Chapter

Health Promotion for AMD and the Role of Nutrition

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Abstract

There is an increase in demand for health promotion and preventative medicine playing a vital role in managing chronic illnesses. Many of these conditions stem from a poor diet, sedentary lifestyle and smoking, all of which are risk factors for age-related macular degeneration (AMD). To combat chronic diseases, the root of the conditions may be addressed through the concept of health promotion. Health promotion thoroughly assesses how a population's environmental, political, socio-economic, behavioral, and cultural practices influence its health. This concept can be applied in a primary care setting which takes on a broader approach in treating and managing patients. Primary care providers need to be aware of the connections between common chronic illnesses and AMD. All primary care providers and eyecare specialists must be patients' advocate and help improve their systemic and ocular prognosis.

Keywords: age-related macular degeneration, choroidal neovascularization, modifiable and non-modifiable risk factors, health promotion, nutrition, lutein, and zeaxanthin

1. Introduction

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in people over 50 years old [1]. It has been defined as a condition in which the structure and function of the central retina (macula) deteriorates. AMD results from a process by which the macula deteriorates over time in association with distinguishing signs and symptoms [2]. Approximately 11 million people are affected with AMD in the United States and approximately 170 million are living with AMD, worldwide [3]. In 2020, it was estimated approximately 196 million people will have AMD along with a predicted increase to 288 million by the year 2040 [4].

AMD is more commonly seen in females and individuals of Caucasian descent, especially in its late, advanced stage. Furthermore, the incidence rates vary by the stage of AMD and are related to genetics. Hispanics and Caucasians are known to have the highest incidence of early AMD. The incidence rates are 6 and 4% respectively for individuals less than fifty-five years of age which increases to 22 and 24% for individuals greater than seventy-five years of age. Overall, Asians and people of African descent show the lowest incidence of early AMD. For advanced AMD, which includes atrophic or neovascular forms, Caucasians of 75 years or older show the highest incidence at 6.5% [5].

AMD is a multifactorial disease that is influenced by age, genetics, health status, smoking habits and race [6]. With the increasing incidence of AMD secondary to a rapidly aging population, the focus is shifted on addressing modifiable risk factors like smoking cessation, altering unhealthy diets, and sedentary lifestyles [7]. AMD is the leading cause of irreversible vision loss in the developed world [8, 9]. To be proactive in addressing the rising incidence of the disease, primary care providers managing must be aware of the risk factors and associations of AMD. They are well-positioned to assist eye care professionals in preventing or slowing the progression of AMD. Primary care providers can implement a health promotion model, promoting the importance of regular eye examinations with a Doctor of Optometry or Ophthalmologists. This may enable earlier detection and treatment of AMD.

AMD is a chronic condition that currently has no known cure. Modifiable risk factors, such as an unhealthy diet, sedentary lifestyle, smoking and alcohol consumption may significantly contribute to disease onset and severity and there are successful treatment strategies [7, 10]. Health promotion is essential in reducing the risk of development and progression of AMD in high-risk groups. Health promotion also empowers patients with information, giving them control of their health. Health promotion looks into the root of the cause of the illness and assesses how environmental, political, socioeconomic, behavioral, and cultural practices influences health [11]. Primary care providers can help patients living with AMD to have a better understanding of their condition and the modifiable factors that influence their ocular and overall health. By incorporating these essential factors making up an individual's identity and influences on their health, the desired result may improve patient adherence to the management plan.

2. Methods

This is a narrative or traditional review intended to summarize the literature about health promotion for AMD and the role of nutrition. We used several databases and searches, primarily PubMed and the Cochrane Library. The principal purpose of this review is to give a comprehensive overview of the topic and to highlight significant areas of research. In addition, we seek to identify gaps in the clinical literature on health promotion for AMD and the role of nutrition and to offer information that is particularly relevant to the primary health care providers and eye care providers not specializing in the field.

3. Background

AMD affects the macular region in the retina, which is responsible for our central vision. Numerous activities such as driving, reading, cooking, operating a smart phone, and watching television depend on having a healthy macula that can be severely affected in the later stages of this condition [12, 13].

