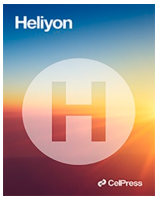
Heliyon 10 (2024) e30578

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Clinical efficacy of dexamethasone parabulbar injection in patients with Nonarteritic anterior ischemic optic neuropathy

Jing Li [*], Guoge Han, Wei Zhang, Yue Zhang [**]

Tianjin Eye Hospital, Tianjin Eye Institute, Tianjin Key Lab of Ophthalmology and Visual Science, Nankai University, Tianjin, 300000, China

ARTICLE INFO

Keywords:
Corticosteroids
Nonarteritic anterior ischemic optic neuropathy
Parabulbar injection
Visual acuity
Visual field

ABSTRACT

Background: Nonarteritic anterior ischemic optic neuropathy (NAAION) is a common optic neuropathy that often leads to significant visual acuity loss in patients. The present study evaluated the effects of parabulbar dexamethasone injection on visual outcomes in patients with NAAION.
Methods: This retrospective case-control study included patients diagnosed with NAAION between January 2019 and December 2022. Thirty-four patients with NAAION (34 eyes) received dexamethasone parabulbar injections, while 39 patients with NAAION (39 eyes) received oral corticosteroid treatment (control group). Best-corrected visual acuity (BCVA), visual field (VF) defect, and retinal nerve fiber layer (RNFL) thickness of the affected eye were compared between groups at baseline and 2, 6, and 12 weeks post-treatment.
Results: Mean BCVA significantly improved after 6 and 12 weeks in the injection groups compared with the control group (all $P < 0.01$). The visual field indices, mean deviation and pattern standard deviation significantly improved in the injection group compared with the control group after 2, 6, and 12 weeks (all $P < 0.01$). The RNFL showed a remarkable decrease in edema after 6 weeks (superior and nasal P values 0.005 and 0.013, respectively) in the injection group compared with the control group. Significant RNFL thinning was also observed in superior, inferior, temporal, and nasal quadrants in the control group after 12 weeks (all P values < 0.01). Also, fewer side effects were observed in the injection group compared to the control group.
Conclusions: The results of this study suggested that dexamethasone parabulbar injection might be a safe and effective intervention for relieving visual acuity and VF in patients with NAAION.

1. Introduction

Nonarteritic anterior ischemic optic neuropathy (NAAION), the most common form of ischemic optic neuropathy, is characterized by sudden painless loss of vision and visual field (VF) defects accompanied by optic disk edema, which leads to optic atrophy in several months [1–3]. In the USA, NAAION affects between 2.3 and 10.3 people over 100,000 individuals per year and may occur at any age; yet, it is particularly common in patients >50 years old [4]. The course of NAAION typically stabilizes within 2–3 months. The acuity improves by up to three lines in 43 % of patients, whereas nearly one-quarter of patients tend to achieve an acuity less than or equal to

* Corresponding author. Tianjin Eye Hospital, Tianjin Eye Institute, Tianjin Key Lab of Ophthalmology and Visual Science, Nankai University, Tianjin, 300000, China.
** Corresponding author. Tianjin Eye Hospital, Tianjin Eye Institute, Tianjin Key Lab of Ophthalmology and Visual Science, Nankai University, Tianjin, 300000, China.
E-mail addresses: jingliwater123@163.com (J. Li), zmoon1976@sina.com (Y. Zhang).

https://doi.org/10.1016/j.heliyon.2024.e30578
Received 18 November 2023; Received in revised form 27 April 2024; Accepted 29 April 2024
Available online 8 May 2024

20/200. Also, in patients with NAAION, VF defects are less likely to improve [5].

