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Suprachoroidal Triamcinolone Acetonide Injection to Treat Macular Edema: A Review

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Abstract

Purpose: To review the available literature on the efficacy and safety of suprachoroidal triamcinolone acetonide for the treatment of chorioretinal diseases. **Methods:** The results of a literature review were analyzed. **Results:** This review included 17 clinical studies of triamcinolone acetonide administration (6, diabetic macular edema; 1, central retinal vein occlusion [RVO]; 2, branch RVO; 7, noninfectious uveitis; 1, cystoid macular edema after cataract surgery). Overall, suprachoroidal triamcinolone acetonide was shown to be effective in decreasing macular thickness and increasing visual acuity (VA) in cases of chorioretinal diseases. The most frequently reported adverse events were eye pain, cataract, and increased intraocular pressure. **Conclusions:** Except for 3 sufficiently powered trials of suprachoroidal triamcinolone acetonide for macular edema associated with noninfectious uveitis, most other studies were clinical trials with small samples. These studies found that suprachoroidal triamcinolone acetonide has a satisfactory safety and efficacy profile. Further research with sufficiently large samples is required to confirm the potential role of suprachoroidal triamcinolone acetonide in retinal diseases.

Keywords

suprachoroid, steroids, triamcinolone acetonide, macular edema

Introduction

Pharmacological treatments for posterior segment ocular diseases have evolved rapidly in the past few years. At present, intravitreal (IVT) administration is the favored method to inject medications for posterior segment disease. However, IVT administration is invasive and medications injected intravitreally diffuse into the anterior segment of the eye, resulting in quick clearance and adverse events (AEs).[1] The suprachoroidal space is being explored as a potential site for local delivery of ophthalmic drugs. Drugs injected in the suprachoroidal space are compartmentalized from the anterior segment, thus providing the benefit of targeting the chorioretina without the unnecessary side effects caused by drug diffusion into the anterior segment.[2]

The role of steroids in the treatment of macular edema (ME) is well established. Triamcinolone acetonide injected intravitreally is known to be effective.[3–5] In a preclinical study, triamcinolone acetonide injected in the suprachoroidal space in rabbits achieved a higher concentration in the posterior segment than IVT injection and did not accumulate in the anterior segment.[6] Furthermore, other preclinical studies have shown that triamcinolone acetonide can stay in the suprachoroidal space for extended periods, acting as a slow-release drug-delivery system.[7]

As clinicians move to adopt suprachoroidal triamcinolone acetonide injections in their practice, it is important to understand the efficacy and safety profile of this procedure. In this article, we review the available literature on the administration of suprachoroidal triamcinolone acetonide for the treatment of ME.

Methods

The literature search for this review was conducted using PubMed. The primary search included articles published between 2000 and 2023, and other articles were added because of their relevance. The following search terms were included: "suprachoroid", "triamcinolone acetonide", "suprachoroidal triamcinolone acetonide", and "suprachoroidal steroids". Original articles and literature reviews were included.

