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ORIGINAL ARTICLE

Intravitreal triamcinolone injections in non-arteritic anterior ischemic optic neuropathy — A retrospective report

Injection intravitréenne de triamcinolone dans les neuropathies optiques ischémiques antérieures aiguës non-artéritiques — Une étude rétrospective

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NAION;
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Summary
Background. — Non-arteritic anterior ischemic optic neuropathy (NAION) is a common cause of vision loss but no treatment has demonstrated its efficiency. A preliminary study showed an improvement on the visual acuity (VA) in a group of patients who received intravitreal administration of triamcinolone acetonide (IVTA) versus a non-treated group. In the present series, the visual outcome of IVTA in NAION was evaluated on a larger group of patients.
Methods. — This retrospective, unmasked and non-randomized study took place at Reims University Hospital between 2009 and 2017. The data of consecutive patients presenting with isolated optic disc edema characteristic of recent NAION (< 1 month of visual acuity loss) were included. After informed consent, a single intravitreal injection of filtrated 4 mg/0.1 mL triamcinolone acetonide were administered. Twenty-seven control patients chose not to be injected and therefore served as controls. LogMar visual acuity (VA), VA rating (VAR) (1 line = 0.1LogMAR = 5 VAR letters), retinal nerve fiber layer thickness assessed by OCT and static visual field were evaluated at presentation, after 7 days, after 3 months and after 6 months.
Results. — Sixty-eight patients with NAION were evaluated. Forty-one received IVTA, 29 were injected within 15 days after the onset of symptoms and 12 after 15 days. There was a higher

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proportion of patients improving VA of 2 lines or more (10 or more VAR letters) in the injected group (49%) compared with the non-injected group (11%, $P = 0.019$). Among the patients injected before 15 days, the proportion improving for 2 lines or more (55% vs. 11%, respectively, $P = 0.013$) and for 3 lines or more (45% vs. 11%, respectively, $P = 0.035$) were significantly higher than in the non-injected group. Also, comparing the VA at presentation with the VA after 6 months in the injected eyes, it improved significantly ($P = 0.003$) and also in the subgroup injected within 15 days ($P = 0.0007$) but not in the injected group after 15 days ($P = 0.801$). Visual field improvement was only observed in the subgroup of patients injected within 15 days with a significant improvement of the mean deviation (dB) within 6 months ($P = 0.015$).
Conclusions. — This follow-up study confirms the results of the previous series displaying an apparent benefit of intravitreal steroids injected in the acute phase of NAION. Only patients receiving IVTA within 15 days from onset of NAION have a significant improvement of VA and visual field during the follow-up period of 6 months.

MOTS CLÉS
Neuropathie optique ischémique ;
Triamcinolone ;
Injections intravitréennes

Résumé
Objectifs. — La neuropathie optique ischémique antérieure aiguë (NOIAA) est une cause de cécité courante cependant aucun traitement n'a prouvé pour l'heure son efficacité. Une étude précédente a montré une amélioration de l'acuité visuelle (VA) dans un groupe de patient qui avait reçu une injection intravitréenne de triamcinolone versus un groupe témoin non traité. Cette nouvelle étude inclut un nombre plus important de patients.
Méthodes. — Cette étude rétrospective, non randomisée et contrôlée a lieu à hôpital universitaire de Reims entre 2009 et 2017. Les patients se présentant aux urgences ophtalmologiques avec un tableau œdème papillaire caractéristique d'une NOIAA récente (baisse d'AV < 1 mois) ont été inclus. Une injection unique de 4 mg/0,1 mL de triamcinolone filtrée a été réalisée chez les patients après obtention de leur consentement éclairé. Vingt-sept patients ont choisi de ne pas être injectés et ont donc été inclus dans le groupe contrôle. L'AV en LogMar, le AV rating (VAR) (1 ligne = 0,1LogMAR = 5 lettres VAR), la mesure de l'épaisseur des fibres du nerf optique à OCT et le champ visuel (CV) statique ont été évalué à la première consultation, à 7 jours, à 3 mois et à 6 mois.
Résultats. — Soixante-huit patients ayant présenté une NOIAA ont été inclus. Quarante et un ont reçu une IVTA, dont 29 dans les 15 jours suivant le début des symptôme et 12 au-delà de 15 jours. On observe une proportion de patient ayant amélioré son AV de plus de 2 lignes (> 10 lettres VAR) dans le groupe injecté (49 %) que dans le groupe non injecté (11 %, $p = 0{,}019$). Parmi les patients injectés avant 15 jours, cette proportion est plus importante pour une amélioration de 2 lignes et plus (55 % vs 11 %, $p = 0{,}013$) et ainsi que pour 3 lignes et plus (45 % vs 11 %, $p = 0{,}035$) par rapport au groupe non injecté. De même, en comparant l'AV à la première consultation et à 6 mois, on observe une augmentation significative dans le groupe injecté ($p = 0{,}003$), ainsi que dans le sous-groupe injecté avant 15 jours ($p = 0{,}0007$) mais pas dans le groupe injecté après 15 jours ($p = 0{,}801$). Une amélioration du CV n'a été observé que dans le sous-groupe injecté avant 15 jours avec une augmentation significative de la déviation moyenne à 6 mois ($p = 0{,}015$).
Conclusions. — Cette étude confirme les résultats de la série précédente démontrant un bénéfice apparent de l'injection intravitréenne de corticoïde en phase aiguë de NOIAA. Seul les patients recevant une IVTA dans les 15 jours suivant le début des symptômes ont une amélioration significative de l'acuité visuelle et du champ visuel sur la période de suivi de 6 mois.

