• Clinical Research •

Intravitreal low-dose triamcinolone acetonide for nonarteritic anterior ischemic optic neuropathy

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Abstract

● **AIM:** To evaluate the efficacy and safety of intravitreal low-dose (1 mg) triamcinolone acetonide (TA) in Chinese acute nonarteritic anterior ischemic optic neuropathy (NAION) patients.

● **METHODS:** Twenty-eight eyes of 28 patients with acute NAION (<30d of visual acuity loss) were enrolled and given intravitreal TA (IVTA) once. Visual field (VF), best corrected visual acuity (BCVA), retinal nerve fiber layer (RNFL) thickness, ganglion cell complex (GCC) thickness, radial peripapillary capillary (RPC) density, and intraocular pressure (IOP) were evaluated at baseline and 7d, 1, 3, and 6mo after IVTA.

● **RESULTS:** VF and BCVA were significant improved during the follow-up according to the mean deviation (MD), visual field index (VFI), and Early Treatment Diabetic Retinopathy Study (ETDRS) scores (all P<0.001). There was no significant difference between the group that received an injection less than 14d after illness onset and the group that received an injection more than 14d after illness onset. The RNFL thickness, GCC thickness and RPC density were significantly decreased (all P<0.001). Temporary ocular hypertension was present in five eyes.

● **CONCLUSION:** Low-dose IVTA may be an alternative safe treatment option for some NAION patients in the acute stage. However, optic nerve atrophy still existed.

● **KEYWORDS:** nonarteritic anterior ischemic optic neuropathy; triamcinolone acetonide; intravitreal injections; visual field; visual acuity

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INTRODUCTION

Nonarteritic anterior ischemic optic neuropathy (NAION) is a refractory neuro-ophthalmological disease characterized by sudden and painless vision deterioration[1]. The annual incidence of NAION is estimated to be 1.9 to 8.5 cases per 100 000 persons in the United States[2]. Although less common, NAION is one of the major causes of blindness or seriously permanently impaired vision in people older than 50y[1]. The pathogenesis of the disease is multifactorial. A host of systemic and local factors may disturb optic nerve head (ONH) circulation, with some making the ONH susceptible to ischemia and others acting as the final insult[1].

Despite the lack of evidence from prospective randomized controlled studies, systemic corticosteroid therapy during the early stages of NAION may benefit visual function. A cohort study by Hayreh and Zimmerman[3] showed that systemic corticosteroids given during the very early stages of the disease might help to improve visual function in some patients. Among this cohort, 312 patients in the acute phase of NAION voluntarily opted for systemic steroid therapy, and 301 opted for no treatment. At six months from the onset of treatment, there were visual acuity (VA) and visual field (VF) improvements of 69.8% and 40.1%, respectively, in the treated group compared to 40.5% and 24.5%, respectively, in the untreated group[3]. However, there are certain limitations in clinical practice because systemic corticosteroid therapy may cause significant side effects, including osteoporosis, hyperglycemia, hypertension, and coronary heart disease[4], making patients with cardiovascular and metabolic disturbances unsuitable for or unwilling to use high-dose systemic corticosteroid therapy for a long time.

Triamcinolone acetonide (TA) is a long-acting steroid preparation that is increasingly being used intraocularly to treat a variety of posterior segment ocular pathologies[5-6]. Ophthalmologists have experience using TA off-license *via* periocular administration for over 50y, with the administration *via* the intraocular route being adopted for over 30y[7]. Intravitreal triamcinolone acetonide (IVTA) delivers higher drug concentrations to the targeted eye. It thereby potentially increases the therapeutic response without causing harmful side effects compared with systemic administration, especially in the fragile background of patients with NAION who often have cardiovascular and metabolic disturbances[8]. IVTA could have an efficacy equal to or greater than that achieved with systemic administration. Huang *et al*[8] reported that early administration of IVTA played a role in rescuing retinal ganglion cell survival and improving electrophysiological visual function in a rodent anterior ischemic optic neuropathy (AION) model. Although Pereira *et al*[9] found no therapeutic benefit of intravitreal steroid injection in an AION rodent model, they did declare that the lack of a measurable benefit in a rodent model does not necessarily preclude benefit in humans because AION in animal models are different from NAION in humans. In 2014, a retrospective nonrandomized controlled study was conducted on NAION patients[10]. Twenty-one patients received 4 mg IVTA injection and were compared with 15 non-treated patients. After six months, improved VA was observed in the injected group versus the non-treated group. In addition, the authors mentioned that favorable visual results were associated with only a few side effects during follow-up[10]. However, a prospective study is needed to confirm the potential visual benefit of IVTA in NAION.