Steroid is considered the recommended therapeutic option for NAAION due to its potential role in reducing optic disc edema and improving optic nerve head perfusion [6–8]. Some experts claimed that benefits of systemic steroids in NAAION may be outweighed by the adverse reactions [9,10]. Previous studies reported that up to 90 % of patients treated with systemic glucocorticoids experience adverse reactions, including gastrointestinal reactions, headaches, weight gain, and anxiety [11]. The efficacy of intravitreal triamcinolone injection in patients with NAAION also remains controversial [12]. Some studies [12,13] suggested that intravitreal triamcinolone injection may increase intraocular pressure, further compromising circulation and resulting in further visual loss. Moreover, treatment with intravitreal triamcinolone injection also causes complications such as accelerated cataract progression and endophthalmitis [14,15]. Thus, searching for safer ways to treat NAAION is of essential importance.

Parabulbar injections of steroids have a long history of use in ophthalmology for treating inflammatory conditions. This type of injection can provide long-term efficacious therapy while minimizing side effects compared with systemic glucocorticoids in uveitis, thyroid-associated ophthalmopathy, and ocular myasthenia gravis [16–18]. Nevertheless, few studies have reported the effectiveness and safety of parabulbar glucocorticoids in patients with NAAION.

The present study aimed to explore the visual outcomes in patients with NAAION treated with parabulbar dexamethasone injection compared with those treated with systemic glucocorticoids. Additionally, we also reported the adverse effects of such treatments.

2. Materials and methods

2.1. Study design

This retrospective case-control study involved patients diagnosed with NAAION in Tianjin Eye Hospital between January 2019 and December 2022. The study was performed according to the Declaration of Helsinki. The institutional review board or ethics committee approval was obtained (approval no. KY2023021), and all patients provided written informed consent.

Patients were with acute NAAION if they (1) had a history of sudden visual field loss and/or painless vision loss. (2) showed visual field defects corresponding to optic nerve damage. (3) showed localized or diffuse optic disc edema, often accompanied by peripheral linear bleeding. (4) showed relative afferent pupillary dysfunction and/or visual evoked potential abnormalities. (5) showed no neurologic, systemic or ocular disorders, that could contribute to optic disc edema and visual impairment [7]. The inclusion criteria were as follows: (1) patients diagnosed with NAAION for the first time; (2) within 2 weeks of the onset of symptoms and not having treatment for NAAION prior to evaluation. The exclusion criteria were: (1) other serious eye diseases affecting visual function, such as obvious cataracts and retinal vascular occlusion; (2) patients with symptoms and signs suggestive of an arteritic anterior ischemic optic neuropathy such as scalp tenderness, jaw claudication, temporal headaches, presence of an elevated erythrocyte sedimentation rate, and high Creactive protein levels; (3) patients with glaucoma with VF loss; (4) serious organic diseases, such as cancer, heart failure, and hemophilia; (5) mental disorders; (6) patients with diabetes or diabetic retinopathy; (7) eyes with unreliable VFs; and (8) follow-up in less than 3 months.

2.2. Enrollment of participants and intervention

Thirty-four patients diagnosed with NAAION (34 eyes) between December 2020 and December 2022 received dexamethasone parabulbar injections and were designated the injection group. In addition, 39 patients diagnosed with NAION from January 2019 to November 2020 received oral corticosteroid treatment and were categorized as the control group. The injection group patients received a 5-mg dexamethasone parabulbar injection every 3 days for 36 days. The dexamethasone was injected from the outer and outer one-third of the skin surface of the lower orbital margin. The basis for the administration plan of dexamethasone injection is that the half-life of dexamethasone is 36–54 h. After 5 weeks, optic disc edema in most patients basically subsidedA 5-mg dexamethasone parabulbar injection is a safe dose that is commonly used in clinical practice [16–18]. After reviewing the literature [6,7], the control group patients were started on 80 mg of prednisone daily (irrespective of their weight). After 2 weeks, the therapy was gradually tapered (70 mg, 60 mg, and then reduced by 5 mg every 5 days until drug withdrawal). Patients in both groups were given Ginaton injection (Ginkgo biloba extract, Chi Sheng Chemical Cooperation, Taiwan, China) 70 mg QD intravenously for 10 days and mecobalamin (Eisai China Inc.) 0.5 mg TID orally for 6 months to improve circulation and protect the optic nerve.

Blood glucose tests (fasting and 2 h after a meal) were conducted at the beginning and end of glucocorticoid treatment in both groups.