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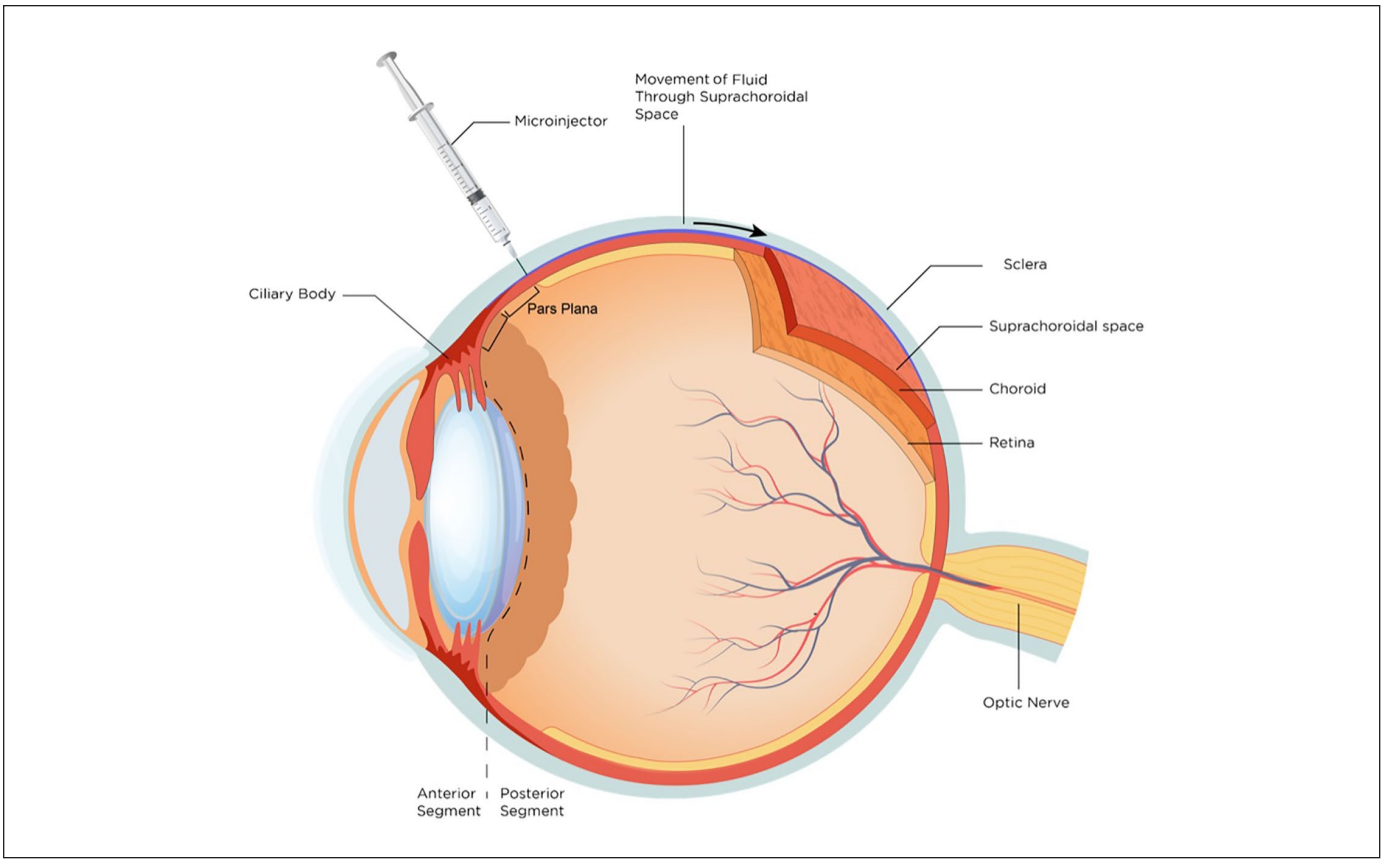

Figure 1. Suprachoroidal administration of a drug and movement of fluid through the suprachoroidal space.

Results

How Suprachoroidal Triamcinolone Acetonide Injection Works

Anatomy of the Suprachoroidal Space. The suprachoroidal space is a potential space that exists between the sclera and the choroid.[8] The suprachoroidal layer consists of expandable collagenous lamellae, and intraocular pressure (IOP) causes the suprachoroidal space to remain collapsed. The suprachoroidal space expands to accommodate fluid, such as in pathologic states (eg, suprachoroidal effusion or suprachoroidal hemorrhage), or when fluid is injected into it. The suprachoroidal space then reverts to its original collapsed state in which the sclera and choroid are apposed to each other (Figure 1).[9] The space is limited anteriorly by the scleral spur, which limits fluid flow to the anterior segment of the eye. Posteriorly, it is limited by the optic nerve and the short ciliary vessels.[10]

The suprachoroidal space can be visualized using advanced optical coherence tomography (OCT) techniques.[2] Hanhart and Rozenman[11] found that by using enhanced depth imaging in swept-source OCT, they were able to increase the proportion of eyes in which the suprachoroidal space was visible as well as the total visible area of the suprachoroidal space.

Access to the Suprachoroidal Space. The suprachoroidal space is accessed using microneedles.[12] Alternative methods of access include creating a scleral flap, using a standard hypodermic needle, and performing cannulation.[13] However, the minimal invasiveness, reduced risk for hemorrhage, and rapid sealing of the injection site favor the use of microneedles.[14]

Most studies included in this review used the Clearside Biomedical suprachoroidal space microinjector. It is supplied with two 30-gauge microneedles that are 900 µm and 1100 µm in length, respectively. The microneedle enters the suprachoroidal space by puncturing the sclera. The flow of the injection into the suprachoroidal space results in expansion of the space with a loss of resistance. If a loss of resistance is not felt, the user is advised to switch to the 1100 µm needle.

In a retrospective analysis of data from 6 clinical trials, Wan et al[15] assessed the user experience with the suprachoroidal space microinjector in eyes with retinal disorders and found that the 900 µm needle was used in 70.9% of the procedures. Sex and the quadrant of administration were the only statistically significant variables that correlated with the length of the needle. The 900 µm needle was used in 76% of surgeries in women and in 66% of surgeries in men. It was also used for 78% of injections in the superotemporal quadrant vs 65% in the inferotemporal quadrant.

