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Clinical characteristics and prognosis of bilateral nonarteritic ischemic optic neuropathy patients in 61 cases

Liang Liao, Qi-Ping Wei, Jian Zhou, Yan-Hong Sun, Yan-Ting Xia

Department of Ophthalmology, Dongfang Affiliated Hospital of Beijing University of Chinese Medicine, Beijing 100078, China

Correspondence to: Qi-Ping Wei. No. 6, District 1, Fangxingyuan, Fangzhuang, Fengtai District, Beijing 100078, China. 58273677@qq.com

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双眼非动脉炎性前部缺血性视神经病变患者的临床特点和预后分析

廖 良,韦企平,周 剑,孙艳红,夏燕婷
(作者单位:100078 中国北京市北京中医药大学东方医院眼科)
作者简介:廖良,毕业于北京中医药大学,博士,主治医师,研究方向:视神经疾病。
通讯作者:韦企平,毕业于北京中医药大学,学士,主任医师,教授,研究方向:视神经疾病. 58273677@qq.com

摘要

目的:研究双眼非动脉炎性前部缺血性视神经病变(nonarteritic ischemic optic neuropathy, NAION)患者的临床特点及其预后的影响因素。

方法:回顾 2006 年以来我院收治的双眼发病 NAION 患者的临床资料,包括发病特点、治疗方法、人口统计学特征、病史、视功能指标(视力、视野)等,并对影响视功能预后的相关因素进行统计分析。

结果:研究共纳入 61 例(122 眼)双眼 NAION 患者,其中男性 39 例,女性 22 例,平均年龄 58.0±11.0 岁,就诊时平均病程 12.5mo(IQR 4.75~26.5),初诊时最佳矫正视力中位数为 0.7 LogMAR(IQR 0.2~1.3)。就诊时 38 眼仍有不同程度视盘水肿,76 眼视盘色淡或苍白。典型的视野缺损类型分别为下方近水平半盲(38 眼)、鼻上方缺损(21 眼)、鼻下方缺损(16 眼)、上方近水平半盲(13 眼),以及近管状视野(12 眼)。纳入患者中 31 例伴有高血压、高血脂、糖尿病或其他心脑血管疾病。患者随访时间的中位数为 12mo(IQR 6.0~23.5),随访期间视力中位数由 0.7 LogMAR(IQR 0.2~1.3)提高至 0.4 LogMAR(IQR 0.175~1.1),其中 45 眼(36.9%)的视力提高了 2 行或以上。男性患者和女性患者的视力比较,初诊时及随访后两者均无统计学差异($Z=-0.521$, -1.600, $P>0.05$)。伴有心脑血管疾病的患者与不伴心脑血管疾病者比较,初诊时两组患者视力无统计学差异($Z=-1.103$, $P>0.05$),但末次随访时不伴有心脑血管疾病的患者的视力明显优于伴心脑血管疾病的患者($Z=-2.090$, $P<0.05$)。首发眼和后发病眼的末次随访视力均优于初诊视力($P=0.003$, 0.019),且首发眼的视力在随访期间的提高幅度高于后发病眼的视力提高幅度(分别为 0.2 LogMAR 及 0.1 LogMAR),但差异尚无统计学意义($P=0.195$)。

结论:本研究统计分析了双眼 NAION 患者的人口统计学特征、发病率、病史、视功能指标(视力、视野)等,现有随访数据表明,不伴心脑血管疾病的双眼 NAION 患者视力改善幅度优于患心脑血管疾病者,且首发眼视力预后可能优于后发病眼。但目前尚缺乏足够证据,仍需进一步研究。

关键词:临床特点;预后;非动脉炎性前部缺血性视神经病变

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Abstract

• AIM: To evaluate the clinical characteristics of patients with bilateral nonarteritic ischemic optic neuropathy (NAION) and the prognosis of NAION's impact factors.

• METHODS: NAION patients with both eyes onset from 2006 were included in this study, their clinical characteristics, treatment methods, the demographic index, medical history, visual acuity, visual field and other clinical data of NAION, including the impact factors of the prognosis, were obtained statistically.

