Age-related macular degeneration and its possible prevention

Despite well publicised claims of the therapeutic value of dietary supplements and other new treatments, the evidence for their effectiveness is modest

The distinction between conventional and alternative medicine is often based on the presence or absence of scientific evidence. However, this evidence is expensive to gather, and often difficult to interpret and reduce to practical advice. Age-related macular degeneration (ARMD), the dominant and rapidly increasing cause of permanent visual loss in Australia, is an important case in point. Its prevalence rises from 0.7% in the 65–74-years age group to 5.4% at 75–84 years and 18.5% in people over 85.[1] Definitive treatment does not yet exist. While we have some knowledge of risk factors, this knowledge is imperfect and has recently been muddied by well publicised claims (discussed below) that, although evidence-based, are preliminary and need to be interpreted with caution.

The early signs of ARMD include hypo- or hyperpigmentation of the retina and large yellow drusen (> 63 μm) or soft drusen with indistinct margins.[2] A few small hard drusen can be found in almost everyone over 50 years of age, and, in contrast to large or soft drusen, do not appear to progress with age.[1]

Loss of vision from ARMD occurs either as a result of choroidal neovascularisation with exudation and haemorrhage (the "wet" form) or by slow atrophy of the retinal-pigment epithelium and overlying receptors (the "dry" form). Wet ARMD is twice as common as the dry type and causes rapid vision loss. About 10% of patients with wet ARMD who present early with distorted vision and an eccentric neovascular lesion can be treated successfully with laser photocoagulation.[3] However, the recurrence rate is over 60%, and further vision is then usually lost. Another small proportion of patients can be treated with photodynamic therapy (involving low-intensity red laser treatment after intravenous verteporfin infusion), but the functional benefit is usually modest.[4] There is no treatment yet for the dry form of ARMD.

Elderly people fear blindness and the loss of independence greatly, and the prevalence of ARMD is rising dramatically. It is no surprise that recent studies of possible risk factors have attracted a lot of public interest. People with an ARMD-affected first-degree relative have a 50% lifetime risk of experiencing advanced ARMD and vision loss, and tend to develop it earlier.[5] Smoking is associated with a fourfold increase in the risk of ARMD and visual loss and, again, tends to promote earlier occurrence.[6] Weaker associations have been found with obesity, hypertension, macrovascular disease, raised cholesterol and fibrinogen levels, cumulative light exposure and cataract surgery.

Retinal images showing age-related macular degeneration (ARMD)

A. "Dry" ARMD. Large soft macular drusen, signifying a high risk of progressive visual loss.

B. "Wet" ARMD. Arrowed area delineates advanced wet macular degeneration with subretinal exudation and neovascular scar tissue. These changes result in blindness.

Dietary associations have also been found both with the signs of ARMD and with progression to vision loss.[7-9] In a well conducted, prospective study, dietary fat intake was systematically analysed after correcting for other risk factors.[9] Vegetable fat intake had the strongest relationship with ARMD progression, with a relative risk of 3.82 for the highest fat-intake quartile compared with the lowest quartile. Higher intakes of total fat and of saturated, monounsaturated, polyunsaturated and transunsaturated fats all raised the relative risk of ARMD progression about twofold. Weekly fish intake and eating nuts two to three times a week were mildly protective. The implication is that a large shift away from vegetable oils, margarine and fat-containing processed foods might reduce this epidemic of blindness in the elderly. Some of these measures conflict with conventional advice on controlling cardiovascular conditions and need further research.[10] Definitive evidence for the effectiveness of certain interventions might be obtained by randomly assigning those in the top quartile of risk to receive either a diet with low vegetable fat, fish, nuts and fruit, or a normal diet.

There is also evidence from a randomised controlled trial that high-dose dietary supplements of the antioxidants vitamin C, vitamin E, beta-carotene and zinc can reduce the risk of progression from large or soft drusen to advanced ARMD and visual loss by about 20% compared with controls over 6 years.[11] However, high-dose zinc can cause gastric irritation or anaemia, and beta-carotene may possibly be associated with an increased risk of lung cancer among smokers. Uncontrolled studies suggest the antioxidants selenium, lutein and zeaxanthin, which localise in the normal macula, may also help. There are as yet no studies to show whether dietary supplements are protective in patients with only small drusen or in the 20% of patients who are at genetic risk.

It is not yet known whether major dietary adjustment and/or introduction of dietary supplements for large numbers of elderly people will be justified in terms of preventing blindness. On present evidence, we should identify people at increased risk of ARMD (ie, those with a family history, large or soft drusen, or vision loss in one eye from ARMD), encourage them to stop smoking, and promote a diet that includes vegetables, fish and

nuts and reduces fatty foods laced with vegetable oils. Antioxidant supplements should be recommended if a fresh diet is impractical and if retinal signs of progression are present. For people of advanced age with a lower risk of ARMD, we might compliment them on reaching seniority and note that, in the dietary supplement study mentioned above,[11] only 1.3% of patients with small drusen experienced ARMD progression over a 6-year period.

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