Role of aspirin in reducing the frequency of second eye involvement in patients with non-arteritic anterior ischaemic optic neuropathy

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CLINICAL STUDY

Abstract

Purpose **To retrospectively evaluate in patients with non-arteritic ischaemic optic neuropathy (NAION) whether aspirin reduces the frequency of second eye involvement.**
Methods **In 52 patients who presented with NAION between 1984 and 1997 adequate information was available regarding use of aspirin, presence of risk factors and second eye involvement.**
Results **Second eye involvement was noted in 8 of 16 patients (50%) who did not receive aspirin, in 3 of 8 patients (38%) who received 100 mg/day aspirin and in only 5 of 28 patients (18%) who received aspirin 325 mg/day. Moreover, mean time to second eye involvement was 63 months in patients who did not receive aspirin versus 156 months in patients who received aspirin 325 mg/day.**
Conclusion **Our results strongly suggest that aspirin at 325 mg/day may be effective in reducing the frequency of second eye involvement with NAION.**

Key words Anterior ischaemic optic neuropathy, Aspirin

Non-arteritic ischaemic optic neuropathy (NAION) is a devastating form of visual impairment that probably results from inadequate blood supply by the posterior ciliary arteries.[1,2] The estimated incidence of NAION is 2.3 per 100 000 in patients over 50 years of age.[3] Hypertension, diabetes mellitus and/or hypercholesterolaemia have been identified as risk factors for NAION.[4–8] In a recent study thrombophilia was not shown to constitute a predisposition for NAION.[8]

Twenty-four per cent[4] to 48%[9] of patients with NAION exhibit a recurrent event in the second eye within a period of 5–11 years. Aspirin administration following a first episode of NAION has been advocated, but its apparent effect on reducing the incidence of second eye involvement has been demonstrated in only one study.[10] The objective of this study was to evaluate retrospectively the effect of aspirin in the treatment of patients who have presented at the Eye Institute with NAION over a period of 13 years.

Patients and methods

The study group consisted of 66 consecutive patients who presented with NAION between September 1984 and July 1997 at the Goldschleger Eye Institute. Inclusion criteria were sudden visual loss, optic disc oedema followed by pallor, evidence of relative afferent pupillary defect and a visual field defect consistent with optic neuropathy. Patients younger than 45 years underwent magnetic resonance imaging for exclusion of a demyelinating or other neurological disease. Patients with clinical symptoms suggestive of giant cell arteritis were excluded. Patients with an erythrocyte sedimentation rate over 40 mm/h underwent biopsy of the temporal artery to exclude giant cell arteritis.

A detailed medical history was obtained from all patients. Particular attention was paid to arterial hypertension, diabetes mellitus, hypercholesterolaemia, ischaemic heart disease, arrhythmias, arterial thromboembolism, smoking at the time of the initial NAION event, and use of drugs. Fourteen of the 66 patients with NAION were not included: 9 patients had taken aspirin prior to the first event, 1 patient was affected by a myeloproliferative disorder, and 4 patients have been lost to follow-up.

Mean time to second eye involvement was estimated by the total time at risk divided by the number of cases with bilateral involvement. Patients who had only unilateral involvement were considered as censored observations. The effect of potential risk factors and aspirin

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Table 1. *Effect of aspirin treatment following the first event of NAION on recurrence rate and time interval between first and second events*

Aspirin treatment	*n*	Second eye involvement		Mean interval between first and second events (months)
		n	%	
None	16	8	50	63.4
Aspirin 100 mg/day	8	3	38	80.3
Aspirin ⩾ 325 mg/day	28	5	18	156.5

treatment on the time interval between a first and a second episode of NAION was assessed by survival analysis (log rank tests and Cox proportional hazard regression).

Results

Sixteen of the 52 patients included in the study had bilateral NAION as shown in Table 1. The mean time from the first episode to the second episode of NAION in the 16 patients was 95.7 months. This interval was not influenced statistically by gender, age of onset of the first NAION episode, visual acuity, presence of ischaemic heart disease, arrhythmia, hypertension or crowded disc. Patients with hypercholesterolaemia had a lower incidence of second eye involvement: 3 of 12 patients with hypercholesterolaemia had a second event in comparison with 13 of 33 patients whose cholesterol level was normal. However, the difference was not statistically significant ($p = 0.09$).

Thirty-six patients took aspirin following the first episode of NAION and 16 patients did not. The number of patients with a second event was lower among patients who took aspirin following the first episode. Table 1 shows that among patients who did not take aspirin after the first episode 50% had a recurrent event with a mean time to second event of 63 months. This contrasted with an 18% recurrence rate with a mean time to second event of 156 months in patients who took aspirin at a dose of 325 mg/day following the first event. In patients who took 100 mg aspirin/day after the first event, the recurrence rate and mean time to second event were intermediate (Table 1). However, none of these observed differences reached statistical significance, probably due to the small sample sizes.

Fig. 1 is a Kaplan–Meier plot describing the NAION-free time interval for second eye involvement in patients who took aspirin at a dose of ⩾ 325 mg/day or 100 mg/day and patients who did not take aspirin. The plots of the three groups were similar for the first 8 months after the first event of NAION. Thereafter, the curve representing patients on aspirin ⩾ 325 mg/day is noticeably higher than the curves representing the two other groups of patients. The sharp drop in NAION-free survival at about 9 years for the no-treatment group should be regarded with caution as it is based on just a single patient who had follow-up of more than 6 years.