• RESULTS: A total of 61 patients (122 eyes) have been diagnosed with NAION bilaterally, including 39 males and 22 females, with an average age of 58.0±11.0 years old, and the duration of the first onset was 12.5mo (IQR 4.75-26.5). The median of the best log MAR corrected visual acuity of the 122 eyes at initial visit were 0.7 logMAR (IQR 0.2-1.3), optic disc edema was seen in 38 eyes while optic disc saw in 76 eyes were pale or white. The most common types of visual field defects were inferior altitudinal visual field defect (38 eyes), supero-nasal defect (21 eyes), infero-nasal defect (16 eyes), superior altitudinal visual field defect (13 eyes), and tubular visual field defect (12 eyes). Among all the patients, there were 31 accompanied with hypertension, hyperlipidemia, diabetes, or a history of other cardiovascular and cerebrovascular diseases. After an median of 12mo (IQR 6-23.5) of follow-up observation, the visual acuity has been increased from 0.7 logMAR (IQR 0.2-1.3) to 0.4 logMAR (IQR 0.175-1.1), in which 45 eyes (36.9%) increased 2 lines or more. Best corrected visual acuity

(BCVA) had no significant differences ($Z=-0.521$, -1.600, $P>0.05$) between the male and female patients at initial visit and during follow-up. BCVA of patients accompanied with cardiovascular or cerebrovascular disease had no significant differences ($Z=-1.103$, $P>0.05$) from those without cardiovascular or cerebrovascular disease before the treatment, while there were significant differences ($Z=-2.090$, $P<0.05$) between the two type of patients at their last follow-up visit. The visual acuity of the earlier onset cases and the later onset cases were both significantly higher ($P=0.003$, 0.019) than that at last visit, while BCVA of earlier onset cases improved more than later onset cases (median with 0.2 and 0.1 logMAR respectively, $P=0.195$) though there was no significant differences.

• CONCLUSION: After summarizing the demographic index, incidence, medical history, visual acuity, and visual field characteristics of the bilateral NAION patients, we found that patients who were accompanied with cardiovascular or cerebrovascular disease and the later onset eyes might had a poor prognosis than the others, though there were further evidence needed to support this finding.

• KEYWORDS: clinical characteristics; prognosis; nonarteritic ischemic optic neuropathy
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INTRODUCTION

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common type of optic neuropathy seen in the middle-aged and elderly population. A population-based study has shown people who were 50 or older are the common population of NAION. The estimated mean annual incidence rates of NAION per 100000 population were 2.3-10.2 in California[1]. Moreover, the incidence of NAION has shown a rising trend as the incidence of hypertension, diabetes, hyperlipidemia, cardiovascular and cerebrovascular disease increased[2-4]. Many patients with bilateral involvement have difficulties in handling their daily life than that unilateral involved. This study was conducted retrospectively in 61 patients (122 eyes) diagnosed with NAION bilaterally since January, 2006 and the author aimed to investigate their clinical features and prognosis of the patients.

SUBJECTS AND METHODS

Patients The study was conducted at the Dongfang Hospital of Beijing University of Chinese Medicine in Beijing, where all patients diagnosed with NAION bilaterally had been regularly followed-up since 2006. The study followed the tenets of the Declaration of Helsinki. Written or verbal informed consent was obtained from all participants. Patients' clinical characteristics, treatment rendered, visual acuity, visual field (VF) index, the demographic index, medical history, visual acuity, VF and other clinical data of NAION, as well as the impact factors of the prognosis, were obtained statistically.

Diagnosis and Inclusion Criteria ANION diagnostic and inclusion criteria are: 1) chief complaint of sudden painless visual loss or vision deterioration; 2) relative afferent pupillary defect during the onset is positive; 3) optic disc edema (ODE) can be seen by ophthalmoscope or documented at onset; 4) the affected eye had optic disc-related VF defects; 5) pattern visual evoked potential or flash visual evoked potential anomalies were encountered; 6) there wasn't any neurology, systemic factors, nor ocular disorder that could be responsible for ODE and visual impairment; 7) patients have been treated at other hospital with sufficient diagnostic evidences as NAION are included at this retrospective study.

