

A simple technique for suprachoroidal space injection of triamcinolone acetonide in treatment of macular edema

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Abstract

• **AIM:** To introduce a simple resistance controlled suprachoroidal space (SCS) injection technique using a disposable 30-gauge needle connected to a 1 mL syringe and evaluate the effectiveness and applicability of this technique in the treatment of macular edema.

• **METHODS:** A total of 20 patients with various types of macular edema were subjected to a resistance controlled SCS injection of triamcinolone acetonide (TA) with a disposable 30-gauge needle connected to a 1 mL syringe. This technique allows the easy and smooth injection of the TA only once the tip of the needle reached the potential SCS which was indicated by the lower resistance on the plunger. The main outcome measures were anterior segment spectral-domain optical coherence tomography (AS-OCT) measurements post-operation immediately and central subfield thickness (CST), best-corrected visual acuity (BCVA), and intraocular pressure (IOP) measurements at 3mo post-operation.

• **RESULTS:** AS-OCT examination showed the expansion of the SCS near the injection site immediately after SCS injection. At three months of follow-up, as compared to the baseline, the mean CST was significantly decreased from 535.0 ± 157.24 to 319.55 ± 127.30 μm ($P < 0.001$), the mean BCVA was significantly improved from 1.05 ± 0.41 to 0.73 ± 0.41 logMAR ($P < 0.001$), and the mean IOP was not significantly different, from 15.05 ± 2.54 to 15.85 ± 3.60 mm Hg ($P = 0.185$). Any complication related to the injection procedure including cataract, choroidal and retinal hemorrhage, retinal

detachment, or endophthalmitis was not observed in this study.

• **CONCLUSION:** The simple and minimally invasive technique of SCS injection of TA with a disposable 30-gauge needle connected to a 1 mL syringe is useful and applicable for macular edema.

• **KEYWORDS:** suprachoroidal space; injection; needle; macular edema; triamcinolone acetonide

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INTRODUCTION

Although intravitreal injection of anti-vascular endothelial growth factor (VEGF) drugs, steroids, and anti-infective agents is currently the dominant delivery technique for a variety of posterior segment diseases, its use has been associated with severe ocular adverse effects, such as cataracts and glaucoma^[1]. Furthermore, the high frequency and cost imposes increasing burden on the patients^[2].

Recently, the suprachoroidal space (SCS) has emerged as a potential pathway for local drug administration and delivery to the posterior segment of the eye^[3-4]. Studies showed suprachoroidal injection achieved more than 10-fold higher chorioretinal concentrations and lower concentrations in nontarget areas (lens, anterior chamber), compared to intravitreal administration^[5]. This increased selectivity may potentially allow for lower dosage or frequency of drugs, and reduce the risk of cataract formation or elevated intraocular pressure (IOP) associated with corticosteroid delivery^[6-7]. The utilization of the SCS injection has shown successful outcomes in a limited range of ophthalmic diseases, including non-infectious uveitis, retinal vein occlusion (RVO) with macular edema and diabetic macular edema^[7-9].

Access to the SCS is difficult because it is a potential space between the choroid and the sclera. Previous methods include surgically introducing catheters into this space, using a custom-made hollow microneedle or a Hamilton glass syringe^[10-11]. These techniques are invasive or too complex to be performed

as a simple office procedure. Recently, a proprietary microinjector was developed for administering triamcinolone acetonide (TA) suspension through the SCS^[12-13], however, this is expensive and is limited by a lack of widespread availability. We recently developed an easy and minimally invasive technique to inject TA suspension into the SCS using a disposable 30-gauge needle attached to a 1 mL syringe, which is regularly available in clinical practice. This technique allows the easy and smooth injection of the TA only once the tip of the needle reached the potential SCS which was indicated by the lower resistance on the plunger and achieved desired outcomes in the treatment of macular edema. We believe that this resistance controlled SCS injection technique holds promise as an alternative to intravitreal injection and as a routine office procedure.

SUBJECTS AND METHODS

Ethical Approval The study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine. Written informed consent was obtained from all patients before inclusion in the study.