2.3. Primary and secondary outcome

The primary outcome measure was the best-corrected VA (BCVA). The secondary objectives included evaluating any possible benefit on VF defects or retinal nerve fiber layer (RNFL) thickness and documenting any adverse effects of therapy.

2.4. Data collection and follow-up

The ophthalmic evaluation included BCVA assessment using the Early Treatment Diabetic Retinopathy Study (ETDRS) charts with logarithm of the minimal angle of resolution (logMAR) values, intraocular pressure measurement, slit-lamp and dilated fundus examinations. Visual field examinations were performed using the Humphrey visual field test (30-2 SITA program), primarily collecting

parameters of visual field indices (VFIs), mean deviation (MD) and pattern standard deviation (PSD). Optical coherence tomography (OCT) (Optovue, Inc., CA, USA) imaging was used to obtain RNFL thickness, disc area, and central macular thickness. The analysis data included examinations conducted at baseline and after 2, 6, and 12 weeks. Additionally, a detailed consultation session was conducted at each follow-up examination to look for any adverse effects of steroids.

SPSS Statistics 19.0 software was used for statistical analysis (SPSS, Inc., IL, USA). Quantitative data were expressed as mean ± standard deviation or median value with range, as appropriate. Qualitative variables were expressed as percentage. The normality of data was assessed using the Kolmogorov-Smirnov test and Q-Q diagrams. Manne-Whitney *U* test was used to compare quantitative variables and chi-square test was used to compare qualitative variables. The Friedman test was used to evaluate the changes within groups. *P* value of <0.05 indicated statistical significant.

3. Results

3.1. General data

The main demographic and clinical data of the two groups were statistically compared with reference to baseline (Table 1). Thirty-four patients [18 men (18 eyes) and 16 women (16 eyes) aged 47–76 (63.85 ± 8.496) years] received dexamethasone parabulbar injection, while 39 patients [18 males (18 eyes) and 21 females (21 eyes) aged 46–76 (63.21 ± 8.189) years] received systemic corticosteroid treatment (Table 1). Age and sex in both groups were similar ($P = 0.846$ and $P = 0.566$). The median duration between the onset of symptoms and presentation was 6 days in both the injection (range: 1–12 days) and control groups (range: 1–13 days), with mean duration showing no significant difference between the two groups ($P = 0.920$) (Table 1). There was no statistically significant difference between the fasting blood glucose levels (5.09 ± 0.59 vs 5.08 ± 0.58 mmol/L, $P = 0.943$) and the 2-h postprandial blood glucose levels (6.46 ± 0.73 vs 6.19 ± 0.77 mmol/L mmol/L, $P = 0.107$) in the injection and control groups.

3.2. Visual acuity

At baseline, the mean initial BCVA showed no difference between the injection and control groups ($P = 0.656$) (Table 1 and Fig. 1A). After 2 weeks of treatment, no significant change in optic disc edema and visual acuity was visible in the two groups, yet BCVA was marginally reduced from baseline in both groups ($P = 0.184$ and $P = 0.291$, respectively).At week 6, BCVA further increased in both groups compared to baseline, yet the optic disc edema resolution in the injection group was significantly better than in the control group (all $P < 0.01$), as shown in Fig. 1A. From week 12, the optic disc atrophy and visual acuity decreased significantly in the control group compared to the injection group ($P < 0.01$). Both groups showed a statistically significant improvement in BCVA from baseline during a 12-week follow-up (both $P < 0.01$).