Visual Status Evaluation Visual acuity was examined using the standard logarithmic visual acuity chart and under identical testing conditions. The following steps of visual acuity were checked: every interval of 0.10 from -0.30 LogMAR to 1.90 LogMAR, fingers counting, hand motion, light perception, and no light perception. We use automated perimetry (OCTOPUS101 Perimeter, Switzerland, Program N1 or LVC depending on patients' coordination) to obtain static vision field index, such as MS and MD. Other ophthalmology examinations had included color vision, intraocular pressure (IOP, pneumatic tonometer, Canon, Japan), pupillary light response, and most he cases were examined with visual electrophysiological instrument (dual channels, Roland, Germany), optical coherence tomography or fluorescence fundus angiography. All 61 cases also underwent CT and/or brain MRI examination, as well as blood cell and urine analysis, blood biochemical examination, Transcranial Doppler and color Doppler angiography examination.

Treatment and Follow-up All patients were treated 2-4wk with integrated traditional Chinese medicine and western medicine. The prescriptions of herbal medicine were based on pattern differentiations of traditional Chinese medicine. Besides, patients were injected with compound Anisodine subcutaneously closed to superficial temporal artery, 4ml per day, and vitamin B1 tablets were administered three times daily. Patients were given acupuncture once a day. All patients were told to revisit every 4wk in the first 6mo after discharging from the hospital, there after return visit in every 3mo interval would be arranged. Patients who did not return visit on time were followed up with telephone interview if possible. The last follow-up was scheduled on April 30, 2014.

Statistical Methods Statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, Illions, USA). Descriptive statistics modules (means, standard deviations, median, and percentages) were computed for the demographic and clinical variables, visual acuity, and MS of VF at initial visit. A change of $\geqslant 2$ lines in the international standard visual acuity chart or 0.20 logMAR was considered a

Table 1 Systemic condition of bilateral and unilateral NAION patients

Systemic condition	Diabetes mellitus		Arterial hypertension		Atherosclerosis		Cerebrovascular disorder	
	Y	N	Y	N	Y	N	Y	N
Bilateral NAION (n=61)	12	49	22	39	20	41	11	50
Unilateral NAION (n=49)	16	33	21	28	13	36	6	43
Chi-square	2.413		0.526		0.506		0.697	
Significance (P)	0.120		0.468		0.477		0.404	

significant change in either improvement or deterioration. Measurement data of normal distribution (age, IOP) were described by the mean±standard deviation and compared by t-test, while data not fit the normal distribution were described by median (IQR) and compared by Wilcoxon signed-rank test (independent samples) or Mann-Whitney test (related samples). Categorical data was assessed with chi-square statistics. The level of statistical significance was defined as P <0.05.

RESULTS

Clinical Characteristics of Bilateral Nonarteritic Ischemic Optic Neuropathy

Gender and age There were 110 patients in Dongfang hospital diagnosed with NAION since 2006 January, among them 61 cases (55.5%, 122 eyes) were bilateral onset. There were 39 males and 22 females. Patients average age were 58±11 (39-90) years old, of which 5 cases aged below 40 years old, 9 cases aged 41-50 years old, 25 cases aged 51-60 years old, 15 cases aged 61-70 years old, 4 cases aged 71-80 years old, and 3 cases aged older than 80 years.

Details of onset The median durations of the 61 cases were12.5mo (IQR 4.75-26.5) since the first onset. Among them 44 patients were presented with acute onset (within 1d) and complained of a sudden "vision deterioration" or "shadows in the field", onset of 18 cases occurred in the early morning upon waking up, 17 cases onset of symptoms during the day, and 9 cases onset of symptoms casually happened without any recall of time. The balance of 17 cases presented with a sub-acute (1-5d) or progressively vision (over 5d) deterioration. 7 cases were reported as having bilateral onset simultaneously but only 2 cases has shown consistent ODE in their fundus examination, while 54 cases reported one eye onset earlier and the other eye was later with an median interval time of 10.0mo (3d-26y, IQR 3-22.5mo). The average interval time of 10 cases of patients with diabetes mellitus was 4.25mo (3d-12mo, IQR 2.0-11.5mo), which was shorter than that of 44 patients without diabetes mellitus whose median interval time was 10.5mo (7d-26y, IQR 3.0-31.875mo) though the differences was not significant ($Z=-1.745$, $P=0.081$).