The other commonly used technique was to modify a needle, such as cutting the cannula of a 30-gauge insulin syringe so that only 1000 µm of the syringe is exposed.[16–18]

Pharmacokinetics of the Suprachoroidal Space. In a review of the suprachoroidal space as a route of drug administration, Chiang et al[19] summarized the distribution, clearance, and bioavailability of drugs injected in the suprachoroidal space. Although they found higher levels of the drug in the chorioretina with suprachoroidal injections than with IVT injections, the rate of clearance increased as well.

Fluid flow in the suprachoroidal space has been described as circumferential and not uniform.[20] Animal studies have shown that the flow is toward the back of the eye and that the pressure in the eye decreases posteriorly. Distribution is related to the volume and viscosity of the formulation injected, and particle size and molecular weight affect the clearance rate.[21–23]

Change in the Suprachoroidal Space After Injection of Fluid. To investigate whether injecting a therapeutic agent in the suprachoroidal space causes permanent transformation, HULK study researchers conducted a post hoc analysis.[24] They compared the thickness of the suprachoroidal space in the study eye (injected with CLS-TA) with that in the fellow eye. Images were taken before and 30 minutes after each injection using anterior segment spectral-domain OCT. Images in which the choroid was not clearly visible were excluded. The researchers found a statistically significant enlargement of the superior–temporal quadrant 30 minutes after injection, which was not noted in other quadrants. However, the mean suprachoroidal width returned to baseline levels 1 month after the last injection.

Willoughby et al[25] evaluated changes in the choroidal thickness in eyes of patients enrolled in the TANZANITE study. They acquired enhanced depth imaging OCT images to measure the vascular choroidal thickness, stromal choroidal thickness, and total choroidal thickness. There was no significant change in these measurements 3 months after the last treatment. The authors calculated the thickness of the suprachoroidal space by subtracting the stromal choroidal thickness from the total choroidal thickness and found that there was a trend toward thickening of the space in eyes treated with CLS-TA.

Triamcinolone Acetonide

Mechanism of Action. ME in retinal vascular diseases is caused by up-regulation of gene products that cause retinal vascular leakage, including vascular endothelial growth factor (VEGF).[26] For this reason, anti-VEGF agents are usually the first line of treatment for retinal vein occlusions (RVOs) and diabetic ME (DME). However, anti-VEGF may be ineffective in some patients.[27] In addition, because of cost and compliance issues, triamcinolone acetonide is being used as an alternative.[28]

Triamcinolone acetonide is a small, synthetic, lipophilic glucocorticoid receptor agonist.[29] It reduces ME and improves VA (1) by decreasing the levels of VEGF and other factors that promote permeability, which decreases vascular permeability and proliferation,[30] and (2) by inducing lipocortin synthesis, which inhibits phospholipase A2, leading to reduced arachidonic acid release and thus reduced formation of prostaglandins and leukotrienes, both of which are inflammatory mediators.[31]

Current Formulations. The injectable formulations of triamcinolone acetonide used in the studies included in this review are as follows: CLS-TA (Xipere, Bausch + Lomb) (40 mg/mL), Triesence (Alcon) (40 mg/mL), Kenacort (GlaxoSmithKline) (40 mg/mL), and Epirelefan (EPICO) (40 mg/mL). Most clinical trials included in this review used CLS-TA.

Indications for Triamcinolone Acetonide

Diabetic Macular Edema. The HULK phase 1/2 clinical trial was the first use of CLS-TA for DME and the first use as monotherapy in previously treated patients with any retinal vascular disease.[32] Patients were divided into the following 3 arms: previously treated, treatment-naïve, and combination. At baseline, all 20 patients received 0.1 mL (4 mg) of CLS-TA; treatment-naïve patients also received a single IVT injection of aflibercept 0.05 mL (2 mg). Pro re nata CLS-TA was given if the retreatment criteria were met. At 6 months, the previously treated arm had a mean improvement in best-corrected visual acuity (BCVA) of 1.1 letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart and a mean reduction in central subfield thickness (CST) of 128 μm. The treatment-naïve arm had a mean improvement in BCVA of 8.5 letters and a mean reduction in CST of 331 μm. The combination arm had a mean improvement in BCVA of 5.2 letters, and 89% these patients had a greater than 50% reduction in CST.