Introduction

Anterior ischemic optic neuropathy (AION) is a relatively common cause of vision loss in the population aged 50 or older. The annual incidence of AION is 2.3 to 10.2 per 100,000 population in the United States [1,2]. Non-arteritic AION (NAION) is the result of hypoperfusion and ischemia of the optic nerve head by transitory occlusion of capillaries of the posterior ciliary arteries [3,4], but the root cause remains unknown.

NAION is clinically characterized by a sudden and painless loss of vision mostly frequently involving the upper or

the lower half of the visual field [5,6] in one eye, commonly noticed on awakening [7] and associated with an edema of the optic nerve head. There are two main risk factors for NAION. First, there is a mechanical factor related to overcrowding of the optic nerve by optic disc drusen or small-sized optic discs with small cup-to-disc ratio [8,9], and then, a vascular factor, as NAION is often associated with predisposing cardiovascular risk factors [10]. The risk of sequential NAION is estimated at 15% within 5 years [11]. The natural history of the disease is rather uncertain; generally, after progressive vision loss during the initial evolution period of several weeks, the visual acuity can improve for up to 6 months, and the optic disc edema evolves into pallor and atrophy. Histologically, experimental models of NAION reveal a loss of retinal ganglion cells (RGC) through apoptosis induced by inflammation, which induced by ischemia in a vicious cycle [12].

A specific modulation of inflammation in the early stage of NAION might reduce the apoptosis in the RGC.

Thus, to reduce the vicious cycle of ischemia, the use of steroids appears to be the most logical treatment. The use of intravitreal injections reduces potential side effects compared to systemic administration of steroids. A preliminary study including 36 patients published in 2014 showed a higher proportion of patients with improvement of visual acuity (VA) in the group given intravitreal triamcinolone acetonide (IVTA) versus the non-treated group over a six-month follow-up period [13].

The purpose of this controlled study was to reevaluate the benefit of intravitreal steroids on a larger number of patients.

Patients and methods

Inclusion criteria

Consecutive patients with no age limitation presenting with isolated optic disc edema characteristic of recent NAION (< 1 month of visual acuity loss) at Reims University hospital between 2009 and 2017.

For the analysis, the patients were retrospectively divided into two groups: one ''injected group'' of patients who received IVTA and a ''control group'' of patients who did not receive injection. The first group was further split into two subgroups depending on whether they received injections within 15 days from the onset of symptoms or after 15 days.

Exclusion criteria

Patients with a history or clinical symptoms of arteritic AION or elevated C-reactive protein and erythrocyte sedimentation rate levels were excluded. If a temporal artery biopsy was performed, the patient was only included if pathological examination showed neither inflammation nor giant cells. Patients with an onset of symptoms over one month previously, associated blinding ocular diseases (glaucoma, macular disorders, diabetic retinopathy, lens opacities), or previous intravitreal or systemic steroid treatments were not included in this analysis.

Intraocular injection protocol

In the acute phase of NAION, once the diagnosis was established, the patients were informed of the option of treating them with intravitreal steroids, and they decided whether to be injected or if simple follow-up was performed as a standard procedure. Patients who gave their consent for IVTA were also informed that the treatment was off label. A single intravitreal injection of 4 mg/0.1 mL triamcinolone acetonide (IVTA) was then administered. Triamcinolone was filtered to eliminate the excipients of the available solution. Systematic treatment with brinzolamide was administrated in all cases after the injection in order to prevent ocular hypertension caused by triamcinolone acetonide.

Unmasked follow-up

Examinations were conducted only by ophthalmologists from the department; the same ophthalmologist generally performed the entire 6 months of follow-up.