Visual functions During patients first visit at Dongfang hospital, visual function of the 61 cases were as follows: 1) visual acuity in patients with bilateral NAION varies considerably, from no perception of light to -0.3 logMAR, the median best corrected visual acuity (BCVA) was 0.7 logMAR (IQR 0.2-1.3); 2) the average IOP was 15.51±2.37mmHg; 3) diffuse and hyperaemic ODE were seen in 18 eyes, segmental and hyperaemic ODE in 17 eyes, mild ODE with shallow white disc in 13 eyes, while pale disc was seen in 71 eyes indicated that most of the patients had gone through a long period since their first onset. Shallow white or pale disc was seen at the first onset and the subsequent fellow eye with diffuse and hyperaemic or segmental ODE; 4) VF were of many kinds of patterns which were related to optic nerve damage. The most common types of VF defects were inferior altitudinal VF defect (38 eyes), supero-nasal defect (21 eyes), infero-nasal defect (16 eyes), superior altitudinal VF defect (13 eyes), and tubular VF defect (12 eyes), other types of visual defect, such as central scotoma, paracentral scotoma, island, *etc.* were rarely seen, where as 15 eyes with very poor BCVA could not coordinate with VF examination in OCTOPUS perimetry.

Systemic conditions Among the 61 cases of bilateral NAION patients, 31 cases were accompanied with cardiovascular or cerebrovascular diseases: 22 cases were with arterial hypertension, 20 cases were with hyperlipidemia, 12 cases were with diabetes mellitus, 11 cases were with cerebrovascular disorder, 11 cases were with atherosclerosis, 5 cases were with ischemic heart disease, and 2 cases were with hypotension and 2 cases were with sleep apnea. Those morbidity rates of cardiovascular or cerebrovascular disease had no significant differences (chi-square test, details of P values showed in Table 1) in 61 cases of bilateral NAION contrast with 49 cases of unilateral NAION in Dongfang hospital at the same period. More details are given in Table 1.

Follow-up and Prognosis of Best Corrected Visual Acuity and Visual Field

Follow-up All the 61 cases had 2mo or more (median of 12mo, IQR 6-23.5mo) follow-up from the first initial visit, BCVA of all the 122 eyes were followed up, while only 89 eyes of VF (71 were with program N1 and 18 were with program LVC) were followed up for 2mo or more, as for some reasons such as BCVA was too bad to coordinate (15 eyes), or patients had financial difficulties for further examinations (8 eyes) *etc.* While the high reliability factor (RF) values in LVC were unreliable in statistic analysis. Thus there were 23 eyes lack of data and 18 eyes with VF follow-up in program LVC, and these eyes were included only in the analysis of VF baseline features but not in VF prognosis analysis.

BCVA during follow-up time, BCVA has significantly improved from 0.7 logMAR (IQR 0.2-1.3) to 0.4 logMAR (IQR 0.175-1.1) at the last follow-up visit, in which 45

Table 2 Distribution of BCVA of the bilateral NAION patients at initial visit and last follow-up

Parameters	Normal	Minor damage	Moderate damage	Severe damage	Chi-square	*P*
BCVA (logMAR)	≤0.1	0.2-0.5	0.6-1.3	≥1.3	1.547	0.665
Initial(n=122)	24	34	35	29		
Follow-up(n=122)	29	37	34	22		

Table 3 BCVA at initial visit and last follow-up in different genders

Parameters	Initial BCVA	Follow-up BCVA	Increase of BCVA	Z^a	P^a
M (n=39)	0.5 (0.2, 1.1)	0.4 (0, 0.875)	-0.1 (-0.375, 0)	-3.019	0.003
F(n=22)	0.75(0.2, 1.325)	0.4(0.124, 1.275)	-0.3(-0.55, 0)	-2.274	0.023
Z^b	-0.521	-1.600	-0.711		
P^b	0.602	0.110	0.477		

BCVA was given asmedian (IQR). [a]Mann-Whitney test, two related samples; [b]Wilcoxon Signed Ranks test, two independent samples.

Table 4 BCVA at initial visit and last follow-up in different ages

Parameters	Initial BCVA	Follow-up BCVA	Z^a	P^a
Younger group (<60, n=31)	0.55 (0.2, 1.225)	0.4 (0.1, 1.1)	-2.550	0.011
Older group (≥60, n=30)	0.9 (0.2, 1.4)	0.5 (0.2, 1.0)	-2.728	0.006
Z^b	-0.974	-0.509		
P^b	0.343	0.611		

BCVA was given asmedian (IQR). [a]Mann-Whitney test, two related samples; [b]Wilcoxon Signed Ranks test, two independent samples.

eyes (36.9%) have improved 0.2 logMAR or more, while 57 eyes (46.7%) remain unchanged or improved only 1 lines and 20 eyes (16.4%) have been worsened. More details about BCVA at initial visit and last follow-up are given in Table 2.

