Prevention and Management of Age-Related Macular Degeneration

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Abstract

Age-related Macular Degeneration (AMD) is a major cause of blindness in the elderly. It is more prevalent in people above 65 years of age. Blindness caused by AMD is usually irreversible. Visual function in AMD patients deteriorates progressively and significantly impacts on their quality of life. The social costs of AMD are also on the high side. While treatment modalities like anti-VEGF treatment have been designed for neurovascular age-related macular degeneration, no treatment has yet been developed for geographical atrophy, and as such, prevention stands as the most cost-effective management of age-related macular degeneration. Current therapies are only capable of slowing the disease’s natural course, but is incapable of stopping the progression of the disease. It is therefore important to have an in-depth understanding of the possibilities in order to be able to prevent disease progression. Pertaining to this, therefore, identification of risk factors plays a major role. A lot of research has been carried out on such risk factors as diet, light exposure, and lifestyle. Many studies have shown that an increased intake of nutrients, including zeaxanthin, lutein, omega-3 fatty acids, beta carotene, and zinc, drastically reduces the risk of age-related macular degeneration. With respect to lifestyle habits, the relationship between AMD and smoking has been studied and accepted. It is also important to note that retinal damage due to blue light and ultraviolet rays should be considered. This review aims to summarize current knowledge on steps towards the prevention and management of AMD.
Keywords: Age-related macular degeneration; Geographic atrophy; Nutrients; Prevention; Lifestyle

Introduction

Age-related Macular Degeneration (AMD) is the primary cause of irreversible loss to central vision in the Western hemisphere [1]. Many researchers have postulated that with the increasing geriatric population, AMD will continue to have an increasing burden and prevalence. Visual defects that occur in the initial stages of the disease include impaired dark adaptation. With the progression of the disease, vision loss become more pronounced, the retinal tissue undergoes serious degeneration, and suffers permanent damage.

AMD currently represents the primary cause of irreversible blindness in the geriatric population. Most cases occur after the age of 65 [2]. According to recent studies, there will be at least 288 million affected people by 2040 [1]. Also, the progressive increase in global life expectancy, especially in developing nations will cause an increase in the geriatric population [3]. It has been estimated that by 2025, the global geriatric populace will be over 1.2 billion strong, 70% of whom will be in developing countries [4]. This process contributes immensely to an increase in the number of AMD cases, even surpassing the number projected by previous studies.

AMD usually affects the macula, resulting in the gradual loss of central vision [5]. Early-stage AMD may be recognized by clinical symptoms like alteration of the retinal pigment epithelium and drusen. AMD at the late stage can assume a dual state namely: neovascular or non-neovascular. The progression of AMD to the late stage can also affect central vision, resulting in persistent and severe visual impairment and blindness, and impacting significantly on the quality of life and also affecting the ability of the affected individual to live independently [6].

Clinical characteristics of early AMD include typical disturbances, like reduced reading capacity and mild central distortion. Additional signs that may appear include central scotoma and difficulty in recognizing faces. It is important to note that most people are asymptomatic at this stage. Late AMD progresses to a sudden deterioration in event of a neovascular form, but the non-neovascular form may be characterized by a gradual and slow decline of central vision function.

The primary feature of neovascular AMD is the occurrence of choroidal neovascularization and its consequences, including subretinal and intra fluid, epithelial detachment of the pigments, hemorrhages, fibrotic tissues and hard exudates. Outer retinal thinning is a major characteristic of geographic atrophy. According to studies, the rate of progression corresponds to 2 mm2/year on average.

Although the treatment of neovascular AMD has been improved through the use of intravitreal anti-vascular endothelial growth factor injections, no standard gold-line treatment has yet been discovered for both geographic atrophy and early AMD. The lack of a therapy that can pause the progression of the clinical course determines a limitation in activities of daily living and consequently, a poor quality of life for the patients.

Over the past few years, researchers have attempted to define modified risk factors, with emphasis on how to tackle retinal oxidative alterations related to disease onset and progression. In particular, positive lifestyle modifications such as exercise, cessation of smoking, and a healthy diet with occasional intake of nutritional supplements are very helpful [7]. These studies have placed more emphasis on intervention on the progression of early AMD towards advanced stages of the disease and geographic atrophy, thus modifying the risk factors.

