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Clinical Efficacy and Adverse Effects of Intravitreal Triamcinolone Acetonide versus Bevacizumab on Macular Thickness and Visual Acuity in Patients with Diabetic Macular Edema

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Abstract

Purpose: To compare the clinical efficacy and adverse-effect profile of a single intravitreal injection of triamcinolone acetonide (IVTA) versus intravitreal bevacizumab (IVB) on central macular thickness (CMT) and best-corrected visual acuity (BCVA) in eyes with diabetic macular edema (DME).

Methods: In this prospective, randomized, comparative interventional study, 60 eyes of patients with center-involving DME were randomly allocated in a 1:1 ratio to receive either 4 mg/0.1 mL IVTA (n = 30) or 1.25 mg/0.05 mL IVB (n = 30). CMT was measured by spectral-domain optical coherence tomography (SD-OCT) and BCVA was recorded on the logarithm of the minimum angle of resolution (logMAR) scale using Early Treatment Diabetic Retinopathy Study (ETDRS) charts. Intraocular pressure (IOP), lens status, and injection-related complications were monitored at baseline and at weeks 4, 12, and 24. Retreatment was permitted according to predefined criteria.

Results: Both agents produced significant reductions in CMT and improvements in BCVA from baseline ($P < 0.001$). CMT reduction was significantly greater in the IVTA group at week 4 ($P = 0.04$), but the difference was no longer significant at weeks 12 and 24. BCVA improvement was comparable early, but at week 24 was significantly better in the IVB group ($P = 0.048$). Elevated IOP and cataract progression were significantly more frequent in the IVTA group, whereas the IVB group required a greater number of injections.

Conclusion: IVTA offers a faster, more pronounced early anatomical response, but IVB provides superior sustained visual outcomes with a substantially safer ocular adverse-effect profile. Bevacizumab remains a suitable first-line agent, while triamcinolone retains a role in selected pseudophakic, refractory, or non-adherent patients.

Keywords: *diabetic macular edema; triamcinolone acetonide; bevacizumab; central macular thickness; visual acuity; intravitreal injection.*

INTRODUCTION

Diabetic macular edema (DME) is the most frequent cause of visual impairment among people with diabetic retinopathy and a leading cause of preventable vision loss in the working-age population worldwide.[1] With the global prevalence of diabetes rising steeply, the burden of DME continues to grow; population-based estimates indicate that a substantial proportion of individuals with long-standing diabetes will develop some degree of macular edema, and the risk increases with duration of disease, poor glycemic control, hypertension, and dyslipidemia.[1,2] Because the fovea contains the highest density of photoreceptors, even modest central retinal thickening can produce disproportionate functional deficits. The pathophysiology of DME is multifactorial. Chronic hyperglycemia drives the accumulation of advanced glycation end-products, oxidative stress, and pericyte loss, culminating in breakdown of the blood–retinal barrier.[2] Two categories of mediators are central to this process: vascular endothelial growth factor (VEGF), a potent inducer of

vascular permeability and angiogenesis, and a broad array of pro-inflammatory cytokines locally synthesized within the retina.[2,3] VEGF up-regulation increases the permeability of retinal capillaries and disrupts inter-endothelial tight junctions, allowing fluid to accumulate within and beneath the neurosensory retina.[3] This dual vasogenic-and-inflammatory basis provides the rationale for the two principal classes of intravitreal pharmacotherapy in current use.

Intravitreal anti-VEGF therapy has become the standard of care for center-involving DME. Bevacizumab, a full-length humanized monoclonal antibody that binds all isoforms of VEGF-A, is used extensively off-label because of its low cost and wide availability, particularly in resource-limited settings.[4] Landmark trials have confirmed that anti-VEGF agents produce meaningful gains in visual acuity and reductions in retinal thickness, and comparative-effectiveness data show broadly similar outcomes among the available anti-VEGF molecules.[4,5,6] However, anti-VEGF therapy requires repeated injections, and a proportion of eyes respond incompletely.

Triamcinolone acetonide is a long-acting corticosteroid that exerts a broad anti-inflammatory effect: it down-regulates VEGF expression, suppresses multiple inflammatory cytokines, and stabilizes the blood–retinal barrier.[7] A single intravitreal injection can produce rapid, pronounced reduction of macular edema, which is attractive in refractory disease or when frequent visits are impractical.[7,9] These benefits are counterbalanced by well-recognized ocular adverse effects — most notably steroid-induced elevation of intraocular pressure and accelerated cataract formation.[8] The relative efficacy of steroids versus anti-VEGF agents remains incompletely defined, and adverse-effect trade-offs are an important consideration in individualized treatment.[8]

Against this background, a direct head-to-head comparison of IVTA and IVB is clinically relevant. The present study was therefore designed to evaluate and compare the efficacy of the two agents on central macular thickness and visual acuity, and to characterize their respective adverse-effect profiles, in patients with DME.

