

Comparative Efficacy Of Intravitreal versus Posterior Sub-Tenon Triamcinolone Acetonide Injections For Diabetic Macular Edema

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Abstract:

Objectives: To evaluate and compare the efficacy and safety of intravitreal versus posterior sub-tenon injections of triamcinolone acetonide in treating diabetic macular edema among patients with diabetic retinopathy (DR).

Methods: A total of 66 participants were enrolled in this randomized controlled trial conducted at Al Shifa Trust Eye Hospital in Rawalpindi. The participants were randomly allocated into two equal groups of 33 each.. The IVTA group received a 4 mg intravitreal injection of triamcinolone acetonide, while the STTA group received a 40 mg posterior sub-tenon injection. Follow-up was conducted one- and three-months post-injection.

Results: Pre-injection central macular thickness (CMT) was similar between groups (IVTA: $375.9 \mu\text{m} \pm 103 \mu\text{m}$ vs. STTA: $380.3 \mu\text{m} \pm 101 \mu\text{m}$, $p = 0.921$). Post-injection, CMT significantly improved in both groups, with a more prominent effect in the IVTA group ($223 \mu\text{m} \pm 59$ vs. $299 \mu\text{m} \pm 79$, $p = 0.01$). Pre-injection best-corrected visual acuity (BCVA) was comparable (IVTA: 0.83 ± 0.1 vs. STTA: 0.80 ± 0.17 LogMAR, $p = 0.334$), but the IVTA group showed significantly better BCVA post-injection (0.38 ± 0.08 vs. 0.67 ± 0.08 LogMAR, $p < 0.001$). While pre-injection intraocular pressure (IOP) was similar ($p = 0.753$), post-injection IOP was lower in the STTA group (15.8 ± 0.59 mmHg) compared to the IVTA group (18.3 ± 1.7 mmHg, $p < 0.001$).

Conclusion: Both injection methods effectively treated diabetic macular edema, with the posterior sub-tenon approach showing a lower risk of raised IOP. *Al-Shifa Journal of Ophthalmology 2025; 21(2): 63-69. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

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Introduction:

Diabetic retinopathy (DR) is a microvascular complication of diabetes mellitus, often leading to progressive retinal damage and potential blindness.¹ As the leading cause of vision loss in working-age adults worldwide, it demands timely diagnosis and intervention. Projections indicate that by 2050, 16 million Americans will have DR, with 3.4 million at risk for vision-threatening complications.^{1,2} Strict glycemic control is crucial for delaying DR progression, as established by studies such as the UK Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complication Trial (DCCT).³

Diabetic macular edema (DME), a common complication of DR, results from compromised hemato-retinal barriers leading to fluid accumulation.

Corticosteroid injections, whether intravitreal Triamcinolone Acetonide (IVTA) or posterior sub-tenon Triamcinolone Acetonide (STTA), have been shown effective in decreasing central macular thickness (CMT) and enhancing visual acuity. IVTA, while efficacious, has concerns such as increased intraocular pressure (IOP) and endophthalmitis. Conversely,⁴ STTA provides a less intrusive option with fewer problems.⁵ This study aims to elucidate the beneficial effects of intravitreal and posterior sub-tenon injections on the alleviation of diabetic macular edema throughout the therapy phase. Post-injection improvements will be observed in visual acuity, central macular thickness (CMT), and intraocular pressure (IOP) in both cohorts. While both methodologies are advantageous, the results will elucidate that their impact on certain clinical parameters may differ, notwithstanding the efficacy of both procedures.