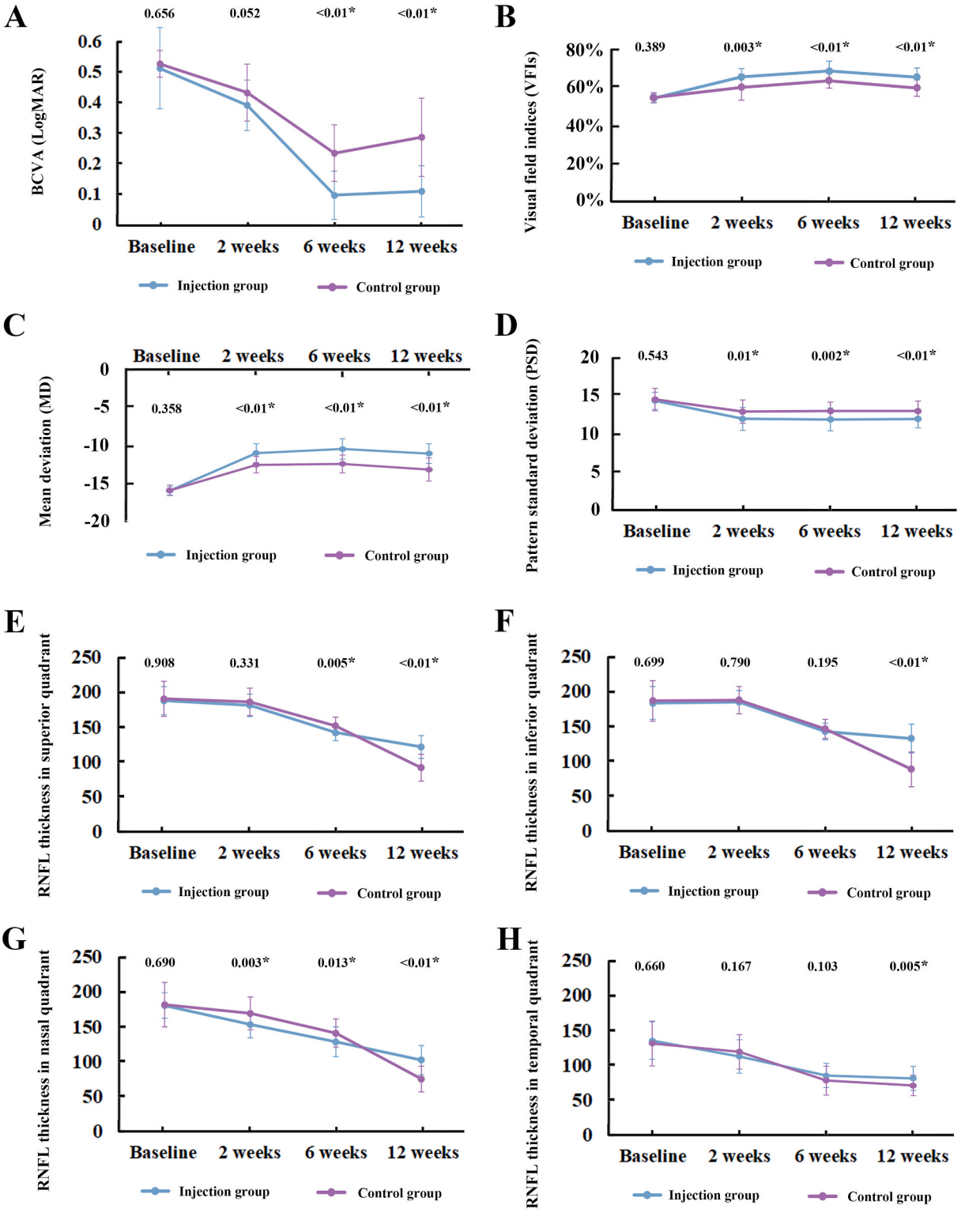
3.3. Visual fields

There were no significant differences in VFI (injection group: 54.71 % ± 2.406 %; control group: 54.69 % ± 2.261 %; $P = 0.389$), MD (injection group: 15.79 ± 0.528 dB; control group: 15.744 ± 0.651 dB; $P = 0.358$), and PSD (injection group: 14.335 ± 1.07 dB; control group: 14.485 ± 1.387 dB; $P = 0.543$) between groups at baseline (Table 1 and Fig. 1B–D). The VFI, MD and PSD in both groups showed significant improvement during the first 2 weeks of treatment (both $P < 0.01$). The injection group improved to a greater degree than the control group ($P < 0.01$) (Fig. 1B–D). From week 6–12, there were no significant changes in VFI, MD, and PSD in either group. However, the values for VFI, MD, and PSD in the injection group remained higher than those in the control group (Fig. 1B–D).