Visual acuity evaluation

Best-corrected visual acuity (VA) was evaluated using the Monoyer scale and presented as LogMAR equivalent at inclusion and after 7 days, 1 month and 6 months. VA rating (VAR) was used to compare the change in VA between the first visit and the various follow-up visits. VAR is an inversion of the LogMAR scale, based on the formula $VAR = 100 - 50 \times LogMAR$. This scale avoids decimal values, and higher values represent better VA. Thus, the change in VA is expressed in VAR letters or lines (1 line = 0.1LogMAR = 5 VAR letters).

Visual field evaluation

FAST 30 static perimetry (Ophthalmic Monitor, Metrovision, France) was performed at onset, 1 month, and 6 months after presentation, except in cases of severe vision loss where visual fields could not be performed. Corrected mean deviation was analyzed to evaluate visual field progression. When available in the patients' charts, the change in mean deviation between baseline and 6 months was calculated.

Retinal nerve fiber layer thickness

Prior to 2012, Time-domain OCT (Stratus, Carl Zeiss Meditec, Dublin, CA, USA), and after 2012, spectral domain OCT (OCT Spectralis, Heidelberg), of the retinal nerve fiber layer (RNFL) was performed at presentation and after 7 days, 1 month, and 6 months. The decrease in optic disc edema was evaluated by comparing the initial mean RNFL thickness with the measurements performed after 7 days, 1 month, 3 months, and 6 months.

Statistical methods

For descriptive analysis, quantitative variables were expressed as mean values with standard deviation; qualitative variables were expressed as percentage. The VA and mean deficit of the visual field were compared between the

Table 1 Demographic characteristics and history of the patients of the study.

	IVTA group	Non-IVTA group	All patients
n	41	27	68
Mean age (in years)	66	68	67
History			
HBP (%)	60	75	64
Diabetes (%)	35	13	28
OSA (%)	15	13	14
Atrial fibrillation (%)	15	25	18
Phakic (%)	76	83	76
Pseudophakic (%)	24	17	21
NAION on controlateral eye (%)		14	

IVTA: intravitreal administration of triamcinolone acetonide; HBP: high blood pressure; OSA: obstructive sleep apnea; NAION: non-arteritic anterior ischemic optic neuropathy.

injected and the non-injected eyes. Also, the subgroups of patients injected before and after 15 days from the onset of symptoms were compared separately with the non-injected group. Mann—Whitney tests were used to compare quantitative variables with $n < 30$. Changes with time were analyzed with the repeated-measure *t*-test. The correlations were performed with a Pearson's linear regression. Results were considered as statistically significant when $P < 0.05$.

Results

Demographic characteristics

Sixty-eight patients were included: 41 received IVTA, of whom 29 were injected before 15 days and 12 after 15 days. Twenty-seven patients did not receive IVTA. The patients were all Caucasians, aged from 59 to 91 years, with a mean age of 67.2 years. Sixty-four percent of the patients had a history of high blood pressure (HBP), 29% diabetes, 18% atrial fibrillation, 14% obstructive sleep apnea (OSA), and 14% had a history of NAION in the fellow eye (Table 1).

Visual acuity (VA)

At presentation, there was no statistical difference in VA at baseline between the group of injected patients and the group of non-injected patients ($P = 0.447$), between the group of injected patients within 15 days and the non-injected group ($P = 0.774$), or between the non-injected group and the group injected after 15 days group ($P = 0.184$) (Table 2).

At the end of the study period (6 months), there was a higher proportion of patients with VA improvement of 2 lines or more (10 or more VAR letters) in the injected group (49%) compared with the non-injected group (11% $P = 0.019$) (Table 3). The proportion of patients receiving IVTA within 15 days experiencing VA improvement of 2 lines or more and 3 lines or more was also significantly higher compared with the non-injected group, respectively 55% ($P = 0.013$) and 45% ($P = 0.035$). There was no significant VA improvement in the non-injected group or the group injected after 15 days.

Comparing the VA at presentation with the VA at 6 months, visual acuity improved significantly in the entire group of injected eyes ($P = 0.003$) and in the subgroup injected within 15 days ($P = 0.0007$), while it remained unchanged if the injection was performed after 15 days from onset ($P = 0.801$), and significantly decreased in the non-injected group ($P = 0.048$) (Table 4).

The complete analysis of the visual outcomes is displayed in Table 3.

Moreover, the timing of the injection appears to correlate with the VA improvement. A regression analysis confirmed the importance of the timing; there was a significant correlation between delay of injection and the change in LogMar VA ($R = 0.52$, 95% CI [0.25; 0.72], $P = 0.0006$ using Pearson's test). The statistical analysis confirms the linear relationship between delay of injection and VA outcome (Fig. 1).