Methodology:

This randomized controlled, clinical trial was conducted over six months, from February 28, 2021, to August 28, 2021, in the Outpatient Department of Al Shifa Trust Eye Hospital, Rawalpindi, after obtaining ethical approval from the hospital's review board. Using Open Epi sample size calculator, keeping the mean difference of intraocular pressure (IOP) as 18.44 ± 3.76 mm/Hg in intravitreal approach and 16.28 ± 2.23 mm/Hg in the sub-tenon approach for diabetic macular edema, after 3rd month of Triamcinolone acetonide injection,¹³ 95% of two-sided significance level and power of 80%, the sample size in group 1 (intravitreal triamcinolone acetonide) will be 33 and in group 2 (posterior sub-tenon triamcinolone acetonide) were 33 making total sample size of 66. Participants were recruited using a computer-generated randomization sequence and allocated into groups using concealed allocation. Eligibility criteria required patients aged 30 to 80 years with

diabetic macular edema (DME) diagnosed according to the Early Treatment Diabetic Retinopathy Study (ETDRS) guidelines, with a retinal thickness of more than 300 μ m in the central macular area confirmed by optical coherence tomography (OCT). Both male and female patients were included. Patients with a history of unrelated chorioretinal diseases, including uveitis or glaucoma, severe cataracts, significant macular ischemia, or previous ocular treatments including intravitreal injections or laser photocoagulation, were excluded.

Randomization was performed using a computer-generated random sequence. Allocation concealment was ensured by sealed, opaque envelopes, which were opened sequentially only after a participant was enrolled. Participants were allocated into one of two treatment groups. Group 1 received intravitreal injections of 4 mg of triamcinolone acetonide, while Group 2 received posterior sub-tenon injections of 40 mg of triamcinolone acetonide. All injections were administered under aseptic conditions by experienced ophthalmologists. The intravitreal injections were delivered using a 27-gauge needle, while posterior sub-tenon injections were performed using a 25-gauge cannula under topical anesthesia.

Baseline evaluations included central macular thickness measured by OCT, intraocular pressure assessed with Goldman applanation tonometry, and visual acuity evaluated using the LogMAR scale. Additional data on demographics, type of diabetes, duration of diabetes, and BMI were also collected. Follow-up assessments were conducted one and three months after the injections, where the same parameters—central macular thickness, intraocular pressure, and visual acuity—were reevaluated. Any adverse events, such as increased intraocular pressure, endophthalmitis, or other complications, were recorded during follow-up visits.

This study employed single blinding, where the outcome assessors were blinded to the

treatment groups to minimize observer bias. However, participants and clinicians administering the treatment were not blinded due to the visible differences in the injection techniques. Statistical analysis was conducted using SPSS version 20. Continuous variables, such as central macular thickness, intraocular pressure, and visual acuity, were expressed as mean \pm standard deviation (SD). Categorical variables, such as gender and type of diabetes, were summarized as frequencies and percentages. Group comparisons for continuous variables were performed using independent t-tests after confirming normality assumptions, and a p-value of <0.05 was considered statistically significant.

Results:

In total, 66 patients participated in the study, evenly distributed between the two groups (33 each). Of these, 48.5% were male and 51.5% were female, with an average age of 45.1 ± 8.6 years. Among the participants, 28.8% had type I diabetes, and 71.2% had type II diabetes. The average duration of diabetes was 3.4 ± 1.7 years, and the mean body mass index (BMI) was 30.2 ± 2.3 kg/m². Baseline intraocular pressure (IOP) was similar across the groups, with an overall mean of 16.1 ± 1.1 mmHg. After treatment, the average IOP rose to 17.1 ± 1.1 mmHg. Best corrected visual acuity (BCVA) improved significantly post-injection, decreasing from 0.81 ± 0.1 LogMAR to 0.53 ± 0.1 LogMAR. Central macular thickness (CMT) showed a marked reduction, with an average decrease from 376.1 ± 103 μ m

before injection to 231.3 ± 60.2 μ m after injection.

Both groups demonstrated significant improvements in CMT post-injection. While pre-injection CMT values were comparable (IVTA: 375.9 ± 103 μ m vs. STTA: 380.3 ± 101 μ m; $p = 0.921$), the IVTA group exhibited a greater reduction in CMT compared to the STTA group (post-injection: 223 ± 59 μ m vs. 299 ± 79 μ m; $p = 0.01$). This indicates a more pronounced effect of intravitreal triamcinolone acetate (IVTA) in resolving macular edema.