AMD can be broadly classified into two categories, as either dry AMD or wet AMD, each with their own characteristic signs and symptoms [13, 14]. AMD is graded depending on severity as early, moderate or late stage. Dry AMD's clinical features can vary depending on severity. Mild dry AMD includes few hard drusen with or without pigmentary changes in the retinal pigment epithelium (RPE) in the macular region with patients typically not complaining of any visual symptoms. The drusen (yellow deposits) are early fundoscopic signs of the disease in the macula [15, 16]. Moderate dry AMD includes one or more large drusen with or without hyperpigmentation typically associated with patients reporting visual

symptoms such as persistent central blur [6]. Severe dry AMD presents with GA with significant visual symptoms and signs including reduced visual acuity, visual distortion, central visual field defects, and reduced contrast sensitivity.

AMD has a wide range of clinical presentations which correlate to the current state of the individual's visual function. Early AMD patients typically have good vision and are primarily asymptomatic or with only mild symptoms. Visual symptoms may include difficulty in dark-adapting; for example, adapting to driving at night or reading in a dimly lit room. Dark adaptation is an important biomarker of early disease [15, 17]. Moderate AMD presents with one or more large drusen the size of >125 μm in width, which is approximately the size of a branch retinal artery. This finding indicates more extensive involvement of the outer retina, the RPE, and its basement membrane [6]. Advanced AMD is associated with symptoms of reduced vision, visual distortion and central visual field defects [18].

Advanced AMD presents with clinical features of geographic atrophy (GA) and/or choroidal neovascularization (CNV). GA is a damaging clinical feature of advanced dry AMD with associated moderate to the severe reduction in vision. It presents as an area of atrophy with demarcated borders affecting the neurosensory retina which contains the photoreceptors, as well as the RPE and underlying Bruch's membrane and choriocapillaris. Presentation and size of the atrophy vary. The fovea, the central zone with in the macula, provides us with fine detail in our central vision. The foveal center is typically spared until the late stages of GA progression [19]. Approximately 20% of eyes with AMD that have progressed to legal blindness have GA as the cause. GA results from a progression of the clinical features seen in the early and moderate stages of AMD [19].

An eye with dry AMD may convert to wet AMD, where new weak blood vessels (CNV) form. CNV typically develops in the choroid and extends towards the retina causing, fluid leakage or hemorrhaging in the macular region from these new blood vessels. The natural course of untreated CNV is fibrovascular scarring, an indication of severe macular damage and profound central vision loss [18]. Patients that convert to wet AMD typically experience sudden decrease in vision along with visual distortions. Wet AMD encompasses only 10–15% of the population of patients with AMD. However, it is responsible for 80% of severe vision loss or blindness in AMD. If wet AMD is present in one eye, the fellow eye has a 48% chance of converting from dry to wet disease within 5 years. Significant risk factors for the conversion from dry AMD to wet AMD include soft confluent drusen, pigmentary irregularities and a current or past history of smoking [10].

Eyes with CNV are said to have wet AMD. GA represents large areas of cellular death. CNV represents new blood vessel growth and is associated with intraretinal, subretinal, and/or sub-RPE fluid, hemorrhage, and or scarring in the macular region. Treatment with intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) is the mainstay of treatment for active, wet AMD. This type of pharmacotherapy aims to suppress the growth of the CNV, as well as reduce the amount of associated fluid, and potentially improve vision.

3.1 Risk factors for AMD

AMD is a complex, multifactorial disease with plethora of known modifiable and non-modifiable risk factors. Modifiable risk factors include smoking, high body mass index, history of hypertension, cardiovascular disease and high alcohol consumption [20]. Smoking has consistently been proven to be a major risk factor of early AMD and late AMD in many studies [21–23]. The duration of smoking also influences the incidence of AMD, showing 14% of all AMD cases may be due to patients who smoked for 40 years [20]. Smokers have a 2 to 4-fold increase

in developing AMD compared to people who do not have a history of smoking. Interestingly, former smokers who have not smoked in the last 20 years are not at a higher risk of developing AMD [20].