Visual field

A significant improvement in MD after 6 months was observed ($P = 0.015$*) only in the eyes injected within 15 days. In every other case, the visual field remained stable or deteriorated (Table 5).

Retinal nerve fiber layer (RNFL)

A decrease in RNFL thickness was noted in both groups, with no significant difference in the change in RNFL thickness (Fig. 2). After 3 months of observation in all eyes, injected or not, the optic disc displayed atrophy.

Intraocular pressure (IOP) and other side effects

There was no statistically significant difference in IOP in the treated group versus the non-treated group ($P = 0.797$) at presentation. The intraocular pressure change from baseline was significantly higher in the treated group throughout the follow-up at months 1 and 3 when applying a Wilcoxon Mann—Whitney test (respectively, $P = 0.017$ and $P = 0.015$). In the treated group, 5 eyes presented with an IOP above 21 mmHg during follow-up (22 to 33 mmHg) despite the

Table 2 Mean baseline visual acuity (MVA) in LogMar between the patients of the IVTA groups and the non-IVTA group — Mann—Whitney Test.

	IVTA	*n*	Non-IVTA	*n*	*P*
	0.92 ± 0.72	41	0.76 ± 0.67	27	*P* = 0.447
IVTA < 15d	0.87 ± 0.77	29	*P* = 0.774		
IVTA > 15d	1.06 ± 0.61	12	*P* = 0.194		

IVTA: intravitreal administration of triamcinolone acetonide.

Table 3 VAR letters improvement in lines after 6 months for the patients of the IVTA groups and the non-IVTA group.

	Non-IVTA	IVTA	*P*	IVTA < 15d	*P*	IVTA > 15d	*P*
n	27	41		29		12	
> 1 line (%)	11	49		55		33	
n	3	20	*P* = 0.019*	16	*P* = 0.013*	4	*P* = 0.177
> 2 lines (%)	11	37		45		17	
n	3	15	*P* = 0.068	13	*P* = 0.035*	2	*P* = 0.676
> 3 lines (%)	11	29		38		8	
n	3	12	*P* = 0.150	11	*P* = 0.070	1	*P* = 0.810

VAR: visual acuity rating; IVTA: intravitreal administration of triamcinolone acetonide.
* Chi^2 test $P < 0.05$.

Table 4 Visual acuity variation between presentation and at 6 months in LogMAR.

	MVA D0	MVA M6	Δ MVA M6-MVA D0	*P*
Non-IVTA *n* = 27	0.76 ± 0.67	1.00 ± 0.78	0.23 ± 0.58	0.048*
IVTA *n* = 41	0.92 ± 0.73	0.63 ± 0.63	−0.30 ± 0.60	0.003**
IVTA < 15d *n* = 29	0.87 ± 0.77	0.43 ± 0.50	−0.44 ± 0.62	0.0007***
IVTA > 15d *n* = 12	1.07 ± 0.61	1.10 ± 0.67	0.09 ± 0.46	0.801

MVA: mean baseline visual acuity; IVTA: intravitreal administration of triamcinolone acetonide.
* Repeated-measure *t*-test $P < 0.05$.
** Repeated-measure *t*-test $P < 0.005$.
*** Repeated-measure *t*-test $P < 0.001$.