Similarly, BCVA significantly improved in both groups, with no difference observed at baseline (IVTA: 0.83 ± 0.1 vs. STTA: 0.80 ± 0.17 ; $p = 0.334$). However, post-injection BCVA was superior in the IVTA group (0.38 ± 0.08 vs. 0.67 ± 0.08 ; $p < 0.001$). This suggests that the reduction in macular thickness achieved with IVTA translated into more substantial improvements in visual function, a key outcome for patients with diabetic macular edema.

Regarding IOP, baseline measurements were comparable between the groups ($p = 0.753$), as shown in Table 1. Post-injection, the IVTA group showed a higher mean IOP compared to the STTA group (18.3 ± 1.7 mmHg vs. 15.8 ± 0.59 mmHg; $p < 0.001$). While the increase in IOP following IVTA was significant, it remained within clinically manageable limits, emphasizing the importance of monitoring in these patients. In contrast, the STTA group exhibited a safer IOP profile, suggesting it may be more appropriate for patients at risk of elevated IOP.

Table 1: Demographic and Clinical Characteristics of the Study Participants

Demographic characteristics	Frequency (N=66)	Percentage
Gender		
Male	32	48.5%
Female	34	51.5%
Type of diabetes mellitus		
Type I	19	28.8%
Type II	47	71.2%
	Mean	Standard deviation
Age (years)	45.1	8.6
Duration of diabetes mellitus (years)	3.4	1.7
BMI (Kg/m2)	30.2	2.3
Injection IOP		
Pre injection IOP (mmHg)	16.1	1.1
Post injection IOP(mmHg)	17.1	1.1
BCVA		
Pre injection BCVA (Log Mar)	0.81	0.1
Post injection BCVA (Log Mar)	0.53	0.1
CMT		
Pre injection CMT(μm)	376.1	14.7
Post injection CMT(μm)	231.3	13.9

Table 2: Comparison of CMT, BCVA and IOP pre and post injection in both groups

Outcomes	Groups	N=66	Mean ± SD	P value
CMT				
Pre CMT	IVTA	33	375.9±103	0.921
	STTA	33	380.3±101	
Post CMT	IVTA	33	223.2±59	0.01
	STTA	33	299.1±79	
BCVA				
Pre BCVA	IVTA	33	0.83±0.1	0.334
	STTA	33	0.80±0.17	
Post BCVA	IVTA	33	0.38±0.08	0.000
	STTA	33	0.67±0.08	
IOP				
Pre IOP	IVTA	33	17.09±1.1	0.753
	STTA	33	17.18±1.15	
Post IOP	IVTA	33	18.3±1.7	0.000
	STTA	33	15.8±0.59	

Discussion:

Macular oedema is the most common reason for diabetics to have a decline in their visual acuity.⁶ This condition may manifest itself at any point in the progression of the retinal disease and is the most prevalent reason for vision impairments in these individuals. The hemato-retinal barrier is compromised in oedema as a result of a modification in the tight connection that exists between the pigmented epithelial cells and the retinal capillary endothelial cells. This alteration leads to the loss of water and electrolytes in the retinal tissue.⁷

It has been shown in a number of studies, one of which being the Early Treatment Diabetic Retinopathy Study (ETDRS), that macular photocoagulative therapy is an effective method for treating clinically significant macular oedema. It is thus not possible to recover vision loss that occurred before therapy with laser photocoagulation for macular oedema, despite the fact that it is effective in preventing additional visual loss in 50% percent of treated patients. Additionally, for eyes that have diffuse macular oedema, laser photocoagulation is not a particularly successful treatment option.⁸

Clinical trials have shown that injecting either intravitreal or posterior sub-tenon into diabetic macular oedema patients can alleviate the condition's symptoms. Improvements in intraocular pressure, mean CMT thickness, and visual acuity after injection were significantly different between the two groups.

These findings were comparable to those found in earlier research. At one month and three months after receiving an intravitreal injection of triamcinolone, Martidis et al⁹ found that the percentage of CMT that had reduced was 55% and 57.5%, respectively. A reduction of 42% and 46.4% was found by Ciardella et al¹⁰ respectively. Visual acuity (LogMAR) was found to have increased by 0.15 (15.3%) and 0.19 (19.3%) after one and three months following intravitreal triamcinolone

injection, respectively, according to Jonas et al's¹¹ findings.