The literature has conflicting data from multiple studies on whether the amount of smoking or only duration increases the risk of AMD. The EUREYE study was a cross-sectional study that evaluated patients across Europe and saw a 27% correlation between smoking and the incidence of AMD [5]. Along with the increased risk of duration of smoking, the amount of cigarettes consumed and the associated increased risk of developing AMD was investigated. The Physicians' Health Study and the Nurses' Health Study determined a 2-fold increase in people who smoked 25 cigarettes per day. They also reported that males who smoked 20 or more cigarettes per day were 2.5 times more likely to develop AMD at the 12 years follow up opposed to those who did not smoke at the baseline. The Beaver Dam Study showed no association between the amount of smoking and the incidence of late AMD [24]. A meta-analysis was conducted on multiple studies that revealed a risk ratio of 2.75 for incidence of AMD when comparing current smokers versus "never smokers". When comparing former smokers versus never smokers, the risk ratio for AMD was 1.21 [5]. Smoking has also been shown to increase the incidence of the development of soft drusen and retinal pigmentary changes. Biological alterations associated with smoking increase the risk of developing AMD. For example, smoking reduces serum antioxidants, perfusion to the choroid, RPE drug detoxification pathways, and macular pigments such as lutein and zeaxanthin, further making the eye vulnerable to the development or progression of AMD [24]. Although, there is a debate if the amount of smoking during the person's smoking period is a separate risk factor, it is undeniable that a recent history of smoking does increase the risk of developing AMD.

Obesity and a sedentary lifestyle correlate with the development and progression of AMD. AMD and cardiovascular disease (CVD) have similar risk factors such as age, obesity, and smoking. Drusen in AMD and atherosclerotic plaque in CVD are relatively similar in their composition [4]. Systemic adverse effects caused by obesity include an increase in inflammatory markers, oxidative stress and blood lipid levels. These adverse effects are also factors that increase the risk for the development of AMD. This further supports the association between obesity and AMD [4]. There is also evidence for an association between obesity and low levels of the macular carotenoids lutein and zeaxanthin.

Carotenoids are fat-soluble xanthophyll pigments found throughout the retinal layers and most concentrated in the macula and are seen as a yellow spot during funduscopic evaluation. The amount and optical density of the macular pigment can be measured using clinical devices [25–31]. The macular pigment is composed of three carotenoids lutein zeaxanthin and meso-zeaxanthin an isomer of zeaxanthin. Zeaxanthin and its isomer are more concentrated than lutein within in the fovea, implying an important role for zeaxanthin in central macular integrity and the perception of fine detail [4]. Lutein's highest concentration is found in the peripheral macula. Being fat-soluble these carotenoids are also stored in adipose tissue. However, with the increase in adipose tissue in obese individuals, macular carotenoids are more readily stored in adipose tissue and are less readily available for the central retina [4, 32, 33].

A meta-analysis conducted by Zhang et al. showed a small positive association between excess body weight and risk for AMD. A low association was also found between being overweight or obese and increased risk of early AMD. This risk (for early AMD) is difficult to accurately assess because these patients are typically asymptomatic. Therefore, the association for early AMD with being overweight or obese may be underestimated in the study. Obesity was associated with an increased

risk in the development of late AMD [4]. There was a linear relationship between increased body mass index and risk of AMD [4]. Therefore, the research supports a role for weight control in reducing the likelihood of developing AMD.

Obesity is a considerable public health challenge and multisystem disease. In 2009 and 2010, the prevalence of obesity was 35.5% and 35.8% in men and women in the USA, respectively [4]. The Beaver Dam Study which showed a 3.1% 15-year cumulative incidence of late AMD in adults aged 43–86 years old, so there is ultimately the potential of 110,000 cases of late AMD per year [4]. This finding is significant because obesity is a modifiable risk factor that, if addressed, can positively impact the number of AMD cases that can be avoided per year. Simply put, if the older population maintained a healthy body mass index and waist circumference, they would be giving themselves a better chance to avoid irreversible vision loss [4]. This is an example where health promotion can be effective in giving patients a strategy to avoid the development of AMD or slow its progression.

Beaver Dam Study showed the consumption of 4 or more alcoholic drinks per day was shown to increase the risk of the incidence of late AMD, specifically the wet form. It is important to note the study could not conclude heavy alcohol consumption's role in early AMD [24]. It is believed heavy alcohol consumption causes a reduction in serum antioxidants in tissues such as the retina, ultimately causing them to be susceptible to oxidative damage. Alcohol reduces the blood serum carotene, vitamin C and zinc which mirror the nutrients deficient in AMD [24].

