2008

Vision and maintaining eye sight

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Publication Details
Vision and maintaining eye sight

Abstract
The most important diseases causing visual impairment in people as they age include age-related macular degeneration, cataract, glaucoma, diabetic retinopathy and retinal vein occlusion. This discussion paper will limit itself to reviewing common eye diseases which have investigated the relationship to the consumption of omega-3s and fish: age-related macular degeneration (AMD), cataract and retinal vessel changes.

Keywords
vision, sight, maintaining, eye

Disciplines
Arts and Humanities | Life Sciences | Medicine and Health Sciences | Social and Behavioral Sciences

Publication Details
Omega-3s for the body?

Vision and maintaining eye sight
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The most important diseases causing visual impairment in people as they age include age-related macular degeneration, cataract, glaucoma, diabetic retinopathy and retinal vein occlusion. This discussion paper will limit itself to reviewing common eye diseases which have investigated the relationship to the consumption of omega-3s and fish: age-related macular degeneration (AMD), cataract and retinal vessel changes.

Figure 10: Structure of the eye

From www.cvr.org.au/amd.htm

Impaired Vision

Normal or good vision is considered to be 6/6: this refers to the ability to read at 6 metres the line a person with good vision can read at that distance. The term 20/20 actually represents the same level but is measured in feet, for the United States. Visual impairment is generally defined from the better eye as mild (6/12 to 6/18 vision), moderate (6/24 to 6/60) or severe (legal blindness; worse than 6/60).

In a population-based cohort of older Australians (aged 49 and over) AMD was the overwhelming cause of blindness (less than 6/60 vision in both eyes) and of moderate visual impairment, while cataract was the leading cause of mild impairment (Mitchell et al 2002).

Age-related macular degeneration

AMD is a term describing disease of the macula, the most central part of the retina at the back of the eye. When we look directly at someone or at text in a book, we are using our macula. When the macula is damaged, it is like having a dark, grayish or distorted patch in the centre of everything you view. AMD is the most frequent cause of severe vision loss and blindness in elderly people (Klein et al 2002, Mitchell et al 2002, Tornamby et al 2004). Although new treatments targeting vascular endothelial growth factor (VEGF) have revolutionized the management of this condition, this therapy is not possible for many cases, requires regular injections into the eye and is costly. Therefore, identifying risk factors that could be targeted in preventive strategies has the potential to reduce the burden of macular degeneration in our ageing populations (Flood & Mitchell 2008).

Omega-3s, particularly DHA, constitute a high proportion of the human retina and macular composition, and may be important in cell membrane maintenance and retinal repair following oxidative stress. They may also protect against retinal inflammation (SanGiovanni & Chew 2005, Connor 2000). It is believed that AMD shares some aspects of the pathogenesis as cardiovascular disease (Hu et al 1997, Snow & Seddon 1999). Several recent reports have examined possible associations between dietary fat and progression of macular degeneration.

The Blue Mountains Eye Study (BMES) examined the association between dietary fat and fatty acid components and the 5y incidence of AMD (Chua et al 2006). This is a population-based cohort study of vision and common eye diseases in non-institutionalised residents, 49 years or older, living in the Blue Mountains region, west of Sydney, Australia. Dietary data were collected from 2895 people at baseline using a validated food frequency questionnaire. Incidence of early and late AMD was assessed after a mean follow-up of 5.1 y. Participants with the highest versus the lowest quintile of omega-3s had a lower risk of AMD (pooled odds ratio (OR), 0.41, 95% confidence interval (CI) 0.22-0.75). A 40% reduction of incident early AMD was associated with fish consumption of at least once a week (OR 0.58, 95% CI 0.4-0.9), and fish consumption of at least 3 times a week reduced the incidence of late AMD by 75% (OR 0.25, 95% CI 0.06, 1.0) – see Table 5. Although not statistically significant, the trend for long-chain omega-3s also suggested protection. Low intakes of the shorter chain omega-3, alpha-linolenic acid (ALA), were associated with increased risk, suggesting it too may be protective for AMD. This
study confirmed an earlier cross-sectional report in the same cohort of 50% protective effect of fish consumed more than once per week compared to less than once per month (Smith et al 2000).

**Table 5: Incident cases of age-related macular degeneration (AMD) in BMES (5y)**

<table>
<thead>
<tr>
<th>Total Fish* §</th>
<th>Early AMD</th>
<th>Late AMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1/month</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>≥1/week</td>
<td>0.58 (0.37-0.90)</td>
<td>0.44 (0.16-1.21)</td>
</tr>
<tr>
<td>≥3/week</td>
<td>0.62 (0.38-1.03)</td>
<td>0.25 (0.06-1.00)</td>
</tr>
</tbody>
</table>

* Includes sardines, tuna, other fish
§ adjusted for age, sex, current smoking, antioxidants (diet & supplements)

From: Chua et al 2006

In a more recent study reported by the Age-Related Eye Disease Study (AREDS) group in which participants with varying levels of AMD severity were compared to a control group, people who consumed a higher intake of total long-chain omega-3s had a lower risk for neovascular AMD (OR 0.6, 95% CI 0.4-0.9), with a similar finding for DHA and fish intake. Arachidonic acid (AA), an omega-6, increased the risk of neovascular AMD by about 50% (OR 1.5, 95% CI 1.0-2.3) (SanGiovanni et al 2007). There were no other statistically significant associations with other sub-types of fatty acids and AMD.

In a recently published systematic review and meta-analysis of omega-3s and fish intake and the prevention of AMD (Chong et al 2008), 9 studies were identified for analyses (3 prospective cohorts, 3 case-control studies and 3 cross-sectional studies). A high dietary intake of omega-3s was associated with a 38% reduced risk of overall AMD (pooled OR 0.62, 95% CI 0.48-0.82). Fish intake of at least twice a week was associated with a reduced risk of both early AMD and late AMD (pooled OR 0.76, 95% CI 0.64-0.9; 0.67, 95% CI 0.53-0.85).