Some randomized studies have suggested that 4 mg of TA may result in a higher incidence of side effects, such as cataracts or increased intraocular pressure (IOP), than 1 mg of TA[11]. A prospective randomized clinical trial compared the efficacy and safety of 4 and 1 mg of TA for eyes with branch retinal vein occlusion[11]. No significant differences were found among the two groups for a gain in VA at 12mo, while the rates of elevated IOP and cataracts were higher in the 4 mg group. In view of side effects, an intravitreal injection of 1 mg of TA was administered in our study. Due to the particularity of this disease, which was often accompanied by systemic disease, most NAION patients had complex systemic diseases and were unsuitable for systemic steroid therapy. According to the recommendations of the Ethics Committee of Shanghai General Hospital, this study was designed as a single-arm clinical study to preliminarily confirm the efficacy and safety of low-dose IVTA for the treatment of acute-phase NAION.

PARTICIPANTS AND METHODS

Ethical Approval The study was registered with the identifier ChiCTR1800019525 in the Chinese Clinical Trial Registry on 16/11/2018. The study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of Shanghai General Hospital (No. of ethics committee approval: 2018–67). A written informed consent was obtained from each participant.

Study Design This open-label, single-center, single-arm trial evaluated the efficacy and safety of IVTA (1 mg) injection in Chinese patients with NAION during the acute phase. Twenty-eight adult participants with NAION were recruited from the Department of Ophthalmology, Shanghai General Hospital, from December 2018 to January 2021.

Participants Adults ≥18y diagnosed with acute NAION (<30d of onset) in one eye were enrolled. NAION is characterized by an acute, painless decrease in vision, optic disc edema, and VF loss. All cases were divided into groups according to the onset time, and subgroup analysis was performed. Group 1 received an injection less than 14d after illness onset, and group 2 received an injection more than 14d after onset.

Key inclusion criteria included an optical coherence tomography (OCT), a funduscopic examination, and/or a fluorescein angiography diagnosis of definite optic disc edema; VA no less than light perception; no severe refraction medium opacity or miosis that interfered with fundus examination; and an initial diagnosis of acute-phase NAION without any intravitreal treatment. Patients who already received systemic corticosteroids (<1wk) but were intolerant were also included.

Key exclusion criteria included evidence of any other ocular fundus diseases or optic neuropathy; a history of intravitreal injection or ocular surgery in the study eye; a history or evidence of inflammation, arteritis, or uveitis in either eye; an ocular condition in the study eye likely to impact vision and confound study outcomes.

Interventions The eye was intravitreally injected with 1 mg/0.025 mL TA once within three days after enrolment. The injection site was selected in the inferior temporal region for the best exposure and at a 3.5-4.0 mm distance from the limbus. The needle was advanced transconjunctivally towards the center of the vitreous cavity, and TA (1 mg/0.025 mL) was then slowly injected into the vitreous cavity. Tobramycin eye drops were used for three days after injection (three times daily, one drop each time). Carteolol hydrochloride eye drops were used in case of significant IOP elevation.

Participants were followed up at baseline, as well as 1wk, 1, 3, and 6mo after injection. At each visit, all prespecified evaluation indexes were recorded, including VF, VA, IOP, retinal nerve fiber layer (RNFL) thickness, ganglion cell complex (GCC) thickness, and radial peripapillary capillary (RPC) density. Symptomatic treatment was provided as needed when side effects such as increased IOP occurred.

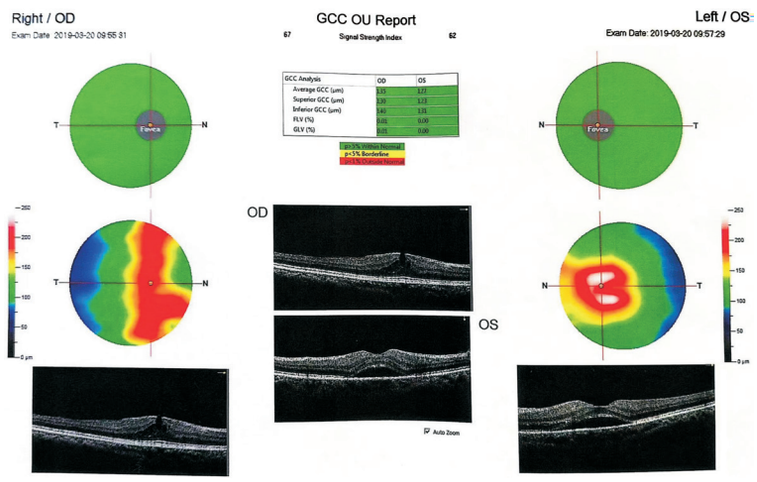

Figure 1 GCC report provided by AngioVue image system GCC: Ganglion cell complex; FLV: Focal loss volume; GLV: Global loss volume; N: Nasal; T: Temporal.

Outcome Evaluation The key efficacy outcome measures were patients' VF and best corrected visual acuity (BCVA) shift from baseline to 6mo. Secondary outcomes included RNFL thickness, GCC thickness, and RPC density changes. Safety assessments included high IOP and other adverse events occurring during the entire period.