Table 1
Clinical and demographic profile of patients.

Parameter	Injection Group	Control Group	P Value
Age (yrs); mean ± SD	63.85 ± 8.496	63.21 ± 8.189	0.846
Gender (M: F)	18:16	18:21	0.566
Duration between onset of symptoms and presentation (days), mean ± SD	6.21 ± 2.794	6.28 ± 3.06	0.920
Median	6	6	
Range	1–12	1–13	
Fasting blood glucose (mmol/L); mean ± SD	5.09 ± 0.59	5.08 ± 0.58	0.943
2-h postprandial blood glucose (mmol/L); mean ± SD	6.46 ± 0.73	6.19 ± 0.77	0.107
Visual acuity (logMAR), mean ± SD	0.521 ± 0.140	0.536 ± 0.143	0.656
Visual field indices (VFIs)	54.21 % ± 2.358 %	54.64 % ± 2.549 %	0.389
Mean deviation (MD), (dB)	15.79 ± 0.528	15.744 ± 0.651	0.358
Pattern standard deviation (PSD), (dB)	14.335 ± 1.07	14.485 ± 1.387	0.543
OCT RNFLT (μm), mean ± SD			
Superior	188.91 ± 20.306	191.62 ± 25.226	0.908
Inferior	183.47 ± 23.215	186.33 ± 28.393	0.699
Temporal	181.29 ± 18.785	182.64 ± 32.383	0.6602
Nasal	133.82 ± 25.892	129.72 ± 30.922	0.690

M = male; F = female; logMAR = logarithm of the minimum angle of resolution; RNFLT = retinal nerve fiber layer thickness; SD = standard deviation.



(caption on next page)

Fig. 1. (A–H) BCVA (A), VFIs (B), MD (C), PSD(D), RNFL thickness of superior (E), inferior (F), nasal(G), and temporal (H) quadrants for both the injection and control groups. At baseline and at 2 weeks, mean BCVA showed no difference between the groups. However, a significant difference in mean BCVA was observed between the injection and control groups at 6 weeks ($P < 0.01$) and 12 weeks ($P < 0.01$). Initial assessments of VFI, MD, and PSD showed no statistical difference between the groups. Yet, the differences in VFI, MD, and PSD were statistically significant between the injection and control groups from 2 to 12 weeks ($P < 0.01$). No difference was noted in the thickness of superior, inferior, temporal, and nasal RNFL between the groups at baseline. Similarly, no difference was observed in the superior, inferior, and temporal RNFL parameters between the two groups after 2 weeks, but a significant difference was found in nasal RNFL thickness ($P = 0.003$). Moreover, the superior and nasal RNFL showed a more pronounced reduction in edema after 6 weeks in the injection group compared with the control group ($P = 0.005$ and $P = 0.013$, respectively). Changes in the inferior and temporal quadrants were similar in both groups after 6 weeks ($P = 0.195$ and $P = 0.103$, respectively). Significant RNFL thinning was also observed in superior, inferior, temporal, and nasal quadrants in the control group after 12 weeks (all $P < 0.01$).

3.4. RNFL thickness

Baseline OCT showed increased thickness and edema in the superior, inferior, temporal, or nasal RNFL, or all, in most patients who showed improvement and RNFL thinning at the follow-up visit. No difference was observed in the thickness of superior, inferior, temporal, and nasal RNFL between the injection and control groups at baseline ($P = 0.908$, $P = 0.699$, $P = 0.660$, and $P = 0.690$, respectively) (Table 1 and Fig. 1E–H). Also, no difference was observed in the superior, inferior, and temporal RNFL parameters between the two groups after 2 weeks ($P = 0.331$, $P = 0.790$, and $P = 0.167$, respectively), but there was a significant difference in nasal RNFL thickness ($P = 0.003$) (Fig. 1E–H). However, the superior and nasal RNFL showed a greater reduction in edema after 6 weeks in the injection group compared with the control group ($P = 0.005$ and $P = 0.013$, respectively) (Fig. 1E–H). The change in the inferior and temporal quadrants was similar in both groups after 6 weeks ($P = 0.195$ and $P = 0.103$, respectively). The optic atrophy was more obvious in the control group after 12 weeks, manifested by significant RNFL thinning in the superior, inferior, temporal, and nasal quadrants, and the difference was statistically insignificant between the two groups (all P values < 0.01) (Fig. 1E–H).