Visual Field This analysis included only 71 eyes both checked at initial visit and last follow-up visit with OCTOPUS101 Perimeter test in program N1. Those checked with program LVC were not included because the high RF values in LVC were unreliable in statistic analysis. Patients MS of the 71 eyes were significantly increased from 13.1 dB (IQR 8.3-19.1) at initial visit to 13.6dB(IQR 8.9-20.8; $Z=-2.651$, $P=0.009$, Wilcoxon Signed Ranks Test, two related samples) at last follow-up visit.

Factors Affecting the Prognosis of Best Corrected Visual Acuity For potential high selection bias and the lack of enough sample size to analysis the influence factors of VF, this study only analyzed the factors might affect the prognosis of BCVA, including gender, age, systemic condition, time sequence of eye onset.

Gender BCVA of the 122 eyes had no significant differences (P=0.602, 0.110) between the males and females at initial visit and follow-up visit. Yet BCVA at the last follow-up visit has increased significantly (P=0.023, 0.003) compared with that at initial visit, both in the male and the female patients. The median BCVA of female patients during the follow-up period increased by 0.3, while the male patients increased only 0.1, though there were no significant differences (P=0.477) between them. More details are given in Table 3.

Age Patients were divided into two groups according to age: younger group (Y) aged below 60, and older group (O) aged 60 or above. There were no significant differences (P=0.343, 0.611) in BCVA between the Y group and O group. Furthermore BCVA of Y group and O group at last follow-up visit were both increased significantly (P=0.011, 0.006) compared with that at initial visit. More details are given in Table 4.

Systemic condition Patients were divided into two groups according to systemic conditions: systemic disease group (S) who were accompanied with artery hypertension, hyperlipidemia, diabetes mellitus, cerebrovascular disorder, atherosclerosis, or ischemic heart disease, and no-systemic disease group (N) who were NOT accompanied with systemic diseases mentioned above. There were no significant differences (P=0.270) in BCVA between the S group and N group at initial visit. But BCVA of N group were significantly higher (P=0.037) than S group at their last visit. Furthermore BCVA of S group and N group at their last follow-up visit had increased significantly (P=0.033, 0.001) compared with that at initial visit. More details are given in Table 5.

Time sequence of onset Eyes were divided into two groups: earlier onset group (E) and later onset eye group (L). There were no significant differences (P=0.500, 0.785) in BCVA between the E group and L group not only at initial visit but also at last follow-up visit. BCVA of E and L group at initial visit were both significantly higher (P=0.003, 0.019) than that at last visit suggests BCVA improved during follow-up. While BCVA of E group improved more than L group (median

Table 5 BCVA at initial visit and last follow-up in patients with or without systemic disease

Parameters	Initial BCVA	Follow-up BCVA	Z[a]	P[a]
Systemic disease group (n=31)	0.65 (0.225, 1.4)	0.525 (0.2, 1.25)	-2.135	0.033
No-systemic disease group (n=30)	0.55 (0.175, 1.2)	0.3 (0.1, 0.75)	-3.267	0.001
Z[b]	-1.103	-2.090		
P[b]	0.270	0.037		

BCVA was given asmedian (IQR). [a]Mann-Whitney test, two related samples; [b]Wilcoxon Signed Ranks test, two independent samples.

Table 6 BCVA at initial visit and last follow-up in earlier onset eyes and later onset eyes

Parameters	Initial BCVA	Follow-up BCVA	Increase of BCVA	Z[a]	P[a]
Earlier onset eye group (n=61)	0.7 (0.2, 1.35)	0.5 (0.2, 0.95)	-0.2 (-0.3, 0)	-2.951	0.003
Later onset eye group (n=61)	0.5 (0.2, 1.25)	0.4 (0.1, 1.1)	-0.1 (-0.2, 0)	-2.347	0.019
Z[b]	-0.675	-0.273	-0.1297		
P[b]	0.500	0.785	0.195		

BCVA was given asmedian (IQR). [a]Mann-Whitney test, two related samples; [b]Wilcoxon Signed Ranks test, two independent samples.

with 0.2 and 0.1 logMAR respectively) though there was no significant differences (P=0.195) between the two groups during fellow-up. More details are given in Table 6.