Visual field evaluation VF was evaluated using a central 30-2 thresholds test with a Humphrey field analyzer II model 750 (Carl Zeiss Meditec, Dublin, California, USA). The mean deviation (MD), pattern standard deviation (PSD), and visual field index (VFI) were collected and analyzed.

Visual acuity evaluation BCVA was examined using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart at 4 or 1 m, and the changes in ETDRS scores at baseline and each visit were determined.

Retinal nerve fiber layer thickness RNFL thickness was measured by Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) built-in software (version 6.15.7). The optic disc was fast-scanned at a scanning angle of 12°, projecting a 3.4 mm diameter circle centered on the ONH. This circle scan contained 768 A-scans, yielding 768 data points, and was divided into four 90° quadrants. The average RNFL thickness and the four-quadrant [superior (S), inferior (I), nasal (N), and temporal (T)] RNFL thickness were recorded.

Ganglion cell complex thickness GCC scan was performed by AngioVue (Optovue, Fremont, CA, USA) and consisted of 15 vertical lines with a 7 mm scanning length and a 0.5 mm interval and one horizontal line with a 7 mm scanning length. The AngioVue Image System (Optovue, version 2018.1.0.43) automatically recognized the GCC thickness as the distance between the internal limiting membrane and the external boundary of the inner plexiform layer and then generated three different values: the superior sector GCC thickness (SupGCC), the inferior sector GCC thickness (InfGCC) and the average thickness of both sectors (AvgGCC). The global loss volume (GLV) and the focal loss volume (FLV) were calculated simultaneously to reflect GCC loss (Figure 1).

Radial peripapillary capillary density RPC density was measured by the AngioVue image system (Optovue). RPC network is distributed radially around the ONH and represents the main blood supply to the RNFL. The AngioVue system provides a quantitative analysis of RPC density at all vessels and specifically small vessels (Figure 2). This study collected and analyzed data on small vessel density in the whole image and in peripapillary regions and their superior-hemi and inferior-hemi parts.

Intraocular pressure IOP examination was performed by Auto Non-Contact Tonometer (NT-3000, Nidek, Japan) at baseline and each follow up. Three measurements were obtained each time, and the average IOP was recorded.

Statistical Analysis All statistical analyses were completed using SPSS 20.0 software (SPSS, Chicago, IL, USA). For descriptive statistics, quantitative variables were expressed as the means and standard deviations (SDs), and qualitative variables were expressed as frequencies. Repeated measures analysis of variance was used to compare the change in normally distributed quantitative variables. In contrast, the Friedman test was used to compare the change in nonnormally distributed quantitative variables between 1wk, 1, 3, and 6mo after intervention and baseline. Linear mixed-effects models were conducted to evaluate the difference in nonnormally distributed quantitative variables between groups. A value of $P<0.05$ was considered as statistically significant.

RESULTS

Demographic Characteristics As shown in Figure 3, 28 eyes of 28 NAION patients were enrolled in this study, and 26 patients completed all five visits (1 baseline evaluation and four follow-up evaluations). Data from all 28 patients

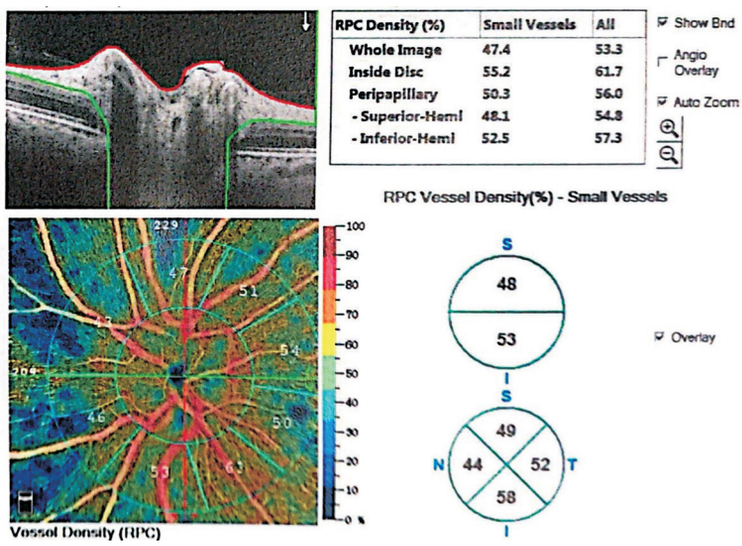

Figure 2 RPC density graph provided by AngioVue image system RPC: Radial peripapillary capillary; S: Superior; I: Inferior, N: Nasal; T: Temporal.

were included in the analysis. The baseline demographics and clinical characteristics of the study patients were shown in Table 1.

