SCIENTIFIC REPORT

Risk of non-arteritic anterior ischaemic optic neuropathy (NAION) after cataract extraction in the fellow eye of patients with prior unilateral NAION

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Aim: To determine the risk of non-arteritic anterior ischaemic optic neuropathy (NAION) after cataract extraction (CE) in the fellow eye of patients with prior unilateral NAION.

Design: Retrospective, cohort study.

Methods: Medical records of patients with NAION evaluated in our institution between 1 January 1986 and 31 December 2001 were reviewed to determine the onset of NAION and the time of CE. Patients were excluded if the date of NAION and CE was unreliable, or if CE in the fellow eye was performed before the unilateral NAION. Statistical analysis was performed by including fellow eye CE as a time-dependent covariate in a Cox proportional hazards regression model of NAION incidence in the fellow eye.

Results: Of the 325 eligible patients, 9 (53%) of 17 patients with NAION who underwent CE in the fellow eye developed fellow eye NAION, and 59 (19%) of 308 patients with NAION who did not undergo CE in the fellow eye developed fellow eye NAION. Cataract extraction in the fellow eye increased the risk of NAION occurrence in the fellow eye by 3.6-fold (Cox regression, $p=0.001$).

Conclusions: Patients with unilateral NAION are at a significantly higher risk of developing NAION in the fellow eye after CE.

The incidence of non-arteritic anterior ischaemic optic neuropathy (NAION) is increased following cataract extraction (CE).¹ Two categories of CE-associated NAION have been reported: an immediate type, occurring within hours of surgery,^{2–3} and a delayed type, occurring days to weeks after surgery.^{4–8} Increased intraocular pressure has been implicated as a causative factor of NAION immediately after surgery.^{2–9} The mechanism underlying delayed cases is undetermined, although substantial evidence supports a causal relationship. The incidence of delayed NAION after CE (1 per 2000) is significantly higher than the annual incidence of NAION (2.3–10.3 per 100 000).¹ In an analysis of 18 patients with NAION occurring within a year after anterior segment surgery, all NAION were found to occur within the first 19 postoperative weeks and none during the remainder of the postoperative year; this is in contrast with an expected uniform distribution if the NAION occurrences were spontaneous.¹⁰ Further, the prevalence of hypertension and crowded optic nerves is significantly lower in subjects with CE-associated NAION than in subjects with spontaneous NAION, suggesting differences in pathophysiology.¹¹

The purpose of this study was to determine the risk of NAION after CE in the fellow eye of patients with prior unilateral

NAION, which has been suggested by previous studies to be increased, but has not been confirmed or quantitated.^{1–2}

METHODS

After institutional review board approval, the computer database at our eye institute (Bascom Palmer Eye Institute, Miami, Florida, USA) was used to identify all cases of NAION between 1 January 1986 and 31 December 2001. Cases were excluded if the following criteria for NAION were not met: (1) an acute decrease in vision; (2) associated nerve fibre layer defect on visual field testing; (3) associated relative afferent pupillary defect; (4) observed optic nerve oedema; and (5) undergone an evaluation for reasonable alternate aetiologies. The eye that had the initial unilateral NAION is referred to as the primary eye. Cases were excluded if the date of occurrence of NAION in the primary eye or the date of CE in the fellow eye could not be determined. Cases were also excluded if fellow eye CE was performed before primary eye NAION.

Kaplan–Meier survival analysis was used to estimate the cumulative incidence of NAION in the fellow eye after primary NAION. A Cox proportional hazards survival regression model was fitted, with CE included as a time-dependent covariate to assess its effect on the development of fellow eye NAION.

RESULTS

Of the 391 patients with NAION identified, those who had no reliable date of primary eye NAION ($n=5$), no reliable date of fellow eye CE ($n=29$) and had fellow eye CE before primary eye NAION ($n=32$) were excluded.

Of the 325 qualified patients with NAION, 180 (55.4%) were men. The median age of onset of the first NAION was 74 (range 34–91) years; the 5th and 95th centiles were 58 and 86 years. The mean (median, range) of follow-up was 30 (5, <1 to 384) months. Of the 309 patients with available hypertension data, 156 (50%) had hypertension. Of the 305 patients with available diabetes data, 73 (24%) had diabetes.