### Gaps in the literature

There are no randomised controlled trials which have evaluated omega-3s and fish intake in the prevention of AMD. A clinical trial has commenced in the US, the Age-Related Eye Disease Study (AREDS-2) which will evaluate the effect of long chain omega-3 supplements compared with a placebo in relation to the progression from early to late AMD, but it will be many years before the findings are available (AREDS2 2008). It is possible that people who consume diets higher in omega-3s, are also eating healthier diets in relation to other dietary factors protective of AMD, such as antioxidants (Kassoff et al 2001) and these factors may have been inadequately adjusted for in the epidemiological literature.

### Conclusions and recommendations

Overall, findings from a range of epidemiological studies and a recent meta-analysis support the hypothesis that increased dietary intakes of omega-3s and regular fish consumption protect against the development and progression of AMD. A plausible mechanism is that long chain omega-3s promote healthy ocular tissue by regulating inflammatory and immune responses in the retina, thereby reducing the risk of AMD.

Given the increasing evidence from prospective cohort studies and the recent meta-analysis, it seems reasonable to recommend that patients with early AMD signs increase their consumption of long chain omega-3s and fish, including about 2 fish meals a week.

### Cataract

Cataract is a term describing opacity that develops in the normally clear lens of the eye. Opacification in the lens causes scattering of light as it passes through the lens, leading to both reduced vision and an increased perception of glare or sensitivity to bright light. There are three types of age-related cataract; nuclear (the most frequent), cortical and posterior subcapsular (least common). Nuclear cataract develops in the nucleus or centre of the lens. As it increases, there is an associated yellow or brown discoloration of the lens. Cortical cataract develops in the outer shell of the lens as spokes and wedges and commonly causes increasing glare sensitivity. Posterior subcapsular cataract develops at the back of the lens, often in the visual axis, and so affects vision rapidly and severely. The majority of people needing cataract surgery have some posterior subcapsular cataract present at that time.

Overall, there has been little epidemiological research investigating omega-3s consumption and cataract. In our BMES dataset, we examined 5y incidence of cataract and macronutrients, and found people with higher intakes of omega-3s had a 42% reduction in incident nuclear cataract (quintile 5 vs quintile 1, OR 0.58, CI 0.35-0.97, p for trend 0.027) (Townend et al 2007) – see Table 6.

### Table 6: Nuclear cataract and omega-3s

<table>
<thead>
<tr>
<th>Omega-3s (quintiles)</th>
<th>Median intake (g/d)</th>
<th>OR* (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.52</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>2</td>
<td>0.7</td>
<td>0.80 (0.49-1.30)</td>
</tr>
<tr>
<td>3</td>
<td>0.85</td>
<td>0.72 (0.43-1.19)</td>
</tr>
<tr>
<td>4</td>
<td>1.03</td>
<td>0.59 (0.35-0.98)</td>
</tr>
<tr>
<td>5</td>
<td>1.42</td>
<td>0.58 (0.35-0.97)</td>
</tr>
</tbody>
</table>

* Adjusted for age, sex, diabetes, use of oral or inhaled corticosteroids, hypertension, body mass index, alcohol and smoking history, myopia and dark brown iris colour.

From: Townend et al 2007
In a cross-sectional study based on Reykjavik Eye Study, Arnarsson et al. (2002) examined risk factors for nuclear lens opacities among 1045 persons, aged 50y and over. They used a 26 item food frequency questionnaire (FFQ) and proxy measures for omega-3s intake (fish consumption) and found no association between these proxy measures and nuclear cataract.

A role for polyunsaturated fatty acids in delaying nuclear cataract formation is biologically plausible, though the exact mechanisms have not been investigated. A potential mechanism may be related to positive effects on cholesterol from elevated serum levels of high-density lipoprotein (HDL) (Chan et al. 2006, Gerassimova et al. 1991, Visioli et al. 2000). Omega-3s may also slow the process of oxidation, which is critical to the pathogenesis of cataract (Hodge et al. 2005). Oxidation is thought to be crucial to the development of nuclear cataract (Truscott 2005). A lens ‘barrier’ is thought to form in middle age, through the oxidation of lens proteins. This virtually compartmentalizes the lens, so that oxidised substances penetrate and remain in the nucleus, and antioxidants cannot enter (Truscott 2005).

**Conclusions**

Further long-term prospective cohort studies and intervention studies are needed to clarify whether omega-3s affect the risk of cataract development.

**Retinal vessel changes**

Retinal vein occlusion occurs when the retinal arteries or retinal veins are blocked, decreasing the oxygen supply to the retina. The blockage is usually caused by a blood clot, fat deposit or atherosclerotic plaque fragment. Omega-3s (particularly DHA) may protect the blood vessels of the eye by inhibiting the development of plaques and blood clots (von Schacky et al. 1999). Other work has investigated the diameter of retinal vessels and found that they may predict systemic vascular and ocular vascular events. For example, narrower retinal arterioles and wider retinal venules predict incident hypertension and coronary heart disease mortality (Kram et al. 2006). In the BMES we have found higher intakes of long chain omega-3s were associated with wider mean retinal arteriolar diameters and narrower mean venular diameters, a ‘protective’ direction. We also showed that fish intake at least twice per week was strongly associated with better retinal vessel outcomes. The findings were independent of blood pressure, past history of stroke and myocardial infarction, smoking, blood lipid levels, inflammatory factors, and socioeconomic status. Stratification by hypertension revealed a greater change in vessel diameter in persons with than without hypertension (Kaushik et al. 2008).

**References**