3.5. Adverse reactions

No serious adverse effects of steroid therapy were observed in this study. A slight increase in intraocular pressure (IOP) without side effects was observed in seven patients in the injection group. Seven patients experienced elevated intraocular pressure (23, 22, 25, 24, 21, and 22 mmHg). After administration of carteolol hydrochloride eye drops for 12 h per drop, IOP dropped below 21 mmHg. Also, 3 cases of subcutaneous congestion appeared after the drug injection, yet, this spontaneously subsided after 2 weeks without causing eye or nerve damage.

In the control group, gastrointestinal reactions, including nausea and heartburn, were observed in 27 patients; 14 reported weight gain, and 5 experienced mild headaches and anxiety. Moreover, abnormal glucose tolerance was seen in 3 control group patients, while blood glucose in the drug injection group was within the normal range. Lifestyle interventions can ameliorate side effects and these side effects diminish after the tapering off of steroid. The incidence of side effects was significant higher in the injection group than in the control group ($P < 0.01$).

4. Discussion

The treatment of NAAION is still controversial. Most current medical therapeutic approaches are empirical. They mainly target ischemia, insufficient blood supply, and inflammation or involve the application of neuroprotective and neuroregenerative agents [2,12,19]. Steroids are by far commonly used therapeutic agents for NAAION [6–10]. Corticosteroids have antiedematous and anti-phlogistic effects, can decrease capillary permeability, and decrease compression of capillaries in the optic nerve head, thus improving blood flow and faster resolution of optic disc edema in NAAION [6–8]. In this study, we evaluated the effects of parabulbar dexamethasone injection on visual outcomes in patients with NAAION and found that dexamethasone parabulbar injection could better affect BCVA and VF defects than systemic glucocorticoid therapy. Moreover, the resolution of optic disk edema was faster, tremendously avoiding the appearance of optic atrophy.

Several studies in the last decade focused on corticosteroid treatment of NAAION [2,6–10,20]. A large cohort of 696 patients over a period of 27 years reported the beneficial effects of oral steroid treatment versus steroid-free treatment, particularly for patients with poor baseline performance [6]. Although flawed by its lack of randomization, the study was considered the best attempt to evaluate the effect of steroids on NAAION [6]. Chen et al. conducted a meta-analysis of studies on treating NAAION with corticosteroids and found that corticosteroids did not significantly improve vision in patients with NAAION [9]. In addition, a randomized controlled trial [10] revealed that oral steroids shorten the duration of disk edema and improve electrophysiological parameters of the optic nerve in patients with NAAION but did not result in a VA benefit. Yet, so far, few studies reported on the effects of corticosteroid parabulbar injection in treating NAAION.

In this study, BCVA and VF defect significantly improved after 6 weeks in the injection group compared with the control group. The difference was statistically significant between the groups. The superior and nasal RNFL showed a substantial reduction in edema after 6 weeks in the injection group compared with the control group. Shi et al. showed that the local injection of dexamethasone had a better treatment response for ocular myasthenia gravis than oral corticosteroids [16]. Moreover, dexamethasone local injections had a faster onset in patients with ocular myasthenia gravis than systemic steroids [16]. Furthermore, research indicates that the parabulbar injection of 5 mg dexamethasone disodiumphosphate resulted in several times higher dexamethasone concentrations in vitreous

compared with an oral dose of 7.5 mg dexamethasone [21] The drug can directly penetrate the posterior ciliary arteries and reach the optic nerve head to help eliminate edema, reduce the crowded state of the optic disk, and improve the degree of nerve ischemia to reduce damage to visual functions [18].