The mean age at the time of the first NAION event was lower in patients who took aspirin (both regimens) than the mean age of patients who did not take aspirin following the event, as shown in Table 2. However, this difference was not significant.

We addressed the question of whether the better outcome of patients who took aspirin ⩾ 325 mg/day following the first event was related to a lower number of NAION-associated risk factors, i.e. ischaemic heart

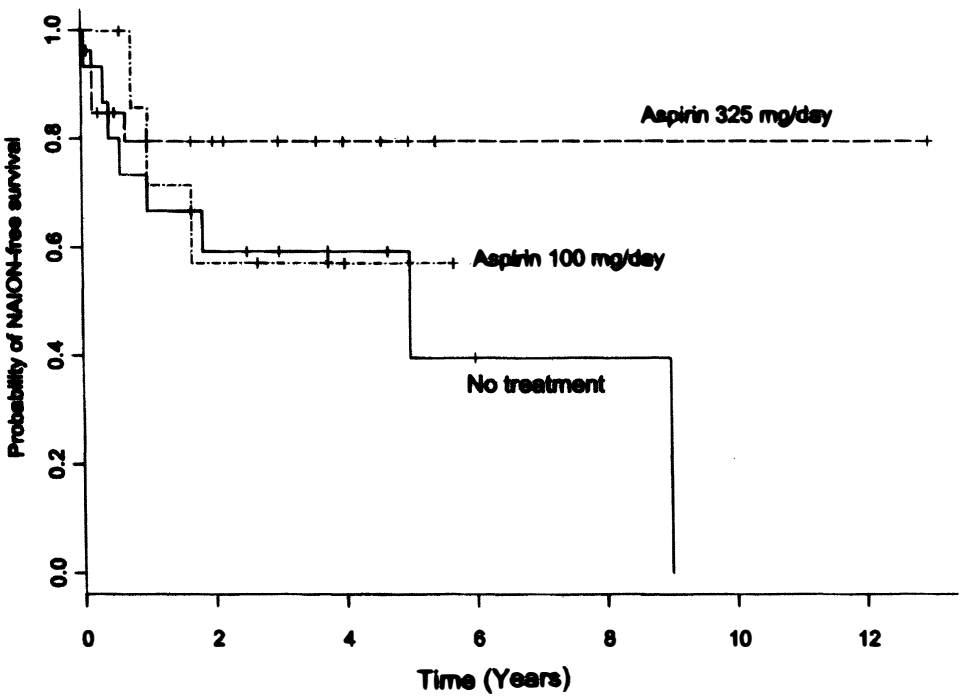

Fig. 1. *Kaplan–Meier curve describing the probability of remaining NAION-free in three subsets of patients. Patients who began treatment with aspirin ⩾ 325 mg/day following the first episode were similar to the two other subsets during the first 8 months, but exhibited a decreased incidence of a second NAION event after 8 months of treatment or more.*

Table 2. *Age (years) and frequency (%) of risk factors in patients with NAION treated or untreated by aspirin*

	Without aspirin	Aspirin 100 mg/day	Aspirin 325 mg/day
Mean age ± SD (years)	65.3 ± 12.2	56.6 ± 16.1	59.8 ± 9.8
Ischaemic heart disease	18.8	25.0	35.7
Hypercholesterolaemia	18.8	37.5	46.4
Diabetes mellitus	18.8	12.5	39.3
Crowded disc	18.8	62.5	39.3
Smokers	18.8	12.5	28.6

disease, diabetes mellitus, hypercholesterolaemia, crowded disc and smoking.[8] No statistically significant differences were found among the three treatment groups with respect to any of these risk factors. However, as shown in Table 2, patients who took 325 mg/day aspirin were not as healthy as those in the other two groups.

Information was also collected about major cardiovascular events during the follow-up period. There were no deaths, but two major events were observed. A male, aged 68 years at the time of NAION onset, suffered a cerebral-vascular accident (CVA) at age 71 years. He began taking aspirin (325 mg/day) after the NAION event. A second male, aged 34 years at the time of NAION onset, suffered a minor coronary event at age 39 years. He began taking aspirin (100 mg/day) after the first NAION event. He suffered a recurrence of NAION in the second eye 12 months after the initial event.

Thus, the protective effect of the 325 mg/day aspirin treatment was observed in spite of the increased burden of risk factors borne by this group of patients.

Discussion

Administration of aspirin for prevention of a second event of NAION has previously been advocated.[10,11] Kupersmith *et al.*[10] showed that patients with NAION who took aspirin several times a week had a low incidence of a second episode within 2 years (odds ratio 0.44). In the present study we found that aspirin at a dose of ⩾ 325 mg/day given following NAION substantially reduced the risk of a second NAION episode. This beneficial effect was noted only after 8 months of follow-up. A dose of 100 mg/day was insufficient to produce a comparable effect.

The dose of aspirin required for secondary prevention of coronary artery or cerebral artery thrombosis is the subject of debate. Doses as low as 35 mg and up to more than 1000 mg per day have been advocated as appropriate.[12–14] Recently, a rationale for using aspirin at a dose greater than 300 mg was reported.[15,16] It was suggested that aspirin exerts an anti-platelet aggregation effect by two different mechanisms: at low doses through inhibition of thromboxane A_2 synthesis in platelets, and at high doses by inhibition of the proaggregating activity of red blood cells. Conceivably, the latter effect is detrimental in patients with NAION.

Clearly, prospective studies need to be designed to further explore the effects of aspirin at a dose over 325 mg/day on secondary prevention of NAION.

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