TYBEE was a phase 2 trial that recruited treatment-naïve patients with DME.[33] The intervention group was administered suprachoroidal CLS-TA 0.1 mL (4 mg) and IVT aflibercept 0.05 mL (2 mg). The control arm received monotherapy of aflibercept 0.05 mL (2 mg). Additional IVT aflibercept was given on a pro re nata basis. The mean change in BCVA from baseline to 24 weeks was measured using ETDRS letters, with no statistically significant difference in improvement between the 2 groups. The reduction in CST was significantly more rapid in the intervention group, which also required fewer additional injections. Although there was an increase in IOP in 3 patients in the intervention group and in 1 patient in the control group, no serious ocular AEs were reported.

Tayyab et al[17] evaluated the use of suprachoroidal triamcinolone acetonide in 24 eyes of 24 patients with DME. At 3 months, the mean increase in BCVA was 12 letters and the mean decrease in CST was 333.84 ± 211.01 μm. Only 1 case of increased IOP was reported.

Zakaria et al[16] compared IVT triamcinolone acetonide with 2 different dosages of suprachoroidal triamcinolone acetonide in 45 eyes of 32 patients for the treatment of DME. They did not specify whether the patients were treatment-naïve or had previously received treatment. Patients were divided into 3 groups; Group I received 4 mg of IVT triamcinolone acetonide. Group II received 4 mg of suprachoroidal triamcinolone acetonide.

Group III received 2 mg of suprachoroidal triamcinolone acetonide. All patients had a follow-up of 6 months. Group II had the greatest improvement in BCVA (−0.14 ± 0.21 logMAR) and reduction in central macular thickness (CMT) (−60.18 ± 117.09 μm). Although the BCVA was improved in all 3 groups at the 3-month follow-up, it reverted to baseline levels in Group I and Group II at the 6-month follow-up. In 1 case in Group II, the cataract showed significant progression. Other adverse effects were comparable between the 3 groups. The authors stated that because the CMT improved at 1 month and 3 months but increased to baseline values at 6 months, suprachoroidal triamcinolone acetonide should be reinjected before 6 months.

In a randomized trial comprising 23 pseudophakic eyes of 23 patients with refractory DME resulting from epiretinal membrane (ERM), Abdelshafy Tabl et al[34] compared 4 mg of suprachoroidal triamcinolone acetonide with 4 mg of IVT triamcinolone acetonide. At 3 months, there was no significant difference in the change in BCVA between the 2 groups (IVT group: mean, 0.9 logMAR [range, 0.8-0.9]; suprachoroidal group: mean, 0.8 logMAR [range, 0.6-0.9]; $P = .313$). However, the mean central foveal thickness (CFT) was significantly greater in the IVT group than in the suprachoroidal group at 3 months (385 ± 72 μm vs 323 ± 54 μm; $P = .028$). The mean increase in IOP was greater in the IVT group at the 3-month follow-up (IVT group, 5 mm Hg; suprachoroidal group, 0 mm Hg). In addition, it took less time for DME to recur in patients treated with IVT triamcinolone acetonide and a greater proportion of these patients experienced a recurrence (IVT group, 70%; suprachoroidal group, 30.8%).

In a retrospective analysis of 11 vitrectomized eyes of 10 patients, Marashi and Zazo[35] analyzed the role of suprachoroidal triamcinolone acetonide in DME after pars plana vitrectomy. At the 8-week follow-up, the mean improvement in BCVA was 0.30 ± 0.52 logMAR and the mean reduction in CMT was 208.82 ± 125.36 μm. The change in IOP was not significant, and no AEs were noted.

Central Retinal Vein Occlusion. TANZANITE was a phase 2 trial (n = 46) that compared aflibercept monotherapy with combination therapy comprising suprachoroidal CLS-TA plus IVT aflibercept for ME resulting from RVO.[36] Treatment-naïve patients were recruited. The combination arm required significantly fewer retreatments (5 patients) than the monotherapy arm (16 patients) ($P = .013$). Also, the mean improvement in BCVA was greater in the combination arm at 3 months ($P = .09$). There were 23 AEs in the combination arm, including 4 cases of increased IOP and 1 case of cataract progression.

A phase 3 clinical trial comparing the use of suprachoroidal CLS-TA with IVT aflibercept in patients with ME resulting from RVO was terminated because the primary efficacy endpoint was not met.[37]

Branch Retinal Vein Occlusion. Nawar[18] assessed the effect of suprachoroidal triamcinolone acetonide with IVT ranibizumab in eyes with ME resulting from branch RVO (BRVO). The study included 60 patients; 1 group received monotherapy of ranibizumab 0.05 mL (0.5 mg), while the other group received 0.05 mL (0.5 mg) of ranibizumab and 0.1 mL (4 mg) of suprachoroidal triamcinolone acetonide. The reduction in CMT was more significant in the combination group after 1 month ($P = .008$); however, the difference in the reduction between groups leveled off after 12 months. The rate of recurrence of ME was higher in the monotherapy group, and the BCVA improvement was more significant in the combination group.