Visual Field As shown in Figure 4, the MD shift was significant throughout the intervention (baseline, 1wk, 1, 3, and 6mo) when applying a Friedman test (P=0.001), indicating a VF improvement of the involved eyes. In addition, the changes were significant in patients who received injections either ≤14d prior to illness onset (group 1, P=0.013) or >14d prior (group 2, P=0.016). Similarly, the VFI shift was significant throughout the intervention. There was a statistically significant difference in the VFI of group 1 (P=0.008) but not group 2 (P=0.066). No significant difference in the PSD of all patients (P=0.325) was determined using repeated measures analysis of variance. The change in the PSD was significant in group 1 (P=0.027) but not in group 2 (P=0.661). The MD, PSD, and VFI were not significantly different between the subgroups of eyes injected before 14d and after 14d (P=0.890, 0.226, 0.922, respectively).

Visual Acuity Figure 5 showed an overall improvement in BCVA (ETDRS score) throughout the intervention using the Friedman test (P=0.043). No significant difference was found between the subgroups (P=0.959). The percentage of eyes that gained ≥15 letters of vision was 17.9% at 3mo and 21.4% at 6mo from baseline. For those who lost ≥15 letters of vision, the proportions were 3.6% and 7.1%, respectively, at 3 and 6mo from baseline (Table 2). Figure 6 showed the resolution of sub-macular fluid in an eye with ETDRS scores below 5 one month after IVTA.

Retinal Nerve Fiber Layer Thickness As shown in Figure 7, OCT results showed a significant reduction in the overall RNFL (G) and the S, I, N, and T sectors (P<0.001, Friedman test). Linear mixed-effects models were used to assess the differences in the RNFL thickness between

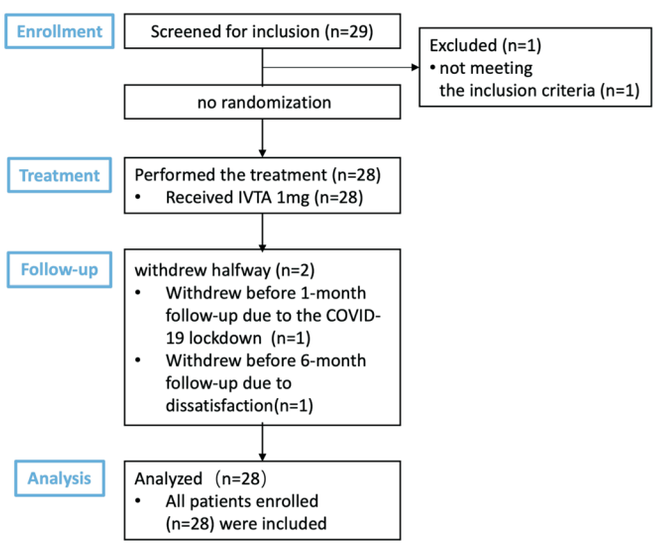

Figure 3 Trial profile.

Table 1 Baseline characteristics of the study patients

Parameters	n=28
Age, y	59±10.18
Male, n (%)	15 (53.6)
Duration of visual loss, d	12.61±2.03
≤14d, n (%)	18 (64.3)
>14d, n (%)	10 (35.7)
Left eye, n (%)	15 (53.6)
Previous disease history, n (%)	
Hypertension	16 (57.1)
Diabetes mellitus	13 (46.4)
Hyperlipidemia	2 (7.1)
Arteriosclerosis	1 (3.6)
Cerebral infarction	4 (14.3)
Previous medication use, n (%)	
Systemic corticosteroids	5 (17.9)