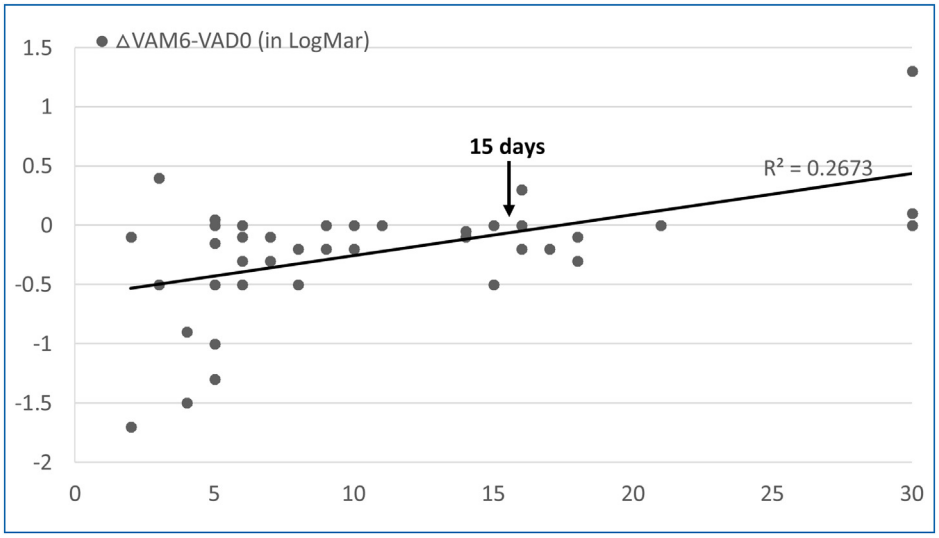

Figure 1. Variation of the visual acuity for each intravitreal administration of triamcinolone acetonide (IVTA) patient (in LogMar) between presentation (VAD0) and 6 months (VAM6) after injection in relation with the delay of injection from onset (in days) (R = 0.52, 95% CI [0.25; 0.72] and *P* = 0.0006*** with Pearson's product moment correlation).

Table 5 Mean deviation (in dB) in visual fields at presentation (MDD0) vs. at 6 months (MDM6).

	MDD0	MDM6	Mean change	*P*
Non-IVTA $n=10$	-8.4 ± 3.8	-8.8 ± 4.4	-0.34 ± 1.8	0.554
IVTA $n=21$	-9.5 ± 4.8	-7.9 ± 4.7	1.70 ± 3.8	0.052
IVTA < 15d $n=18$	-9.8 ± 5.0	-7.6 ± 4.4	2.3 ± 3.6	0.015*
IVTA > 15d $n=3$	-7.9 ± 3.9	-9.6 ± 7.6	-1.7 ± 3.6	0.499

IVTA: intravitreal administration of triamcinolone acetonide.
* Repeated-measure *t*-test $P < 0.05$.

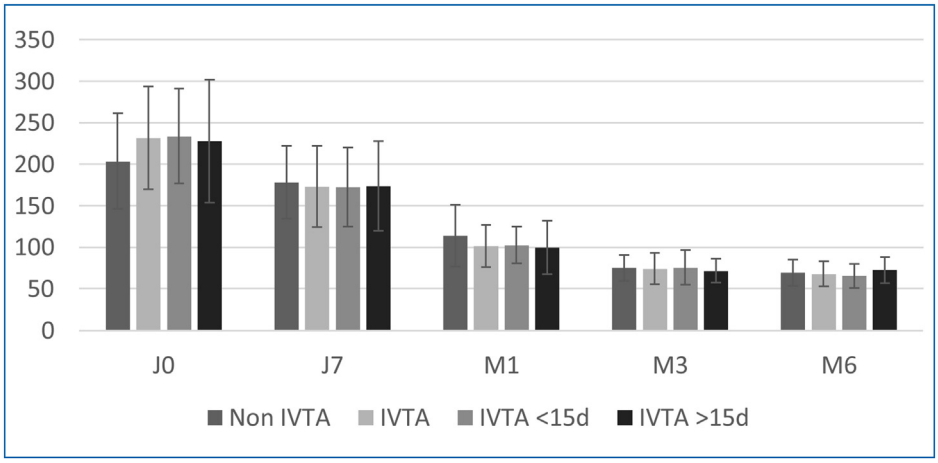

Figure 2. 6 months follow-up of mean retinal nerve fiber layer (RNFL) thickness (in μm) in the different group of patients.

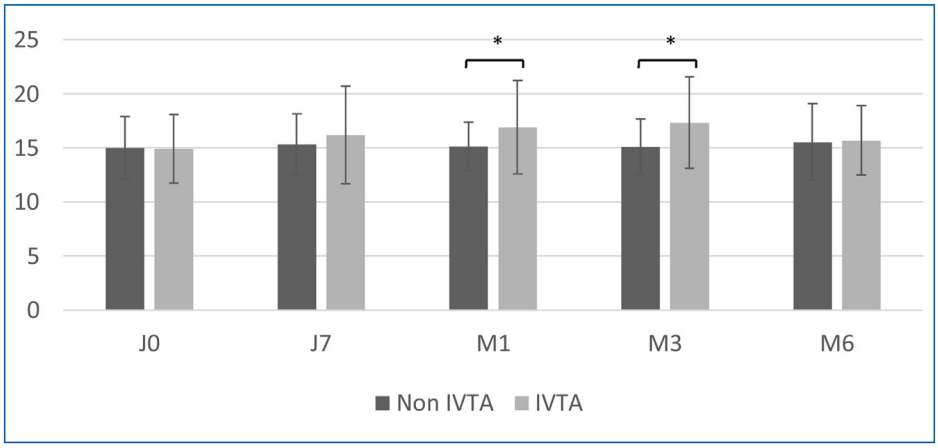

Figure 3. 6 months follow-up of mean intraocular pressure (IOP) (in mmHg) in the different group of patients Wilcoxon Mann—Whitney test $P < 0.05$*.

systematic use of topical brinzolamide, but they all had an IOP below 21 mmHg at 6 months (Fig. 3).