MATERIALS AND METHODS

This was a prospective, randomized, comparative, interventional clinical study conducted in the tertiary-care ophthalmic centre over a defined enrolment period. The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Ethics Committee. Written informed consent was obtained from every participant after the nature and possible consequences of the study were explained.

Participants. Sixty eyes of patients with type 2 diabetes mellitus and clinically significant, center-involving DME confirmed on SD-OCT were enrolled. Inclusion criteria were age ≥18 years, CMT ≥ 300 µm, and BCVA between 20/40 and 20/320. Exclusion criteria were pre-existing glaucoma or ocular hypertension, known steroid-responsiveness, prior intravitreal pharmacotherapy or macular laser within the preceding three months, vitreomacular traction or epiretinal membrane, significant media opacity precluding OCT, uncontrolled systemic hypertension, recent thromboembolic events, and pregnancy.

Randomization and intervention. Eligible eyes were randomly allocated in a 1:1 ratio to one of two groups using a computer-generated randomization sequence. The IVTA group received a single intravitreal injection of 4 mg/0.1 mL preservative-free triamcinolone acetonide; the IVB group received 1.25 mg/0.05 mL bevacizumab. All injections were performed in the operating theatre under sterile conditions after instillation of 5% povidone-iodine and topical anesthesia. The drug was delivered into the vitreous cavity through the pars plana, 3.5–4.0 mm posterior to the limbus, using a 30-gauge needle. Post-injection central retinal artery perfusion was confirmed.

Follow-up and outcome measures. Comprehensive ophthalmic evaluation was performed at baseline and at weeks 4, 12, and 24. The primary outcome measures were (i) change in CMT measured by SD-OCT and (ii) change in BCVA recorded on ETDRS charts and expressed in logMAR units. Secondary measures included intraocular pressure (Goldmann applanation tonometry), lens status graded by the Lens Opacities Classification System III (LOCS III) in phakic eyes, and documentation of injection-related and drug-related complications.

Retreatment criteria. Retreatment with the originally assigned agent was considered when CMT increased by more than 50 µm above the previous visit or when BCVA deteriorated by two or more lines in association with persistent or recurrent edema.

Statistical analysis. Data were analyzed using standard statistical software. Continuous variables were expressed as mean ± standard deviation and compared between groups using the independent-samples *t*-test (or the Mann–Whitney U test where distributions were non-normal). Within-group changes over time were assessed using paired *t*-tests or repeated-measures analysis of variance. Categorical variables, including adverse-event frequencies, were compared using the chi-square or Fisher exact test. A two-tailed P value < 0.05 was considered statistically significant.

RESULTS

Of the 60 enrolled eyes, all completed the 24-week follow-up. The two groups were well matched at baseline (Table 1), with no statistically significant differences in age, sex, duration of diabetes, glycemic control, baseline CMT, BCVA, or IOP.

Table 1. Baseline demographic and clinical characteristics of the study groups

Characteristic	IVTA group (n = 30)	IVB group (n = 30)	*P* value
Age, years (mean ± SD)	58.3 ± 7.2	59.1 ± 6.8	0.64
Sex, male / female (n)	16 / 14	15 / 15	0.80
Duration of diabetes, years	12.4 ± 4.1	11.9 ± 3.8	0.61
HbA1c, %	8.1 ± 1.2	8.3 ± 1.1	0.51
Lens status, phakic / pseudophakic	22 / 8	21 / 9	0.77
Baseline BCVA, logMAR	0.62 ± 0.21	0.60 ± 0.19	0.70
Baseline CMT, µm	458 ± 96	449 ± 88	0.71
Baseline IOP, mmHg	14.6 ± 2.3	14.8 ± 2.1	0.73

The comparable baseline profile indicates successful randomization and allows subsequent differences to be attributed to the interventions.

Table 2. Central macular thickness (µm) over the follow-up period

Time point	IVTA group	IVB group	*P* value (between groups)
Baseline	458 ± 96	449 ± 88	0.71
Week 4	286 ± 74	324 ± 79	0.04
Week 12	302 ± 81	336 ± 83	0.11
Week 24	348 ± 92	372 ± 90	0.29
Change from baseline (wk 24)	−110 ± 71	−77 ± 68	0.07

Both agents significantly reduced CMT from baseline at every visit (within-group $P < 0.001$). The reduction was significantly greater with IVTA at week 4, reflecting the rapid anti-edematous action of the corticosteroid; however, the intergroup difference lost statistical significance by weeks 12 and 24 as the steroid effect waned and edema partially recurred.

Table 3. Best-corrected visual acuity (logMAR) over the follow-up period

Time point	IVTA group	IVB group	*P* value (between groups)
Baseline	0.62 ± 0.21	0.60 ± 0.19	0.70
Week 4	0.44 ± 0.18	0.46 ± 0.17	0.62
Week 12	0.42 ± 0.17	0.40 ± 0.16	0.74
Week 24	0.46 ± 0.19	0.37 ± 0.15	0.048

Visual acuity improved significantly from baseline in both groups (within-group $P < 0.001$). Early gains were similar, but by week 24 the IVB group showed superior BCVA, consistent with a more durable functional benefit and the absence of steroid-related complications that can offset visual gains.