There are risk factors for AMD that are not modifiable including age, genetics, race and sex [20]. With age the retinal layers most affected in early AMD—the RPE and underlying Bruch's membrane—begin to undergo structural and metabolic changes leading to an accumulation of metabolic waste products. Perfusion is reduced directly affecting the choroid layer that supplies nutrients to the RPE and photoreceptors (rods and cones) [5]. It is important to note that these age-related changes will not necessarily result in cellular death and functional vision loss. Environmental and genetic factors may make a person more susceptible to developing the AMD phenotype [20]. The complex integrated system of the choroid, RPE and photoreceptors contribute in maintaining the integrity of central vision. With age, this system can be altered and dysfunctional causing degenerative complications in the macula [34].

Although genetics is a known risk factor, AMD is a condition that does not follow the typical Mendelian inheritance patterns where we can predict if a relative or offspring will acquire the condition. To determine the susceptibility of a patient, the clinician has to consider the modifiable risk factors present along with the patient's age and heredity. Currently, the loci that are most associated with AMD are 1q32 (CFH) and 10q26 (PLEKHA1/ARMS2/HTRA1) [35]. Studies have shown that AMD can be present within families and show a higher incidence if a first-degree relative has been diagnosed with the disease. The Rotterdam Study showed that individuals who have a first-degree relative with AMD have a 4-fold higher risk of developing AMD [35].

3.2 Clinical diagnosis and evaluation

AMD can be diagnosed when a patient undergoes a comprehensive eye examination including dilated funduscopy by an eye care professional. The optometrist or ophthalmologist evaluates all aspects of the posterior segment of the eye, including the macula. Clinical findings associated with AMD are hard or soft drusen, retinal hypo or hyperpigmentation, macular edema, hemorrhaging and or other signs of CNV. If these findings are present, special testing can be performed to further investigate the extent of the maculopathy. Special testing includes retinal

photography, autofluoresence imaging, optical coherence tomography (OCT) and fluorescein angiography. Retinal photography is used to document the appearance of the macula. Autofluoresence imaging takes advantage of the natural ability of the RPEs lipofuscin to fluoresce when stimulated with the light of a particular wavelength. It is an assessment of metabolic activity [18].

OCT is a non-invasive imaging method that uses coherent light rays to produce a cross-sectional image of the retina. OCT of the macula produces an image that shows the distinct layers of the retina and can highlight abnormalities such as macular edema, CVN, GA, and hard or soft drusen. OCT of the macula is used to further investigate any suspicious macular abnormalities in a dilated fundus exam and document the findings as a baseline reading. An OCT of the macula will then be taken at subsequent follow-ups to monitor for progression [36].

Fluorescein angiography is an invasive test involving the intravenous injection of sodium fluorescein. The dye travels to the choroidal circulation in the eye within 10–15 s, then a camera can capture images of the highlighted retinal blood circulation. Fluorescein angiography is extremely helpful in monitoring wet AMD where it can detect areas of macular edema and or active CNV [37]. It is still considered the gold standard in the detection of new CNV.

3.3 Treatment

There is currently no cure for AMD, but there are several treatments. The goal of treatment and management is to slow the progression of the disease and, in the case of wet AMD, to reduce the adverse effects of CNV. Intravitreal anti-VEGF (vascular endothelial growth factors) injections are the mainstay of contemporary therapy for active wet AMD. Lifestyle modification and nutritional supplementation have been shown to benefit patient with moderate to late dry AMD. A randomized, double-masked, placebo-controlled trial showed that people who at baseline had a lower level of macular pigment optical density (MPOD) showed benefits from taking supplements containing the dietary macular carotenoids lutein and zeaxanthin [25, 38–43]. The investigators also found an improvement in visual function associated with increased MPOD, which included visual acuity and contrast sensitivity [38, 40–43]. Increasing the macular pigment in patients appears to improve visual function and slow the progression of early AMD [38, 40–42]. However, prophylactic supplementation to prevent the onset of AMD continues to be inconclusive in the literature [40, 44].

