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Abstract

Age-related macular degeneration (AMD) is a leading cause of vision loss and blindness among older people. It is important to identify modifiable risk factors which could prevent or slow the progression of this chronic disease. Dietary fatty acid intakes have been investigated in epidemiological studies as it is plausible that individual lipids have properties which modulate cellular damage in the eye. This paper reviews epidemiological studies investigating links between fatty acids and AMD. Mixed evidence has related the sub-types of saturated and monounsaturated fatty acids to AMD, but nearly all epidemiological studies have demonstrated some level of AMD protection from omega-3 polyunsaturated fatty acids (particularly long-chain fatty acids) and fish, with a tendency for a corresponding dampening effect with increased dietary omega-6 polyunsaturated fatty acids.

Keywords

dietary, acids, degeneration, macular, age, fatty, related

Disciplines

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Dietary fatty acids and age-related macular degeneration

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ABSTRACT: Age-related macular degeneration (AMD) is a leading cause of vision loss and blindness among older people. It is important to identify modifiable risk factors which could prevent or slow the progression of this chronic disease. Dietary fatty acid intakes have been investigated in epidemiological studies as it is plausible that individual lipids have properties which modulate cellular damage in the eye. This paper reviews epidemiological studies investigating links between fatty acids and AMD. Mixed evidence has related the sub-types of saturated and monounsaturated fatty acids to AMD, but nearly all epidemiological studies have demonstrated some level of AMD protection from omega-3 polyunsaturated fatty acids (particularly long-chain fatty acids) and fish, with a tendency for a corresponding dampening effect with increased dietary omega-6 polyunsaturated fatty acids.

Age-related macular degeneration (AMD) is the most frequent cause of severe vision loss and blindness in elderly people (1-3). 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. Identifying risk factors that could be targeted in preventive strategies therefore has the potential to reduce the burden of macular degeneration in our ageing populations.

Diet has already been identified as an important modifiable risk factor and the management of AMD has been influenced by evidence from the Age-Related Eye Disease Study (AREDS) which demonstrated that a high dose zinc and antioxidant vitamin supplement (vitamin C, E and beta-carotene) slowed AMD progression by around 25 percent in relatively advanced AMD stages (4). Dietary fatty acids are another important potential dietary factor worthy of investigation. Dietary fatty acid intake may be related to AMD development through its effect on atherosclerosis and their presence in retinal and macular cells. Omega-3 polyunaturated fatty acids (PUFA), particularly docosahexaenoic acid (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 (5-6). It is believed that AMD shares some aspects of the pathogenesis as cardiovascular disease (7-8). Several recent reports have examined possible associations between dietary fat and progression of macular degeneration. Earlier epidemiological studies suggested dietary intake of fat and all its subtypes, including vegetable and unsaturated fats, could increase the risk of progression, though this seemed at odds with the known relationship of fatty acids and cardiovascular disease.

In a case-control study of older people attending ophthalmology centres in the US (n=349 cases), people consuming the highest quintile of monounsaturated fat and polyunsaturated fat had a higher risk of AMD compared to those in the lowest quintile (OR 1.71 (95 percent CI 1.0-2.94; 1.86 (95 percent CI 1.1-3.1, respectively), after adjusting for other known risk factors of AMD (9). This same study found that people who consumed higher omega-3 fatty acids (eicosapentoic acid (EPA) and DHA) and higher frequency of fish in the presence of a low linoleic PUFA intake (an omega-6 PUFA) had a reduced risk for ARM (p for trend 0.05), but this was not the case in the presence of a higher linoleic fatty acid intake. In another study of a select group of older people attending an eye clinic for early AMD (n=261), a higher total fat intake (p for trend p=0.01) and higher vegetable fat intake (p for trend p=0.003) was associated with an increased risk of ARM progression, as did other sub-types of fat; saturated, monounsaturated, polyunsaturated and trans-unsaturated fatty acids (10). Statistical models for fatty acid sub-types were adjusted for known confounders of AMD but not simultaneously for other sub-types of fatty acids. As in the previous study, a higher frequency of fish consumption in the presence of low linoleic acid intake reduced the risk of AMD progression (p for trend 0.045). In a study by Cho et al of risk of AMD and fatty acid sub-types among 567 participants of the Nurses Health Study and the Health Professionals Follow-up Study, there was no association between incident late AMD and increasing dietary intakes of vegetable or unsaturated fats (11).

The Blue Mountains Eye Study examined the association between dietary fat and fatty acid components and the 5-year incidence of AMD (12). 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 years. Participants with the highest verses the lowest quintile of omega-3 PUFA had a lower risk of AMD (OR 0.41, 95 percent 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 percent CI 0.4-0.9), and fish consumption of at least 3 times a weeks reduced the incidence of late AMD by 75 percent (OR 0.25, 95 percent CI 0.06, 1.0). There was no significant association between AMD and margarine or butter consumption. There was a non-significant protective effect of nuts consumed at least weekly. Although not statistically significant, the trend for long-chain omega-3 PUFA also suggested protection. Low intakes of the essential fatty acid α-linolenic acid, an omega-3 PUFA, 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 (13). In a more recent study reported by the AREDS group in which participants with varying levels of AMD severity are compared to a control group, people who consumed higher intake of total long-chain omega-3 PUFA had a lower risk for neovascular AMD (OR 0.6, 95 percent CI 0.4-0.9), with similar finding for DHA and fish intake. Arachidonic acid, an omega-6 PUFA, increased the risk of neovascular AMD by about 50 percent (OR 1.5, 95 percent CI 1.0-2.3) (14). There were no other statistically significant associations with other sub-types of fatty acids and AMD.

CONCLUSIONS

Overall, findings from a range of epidemiological studies support the hypothesis that an increased dietary intake of long-chain omega-3 polyunsaturated fatty acids and regular fish in the diet protects against the development and progression of AMD. A plausible mechanism is that long chain omega-3 PUFA promotes healthy ocular tissue by regulating inflammatory and immune responses in the retina, thereby reducing the risk of AMD. It may be that the presence of higher omega-6 fatty acids (mainly linoleic fatty acid and possibly arachidonic fatty acid) dampens the effect of omega-3 PUFA. Evidence for an association between other fatty acid sub-types (monounsaturated and saturated fatty acids) and AMD, however. has been less consistent. In addition to the observational epidemiological studies, it would be valuable to have information from clinical trials about the effect of dietary interventions or supplements with long chain omega-3 PUFA and AMD. Such a study is planned with an extension of the AREDS trial, testing the role of omega-3 PUFA supplementation on AMD progression, though findings will not be available for many years (15).

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