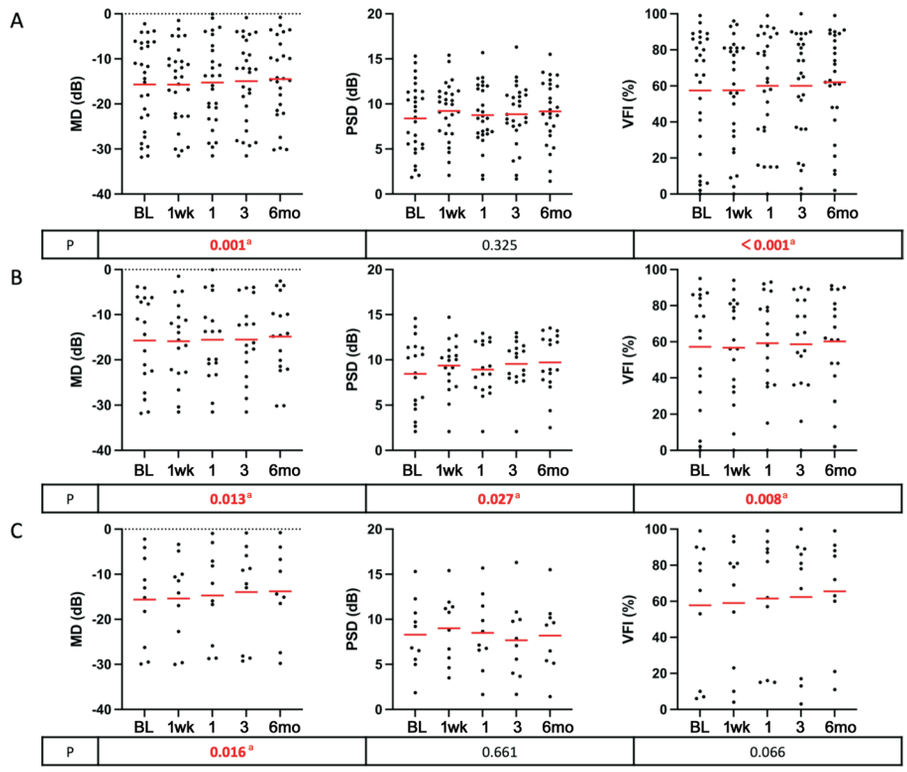

Figure 4 Scatter plots of MD, PSD, and VFI of all cases (A), group 1 (B), and group 2 (C) at baseline and 1wk, 1, 3, and 6mo after injection Red lines at means; [a]Statistically significant. BL: Baseline; MD: Mean deviation; PSD: Pattern standard deviation; VFI: Visual field index.

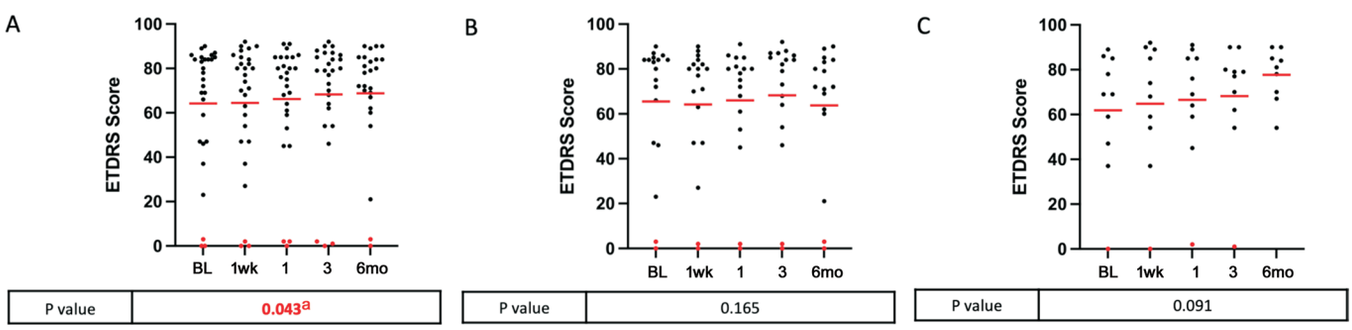

Figure 5 Scatter plots of BCVA ETDRS scores of all cases (A), group 1 (B), and group 2 (C) at baseline and 1wk, 1, 3, and 6mo after injection Red lines at means; red scatter dots represent ETDRS scores of three extremely low vision eyes; [a]Statistically significant. BCVA: Best corrected visual acuity; BL: Baseline; ETDRS: Early Treatment Diabetic Retinopathy Study.

Table 2 Proportion eyes of BCVA change from baseline *n* (%)

BCVA	Month 3	Month 6
Gained ≥10 letters	5 (17.9)	6 (21.4)
Lost ≥10 letters	1 (3.6)	4 (14.3)
Gained ≥15 letters	5 (17.9)	6 (21.4)
Lost ≥15 letters	1 (3.6)	2 (7.1)

BCVA: Best corrected visual acuity.

subgroups. They showed significant differences in the G, S, and T sectors (P=0.007, 0.013, 0.008, respectively) but not in the I and N sectors (P=0.729, 0.095, respectively) between subgroups.

Ganglion Cell Complex Measurement The variation in avgGCC, supGCC, and infGCC was shown in Figure 8. The avgGCC, supGCC, and infGCC were significantly decreased (P<0.001, Friedman tests). Moreover, the FLV and GLV presented significant increase (both P<0.001, Friedman tests).

Radial Peripapillary Capillary Density As shown in Figure 9, the small vessel density in the whole image, peripapillary regions, superior-hemi, and inferior-hemi regions was significantly reduced (all P<0.001). Figure 10 showed the six-month ONH progression of a 47-year-old male patient with acute NAION.

Intraocular Pressure All patients were given IOP-lowering medication before intraocular injection in case of significant IOP elevation. As shown in Table 3, IOP events were summarized as absolute thresholds (≥24 mm Hg, ≥30 mm Hg) and as a ≥10 mm Hg change from baseline. Five patients had IOP≥24 mm Hg during follow-up (Table 4). No patient was