Epidemiology

AMD ranks as the third major cause of blindness just after cataract and glaucoma. Most affected persons reside in developed countries. Generally, advanced AMD rarely occurs before the age of 55. It is also more common in persons over 75 years of age. Geographic atrophy and neovascular AMD have varying prevalence in different racial and ethnic groups globally. Advanced AMD increases in prevalence after the fifth decade of life with the highest prevalence occurring after the 8th decade of life.

Pathogenesis

The underlying cause of AMD is presently elucidated through analysis of genetic linkage and dissection of histopathologic specimens. At the early stage of the disease process, lipids are deposited in the Bruch’s membrane. The deposition may be due to inability of the RPE to process the debris that is associated with outer segment turnover [8]. Drusen becomes visible only in the later stage of the disease. Drusen appearance is the first visible clinical sign of AMD. Laboratory analysis of drusen shows the presence of amyloid, lipid, complement factors, and other cellular components [8].

Drusen’s appearance is concomitant with the thickening of the membranous collagenous layers of Bruch’s membrane, degeneration of elastin and collagen within the Bruch’s membrane along with membrane calcification, increasing amounts of glycation end products, and accumulation of exogenous proteins and lipids. These alterations can act as a hydrophobic barrier to impede the movement of nutrients and fluid between the outer retina and the choroid leading to relative ischemia. Subsequently, the ingrowth of neovascularization may from choriocapillaris may occur through fractures in the Bruch’s membrane.
AMD Management Plans

Until recently, ophthalmologists treated exudative AMD via laser destruction of abnormal capillaries/vessels. Among these procedures were thermal laser photoacoagulation and the use of intravascular photosensitizers like verteporfin employed in photodynamic therapy. However, all that these treatments did was slow the progression of the condition. They did not have any positive effect on vision.

It is worth mentioning that the treatment of exudative AMD underwent dramatic changes with the introduction of Vascular Endothelial Growth Factor (VEGF) inhibitors. Medications have been developed to neutralize or block VEGF in AMD patients. These medications include ranibizumab, pegaptanib, affibercept, and bevacizumab. These medications are administered as intravitreal injections and many doses are usually required. These medications have been shown to stabilize vision in patients with exudative AMD. It is also worth noting that many patients will experience a tremendous improvement in visual acuity [9].

Presently, there are no first-line treatments for atrophic AMD. Clinicians should reassure their patients that the disease progresses slowly and they are likely to retain their independence whether their reading vision is affected or not. Other effective intervention methods include smoking cessation, low vision aids, and rehabilitation. Low vision aids and rehabilitation help improve the patients’ quality of life. Healthcare providers should endeavor to guide patients on these options and how to access them.

AMD Prevention Key Strategies

Nutritional supplementation and dietary modification

Nutritional supplementation plays a vital role in the prevention of AMD progression according to AREDS-1 and -2 studies. On the other hand, there is no data pointing to the possibility of preventing the onset of AMD, either by modification of diet or by adding supplements to the diet.

A 2005 Rotterdam study published in JAMA [10] evaluated the potential association between the intake of antioxidants with diet and the risk of AMD. Results from the study showed that high consumption of antioxidants with the β-carotene diet, both C and E vitamins, and zinc was correlated with a reduced risk of AMD in the elderly.

Drusen formation is influenced by modifications of oxidative protein, as indicated in past studies [11]. And because the onset of drusen is the first obvious sign of AMD, one can argue that antioxidant action exerts maximum effectiveness right before the onset of the condition. As such, an antioxidant-rich diet might affect the onset of AMD which explains why it is highly recommended for people with a family history of the condition [12]. Sources of vitamin E include whole grains, eggs, vegetable oil, and nuts. Foods rich in zinc include dairy products, whole grains, fish, poultry, and meat. β-carotene is present in spinach, kale, and carrots. Juices and citrus fruits, green peppers, potatoes, and broccoli are major suppliers of vitamin C.

Lifestyle modification and smoking

Many studies have associated cigarette smoking with an increased risk of AMD. Cigarette smoking also represent a strong predictor of AMD in two population-based longitudinal studies [13]. Thornton et al. found that cigarette smoking acts as a fundamental risk factor for onset of AMD, estimating precisely that the risk of AMD is two to three times higher in smokers compared to nonsmokers. According to the EUREYE study [14], there was a higher risk of neovascular AMD for smokers. In fact, smoking had a 27% attributable factor for AMD. A comparison between those with a unilateral form of AMD found that those with a bilateral form of AMD tend to be heavy smokers in the previous 25 years. Based on these results, it is important to highlight the possible risks of smoking as well as the benefits derived by quitting smoking. Patients with unilateral AMD should be educated about the risk of developing this condition in the other eye.

