Non-arteritic anterior ischaemic optic neuropathy

Study results suggest omega 3 fatty acids may provide a dose of hope for sufferers

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High doses of omega 3 fatty acids rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) can improve visual acuity in patients with non-arteritic ischaemic optic neuropathy (NAION) within 3 months according to the results of the study detailed below. The treatment can battle neuro-inflammation and improve visual acuity.

NAION is a visually disabling disease involving a segmental or generalized infarction of the optic nerve caused by occlusion of the short posterior ciliary arteries. Optic nerve ischaemia causes permanent loss of vision due to primary damage of retinal ganglion cell (RGC) axons and subsequent death from apoptosis.

NAION makes up 95% of all the cases of anterior ischaemic optic neuropathy and is the most common cause of acute optic neuropathy in people over the age of 50, affecting 2–10 individuals per 100,000. Up to the present time there is no generally accepted, well-proven effective treatment for this condition. The majority of treatments proposed for NAION are empirical and either presume to act on thrombosis, on the blood vessels or on disc oedema. Visual loss is usually sudden and permanent. The Ischaemic Optic Neuropathy Decompression trial is the only randomized control study for the treatment of NAION. It reported no benefit from surgical intervention and suggested that surgical intervention may even be harmful.

A retrospective study by Kinori et al. evaluated the effect of intravenous corticosteroids on patients with NAION with disappointing results — they reported no improvement of the visual outcome of NAION patients treated with intravenous (IV) corticosteroids compared with the untreated patients. Also the data on intravitreal steroid treatment are disappointing, with dangerous ocular side effects such as high intraocular pressures and cataract formation. The side effects of systemic steroids are of concern especially in high risk patient groups due to diabetes instability, mood changes, hypertension and weight gain. We believe, therefore, that randomized control trials to establish the effect of steroids in patients with NAION are essential.

One prospective study evaluated the benefit of intravitreal bevacizumab to patients with NAION. The authors reported no difference between the intervention group and control group in visual field, visual acuity or optic nerve thickness.

Inflammation seems to be involved in the pathogenesis, development and progression of NAION. It results in oligodendrocyte destruction and increased RGC loss, which contributes to the reduced vision in patients with NAION. Elevated concentration of high-sensitivity C reactive protein (hs-CRP) has also been reported in patients after a minimum period of 2 months following NAION.

Cellular inflammation plays a major role following optic nerve infarct, with the involvement of both polymorphonuclear leukocytes and macrophages. Histological tissue analysis from an autopsy obtained 20 days after the onset of NAION revealed tissue inflammation with accumulation of microglia and extrinsic macrophage invasion.

According to recent study data, high doses of omega 3 fatty acids rich in EPA and DHA can improve visual acuity in patients with NAION. Here, the authors present details of the study, highlighting their outcomes.
The resolution of inflammation is now understood to be an active process driven by the pro-resolving mediators derived from the omega 3 fatty acids, EPA and DHA. We have used high doses of omega 3 fatty acids on patients with NAION to study any neuro-rescue effect regarding visual acuity.

**Method**

A retrospective review of 13 patients (13 eyes) with acute NAION following treatment with steroids were used as controls. They are all the patients with acute NAION seen in our clinic within a 2-year period. Patients on steroids received intravenously 1 g/daily of methylprednisolone for 3 days followed by 20 mg of prednisolone orally once a day for a month.

A prospective study of 13 patients (14 eyes) with NAION received daily oral supplements of 5–8 mg of EPA and DHA (ratio 2:1) in liquid form. The mean daily dose was 7.0 g. Patients also received oral polyphenols to act as antioxidants.

Steroids in the control group were given within 2 weeks of the acute reduction of vision. The oral supplement treatment in the EPA/DHA group was given at a mean of 10.8 months (range 1–26 months) following the onset of the disease.

All patients on omega 3 fatty acids had a blood ratio measurement of arachidonic acid/eicosapentaenoic acid (AA/EPA) and the dosage of omega 3 fatty acids was adjusted to ensure a therapeutic ratio between 1 and 2. Visual acuity was measured with an early treatment diabetic retinopathy study (ETDRS) electronic chart.