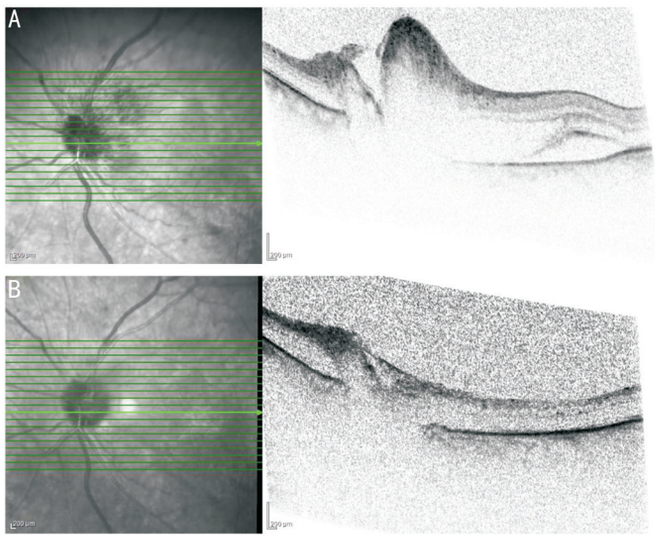

Figure 6 OCT scan of the left eye of a 75-year-old female patient with ETDRS scores below 5 at baseline (A) and 1mo (B) after IVTA OCT: Optical coherence tomography; IVTA: Intravitreal low-dose triamcinolone acetonide; ETDRS: Early Treatment Diabetic Retinopathy Study.

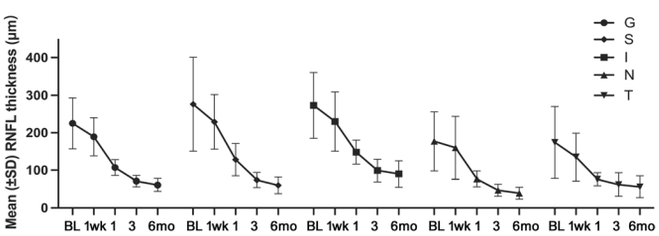

Figure 7 Changes in the average RNFL thickness for the overall RNFL and each 90° quadrant RNFL: Retinal nerve fiber layer; G: General; S: Superior; I: Inferior, N: Nasal; T: Temporal; SD: Standard deviation; BL: Baseline.

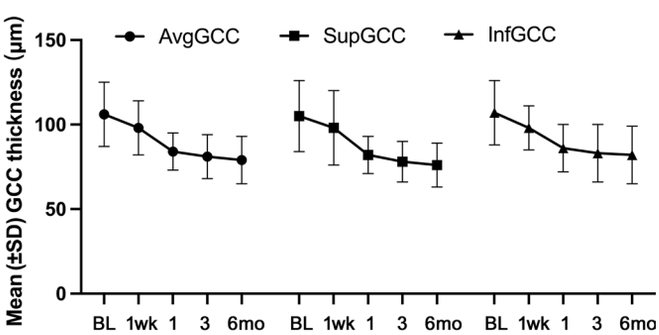

Figure 8 GCC thickness variation GCC: Ganglion cell complex; SupGCC: Superior sector GCC thickness; InfGCC: Inferior sector GCC thickness; AvgGCC: Average thickness of both sectors; SD: Standard deviation; BL: Baseline.

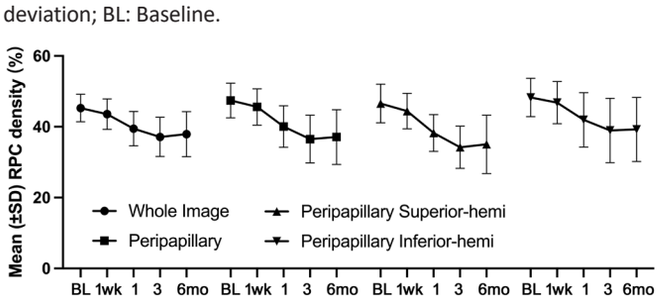

Figure 9 Small vessel density variation RPC: Radial peripapillary capillary; SD: Standard deviation; BL: Baseline.

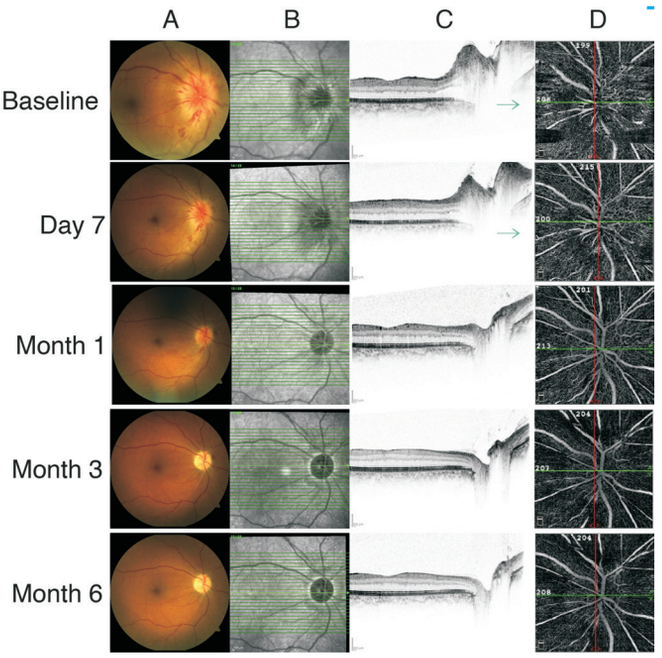

Figure 10 Six months progression of the right eye of a 47-year-old male patient with acute NAION on multimodal analysis A: Color fundus photographs; B, C: OCT scan of the peripapillary retina; D: OCTA vessel density in the peripapillary superficial retina in nerve head mode. NAION: Nonarteritic anterior ischemic optic neuropathy; OCT: Optical coherence tomography; OCTA: Optical coherence tomography angiography.