Reduced sleep duration or excessive sleep has been linked with various negative health conditions, including cardiovascular diseases, total mortality, arterial hypertension, and diabetes [15]. A 2016 study by Khurana, et al. evaluated the association between sleep habits and AMD [16]. 1003 patients were involved in the survey. Their sleep histories were studied with the aim of a specific questionnaire and grading of the patients’ retina as no AMD, early AMD, and geographic atrophy. The researchers concluded that prolonged sleep (minimum of hours) correlated with a 7-fold increase in the risk of geographic atrophy.

Obesity and overweight

Recent studies have identified obesity and overweight as major risk factors for cardiovascular conditions [17]. Being overweight can trigger other physical changes, including a high level of oxidative stress, inflammatory conditions, and blood lipid imbalance, all factors being implicated in the pathophysiology of AMD [18]. According to previous studies, excess body fat can affect the movement and deposition of carotenoids from blood to macula, thus resulting in a reduction of macular pigment at the fovea [19]. According to the AREDS study, a high risk of geographic atrophy presented in individuals with a high BMI. A 2016 study published in the journal Investigative Ophthalmology & Visual Science evaluated the association between the different categories of Body Mass Index (BMI) and the risk of AMD in different stages. The researchers analyzed 1613 cases involving 31,151 subjects. It was concluded that obesity and excess body weight are associated with a higher risk of AMD.
Physical activity

Many scientific reports have shown that physical activity has a positive influence on morbidity and mortality, preserves cognitive function in a much better way, and drastically reduces the biomarkers of aging [20]. Regarding the link between AMD and physical activity, several studies showed that physical activity has a protective role towards the onset of AMD [21]. However, it is also important to note that current evidence is inconclusive owing to the fact that previous studies were carried out in nonhomogeneous populations with varying classifications of AMD. It is also worth noting that there was no uniform assessment of physical activity. A recent meta-analysis and systematic review [22] studied the association between physical activity and AMD among Caucasians. The authors found that physical activity drastically lowered the odds of early and late AMD among members of the Caucasian population and suggested that individuals stayed active throughout life to prevent the onset of AMD.

Reducing light exposure

Several studies have shown that exposure to sunlight may contribute to the onset of AMD [23]. One of the studies, the Beaver Dam Eye Study was a population-based cohort study that measured AMD incidence and the amount of sunlight exposure in 2,764 subjects over a period of 10 years [24]. According to the result by the BDES, extended exposure to sunlight was associated with an increased incidence of early AMD. Sunglasses provided marginal protective effect, and report of data was done on a subjective basis.

More evidence is presented in reports on AMD incidence after intraocular lens implantation and cataract surgery [25-28]. Human crystalline lens assumes a yellow appearance with age and protects the retina from toxic Ultraviolet (UV) or blue-green phototoxicity [28]. After removal of the crystalline lens during surgery, the implanted intraocular lens does not provide adequate intraocular lens in vivo [28]. For patients who have undergone a cataract surgery, wearing sunglasses in the open can provide adequate protection in this regard [29-31].

Conclusions

AMD is a major underlying cause of irreversible blindness in the elderly. Presently, it is a major contributor to economic and social burden for healthcare systems. Dietary supplementation is designed to slow down the advancement of the dry form of AMD. It is important to note that dietary supplementation and intravitreal medications are the mainstay of treatment. AMD has a huge impact on global population in terms of quality of life and visual outcomes. Implementing the aforementioned preventive strategies can help improve the clinical course of this condition. Dietary supplementation with vitamins C and E, zeaxanthin and lutein, β-carotene and zinc, as well as omega-3 fatty acids drastically reduces the risk of AMD. Lifestyle modifications such as cessation of smoking, engaging in physical activity regularly, avoiding obesity and excessive body weight, and having at 7-8 hours of good quality sleep per night, has proven to be effective in decreasing the risk of developing AMD. Finally, intraocular lenses and eye glasses are believed to play a role in AMD prevention although their exact role is still controversial.

Conclusively, a healthy lifestyle without smoking, eating a balanced diet, and engaging in regular physical activity might prevent the development of AMD. Health systems should therefore educate individuals on healthy lifestyle habits while also implementing policies that will encourage the adoption of healthy lifestyles.

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