This is a retrospective, interventional, non-comparative case-series study. Patients, especially those who cannot afford the initial or repeated intravitreal anti-VEGF injection for various types of macular edema associated with RVO, diabetic retinopathy or macular surgery were included. Macular edema was indicated as a central subfield thickness (CST) of greater than or equal to 300 μm as measured by spectral-domain optical coherence tomography (SD-OCT)^[14]. Any patient having intravitreal anti-VEGF treatment within last two months, IOP greater than 21 mm Hg, a history of ocular trauma, or less than three months of follow-up after SCS injection was excluded.

Surgical Technique Eye preparation before SCS injection followed general guidelines for intravitreal injection. TA suspension 0.2 mL of 40 mg/mL (TranstonTM, Kunming Jida Pharmaceutical Co., Ltd., Yunnan, China) was drawn up in a single-use 1 mL syringe with a 25-gauge needle. The needle was exchanged for a 30-gauge, 0.5 inch needle (Becton Dickinson, Franklin Lakes, NJ, USA). The 0.1 mL of TA was kept for injection. After a speculum was placed, the conjunctiva was sterilized with a povidone-iodine soaked cotton-tipped applicator. A globe fixation ring was used to prevent movement of the eyeball. With the needle bevel facing the scleral surface parallel to the limbus, the needle was inserted into the sclera at an angle of about 15°–20°, 3.5–4 mm posterior to the limbus in the superior temporal quadrant of the eye. After the bevel was fully buried in the sclera, the tip of the needle was slightly

redirected posteriorly, and inserted slowly and carefully with a slight wriggling movement. Gentle pressure was applied on the syringe plunger throughout insertion, allowing the easy and smooth injection of the TA only once the tip of the needle reached the potential SCS which was indicated by the lower resistance on the plunger. The needle was removed immediately after the injection without keeping for some time to prevent reflux (Video 1, online supplementary, which demonstrates the SCS injection). All the injection procedures were conducted under a surgical microscope by the same surgeon (Zhu DQ).

Follow-up Examination The fundus was examined after SCS injection to see if TA suspension was mistakenly injected into the vitreous cavity. The patients were examined with an anterior segment spectral-domain optical coherence tomography (AS-OCT, Casia SS-1000; Tomey, Nagoya, Japan) before and immediately after the injection. At every postoperative visit, slit-lamp and fundus examination were conducted. The best-corrected visual acuity (BCVA) recorded in decimal acuity was converted to a Snellen fraction and a logarithm of the minimal angle of resolution (logMAR) value for statistical analyses. CST was evaluated using an SD-OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany). IOP was measured using a non-contact tonometer.

Statistical Analysis SPSS software (version 16.0, SPSS, Inc. Chicago, IL, USA) was used for statistical analysis. The CST, BCVA, and IOP values before and after injection were compared using a Wilcoxon rank-sum test. A value of $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 20 eyes of 20 patients were included between February 2019 and January 2021. The baseline demographic and clinical characteristics were shown in Table 1. Of these 20 patients (male 10, female 10), mean age was 59.7 \pm 13.7y (range: 21–81y). Among them there were 11 eyes with RVO (branch and central RVO, 8 and 3, respectively), 7 eyes with diabetic macular edema (4 eyes after vitrectomy) and 2 eyes after epiretinal membrane peeling surgery. Fifteen (75%) of the cases had phakia and 5 (25%) had pseudophakia. Fifteen eyes had the history of anti-VEGF treatments. The mean duration of follow-up after injection was 4.7 \pm 2.8mo (range: 3–12mo). The SCS injection was reperformed in 7 cases with recurrent edema. Overall, a total of 33 SCS injections were performed and Figure 1 depicted the representative image of SCS injection process.

AS-OCT examination showed the expansion of the SCS near the injection site immediately after SCS injection, compared to that at baseline, which confirmed the successful delivery to the SCS (Figure 2).



Figure 1 The representative image of suprachoroidal space (SCS) injection process.