Table 3 IOP events during follow-up

IOP	*n* (%)
24–30 mm Hg	3 (10.8)
≥30 mm Hg	2 (7.1)
Increase ≥10 mm Hg from baseline	2 (7.1)

IOP: Intraocular pressure.

diagnosed with glaucoma or needed IOP-lowering surgeries during the study.

Other Ocular Complications Topical antibiotic drops were used for 3d after injection. There were no cases of cataract development, retinal detachment, vitreous hemorrhage, endophthalmitis or other serious complications that may have been induced by intravitreal injection or triamcinolone.

DISCUSSION

Several studies have explored the natural history of NAION. According to a retrospective study performed in Taiwan, China[12], various degrees of VF defects were often observed within two weeks after onset, slightly worsened from baseline to three months, and then slowly returned to baseline at six months. It has also been observed by Bialer and Stiebel-Kalish[13] that although most patients have mild changes in VA and VF after the acute phase, a subset of patients (16.4%) can still experience significant progressive deterioration.

Systemic steroid therapy has been controversial in treating acute NAION[14]. It is believed that corticosteroids can reduce

Table 4 IOP fluctuation of 5 patients with high-IOP during the study

Patients	Sex	Study eye	Age (y)	Duration of visual loss at injection (d)	IOP (mm Hg)				
					Baseline	1wk	1mo	3mo	6mo
1	F	Left	71	10	19.6	19.7	30.8	19.2	21.4
2	M	Left	56	21	23.3	22.5	29.2	22.5	20.5
3	F	Right	46	15	18	25.8	18.3	17.7	14.8
4	F	Right	60	22	16.2	16	24.1	22.5	19.7
5	M	Right	62	6	15	11	18.2	32	15.7

IOP: Intraocular pressure.

Table 5 Literature on IVTA in the treatment of NAION

Author, y	Study type	Sample size	Intervention		Onset time	Follow-up	Evaluation	Main outcomes	Adverse reactions
			Treatment	Control					
Kaderli 2007[15]	Retrospective case-control study	10	4 mg IVTA	Untreated	≤22d	9-12mo	VA, VF, regression time of optic disc edema	Improvement in BCVA in IVTA group was higher than control, and the dissipating time of optic disc edema was shortened; No improvement in VF	No increase in IOP, cataracts, endophthalmitis, *etc*.
Jonas 2007[16]	Case report	3	20 mg IVTA	-	≤7d	3-5mo	VA, VF	VA improved in 2 eyes, worsened in 1 eye, VF improved in 1 eye, no obvious change in 2 eyes.	1 eye had high IOP.
Sohn 2009[17]	Case report	1	4 mg IVTA	-	4d	6mo	VA, regression time of optic disc edema	BCVA increased from 0.05 at onset to 0.4 at 6mo after treatment. Optic disc swelling was reduced at 1wk and disappeared at 2wk after treatment.	None
Radoi 2014[10]	Retrospective case-control study	36	4 mg IVTA	Untreated	≤1mo	6mo	VA, VF, RNFL thickness	Improvement in VA and VF in IVTA group was better than control. There was no difference in RNFL thickness. VA was negatively correlated with treatment delay time at 6mo after onset.	Average IOP of the treatment group at 3mo was higher than nontreatment group; there were no differences at baseline, 7d, 1, and 6mo.
Durbant 2021[18]	Retrospective case-control study	68	4 mg IVTA	Untreated	<1mo	6mo	VA, VF, RNFL thickness	Among the patients injected within 15d of onset, the VA improvement rate in IVTA group was better than control, and VF was improved. In patients injected 15d after the onset, VA and VF did not improve. There was no difference in RNFL thickness.	There was no significant difference in IOP between the two groups.

NAION: Nonarteritic anterior ischemic optic neuropathy; IVTA: Intravitreal triamcinolone acetonide; BCVA: Best corrected visual acuity; RNFL: Retinal nerve fiber layer; IOP: Intraocular pressure; VA: Visual acuity; VF: Visual field.

capillary permeability, alleviate exudation and edema, and stop the further aggravation of the condition caused by compartment syndrome after optic nerve ischemia in the scleral canal. However, there is no unified standard for the use of corticosteroids. Additionally, the long-term administration of high-dose systemic steroids can result in many side effects, severely limiting their clinical application. Intravitreal injections could reach high intraocular concentrations and avoid systemic side effects. As a classic steroid preparation, TA has been used intraocularly to treat ocular inflammatory disorders. Several studies have explored TA's efficacy in treating NAION (Table 5)[10,15-18]. A retrospective study by Radoi *et al*[10] showed visual improvement in NAION patients receiving IVTA, but the study had limitations associated with retrospective data collection. Therefore, a prospective trial that systematically tracks and collects data to evaluate the efficacy and safety of IVTA in patients with NAION is essential.

