significant difference was observed among two Groups at baseline CMT (*p*-value =0.587), However, significant difference was noted at 3-month CMT (*p*-value <0.001), as shown in Table-III. Very complications were observed in both Groups. Raised Intraocular pressure (IOP) was found in 15(7.93%) cases in IVTA Group and Subconjunctival Hemorrhage was seen in 30(15.87%) cases in SCTA and 8(4.23%) in IVTA, as shown in Table-IV.

Table-I: Demographic Details of Patients (n=378 Eyes of 189 Patients)

Demographic Details	IVTA Group (Group-A) (n=189 Eyes)	SCTA Group (Group-B) (n=189 Eyes)	*p*-value
Age in years (Mean+SD)	60.12±8.71	62.00±7.42	0.02
Gender			
Male	136(71.9%)	144(76.19%)	0.35
Female	53(28.04%)	45(23.81%)	
Side of the Eye:			
Right	98(51.85%)	91(48.14%)	0.47
Left	91(48.14%)	98(51.85%)	
Etiology			
Diabetic Retinopathy	151(79.89%)	151(79.89%)	1.00
Retinal Vein Occlusion	23(12.16%)	23(12.16%)	
Macular Degeneration	15(7.93%)	15(7.93%)	

DISCUSSION

At three months, CMT considerably decreased in both Groups. In situations of RME, SCTA has recently been employed as minimally invasive therapy because it achieves greater drug concentration that targets retina and choroid with less impact on anterior part of eye.[11,12]

Table-II: Pre-and-post Central Macular Thickness (µm) in Suprachoroidal and Intravitreal Triamcinolone Acetonide (n=378 Eyes of 189 Patients)

Parameter	Suprachoroidal (n=189 Eyes)			
	Baseline	3rd Month	Reduction	*p*-value
Central Macular Thickness (µm)	425.16±139.67	288.79±55.90	136	<0.001
Parameter	Intravitreal Triamcinolone Acetonide (n=189 Eyes)			
	Baseline	3rd Month	Reduction	*p*-value
Central Macular Thickness (µm)	409.91±138.61	253.01±49.16	156	<0.001

P-value: Paired t-test*

Table-III: Comparison of Mean Reduction in Central Macular Thickness (µm) in Suprachoroidal and Intravitreal Triamcinolone Acetonide (n=378 Eyes of 189 Patients)

Pre and Post CMT	IVTA Group (Group-A) (n=189 Eyes)	SCTA Group (Group-B) (n=189 Eyes)	*p*-value
Baseline	409.91±138.61	425.16±139.67	0.29
3rd month	253.01±49.16	288.79±55.90	<0.001

Table-IV: Frequency of Complications in Suprachoroidal and Intravitreal Triamcinolone Acetonide (n=378 Eyes of 189 Patients)

Complications	IVTA Group (Group-A) (n=189 Eyes)	SCTA Group (Group-B) (n=189 Eyes)
IOP Strike	15(7.93%)	Nil
Endophthalmitis	Nil	Nil
Subconjunctival Hemorrhage	8(4.23%)	30(15.87%)
Retinal Detachment	Nil	Nil
Vitreous Hemorrhage	Nil	Nil

SCTA vs IVTA for treatment of DME was subject of randomized trial by Zakaria *et al.*, and at 1 and 3 months, CMT considerably decreased in both Groups. Additionally, after 1 month, both Groups demonstrated the greatest decline in CMT, with statistically major variation between SCTA and IVTA Groups.[13] Like this, our study found statistically noteworthy disparity between two Groups and substantial decline in CMT from baseline in both Groups. In the HULK study, SCTA's effectiveness was examined in 10 patients who had persistent DME.[6] In the previously treated arm of HULK experiment, mean baseline CMT was 473 um; in this study, it was 409.91+138.61 um. In contrast to this research, average CMT in SCTA Group

was decreased to 253+49.16 um after three months, the mean CMT in the HULK Group was reduced to 369 um after six months. Our findings concur with those of Tayyab *et al*., who administered 4 mg SCTA to DME that was resistant to therapy and experienced significant drops in CMT at 1 and 3 months.[10]

There was a statistically significant decrease in CMT in a study by Hanif *et al*., which comprised of 30 patients with non-infectious uveitis who were managed with a single SCTA injection. The mean CMT at presentation was 569.6+170.39 m compared to 266.7+73.127 m at one month, and patients achieved reduction of > 50% of initial thickness, which led to the remission of macular edema in all patients. With a further 22% decrease over the CMT in one month, this drop in CMT was not only persistent but also enhanced after 3 months.[14] Current therapies for refractory macular edema include intravitreal and topical corticosteroid injections, implants, and topical creams. With these therapeutic options, varying degrees of success have been observed, but this achievement has also been linked to hazards of increased IOP, cataract formation, and progression. With up to 17% of individuals suffering from cataract progression after periocular steroid injection and up to 66% of patients experiencing elevated IOP after intravitreal steroids, these unfavorable events are serious concern in patients receiving topical or intravitreal corticosteroids.[15] Current modalities of delivery of long-term ocular steroid therapy have been shown to result in frighteningly high levels of IOP-lowering drugs and interventions, cataract formation, and surgical removal of cataracts.[16] The average IOP remained normal throughout entire follow up in SCTA Group of patients in our study, with none of them experiencing an increase in IOP. However, in IVTA Group, 15(7.93%) eyes had elevated IOP. In the HULK study, eyes treated with SCTA showed an increase in IOP in 10% of participants, which is inconsistent with our data.[17] In another study, there was a greater prevalence of elevated IOP (17.3%), although this could be explained using intravitreal aflibercept in conjunction with SCTA in patients of retinal vein blockage and pre-existing glaucoma.[18]

Thirty (15.87%) eyes in the SCTA Groups and 8(4.23%) in the IVTA Groups experienced subconjunctival hemorrhage, according to our observations of adverse events. Less frequent unfavorable procedures were observed in our research, which is proof of the safety of using suprachoroidal triamcinolone.

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CONCLUSION

The results of the current investigation showed that Triamcinolone can be administered intravitreally and suprachoroidal with equivalent efficacy. In our trial, the Suprachoroidal route showed tolerance of the therapy, noteworthy decline in central macular thickness, and no elevation in IOP. The lasting advantages of SCTA require further larger scale, randomized controlled trials.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MA & TN: Conception, study design, drafting the manuscript, approval of the final version to be published.

RIUH & AA: Data acquisition, critical review, approval of the final version to be published.

SN & NO: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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