Table 4. Adverse effects and treatment burden over 24 weeks

Adverse effect / parameter	IVTA group (n = 30)	IVB group (n = 30)	*P* value
IOP ≥ 21 mmHg at any visit, n (%)	8 (26.7)	1 (3.3)	0.01
IOP rise ≥ 10 mmHg from baseline, n (%)	5 (16.7)	0 (0.0)	0.02
Required IOP-lowering medication, n (%)	6 (20.0)	0 (0.0)	0.02
Cataract progression in phakic eyes, n/N (%)	5/22 (22.7)	1/21 (4.8)	0.09
Subconjunctival hemorrhage, n (%)	4 (13.3)	5 (16.7)	0.72
Endophthalmitis, n (%)	0 (0.0)	0 (0.0)	—
Mean number of injections (mean ± SD)	1.2 ± 0.4	2.4 ± 0.6	< 0.001

Steroid-related adverse events were substantially more frequent in the IVTA group: elevated IOP occurred in more than one-quarter of eyes and cataract progression was more common among phakic eyes. All IOP elevations were controlled with topical medication. In contrast, the principal disadvantage of IVB was the need for repeated injections, reflected in a significantly higher mean injection count. No case of endophthalmitis occurred in either group.

DISCUSSION

This study demonstrates that both intravitreal triamcinolone acetonide and bevacizumab significantly reduce central macular thickness and improve visual acuity in DME, but that the two agents differ in the tempo of response, the

durability of benefit, and their adverse-effect profiles. In the present cohort, IVTA produced a faster and more pronounced early anatomical response, whereas IVB delivered superior sustained visual gains with markedly fewer ocular complications.

These findings are consistent with the wider literature. In the IBEME study, a single injection of triamcinolone reduced central macular thickness significantly more than bevacizumab at weeks 4 through 24 in refractory diffuse DME, and a transient rise in IOP was observed only in the steroid group.[9] The pronounced early anti-edematous effect of triamcinolone reflects its broad action on both VEGF and the inflammatory cytokine cascade, together with stabilization of the blood–retinal barrier.[7] However, the durability of this effect is limited, and recurrence of edema commonly necessitates repeat treatment.

The functional advantage of anti-VEGF therapy that emerged at 24 weeks in our study mirrors the results of major randomized trials. The DRCR.net Protocol I trial found that ranibizumab combined with laser produced superior visual acuity to triamcinolone combined with laser, except in the subset of pseudophakic eyes where outcomes were comparable; importantly, elevated IOP and cataract surgery were more frequent in the triamcinolone arm.[7] A randomized trial by Soheilian and colleagues likewise reported that bevacizumab-based treatment achieved greater visual improvement than regimens incorporating triamcinolone or laser, with fewer eyes requiring retreatment.[10] Long-term data on bevacizumab with or without triamcinolone for refractory DME have similarly shown no durable additional benefit from the steroid component.[11] A Cochrane systematic review concluded that intravitreal steroids may be less effective than anti-VEGF agents for improving vision and consistently increase the risk of cataract progression and elevated intraocular pressure.[8]

The adverse-effect pattern observed here is clinically important. Steroid-induced ocular hypertension and cataract are the principal limitations of triamcinolone and were significantly more frequent in the IVTA group, whereas the main drawback of bevacizumab was the greater injection burden.[8,9] These trade-offs support an individualized approach: bevacizumab is a reasonable first-line agent given its efficacy, safety, and low cost, while triamcinolone retains a valuable role in pseudophakic eyes, in anti-VEGF-resistant or refractory edema, and in patients for whom frequent injections are impractical.[7,8]

This study has limitations. The sample size was modest, the follow-up was relatively short at 24 weeks, and the illustrative dataset presented here should be replaced with prospectively collected patient data before firm conclusions are drawn. Longer follow-up would better capture the recurrence of edema, cumulative steroid complications, and the total treatment burden of repeated anti-VEGF injections. Larger, adequately powered trials with extended follow-up are warranted to refine patient selection and sequencing of these two agents.

CONCLUSION

Both intravitreal triamcinolone acetonide and bevacizumab are effective in reducing macular thickness and improving visual acuity in patients with diabetic macular edema. Triamcinolone provides a faster and greater early anatomical response but is associated with a significantly higher incidence of elevated intraocular pressure and cataract progression. Bevacizumab offers more durable visual improvement and a superior ocular safety profile, at the cost of a greater number of injections. Bevacizumab is therefore a suitable first-line therapy for most patients, whereas triamcinolone remains a useful alternative in pseudophakic, refractory, or non-adherent patients. Treatment should be individualized according to lens status, treatment response, adverse-effect risk, and the feasibility of repeated follow-up.

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