DISCUSSION

NAION is a common eye disease with a sudden visual impairment, usually occurred in an unilateral eye first, while the other eye with a high frequency of involvement in a short period, can be weeks, months or years, especially in patients with systematic conditions[5,6]. With the prolongation of following -up time, the unaffected eyes have shown a rising trend of onset. The incidences of bilateral involvement in NAION were reported diversely from each other. Report from the ischemic optic neuropathy decompression trial follow-up study in 2002 showed that only 14.7% (48/326) unaffected eyes had developed new NAION during a median follow up of 5.1y. This appeared to be less than other researches. There were 25% of 438 NAION patients had developed new NAION in unaffected eyes from Beri and his colleague's study in 1987, while in 1997 other researchers reported 17% of 431 cases during 5y had developed new NAION. These results were consistent with another cohort study where 83 patients (13%) were bilateral affected in 613 cases of NAION[7]. The focused point is through this ischemic optic neuropathy decompression trial follow-up study, the existing NAION or other optic neuropathy cases were present as 21% (88/418) patients at baseline, and 4 patients had developed optic neuropathy in the fellow eye could not be conclusively diagnosed as NAION. Those 92 eyes might be NAION though were not diagnosed. The prevalence and incidence of bilateral NAION may increase to 43% (88/418) if we include these unconfirmed 92 eyes according to the last follow-up data.

Some researches reported on an increase incidence of the second eye onset with diabetes mellitus. Hayreh *et al*[8] reported 655 cases of bilateral NAION, including 206 cases of diabetes mellitus and 449 patients without diabetes mellitus. The results had shown that the risk of developing NAION in the former was significantly higher (P=0.003) than the latter. The study also suggested that in patients with NAION and diabetes, the average time of the fellow eye developing NAION is 6.9 (0.4-16.9) y while the average time in patients without diabetes mellitus is 9.1 (1.8-19.0) y. This study also showed an shorter interval time of the fellow eye onset in diabetes mellitus patients compared with patients without diabetes mellitus (median interval time with 4.25 and 10.5mo, respectively, P=0.081) though the differences was not significant. Which indicate that the onset of fellow eye in NAION patients might be accelerated by diabetes mellitus. Lee *et al*[9] found that Diabetes is associated with the development of NAION at a younger age in most series as well. These results were consistent with another meta-analysis which contains 2096 participants from 12 case-control studies and suggests that DM might be associated with increased risk of NAION recently[10]. An other research found that the fellow eye involvement is more frequent in younger NAION patients with diabetes mellitus because of optic disc ischemia ranging from perfusion delay[11].

Yet Hayreh[12] also has pointed out that onset of NAION in both two eyes at the same time were rare, perhaps only in some very particular circumstances, such as severe hypotension, hemodialysis, or hemorrhagic shock in surgical operation. Some patients complained of sudden vision loss simultaneously, but actually these patients did not realize visual dysfunction at the first onset because the symptoms were painless especially those without any center VF defection are difficult to be aware until the other eye was affected. There were 7 patients complaint of "coinstantaneous" sudden vision loss in this study but fundus examination of optic disc showed only one had a equal morphology of the two optic disc.

According to this study, the demographic characteristics, systemic condition and clinical features of bilateral NAION are similar with that of unilateral NAION reported in other materials[1,2,13]. Bilateral NAION patients often presents with sudden painless visual loss or vision deteriorated typically upon awakening, the visual acuity in patients with NAION

varies considerably while VF defects may follow any pattern but majority present with inferior altitudinal VF defect, and the hemianopia usually have no strict boundaries with horizontal or vertical line. Shallow white or pale disc can be seen in the first onset eye and the fellow eye with diffuse and hyperaemic or segmental ODE. The asymmetry degree of edema or atrophy depends on the interval time between the two eye onsets.

Hayreh *et al*[8] reported that eyes with a visual acuity of ≤20/70 has shown improvement in 41% for up to 6mo after the initial visit. We noticed visual acuity of 36.9% (45/122) eyes of bilateral NAION patients had been improved during our follow-up, while visual acuity of 30 eyes in 49 unilateral NAION patients had been improved, the incidences of visual acuity improvement will be 43.9% (75/171) in total, and this is consistent with what Hayreh has reported. In this study part of the patients treated with corticosteroids and showed a better visual outcome contrast with the untreated patients and Hayreh concluded that corticosteroids were effective in improving visual function compared with the natural history. Whiles an other randomized but much smaller trial revealed no difference in visual outcome between treated and untreated groups[14].