Two of the injected patients in our population underwent cataract surgery during follow-up.

Subgroup of patients with sequential NAION

In the past medical history of 14% ($n=9$) of the included patients, a sequential NAION in the fellow eye was noted. Among them, four patients experienced NAION in the fellow eye during the follow-up period of this study. In all four patients, only the second involved eye was injected. Although the median change in VA was less in the injected eye (−7.5 letters) than the non-injected eye (−15 letters), this difference did not reach statistical significance ($P=0.457$) (Table 6).

Discussion

This study, on a larger sample than our preliminary study, confirms the previous trend of a significant benefit of

Table 6 Variation of visual acuity at presentation and at 6 months in the patient with bilateral NAION during the 7-years follow-up. VA in LogMar.

		IVTA	IVTA delay	VAJ0	VARJ0	VAM6	VARM6	ΔVARM6-VARJ0	Δ in lines
Patient 1	D	No		0.5	75	0.8	60	−15	−3
	G	Yes	6	0	100	0	100	0	0
Patient 2	D	No		0	100	0.3	85	−15	−3
	G	Yes	3	0.3	85	0.7	65	−20	−4
Patient 3	G	No		1	50	2	0	−50	−10
	D	Yes	16	0.7	65	1	50	−15	−3
Patient 4	D	No		0.05	97.5	0.2	90	−7.5	−1.5
	G	Yes	11	0	100	0	100	0	0

NAION: non-arteritic anterior ischemic optic neuropathy; IVTA: intravitreal administration of triamcinolone acetonide; VAR: visual acuity rating.

intravitreal steroids injected in the initial phase of NAION on visual acuity [14].

The two key points are:

- the lack of efficacy when injected more than 15 days after onset of symptoms;
- the concern in patients with bilateral NAION.

No benefit could be demonstrated when the injection was performed more than 15 days after onset of symptoms. However, it must be noted that the number of patients in this group was relatively small, especially since the physicians in the department informed of the results of the previous publication were aware of the importance of early injection. Another important observation in this study concerned the patients with sequential involvement but injection in only one eye. No beneficial effect could be demonstrated for the injected eye. This result remains difficult to analyze, since in NAION, the outcome of the second eye is unpredictable [15].

Our mixed results should be discussed in the context of previously published reports on systemic treatment with steroids: while Hayreh and Zimmerman [16] reported a beneficial effect of oral steroids, another study using high-dose intravenous steroids found no improvement in vision in the treated patients [17]. Our study is, to date, the largest clinical study with intravitreal injection of steroids. Until now, three studies with a small sample of patients have shown promising observations: three injected patients reported by Jonas et al. [18], four injected patients vs. six non-injected patients reported by Kaderli et al. [19], and one injected patient reported by Sohn et al. [20]. While the Jonas et al. study concluded that a high-dose intravitreal injection of triamcinolone acetonide may not be markedly effective in increasing visual acuity after acute NAION, the other two concluded that it may improve visual acuity.

However, in Jonas et al.'s study [18], 20 mg of triamcinolone acetonide was injected, which is four times the dose in our study. The 4 mg/0.1 mL dose was used in our study, because it is the concentration we used to inject in diabetic macular edema (DME) or edema secondary to retinal vein occlusion years ago, and so we were familiar with its tolerability.

This led to another weakness in this retrospective study: the lack of information regarding the previous macular status. Even if there was no statistical difference in VA between the IVTA and non-IVTA group at inclusion, we note a higher proportion of diabetic patients in the IVTA group (35% vs. 13% — Table 1). Indeed, IVTA is effective for DME, and thus, unknown prior DME could bias our results.

The mechanism of action of the treatment remains to be understood. It has been hypothesized that a compartment syndrome induced by optic disc edema inside a confined space is responsible for a vicious cycle of disc edema and peripapillary hemorrhage [21]. This compartment syndrome results in cytotoxic and vasogenic edema, which causes infarction and retinal ganglion cell (RGC) loss. In a rodent NAION model, a previous report demonstrated that 1 week after induced AION, IVTA had a neuroprotective effect on RGC survival, with an increase in the amplitude of visual evoked potentials and a decrease in microglial cell infiltration in the optic nerve [12].