In our study, patients treated with IVTA in the acute phase of NAION showed interesting changes in VF. For all 28 patients, the MD and the mean VFI significantly improved during the follow-up, while the mean PSD did not change significantly. The trend in the MD was in accordance with the trend reported by Radoi *et al*[10], who retrospectively summarized 21 patients injected with TA within one month of onset, suggesting the effectiveness of this treatment for improving VF. We further analyzed 18 patients who received treatment within 14d of onset. The MD and VFI showed comparable improvements to the former in this group. However, the PSD increased, indicating a change in localized defects.

PSD is a global index for detecting localized defects but is entirely insensitive to a decline in the global background VF level[19]. MD, nevertheless, is affected by both diffuse and focal VF loss[20] and would better represent the overall picture of VF defects. VFI is a weighting parameter for which the central VF has a greater weight. Beyond this, the VFI is less affected by cataracts and other age-related media changes[19]. Therefore, the VFI may be an ideal parameter to describe the VF of patients with optic neuropathy.

According to the results of our study, the overall VF showed a trend of improvement, but there was still a deterioration of some local dark spots. This trend is consistent with the treatment outcome reported by Rebolleda *et al*[21], who

launched a clinical trial recruiting NAION patients within 14d of onset to take prednisolone. However, we cannot ascertain whether this change is real or caused by errors, and further research is needed to confirm.

Apart from the VF, VA is also of great concern to AION patients. This study used a nonparametric statistical method to evaluate most indicators due to their nonnormality, including BCVA indicators. Although the data showed a trend towards improved BCVA, these improvements were minor and had no clinical significance for most patients. Several studies reported that BCVA remained almost unchanged or slightly improved after the acute phase[12]. We analyzed the percentage of eyes that changed ≥15 letters at 3 and 6mo after onset, assuming that it was clinically meaningful. Compared with the results of Radoi *et al*[10], our improvement rate (21.4%) was higher than that of the noninjected group (7%) but lower than that of the injected group (29%).

Three of the 28 study eyes had almost lost vision at baseline (ETDRS score<5), and after IVTA, there was no significant improvement in vision. After the case review, we found that these three patients were all diabetes patients and had sub-macular fluid, which may be the reason for their severe vision loss. It should be noted that all enrolled patients have undergone careful fundus examination to ensure that there is no clue related to diabetes retinopathy, such as microvascular aneurysms. Although the sub-macular fluid disappeared completely within one month after IVTA, the vision did not improve.

In the acute stages of NAION, edema of the ganglion cell layer can be observed in the eyes of NAION patients. After about 2-3wk, the edema gradually alleviates[22], and then progresses toward optic atrophy. In our study, we found that most patients showed a rapid resolution of optic disc edema, and over time, RNFL thickness, GCC thickness, and RPC density gradually decreased below normal values[23-24], indicating optic nerve atrophy and peripapillary vessel loss. RNFL measurement is often used in follow-up to evaluate the possibility of retinal swelling and thinning. It has been reported that disc edema and RNFL edema were significantly reduced earlier in the steroid group than in the untreated group. However, for the final outcome of RNFL, both groups showed atrophy without much difference[18,25]. Radoi *et al*[10] noted that IVTA seemed to improve edema in the acute phase, but it did not help the ultimate atrophy of the optic nerve. Hayreh and Zimmerman's study[25] showed that optic disc edema in NAION patients resolved spontaneously at 7.9wk (5.8–11.4wk) after onset.

In our study, the rate of ocular hypertension was within the clinically acceptable range, although slightly higher than that in previous IVTA studies[10,18]. Five patients had IOP≥24 mm Hg at one IOP examination, respectively, and among these five patients, two were over 30. The high IOP of these five eyes is controllable. After using carteolol hydrochloride eye drops as required, the intraocular pressure of all patients returned to normal in the subsequent follow-up. There was no significant difference in VF, VA, RNFL thickness, GCC thickness, and RPC density between cases with high IOP and others.

Our preliminary prospective study showed that 1 mg low-dose IVTA is safe for AION patients at the acute stage, and the VF tended to improve. Therefore, low doses of IVTA could be considered, especially for patients with systemic diseases who are unsuitable for or unwilling to receive systemic corticosteroid treatment, as a focal therapy in the acute phase.

The limitations of our study include the lack of a control group, the small sample size, and the limited follow-up duration of 6mo. In the future, further multicenter randomized controlled studies are needed to explore better treatment solutions.

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