**Results**

The baseline visual acuity of the control group (steroid use) was 6/24+2 (0.560 logMAR) and the visual acuity of the EPA/DHA supplement group was 6/18 (0.50 logMAR). Figure 1 shows the patients on steroids had a mean loss of 1.3 letters at 6 weeks and a mean loss of 1.5 letters at 3 months. It also shows that the patients on oral supplements of EPA/DHA and polyphenols had a mean gain of 9.3 letters at 6 weeks and a mean gain of 15 letters at 3 months.

![Figure 1](image1.png) **(FIGURE 1)** The visual acuity gained or lost in the group treated with steroid (blue line) and the group treated with omega 3 fatty acids (red line).

![Figure 2](image2.png) **(FIGURE 2)** Images of swollen and normal discs using a spectral domain ocular coherence tomography (OCT). A. Swollen disc using a spectral domain OCT. B. Swollen disc using a spectral domain OCT. C. Swollen disc using a spectral domain OCT. D. Normal disc using a spectral domain OCT. E. Normal disc using a spectral domain OCT.
Mean age for the control group was 66.38 years with the ratio of male to female 9:4. Mean age of the EPA/DHA supplement group was 57.75 years with male to female ratio 9:4. Patients in the control group had no significant change of visual acuity at 6 weeks or 3 months (p<0.05). Patients on EPA/DHA, however, had significant improvement on visual acuity measurements during the 6 weeks and 3 months follow up (p<0.01).

**Discussion**

NAION is the most common clinical presentation of sudden reduction of visual acuity secondary to acute ischaemic damage to the optic nerve, with its pathogenesis still remaining perplexing. Currently there is no generally accepted treatment for NAION. According to our results, patients receiving oral supplementation of high doses of EPA/DHA on a daily basis had a remarkable improvement in visual acuity even when the treatment started several months following the initial diagnosis.

Recent studies correlate potential inflammatory response in NAION, which seems to affect the progression of the disease and the resulting reduction in vision. It has been shown that post-infarct inflammation and oedema lead to further compression and additional RGC loss with further reduction of vision.

Inflammation is involved in both the pathogenesis and the progression of NAION. Cheng et al. studied the in vivo inflammatory response of a rodent model of NAION after pure axonal ischaemic infarct. Their findings indicate that inflammatory processes are not only concurrent with early oedema, but persist after the resolution of oedema.

EPA has significant anti-inflammatory properties through the anti-inflammatory eicosanoids, primarily E-series resolvins. It is a structural competitor to AA as a constituent of cell membranes. Once cleaved from the cell membrane, AA is further modified to produce inflammatory eicosanoids. EPA, due to its structure, competes with AA for the active site of phospholipases, an enzyme that cleaves fatty acids from the cell membranes to produce eicosanoids. DHA on the other hand is more powerful than EPA for stimulating neurogenesis.

For neuroprotection, both metabolites of EPA (reduce inflammation) and DHA (neurogenesis) seem to be required. High doses of EPA/DHA in the blood provide a continuous supply of pro-resolving mediators in the brain and consequently in the optic nerve for the resolution of inflammation.

We used a finger stick test for measuring the AA/EPA blood ratio and aimed for a lower limit of AA/EPA ratio of 1 and on upper limit of 2. The ratio would exclude any bleeding concerns and would provide data whether or not the patient is taking the therapeutic dosage of EPA and DHA.

Autoxidation of omega 3 in the blood is prevented by the combination of EPA/DHA with polyphenols. They are powerful anti-oxidants and prevent oxidation of omega 3 fatty acids before entering the brain.

Omega 3 fatty acids are well tolerated by patients and have been shown to be safe, particularly when the AA/EPA ratio is monitored. Administering high doses of EPA/DHA in combination with antioxidants for NAION patients seems to be a promising and innovative approach to managing NAION. As there is no generally accepted treatment to improve the vision in patients with NAION, the positive clinical improvements obtained from this pilot study should be considered significant and demonstrate the value of high doses of EPA and DHA in NAION patients. We are currently supporting a large randomized multicentre study to investigate the benefit of this treatment.

**REFERENCES**