It has been shown that illnesses involving a breakdown of the blood-retinal barrier may be effectively treated with the injection of triamcinolone into the posterior sub-tenon. Intermediate uveitis and cystoid macular oedema are two of these eye diseases. After vitrectomy failed to alleviate widespread diabetic macular oedema, Ohguro et al¹² presented an observational case series showing that infusion of triamcinolone into the posterior sub-tenon was effective. Furthermore, a study conducted by Bakri et al¹³ indicated that after twelve months of treating refractory diabetic macular oedema with injections of posterior sub-tenon triamcinolone, visual acuities were either maintained or improved. New information is often related to what we have been investigating.

For example, Freeman et al¹⁴ shown via the use of ultrasonography B-scan that the supertemporal placement strategy leads to a more precise placement of steroids in close proximity to the macula. In their study, Geroski et al¹⁵ shown that the transscleral route is an effective method for delivering the medication to the retina. Weijtens et al¹⁶ found that the intravitreal concentration of the steroid rose after it was injected into the peribulbar region. On the basis of these data, it is possible to conclude that the sub-tenon macular region is where the injected triamcinolone is situated, and that the transscleral route is the means by which the therapeutic concentration of the drug may be used on the choroid or the retina.

Cardillo et al¹⁷ evaluated the efficacy of injecting intravitreal triamcinolone vs injecting via posterior sub-tenon. After comparing the two injection methods, they determined that the intravitreal injection provided better results in terms of both the structure and function of the improved area. Additionally, Bonini-Filho et al¹⁸ postulated that intravitreal injection, rather than posterior sub-tenon injection, would be the more effective treatment for diffuse and refractive diabetic macular oedema. In

contrast to the results of these two studies, our study shows that injections into the posterior sub-tenon and intravitreal space may be just as well-tolerated and have comparable short-term effects on performance. Cardillo and colleagues performed a trial where a single patient with bilateral symmetric diffuse macular oedema was treated with two separate procedures for each eye. This part of the study was educational. Twelve patients is a tiny sample size, which is one of the research's shortcomings. Patients with diabetic macular oedema were the focus of the study by Bonini-Filho and colleagues. This precludes us from comparing their results to ours directly.

One of the benefits of posterior sub-tenon administration is that it reduces the likelihood of complications. The most frequent consequence that occurs following intravitreal triamcinolone injection is an increase in intraocular pressure (IOP). Despite the fact that it was not statistically significant, intraocular pressure (IOP) increased following intravitreal injection in our research. When compared to the group that received injections into the posterior subtenon, the intravitreal injection group saw a higher change in intraocular pressure three months following the injection. In other investigations, the administration of intravitreal injection was associated with a number of additional problems, including endophthalmitis and retinal detachment.¹⁹ The limitations of this study include its small sample size and single-center design, both of which may influence the generalizability of the findings. A small sample size reduces the statistical power and may increase the risk of random error, potentially impacting the robustness of the results. Furthermore, the single-center design restricts the diversity of the patient population, as participants are drawn from a specific geographic and institutional setting. This limitation may reduce the applicability of the findings to broader, more diverse populations. However, our results align with those of previous studies,

which strengthens their validity and suggests consistency in the observed effects. The convergence of our findings with prior research supports their credibility, even within the context of a smaller sample size. Future studies with larger, more diverse, multicenter cohorts are still needed to confirm these results and further enhance their generalizability.

Conclusion:

Both intravitreal and posterior sub-tenon injections of triamcinolone acetonide effectively reduce central macular thickness and improve visual acuity in diabetic macular edema. Intravitreal injections provide greater improvement but pose a higher risk of elevated intraocular pressure, whereas posterior sub-tenon injections offer a safer, less invasive alternative. Treatment choice should be tailored to patient risk factors, with intravitreal injections preferred for maximizing visual outcomes and posterior sub-tenon injections for patients at risk of ocular complications. Further research is needed to assess long-term effects and broader patient populations.

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