The phase 2 TANZANITE trial assessed patients with ME secondary to BRVO and central retinal vein occlusion.[37]

Noninfectious Uveitis. Suprachoroidal triamcinolone acetonide for noninfectious uveitis was first administered to humans by Goldstein et al[38] in a phase 1/2 trial. Nine patients with ME associated with uveitis were enrolled. Patients were administered a single suprachoroidal injection of 0.1 mL (4 mg) of triamcinolone acetonide (Triesence) and were observed for 26 weeks. No patient had ocular or systemic AEs related to the drug; however, 5 patients reported eye pain at the time of or immediately after the injection. All patients had an improvement in BCVA, with a mean improvement of between 8 letters and 14 letters. There was a reduction in retinal thickness, with the mean reduction in CST ranging from 76 μm to 154 μm at week 26.

After the successful phase 1/2 trial, the phase 2 DOGWOOD trial was conducted.[39] It included 22 patients with ME related to noninfectious uveitis. Four fifths of the participants received 4 mg of CLS-TA, and the rest received 0.8 mg of CLS-TA as an exploratory dose. The mean CST at 2 months was reduced from baseline by 164 μm. At 2 months, there was an increase in BCVA of 9.2 ETDRS letters. Treatment-related adverse effects were reported by 13.6% of the patients, with the most common being conjunctival hemorrhage and eye pain.

Similarly, the AZALEA trial was conducted to determine the safety of 4 mg CLS-TA.[40] The trial included 39 patients with noninfectious uveitis with or without ME. The patients were administered a single suprachoroidal injection of CLS-TA 4 mg (0.1 mL) at day 0 and week 12. Rescue treatments could be administered from week 4. Three patients reported eye pain, and there were 7 ocular AEs. No serious AEs were reported. In all cases, the BCVA improved from a mean of 68.9 letters at baseline to 75.9 letters at week 24. The mean CST decreased from 335.9 μm to 284.0 μm.

PEACHTREE was the first phase 3 trial to assess injection of a therapeutic agent into the suprachoroidal space to treat an ocular disease.[41] The trial included 160 patients with ME secondary to noninfectious uveitis. Patients were randomized to a single unilateral dose of CLS-TA 4 mg at day 0 and week 12 (CLS-TA group) or to sham procedures for masking (control group). The primary outcome measure was an improvement in BCVA of 15 or more ETDRS letters from baseline to week 24. In the CLS-TA group, 46.9% had an improvement of 15 or more letters vs only 15.6% in the control group. The secondary outcome measure was the reduction in CST from baseline to week 24. The reduction in CST was 153 μm in the CLS-TA group and 18 μm in the control group. Rescue therapy was required by 13.5% in the CLS-TA group vs 72% in the control group. Treatment-related AEs occurred in 51% of patients in

the CLS-TA group and in 58% in the control group. Cystoid ME (CME) (0% CLS-TA vs 17.2% control), eye pain (12.5% vs 4.7%), and increased IOP (11.5% vs 15.6%) were the most frequent AEs.

A post hoc analysis of the PEACHTREE trial assessed whether adjuvant systemic corticosteroid treatment boosted the therapeutic effect of CLS-TA.[42] Patients who received systemic treatment had less improvement. However, the authors noted that patients requiring additional medication had more severe disease; therefore, disease severity may have resulted in less improvement.

Another post hoc evaluation of the PEACHTREE trial evaluated the difference in outcomes at week 24 in patients in the control arm who received rescue therapy.[43] Rescue therapy was administered if the patient met prespecified criteria (≥10 letter decrease from baseline; ≥100 μm or 20% increase in CST from baseline; ≥1.5 step increase in the level of inflammation from baseline or an increase from +3 to +4; the uveitic complications in the study eye were not improving). The type and route of rescue therapy administered were decided by the investigator. The first rescue therapies were corticosteroids administered topically (39.1%), intravitreally (30.4%), systemically (13.0%), or periocularly (10.9%). Topical nonsteroidal anti-inflammatory drugs (NSAIDs) were administered to 6.5% of the patients receiving rescue therapy. At week 24, patients in the control arm receiving rescue therapy had a mean increase in BCVA of 10.9 letters and a mean reduction in CST of 148.5 μm. Patients in the CLS-TA arm who did not receive rescue therapy had a mean improvement of 15.7 letters and a mean reduction of 174.0 μm, respectively.