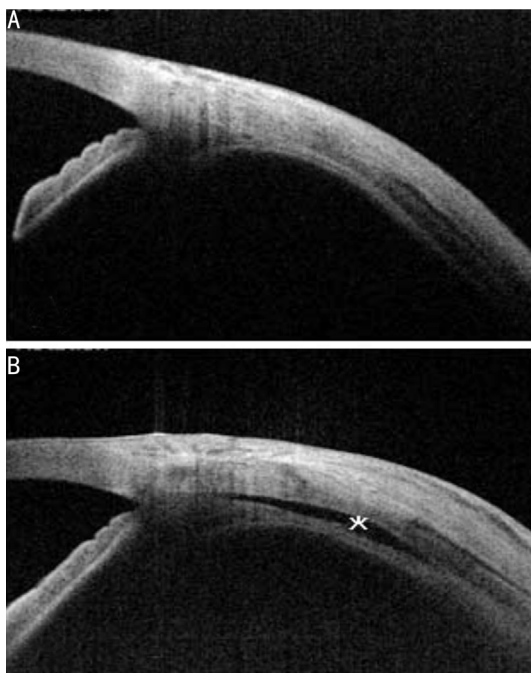


Figure 2 Anterior segment spectral-domain optical coherence tomography images before (A) and immediately after (B) suprachoroidal space (SCS) injection of triamcinolone acetonide (TA) suspension for diabetic macular edema after vitrectomy in a 66-year-old female patient. Expansion of the SCS (asterisk) could be clearly observed after injection, which confirmed the successful delivery of TA to the SCS.

There was no significant difference of the mean IOP before injection (15.05 ± 2.54 mm Hg) and at 1mo after injection (16.10 ± 3.40 mm Hg, $P=0.192$); the mean CST significantly decreased from 535.0 ± 157.24 μm before the injection to 386.3 ± 161.35 μm at one month after injection ($P<0.001$); As shown in Table 2, the mean CST significantly decreased to 319.55 ± 127.30 μm at three months after injection ($P<0.001$); the mean BCVA was significantly improved from 1.05 ± 0.41 to 0.73 ± 0.41 logMAR ($P<0.001$); the mean IOP was 15.85 ± 3.60 mm Hg at three months after injection. The difference was not significant ($P=0.185$). During follow-up, cataract induction was not

Table 1 Baseline demographic and clinical characteristics

Parameters	Patients (n=20)
Age, y, mean \pm SD	59.7 \pm 13.7
Age range, y	21-81
Female, n (%)	10 (50)
Diseases, n (%)	
RVO	11 (55)
Branch RVO	8 (40)
Central RVO	3 (15)
Diabetic macular edema	7 (35)
Epiretinal membrane peeling surgery	2 (10)
Lens state, n (%)	
Phakia	15 (75)
Pseudophakia	5 (2)
Previous anti-VEGF treatment, n (%)	15 (75)
Re-injection, n (%)	7 (35)

RVO: Retinal vein occlusion.

Table 2 The main outcome measures before and after resistance controlled SCS injection

Measures	Mean	SD	95%CI	P
CST (μm)				<0.001
Baseline	535.00	157.24	461.41-608.59	
3mo post injection	319.55	127.30	259.97-379.13	
BCVA (logMAR)				<0.001
Baseline	1.05	0.41	0.86-1.24	
3mo post injection	0.73	0.41	0.54-0.92	
IOP (mm Hg)				0.185
Baseline	15.05	2.54	13.86-16.24	
3mo post injection	15.85	3.60	14.16-17.54	

SCS: Suprachoroidal space; CST: Central subfield thickness; BCVA: Best-corrected visual acuity; IOP: Intraocular pressure; SD: Standard deviation.

observed in the cases with phakia. No additional complications including choroidal and retinal hemorrhage, retinal detachment, or endophthalmitis occurred.

DISCUSSION

This preliminary work demonstrates that the present method can easily and safely enable a minimally invasive injection into the SCS. The good safety and efficacy of SCS injection of TA in improving macular edema in this study suggests that the resistance controlled suprachoroidal injection using a conventional 30-gauge needle attached to a 1 mL syringe may be an alternative to, or to some extent superior to, intravitreal injection. It also demonstrates the promise of SCS injection as a routine administration method for outpatient posterior segment diseases.