Moreover, the BCVA and VF defect showed an obvious deteriorationafter 12 weeks in the control group compared with the injection group. In the control group, significant RNFL thinning was observed in the superior, inferior, temporal, and nasal quadrants, and the difference was statistically significant between the two groups. Published studies showed that dexamethasone had a long biological half-life and high potency [22]. This study also found that a 5-mg dexamethasone parabulbar injection every three days could maintain an effective concentration in paraocular tissues for a long time. Hence, we observed insignificant optic atrophy after 12 weeks in the injection group compared with the control group.

Furthermore, local injections caused fewer side effects than oral hormone treatment [16]. In this study, seven patients exhibited a slight increase in intraocular pressure in the dexamethasone parabulbar injection group without any other side effects. In the oral corticosteroid group, 27 patients suffered from gastrointestinal reactions, including nausea and heartburn, 14 exhibited weight gain, and 5 observed mild headache and anxiety. A prospective trial showed that the parabulbar injection of 5 mg dexamethasone disodiumphosphate resulted in nearly equal dexamethasone concentrations in serum compared with an oral dose of 7.5 mg dexamethasone [21]. In this study, patients in the injection group received a parabulbar injection of 5 mg dexamethasone every 3 days, whereas patients in the control group were started on 80 mg prednisone daily. Clinically, 0.75 mg dexamethasone is equivalent to 5 mg prednisone. Therefore, the serum concentrations of steroids might be lower in the injection group than in the oral corticosteroid group, possibly causing fewer side effects.

However, this study has some limitations. First, this was a retrospective study with small sample size. A prospective study with a larger sample size is required to confirm these findings. Second, the mechanism of dexamethasone parabulbar injection in NAAION treatment was unclear, and the fellow up was relatively short. Therefore, the effects of dexamethasone para-bulbous administration on improving vision and relieving optic atrophy in patients with NAAION should be verified through larger-sample randomized controlled trials and should focus on its hormone adverse reactions.

5. Conclusion

Our data suggest that dexamethasone para-bulbous administration could achieve an excellent VA and VF in patients with NAAION with insignificant optic atrophy as well as fewer side effects compared with oral corticosteroid administration, supporting its use as a replacement for oral drug therapy. The dexamethasone para-bulbous administration may open up novel prospects for treating NAAION in the acute phase and provide hope for patients suffering from this blinding disease.

Data availability statement

Data and materials available on request from the authors.

CRediT authorship contribution statement

Jing Li: Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Guoge Han:** Data curation. **Wei Zhang:** Writing – review & editing, Investigation. **Yue Zhang:** Methodology, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was fully supported by the National Natural Science Foundation of China (82000949), the Natural Science Foundation of Tianjin (20JCQNJC01860) and the Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-016A) and partially supported by grants Natural Science Foundation of Tianjin City (21JCQNJC01800), Tianjin Health Research Project (TJWJ2022QN079), Nankai University Eye Institute (NKYKK202203), and Science Foundation of Tianjin Eye Hospital (No. YKZD1908).

References

[1] M.J. Morrow, Ischemic optic neuropathy, Continuum 25 (5) (2019) 1215–1235.
[2] S.S. Hayreh, Controversies on neuroprotection therapy in non-arteritic anterior ischaemic optic neuropathy, Br. J. Ophthalmol. 104 (2) (2020) 153–156.
[3] E. Gkoumas, G. Bontzos, T. Xirou, E. Chatzispasou, S. Kabanarou, Non-arteritic anterior ischemic optic neuropathy (NAAION) following a Hypovolemic episode of gastric bleeding, Cureus 12 (11) (2020) e11627.
[4] N.R. Miller, A.C. Arnold, Current concepts in the diagnosis, pathogenesis and management of nonarteritic anterior ischaemic optic neuropathy, Eye (Lond). 29 (1) (2015) 65–79.