MAGNOLIA, an extension study of the PEACHTREE trial, continued to evaluate patients for 24 weeks after the trial ended.[44] Patients were enrolled if they had not required rescue treatment in the original trial. The study enrolled 28 patients from the original CLS-TA arm and 5 from the original control arm. After 48 weeks, 14 patients in the CLS-TA arm and 2 patients in the control arm did not require rescue treatment. At least 1 treatment-related ocular AE occurred in 21 patients.

Hanif et al[45] assessed the safety and efficacy of suprachoroidal triamcinolone acetonide for ME associated with noninfectious uveitis in 30 patients, who were administered 0.1 mL of triamcinolone acetonide (Kenacort). All patients had a follow-up assessment at 1 month and 3 months. The CMT decreased from a mean of 569 μm at baseline to 208 μm at 3 months ($P < .001$). The BCVA increased from 0.142 logMAR to 0.469 logMAR ($P < .001$). No significant ocular adverse effects were noted.

Cystoid Macular Edema After Cataract Surgery. Oli and Waikar[46] reported on suprachoroidal triamcinolone acetonide injection for pseudophakic CME in 3 patients who had been using topical NSAIDs for more than 3 months. After the injection, the patients were followed for up to 12 weeks. The BCVA improved from a mean of 1 logMAR to 0.3 logMAR, and the CMT decreased from a mean of 473.5 μm to 287.0 μm. No significant ocular AEs were documented. The authors provided no other details about the study methodology.

To our knowledge, no prospective control studies of pseudophakic ME and the use of suprachoroidal triamcinolone acetonide have been published.

Table 1 summarizes the results of all studies included in our review.[16–18,32–36,38–41,43–46]

Effective Dose of Suprachoroidal Triamcinolone Acetonide: 2 mg vs 4 mg. Only a single study compared different doses of suprachoroidal triamcinolone acetonide. The study by Zakaria et al[16] comprised 45 eyes of 32 patients with DME. As stated above, the patients were divided into 3 groups as follows: Group I, 4 mg of IVT triamcinolone acetonide; Group II, 4 mg of suprachoroidal triamcinolone acetonide; Group III, 2 mg of suprachoroidal triamcinolone acetonide. All patients had a follow-up of 6 months. Group II (higher dose) had a greater reduction in BCVA than Group III (-0.14 ± 0.21 logMAR vs -0.02 ± 0.14 logMAR) and in CMT (-60.18 ± 117.09 μm vs -19.53 ± 86.29 μm) at the 6-month follow-up. Group II and Group III had a similar number of steroid-related side effects, with an IOP increase in 2 patients and 1 patient, respectively, and cataract progression in 3 cases in each group.

Steroid Response: IVT Triamcinolone Acetonide vs Suprachoroidal Triamcinolone Acetonide

Abdelshafy Tabl et al[34] compared the effect of IVT triamcinolone acetonide with that of suprachoroidal triamcinolone acetonide for refractory DME resulting from ERM. They injected suprachoroidal triamcinolone acetonide in 13 eyes and IVT triamcinolone acetonide in 10 eyes. By 3 months, the median BCVA had decreased by 0.2 logMAR in the suprachoroidal group and by 0.1 logMAR in the IVT group ($P = .313$). The mean CFT had decreased by 218 μm and 127 μm, respectively ($P = .028$). Patients in the IVT group had a mean increase in IOP of 5 mm Hg, while no patient in the suprachoroidal group had an IOP increase ($P = .028$).

In the Abdelshafy Tabl et al[34] study, the changes in CFT and BCVA from baseline in the suprachoroidal group were greater than in the IVT group. In addition, the time to recurrence of DME was less in the IVT group, with 50% of patients having a relapse at 1 month and 70% having a relapse by 3 months. In the suprachoroidal group, the recurrence rates were 0% at 1 month and 30.8% at 2 months. Thus, the authors concluded that although IVT triamcinolone acetonide was effective in reducing vision impairment, the faster recurrence timeline and IOP elevation make triamcinolone acetonide administration by IVT injection a less favorable choice.

Zakaria et al[16] compared IVT triamcinolone acetonide and suprachoroidal triamcinolone acetonide to treat DME. They found that the IVT group had the lowest reduction in CMT and the least change in BCVA of the 3 groups. However, the increase in IOP and the rate of cataract progression were comparable between the 2 modes of injection.

Table 1. Summary of Included Studies.