Of the 308 patients who did not have fellow eye CE, 59 (19%) developed fellow eye NAION (table 1). By contrast, 9 (53%) of the 17 patients who underwent fellow eye CE developed fellow eye NAION after CE. These percentages, however, do not account for time elapsed between primary eye NAION and fellow eye CE. Figures 1 and 2 are the Kaplan–Meier graphs displaying the cumulative proportion of patients with incident fellow eye NAION without CE and after CE, respectively. Although useful for descriptive purposes, these incidence estimates from the two graphs cannot be directly compared because the second analysis does not account for the variable time interval between primary NAION and fellow eye CE. To assess the influence of fellow eye CE on fellow eye NAION accounting for this time interval, fellow eye CE was included as a time-dependent covariate in a Cox survival regression model

Figure 1 Kaplan-Meier graph showing the cumulative proportion of patients with NAION having incident fellow eye non-arteritic anterior ischaemic optic neuropathy without cataract extraction.

of fellow eye NAION incidence. Fellow eye CE increased the risk of fellow eye NAION by 3.6 times (95% CI = 1.7 to 7.7, Cox regression, $p = 0.001$). Adjusting for age ($p = 0.31$), diabetes ($p = 0.004$) and hypertension ($p = 0.099$) did not reduce the risk of CE on the incidence of fellow eye NAION (risk ratio = 7.4, $p < 0.001$).

Of the 9 patients with NAION after fellow eye CE, two-thirds developed NAION within 6 months after CE, with a median of 2.8 months (range, 2 days to 6.5 years, fig 2). Five patients had phacoemulsification and four had extracapsular CE. Seven patients received retrobulbar anaesthesia (0.75% marcaine/4% xylocaine mixture) and two had topical anaesthesia (0.5% tetracaine). One patient developed significant macular oedema. Of the eight patients without NAION after fellow eye CE, four had phacoemulsification and four had extracapsular CE; seven received retrobulbar anaesthesia and one had peribulbar anaesthesia (all with 0.75% marcaine/4% xylocaine mixture).

Table 1 Cataract extraction and non-arteritic anterior ischaemic optic neuropathy in the fellow eyes of patients with prior unilateral NAION

Fellow eye: CE/NAION status				
No CE (n = 308)		Yes CE (n = 17)		Total
No NAION n	Yes NAION n	No NAION n	Yes NAION n	
249 (81%)	59 (19%)	8 (47%)	9 (53%)	325

CE, cataract extraction; NAION, non-arteritic anterior ischaemic optic neuropathy.

DISCUSSION

Our data indicate that CE in the fellow eye of patients with previous unilateral NAION significantly increased the risk of NAION in the fellow eye by nearly four times. The 95% CI suggests that the true effect of CE on the risk of NAION in the fellow eye ranges from slightly less than a doubling of the risk to almost eight times the risk as compared to the risk of NAION without CE. This finding was not diminished when the analysis

Figure 2 Kaplan-Meier graph showing the cumulative proportion of patients with non-arteritic anterior ischaemic optic neuropathy (NAION) having incident fellow eye NAION after cataract extraction.

was adjusted for age, diabetes and hypertension. In assessing the effect of CE on the risk of fellow eye NAION, Kaplan-Meier and Cox regression survival analyses accounted for the variable duration of follow-up of the patients as well as the variable time elapsed between primary eye NAION and fellow eye CE. Of interest, the 5-year risk of fellow eye NAION without CE in our study was 26%, and similar to the 15–35% found by previous studies (fig 1).^{12–14}

The potential limitations of our study include its retrospective nature. It is difficult to say how unsuspected selection biases might influence our estimates of incidence. Despite having surveyed over 300 primary NAION cases, the number of cases of post-CE fellow eye NAION was small ($n = 9$). This makes it difficult to evaluate, for example, whether the risk of NAION decreases as the interval after fellow eye CE increases. However, due to the low incidence of NAION after CE, a prospective study would be too large to be practical, and a retrospective study, despite its limitations, seems to be the most feasible.

In this study, only two of the 17 patients with NAION who had fellow eye CE had prior unilateral NAION occurring within 6 months after primary eye CE; therefore, we cannot determine whether the risk of NAION after fellow eye CE is higher in patients with previous CE-associated NAION. We were also unable to assess whether CE in eyes with prior NAION would precipitate another NAION, because few patients underwent ipsilateral CE after NAION owing to poor visual potential.

The purpose of this study was to examine the incidence of NAION after fellow eye CE of patients with prior unilateral NAION and not the pathophysiological mechanisms of immediate and delayed types of NAION after CE, the causes of which remain undetermined. The 17 unilateral patients with NAION who underwent fellow eye CE underwent local anaesthesia and posterior chamber intraocular lens implantation, and it is not possible to identify if any factors related to anaesthesia or operative procedure would have contributed to the development of NAION. Although the findings of this study cannot be readily explained, the results clearly show that CE in the fellow eye of patients with prior unilateral NAION significantly increases the risk of NAION in the fellow eye by nearly fourfold. This information is helpful to clinicians who are treating cataracts of patients with prior unilateral NAION.

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