The reduction of edema by the steroids could be responsible for the observed therapeutic effect. The linear relationship between timing of the IVTA and VA improvement supports the hypothesis of a compartment syndrome involved in the pathogenesis: each passing day was associated with a two-fold reduction of VA improvement. This result is important for patient information, especially in the case of second eye involvement.

It has been shown that axonal loss is associated with microvascular dropout on OCT-A [22—24]. A future OCT-A-based study would enable comparison of the changes and outcomes of optic nerve head vascularization between TA injected eyes and controls, which was not performed routinely in our cohort. This would enable us to evaluate whether or not a vascular mechanism is involved in the observed effect. To further demonstrate the potential action of intravitreal steroids, future studies should focus on induced microvascular changes, comparing injected and non-injected eyes in various stages of the disease. It would be particularly interesting to evaluate the time-dependency of the vascular dropout, especially considering the cut-off at 15 days that was found in the present study and also previously reported by Hayreh et al. [16].

Despite the unclear mechanisms involved, intravitreal steroids appear to be the only treatment having a putative benefit on visual outcome with limited side effects besides the well-known ocular hypertension as previously reported

[25]. Cataract was also a frequently observed complication, although only 2 of the injected patients in our population underwent cataract surgery. Other therapeutic strategies have been reported, but with limited or no effect on visual function. More precisely, two previous studies reporting the effect of intravitreal bevacizumab in NAION demonstrated no benefit either for visual acuity or the visual field [26,27].

It is also important to note that the ischemic optic neuropathy decompression treatment trial (IONDT), which was randomized treatment trial, showed that 42.7% of patients without treatment improved at least 3 lines of Log MAR visual acuity after 6 months [28]. Our untreated group had a worse outcome than that reported in the IONDT study; indeed only 11% of the non-IVTA group had a VA improvement of at least 3 lines of LogMAR (Table 3). This could be a consequence of the retrospective, unmasked and unrandomized design of study. The lack of patient or physician masking to treatment also leads to the following weakness: The volunteer patients could have been randomized into an IVTA group vs. sham injection group. Indeed, patients who choose treatment might be more likely to try harder on visual function testing; additionally, treating physicians may consciously or unconsciously encourage the IVTA patients to try harder than the untreated patients.

Following the publication of our previous results on a smaller cohort [14], the authors attempted to undertake a prospective, controlled randomized multicenter study. There is currently only one commercially available steroid treatment in France designed for intravitreal administration, the dexamethasone implant. However, NAION being relatively rare and the financial impact of such a treatment being relatively low, no support for a multicenter randomized trial could be obtained, as such an implant may lack the loading effect obtained with triamcinolone.

A project for a randomized multicenter study with triamcinolone has also been submitted to the French Ministry of Health. In any event, we strongly believe that intravitreal injection of steroids should be viewed as a promising therapeutic strategy against the poor visual prognosis of NAION.