Indication/Author[a]/Year	Study/Trial Design	Year[b]	Patients (n)	Eyes (n)	Dosage	FU	CFT Change	CFT *P* Value	BCVA Change	BCVA *P* Value	Adverse Event (Cases)
Diabetic macular edema											
Wykoff[32]/2018	Phase 1/2 prospective multicenter randomized controlled trial (HULK)	2016	20	—	4 mg	6 mo	Treatment naïve: −91 μm Previously treated: −128 μm	—	Treatment naïve: +8.5 letters Previously treated: +1.1 letters	—	Cataract progression (3) IOP increase >10 mm Hg (2) Pain (1)
Barakat[33]/2021	Phase 2 randomized double-masked parallel-design controlled study	2017	71	—	4 mg	6 mo	Active ITT: −212.1 μm Control ITT: −178.6μm Active PP: −226.5 μm Control PP: −176.1 μm	.089 .035	Active ITT: +11.4 letters Control ITT: +13.8 letters Active PP: +12.3 letters Control PP: +13.5 letters	.288 .664	Raised IOP (3) Conjunctival hemorrhage (2)
Tayyab[17]/2020	Prospective nonrandomized interventional study	2018	24	24	4 mg	3 mo	−333.84 μm	.00001	+22 letters	.05	Raised IOP (1)
Zakaria[16]/2022	Prospective interventional randomized comparative study	2019	32	45	Group I: 4 mg IVTA Group II: 4 mg SCTA Group III: 2 mg SCTA	6 mo	Group I: +23.36 μm Group II: −60.18 μm Group III: +19.53 μm	.000 .001 .000	Group I: −0.01 logMAR Group II: −0.14 logMAR Group III: −0.02 logMAR	.006 .001 .007	Group I: raised IOP (1); cataract progression (3) Group II: raised IOP (2); cataract progression (3) Group III: raised IOP (1); cataract progression (3)
Abdelshafy Tabl[34]/2022	Randomized clinical trial	2020	23	23	4 mg	3 mo	SCTA: −218 μm IVTA: −127 μm	<.001 <.001	SCTA: −0.2 logMAR IVTA: −0.1 logMAR	.001 .003	None reported
Marashi[35]/2022	Case series	2020	10	11	4 mg	8 wk	−208.82 μm	.003	−0.35 logMAR	.003	None reported
Retinal vein occlusion											
Campochiaro[36]/2018	Phase 2 randomized masked controlled clinical trial (TANZANITE)	2014	46	—	4 mg	3 mo	CRVO: −603 μm BRVO: −343 μm	—	CRVO: +22 letters BRVO: +18 letters	—	Raised IOP (4)
Nawar[18]/2022	Prospective randomized interventional study	2020	60	—	4 mg	12 mo	−330.7 μm	.001	+0.9 log MAR	<.001	None reported

(continued)

Table 1. (continued)

Indication/Author[a]/ Year	Study/Trial		Patients (n)	Eyes (n)	Dosage	FU	CFT		BCVA		Adverse Event (Cases)
	Design	Year[b]					Change	*P* Value	Change	*P* Value	
Noninfectious uveitis											
Goldstein[38]/2016	Phase 1/2 open-label clinical study	2013	11	—	4 mg	26 wk	−107 μm	—	−0.28 logMAR	—	Eye pain (5) No raised IOP- or cataract-related events
Yeh[39]/2019	Randomized controlled masked phase 2 study (DOGWOOD)	2014	16	—	4 mg	2 mo	−164 μm	.0017	+9.2 letters	.004	Eye pain (3) Raised IOP (1) Conjunctival hemorrhage (1)
Henry[40]/2022	Open-label prospective multicenter safety trial (AZALEA)	2017	38	—	4 mg	24 mo	−51.9 μm	—	+7.0 letters	—	Eye pain (3) Raised IOP (5) Cataract (4)
Yeh[41]/2020	Phase 3 masked randomized trial	2015	160	—	4 mg	24 wk	−152.6 μm	<.001	+13.8 letters	<.001	Eye pain (12) Raised IOP (11) Cataract (7)
Singer[43]/2022	Phase 3 randomized controlled trial (PEACHTREE)	2015	129	—	4 mg	24 wk	Unrescued: −174.0 μm Rescued: −148.5 μm	.040	Unrescued: +15.7 letters Rescued: +10.9 letters	.080	Rescued: eye pain (3); raised IOP (2); cataracts (3) Unrescued: eye pain (9); raised IOP (9); cataracts (4)
Khurana[44]/2022	Extension study of phase 3 randomized trial (MAGNOLIA)	2017	33	—	4 mg	48 wk	−174.5 μm	.001	+12.1 letters	.04	Cataract-related AE (4) Raised IOP (4)
Hanif[45]/2021	Prospective nonrandomized interventional study	2019	30	—	4 mg	3 mo	−361.33 μm	.001	−0.33 logMAR	<.001	Lenticular changes (5)
Post-cataract CME											
Oli[46]/2021	Case series	2020	3	—	4 mg	4 wk	−186.5 μm	—	−0.7 logMAR	—	None reported

Abbreviations: AE, adverse event; BCVA, best-corrected visual acuity; BRVO, branch retinal vein occlusion; CME, cystoid macular edema; CFT, central field thickness; CRVO, central retinal vein occlusion; FU, follow-up; IOP, intraocular pressure; ITT, intention to treat; IVTA, intravitreal triamcinolone acetonide; PP, per protocol; SCTA, suprachoroidal triamcinolone acetonide.