[5] J.L. Mercado, V.A. Purvin, A. Kawasaki, D. WuDunn, Bilateral sequential nonarteritic anterior ischemic optic neuropathy: a comparison of visual outcomes in fellow eyes using quantitative analysis of goldmann visual fields, Arch. Ophthalmol. 130 (7) (2012) 863–867.
[6] S.S. Hayreh, M.B. Zimmerman, Non-arteritic anterior ischemic optic neuropathy: role of systemic corticosteroid therapy, Graefes Arch. Clin. Exp. Ophthalmol. 246 (2008) 1029–1046.
[7] Neuroophthalmology Group OSoCMA, Expert consensus on diagnosis and treatment of ischemic optic neuropathy in non-arteritic anterior part of China, Chin. J. Ophthalmol. 51 (5) (2015) 323–326.
[8] A.G. Lee, V. Biousse, Share Should steroids be offered to patients with nonarteritic anterior ischemic optic neuropathy? J. Neuro Ophthalmol. 30 (2) (2010) 193–198.
[9] J. Chen, J. Zhu, L. Chen, C. Hu, Y. Du, Steroids in the treatment of nonarteritic anterior ischemic optic neuropathy: a PRISMA-compliant meta-analysis, Medicine (Baltim.) 98 (46) (2019) e17861.
[10] R. Saxena, D. Singh, M. Sharma, M. James, P. Sharma, V. Menon, Steroids versus No steroids in nonarteritic anterior ischemic optic neuropathy: a randomized controlled trial, Ophthalmology 125 (10) (2018) 1623–1627.
[11] S. Moghadam-Kia, V.P. Werth, Prevention and treatment of systemic glucocorticoid side effects, Int. J. Dermatol. 49 (3) (2010) 239–248.
[12] S.S. Hayreh, Management of ischemic optic neuropathies, Indian J. Ophthalmol. 59 (2) (2011) 123–136.
[13] S.S. Hayreh, The blood supply of the optic nerve head and the evaluation of it - myth and reality, Prog. Retin. Eye Res. 20 (5) (2001) 563–593.
[14] S.A. Gaballa, U.B. Kompella, O. Elgarhy, et al., Corticosteroids in ophthalmology: drug delivery innovations, pharmacology, clinical applications, and future perspectives, Drug Deliv Transl Res 11 (3) (2021) 866–893.
[15] R. Monsellato, E. Trovato, P. Turchetti, et al., Ocular hypertension management in long-term treatments with intravitreal dexamethasone implants: a 3-year experience, Clin. Ter. 170 (1) (2020) e11–e14.
[16] M. Shi, Y. Ye, J. Zhou, A. Qin, J. Cheng, H. Ren, Local use of dexamethasone in the treatment of ocular myasthenia gravis, BMC Ophthalmol. 20 (1) (2020) 432.
[17] Y. Wang, B. Du, M. Yang, Y. Zhu, W. He, Peribulbar injection of glucocorticoids for thyroid-associated ophthalmopathy and factors affecting therapeutic effectiveness: a retrospective cohort study of 386 cases, Exp. Ther. Med. 20 (3) (2020) 2031–2038.
[18] A.T. Fung, T. Tran, L.L. Lim, et al., Local delivery of corticosteroids in clinical ophthalmology: a review, Clin. Exp. Ophthalmol. 48 (3) (2020) 366–401.
[19] S. Berry, W.V. Lin, A. Sadaka, A.G. Lee, Nonarteritic anterior ischemic optic neuropathy: cause, effect, and management, Eye Brain 9 (2017) 23–28.
[20] K. Lantos, Z.R. Domotor, N. Farkas, et al., Efficacy of treatments in nonarteritic ischemic optic neuropathy: a systematic review and meta-analysis, Int. J. Environ. Res. Publ. Health 19 (5) (2022).
[21] O. Weijtens, R.C. Schoemaker, A.F. Cohen, et al., Dexamethasone concentration in vitreous and serum after oral administration, Am. J. Ophthalmol. 125 (5) (1998) 673–679.
[22] K.S. Dixit, P.U. Kumthekar, Optimal management of corticosteroids in patients with intracranial malignancies, Curr. Treat. Options Oncol. 21 (9) (2020) 77.