There was another study in China which has investigated the demographic characteristics and the clinical features of bilateral NAION[15]. The study involved 19 cases of bilateral NAION, with 11 cases of male and 8 cases of female, the average age of the patients was 48.4 (12-66) years old. The interval time between the two eye onsets differs from 20d to 20y and 14 cases in 12mo interval. Nine cases of the 19 patients were accompanied with systematic disease: 4 patients with hyperlipidemia, 9 patients with hypertension, diabetes mellitus or coronary heart disease. The visual acuity of both eyes in these 12 cases were not symmetry in initial visit, of which only 4 cases were with worsened visual acuity in first onset eye while 8 cases of them were with worsened visual acuity in the fellow eye. The visual acuity of two eyes in 8 cases were not symmetry in follow-up visit, of which 6 case were with worsened visual acuity in the fellow eye. This small sample size study has shown a similar demographic characteristics, systemic condition and clinical features with our research of 61 bilateral NAION, and there were also a consistency between the two studies about the circumstances that visual acuity of the fellow eye were worsened than the first onset eye both in initial visit and follow-up visit.

Some researchers found that aspirin may reduce the incidence of fellow-eye involvement after NAION, while a large retrospective study of 431 NAION patients showed no long-term benefit for aspirin in NAION prevention[16]. The disease and ischemic cerebral stroke were very different clinical entities, pathogenetically and in management. NAION was not a disease caused by thrombosis, thus Aspirin has no beneficial effect[17].

In this study we found both BCVA and MSof VF had significantly improved during follow-up visit, this might because of our treatment with integrated traditional Chinese medicine and western medicine, but might also because of spontaneous recovery. As the Ischemic Optic Neuropathy Decompression Trial Research Group says, 31.0% of patients in the careful follow-up group experienced an increase of 3 or more lines of vision acuity compared with baseline acuity at 24mo of follow-up, while superior and inferior VF defects present at baseline in non-study eyes improved at follow-up[18,19]. Yet there is insufficient evidence to evaluate the curative effect of our treatment.

We also have done some analysis about the factors affecting the prognosis of bilateral NAION, which listed here as follows.

Gender The improvement of average BCVA in female patients might be (P = 0.477) higher than male patients (medians were 0.3 and 0.1 logMAR respectively). Possible reasons may include: 1) there was a higher prevalence in male patients than female patients with systematic diseases (in 25 of 39 cases of male patients and 11 of 22 female patients respectively) which may be an important risk factor of NAION as discussed. We also found that systematic diseases in female patients were often lesser than in male patients which might be related to lower smoking rate and healthy diet in females; however there is still no definite evidence on this. 2) It might be a statistical bias for the small sample size of the in females.

Age There were no significant differences in BCVA between patients aged below 60 and aged 60 or older not only at initial visit but also at last follow-up visit, thus there were still no evidences to show the relationship between age and prognosis in NAION patients in this study.

Systematic Conditions There were no significant differences (P = 0.270) in BCVA between the patients accompanied with cardiovascular and cerebrovascular diseases and patients without systematic disease at their initial visit. But BCVA of patients without systematic disease were significantly higher (P = 0.037) during follow-up. Which means the prevention and control of cardiovascular and cerebrovascular diseases might be benefit for NAION prevention and treatment.

Best Corrected Visual Acuity Difference in the First Onset Eye and Fellow Eye Something might be interesting was BCVA of the earlier onset eyes in bilateral NAION patients has improved better than the later fellow eye (median with +0.2 and 0.1 logMAR, respectively), which possibly because the earlier onset eyes had a longer history than the fellow eye while BCVA of NAION would improve during long follow-up time as discussed. The other possible reasons might be the same direction as Hayreh and Zimmerman's speculation[20,21] that in some patients with bilateral NAION, when the fellow eye developed NAION with marked deterioration of visual acuity, the earlier onset eye with comparatively better visual acuity may showed spontaneous improvement. Yet there is insufficient evidence till date and further research is needed to support such view.

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