[a]First author.

[b]Year of study/trial commencement.

Macular Edema in Vitrectomized Eyes

ME after vitrectomy may be secondary to the effect of surgery or to the presence of silicone oil (SO), when used. To our knowledge, no study evaluating the efficacy of suprachoroidal triamcinolone acetonide to treat ME in silicone-filled eyes has been published. SO-induced ME is a frequent complication,[47] and suprachoroidal injection of triamcinolone acetonide may prove a useful route in these difficult cases.

Conclusions

Treating ME with IVT anti-VEGF is costly. In addition, IVT anti-VEGF must be injected frequently, and multiple injections lead to low patient compliance. In some patients, anti-VEGF is ineffective because of an insufficient response to treatment. Anti-VEGF therapy yields a limited response, most likely because of the multiple disorders that can lead to ME.[48] Steroids target alternate pathways to those anti-VEGF targets. Multiple clinical trials with small samples that studied suprachoroidal triamcinolone acetonide have shown the safety of both the drug and the suprachoroidal route of delivery. Suprachoroidal triamcinolone acetonide treatment could benefit patients in terms of fewer clinic visits, swift improvement, longer lasting effects, and cost savings.

The absence of high-quality clinical trials means there is still uncertainty about the role of suprachoroidal triamcinolone acetonide in retinal disorders. Although a number of trials have been conducted, they are limited by their modest sample sizes. ME in noninfectious uveitis has been studied in a phase 3 trial involving 160 patients. No such large-scale studies that evaluated the safety and efficacy of suprachoroidal triamcinolone acetonide in DME, ME associated with RVO, and CME have been published. The existence of distinct pathways of ME pathogenesis in each disease means steroids work to a varying extent in each disease. Future research should seek to evaluate suprachoroidal triamcinolone acetonide in diseases other than noninfectious uveitis.

The clearance rate of drugs injected in the suprachoroidal space has been shown to be related to the solution's viscosity and particle size; thus, the formulation of triamcinolone acetonide determines the duration of its therapeutic effect. Current aqueous formulations have a comparatively faster clearance rate. Results in animal studies of controlled-release drug-delivery systems are promising.[19] Because injection in the suprachoroidal space is confirmed by a tactile loss of resistance felt by the clinician, pressure optimization of the injector by lowering the variability in glide force is important.

The pharmacokinetics of vitrectomized eyes indicate that the effects of IVT injections are short lived.[49] A randomized control trial evaluating suprachoroidal triamcinolone acetonide for the treatment of ME in vitrectomized eyes or eyes filled with SO is needed. Further research could also study the long-term effects of suprachoroidal triamcinolone acetonide. The longest current follow-up is 1 year after injection (MAGNOLIA study). Additional studies will help determine whether the side effects of steroid injection appear later and whether a reduction in efficacy occurs after repeated injections. It is important to ascertain where suprachoroidal triamcinolone acetonide will fit in the clinical pathway of ME. It is also important to determine whether suprachoroidal triamcinolone acetonide will play a role as a standalone treatment or as an adjunct to other treatments for ME. With the introduction of newer anti-VEGF agents, it is likely the treatment of ME will become more multimodal, with suprachoroidal triamcinolone acetonide playing a pivotal role.

In conclusion, except for 3 sufficiently powered trials of suprachoroidal triamcinolone acetonide for ME associated with noninfectious uveitis, most other studies were small-group clinical trials. Nonetheless, these studies have shown that suprachoroidal triamcinolone acetonide has a satisfactory safety and efficacy profile. Although it is a promising treatment, further research is needed through sufficiently powered trials to evaluate the efficacy and safety of suprachoroidal triamcinolone acetonide compared with other pharmaceutical agents. Particularly interesting would be the role of suprachoroidal triamcinolone acetonide in treating ME in vitrectomized eyes. Future studies should also assess the role of suprachoroidal triamcinolone acetonide as a primary or adjuvant treatment to reduce ME.

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki.

Statement of Informed Consent

Informed consent was waived for the present study because the analysis consisted of de-identified data obtained through a retrospective review.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article.

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