Many studies have investigated the localization and distribution of the injected fluid within SCS after SCS injection by visual assessment using India ink, indocyanine green (ICG), TA suspension or fluorescence, ultra high resolution-optical coherence tomography at posterior pole, or

ultrasound biomicroscopy (UBM) in animal eyes or human eyes *ex vivo*^[5,10-11,15-16]. In clinical investigation, thickening or expansion of the SCS could be detected in the central macula using enhanced-depth imaging optical coherence tomography 1mo after an SCS injection of TA suspension with an intravitreal injection of aflibercept, as compared to only an intravitreal injection of aflibercept^[17]. However, it is unclear whether the SCS expansion results from the mechanical effect of the suprachoroidal fluid injected or a pharmacologic effect of the drug suspension. In AS-OCT, anterior SCS width was found increased following the SCS injection^[18]. In this study, we also used AS-OCT examination to determine the SCS morphology at baseline and changes immediately after SCS injections. Expansion of the SCS near the injection site could be clearly observed after injection, which confirmed the successful delivery to the SCS. Limited by the ability of AS-OCT, we could not assess the posterior area over which the TA suspension spread within the SCS. Although the fluid delivered into the SCS may distribute circumferentially around the eye within the SCS^[19], multiple elements, including injection volume, formulations and IOP, have been shown to influence the distribution and delivery to targeted tissues^[15-16]. Regardless of the distribution of TA suspension within SCS in this study, the reduced macular edema after the injection provided strong supporting evidence for the effectiveness of the present injection.

SCS injection using the present method appears challenging. One may worry that the needle would possibly penetrate through the ciliary body, leading to an intraocular injection. Actually, we inadvertently penetrated through the ciliary body in 2 eyes, which occurred in the early phase without the use of a fixation ring. We believe that the learning curve to get accurate and skilled is not expected to be steep, providing that some details of the procedure are carefully concerned. The first critical step is to make sure that the eyeball is stable. A fixation ring could help to control the eye movement. The second step is to appropriately bury the tip of the needle into the sclera with the bevel parallel to the scleral surface. This procedure requires a certain level of experience and has better to be performed under microscope. The third step is to gently wriggle the insertion to facilitate it in a controllable manner to prevent penetration through ciliary body. Lastly, maintaining the pressure on the plunger during the insertion until the smooth injection contributed to accurate SCS injection. Since the expandable SCS has a much lower resistance to flow than the relatively incompressible sclera, the injected fluid could be naturally infused into and expand the SCS before the needle punctured the ciliary body, as long as the gentle pressure was kept. We did not observe any complication related to the injection procedure including choroidal and retinal hemorrhage,

retinal detachment, or endophthalmitis in this study. The post operative process appeared not different from that with an intravitreal injection. There was no increase in IOP and cataract induction during the follow up period, which, on the contrary, is commonly seen with intravitreal steroid use. Our results are in accordance with those observed in the previous investigations that treated macular edema secondary to uveitis or RVO with SCS injection using a proprietary microinjector. To date, anterior SCS is the most accessible location of the SCS. Adequate drug volume should be injected into anterior SCS to allow the distribution of drugs to a large area of the ocular posterior segment. However, increasing injectate volume results in transient IOP elevation likely sufficient to damage retinal perfusion and optic nerve. An additional advantage of the present technique is that there was no fluid reflux occurred after injection because of the oblique insertion of the needle, compared to the perpendicular insertion required with current microneedles. Hence, less volume of drugs, leading to lower incidence of IOP spike, was required to be administered with this injection technique.

Limitations of this study include small number of subjects, short follow-up period, lack of a control or comparison group, and heterogeneity of the indications included. Despite these limitations, the fact that the easy and minimally invasive technique of SCS injection of TA safely and effectively improved macular edema in this study is very encouraging. Further exploration for more cases, better accessible devices and more detailed indications is planned in our future study.

In conclusion, the easy and minimally invasive technique of resistance controlled SCS injection of TA with a disposable 30-gauge needle connected to a 1 mL syringe is effective and applicable for macular edema. This injection technique could be explored as a suitable alternative to intravitreal injection. Long-term stability and efficacy of the resistance controlled SCS injection method warrant further exploration.

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Conflicts of Interest: Zhang DD, None; Che DY, None; Zhu DQ, None.

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