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Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Johnson LN, Arnold AC. Incidence of nonarteritic and arteritic anterior ischemic optic neuropathy. Population-based study in the state of Missouri and Los Angeles County, California. J Neuroophthalmol 1994;14:38—44.
[2] Hattenhauer MG, Leavitt JA, Hodge DO, Grill R, Gray DT. Incidence of nonarteritic anterior ischemic optic neuropathy. Am J Ophthalmol 1997;123:103—7.
[3] Arnold AC, Helper RS. Fluorescein angiography in acute nonarteritic anterior ischemic optic neuropathy. Am J Ophthalmol 1994;117:222—30.
[4] Olver JM, Spalton DJ, McCartney ACE. Microvascular study of the retrolaminar optic nerve in man: the possible significance in anterior ischaemic optic neuropathy. Eye 1990;4:7—24.
[5] Hayreh SS, Zimmerman B. Visual field abnormalities in nonarteritic anterior ischemic optic neuropathy: their pattern and prevalence at initial examination. Arch Ophthalmol 2005;123:1554—62.
[6] Traustason OI, Feldon SE, Leemaster JE, Weiner JM. Anterior ischemic optic neuropathy: classification of field defects by Octopus automated static perimetry. Graefes Arch Clin Exp Ophthalmol 1988;226:206—12.
[7] Hayreh SS, Podhajsky PA, Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: time of onset of visual loss. Am J Ophthalmol 1997;124:641—7.
[8] Burde RM. Optic disk risk factors for nonarteritic anterior ischemic optic neuropathy. Am J Ophthalmol 1993;116:759—64.
[9] Beck RW, Savino PJ, Repka MX, Schatz NJ, Sergott RC. Optic disc structure in anterior ischemic optic neuropathy. Ophthalmology 1984;91:1334—7.
[10] [No authors listed]. Characteristics of patients with nonarteritic anterior ischemic optic neuropathy eligible for the ischemic optic neuropathy decompression trial. Arch Ophthalmol 1996;114:1366—74.
[11] Hayreh SS, Podhajsky PA, Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: time of onset of visual loss. Am J Ophthalmol 1997;124:641—7.
[12] Newman NJ, Scherer R, Langenberg P, Kelman S, Feldon S, Kaufman D, et al. The fellow eye in NAION: report from the ischemic optic neuropathy decompression trial follow-up study. Am J Ophthalmol 2002;134:317—28.
[13] Huang T-L, Wen Y-T, Chang C-H, Chang S-W, Lin K-H, Tsai R-K. Efficacy of intravitreal injections of triamcinolone acetonide in a rodent model of nonarteritic anterior ischemic optic neuropathy. Invest Ophthalmol Vis Sci 2016;57:1878—84.
[14] Radoi C, Garcia T, Brugniart C, Ducasse A, Arndt C. Intravitreal triamcinolone injections in non-arteritic anterior ischemic optic neuropathy. Graefes Arch Clin Exp Ophthalmol 2014;252:339—45.
[15] Keren S, Zanolli M, Dotan G. Visual outcome following bilateral non-arteritic anterior ischemic optic neuropathy: a systematic review and meta-analysis. BMC Ophthalmol 2017;17:155, http://dx.doi.org/10.1186/s12886-017-0543-y.
[16] Hayreh SS, Zimmerman MB. Non-arteritic anterior ischemic optic neuropathy: role of systemic corticosteroid therapy. Graefes Arch Clin Exp Ophthalmol 2008;246:1029—46.
[17] Pakravan M, Sanjari N, Esfandiari H, Pakravan P, Yaseri M. The effect of high-dose steroids, and normobaric oxygen therapy, on recent onset non-arteritic anterior ischemic optic neuropathy: a randomized clinical trial. Graefes Arch Clin Exp Ophthalmol 2016;254:2043—8.
[18] Jonas JB, Spandau UH, Harder B, Sauder G. Intravitreal triamcinolone acetonide for treatment of acute nonarteritic anterior ischemic optic neuropathy. Graefes Arch Clin Exp Ophthalmol 2007;245:749—50.
[19] Kaderli B, Avci R, Yucel A, Guler K, Gelisken O. Intravitreal triamcinolone improves recovery of visual acuity in nonarteritic anterior ischemic optic neuropathy. J Neuroophthalmol 2007;27:164—8.
[20] Sohn BJ, Chun BY, Kwon JY. The effect of an intravitreal triamcinolone acetonide injection for acute nonarteritic anterior ischemic optic neuropathy. Korean J Ophthalmol 2009;23:59—61.
[21] Arnold AC. Pathogenesis of nonarteritic anterior ischemic optic neuropathy. J Neuroophthalmol 2003;23:157—63.
[22] Gaier ED, Gilbert AL, Cestari DM, Miller JB. Optical coherence tomographic angiography identifies peripapillary microvascular dilation and focal non-perfusion in

giant cell arteritis. Br J Ophthalmol 2018;102:1141—6 https://doi.org/10.1136/bjophthalmol-2017-310718.
[23] Sharma S, Ang M, Najjar RP, Sng C, Cheung CY, Rukmini AV, et al. Optical coherence tomography angiography in acute nonarteritic anterior ischaemic optic neuropathy. Br J Ophthalmol 2017;101:1045—51.
[24] Augstburger E, Zéboulon P, Keilani C, Baudouin C, Labbé A. Retinal and choroidal microvasculature in nonarteritic anterior ischemic optic neuropathy: an optical coherence tomography angiography study. Invest Ophthalmol Vis Sci 2018;59:870—7.
[25] Tammewar AM, Cheng L, Kayikcioglu OR, Falkenstein IA, Kozak I, Goldbaum MH, et al. Comparison of 4 mg versus 20 mg intravitreal triamcinolone acetonide injections. Br J Ophthalmol 2008;92:810—3.
[26] Prescott CR, Sklar CA, Lesser RL, Adelman RA. Is intravitreal bevacizumab an effective treatment option for nonarteritic anterior ischemic optic neuropathy? J Neuroophthalmol 2012;32:51—3.
[27] Rootman DB, Gill HS, Margolin EA. Intravitreal bevacizumab for the treatment of nonarteritic anterior ischemic optic neuropathy: a prospective trial. Eye 2013;27:538—44.
[28] The Ischemic Optic Neuropathy Decompression Trial Research Group. Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy is not effective and may be harmful. JAMA 1995;273:625—32.