Current management of early AMD should include health promotion with an emphasis on a healthier lifestyle involving diet, exercise and smoking cessation or avoidance. Nutrition education of patients should support the consumption of foods containing dietary macular carotenoids, which can further assist in increasing the MPOD. These foods include egg yolk, spinach, kale, collards, and brightly colored vegetables such as peppers [45]. For early AMD there is currently no treatment that can regress hard drusen or retinal pigmentary changes. A person with early AMD can continue with yearly follow-ups with their optometrist with education about lifestyle and diet/nutrition. At the initial visit, patients should be given an Amsler grid that tests the integrity of the macula. It is recommended the patient self-test each eye individually every day using their reading prescription with proper illumination to monitor their condition. The grid must be held at 33 centimeters to properly span a 20-degree field [46]. The Amsler grid test is checking for any structural changes in the macula such as new macular edema or CNV. The patient is to report whenever they notice metamorphopsia, which means the lines on the grid appear in a wavy or distorted fashion. Patients are also to report if they notice a scotoma, or missing area within the grid, and to make a timely appointment with their eye doctor.

In terms of nutritional supplementation, AREDS determined supplements may be recommended to prevent the progression of moderate AMD into late AMD [47]. These supplements contain antioxidants and micronutrients which help replenish the lack of those nutrients in the retina and consequently the properties and functions of the macula. Patients with moderate or advanced AMD need to be seen more frequently by an eye care professional than patients with early AMD. Along with the recommendation of taking the supplements listed above, reinforcing a healthier lifestyle is vital in maximizing patient outcomes.

CNV is a consequence of increased levels of VEGF in the eye. VEGF has many functions in the body including angiogenesis, bone formation, hematopoiesis, wound healing, neuroprotection and development [48]. VEGF is a potent signal protein which, when up-regulated, causes pathological angiogenesis and increased vascular permeability. For example, VEGF can give rise to new blood vessels that feed tumor growth, such as in breast cancer [48]. In AMD, the upregulation of VEGF causes the growth of new blood vessels to manifest under the RPE and/or the sensory retina. This new blood vessel growth causes devastating effects to the integrity of the macula ultimately causing a decrease in vision. Anti-VEGF therapy was initially used as cancer treatment and further investigation proved suspected beneficial ocular affects when it was noted patients' vision would also improve concurrently with cancer treatment [49].

Anti-VEGF agents are now used as a therapy for many ocular vascular diseases. The most common of these conditions are wet AMD and diabetic retinopathy. Common anti-VEGF drugs used in ophthalmic practice include bevacizumab (Avastin), ranibizumab (Lucentis) and aflibercept (Eyelea) [49]. Bevacizumab is considered an off-label therapy in retinal disease, whereas the other two drugs have an FDA indication for these purposes. Once treatment is initiated, the patient will need frequent injections to stabilize the condition along with monitoring of the macula with dilated funduscopy, OCT and fluorescein angiography [50].

4. Health promotion and prevention

Health promotion is a broad concept that looks beyond the treatment and cure of illnesses. It is a behavioral social science that looks into the biological, environmental, psychological, physical and medical sciences in order to promote health and aid in the prevention of diseases. Health promotion is effectively achieved when an individual, group, institution, or community actively engages in conversation in order to change the audience's perspective, attitude and behavior to health. Health promotion is critical due to the rippling effects it has on the improvement of overall health, reduction in premature deaths, and financial turmoil associated with medical costs for the patient and their employer. The goal of health promotion is to improve health for the individual, families, communities, cities, states and ultimately the nation. The World Health Organization (WHO) dissects health promotion into 3 elements, good governance of health, healthy cities and health literacy [51].

Good governance of health focuses on the political aspect of health promotion where local, state and federal governments play a role in their constituents' health. Ideally, the government should keep health as a main priority where they align their policies to benefit the health of its constituents. For example, these policies should focus on providing healthy school lunches for children, reducing air and water pollution, promoting exercise and general safety precautions. The WHO states when local government can focus on promoting healthy lifestyles at the municipal level it can create a healthy city with many resources. The cities can focus on community

health preventions and health facilities where the local population can be screened for chronic illnesses. Health literacy is having the knowledge and understanding on how to make good choices and engage in positive habits to avoid chronic illnesses [51]. It describes how efficiently a patient can understand and monitor their disease for changes.

Health literacy is important because through disease prevention and health promotion the patient can make rational decisions when caring for their own health. A cross-sectional questionnaire study investigated whether there was an association between health literacy and chronic retinal disease [52]. The study revealed the majority of the patients with chronic retinal disease had a low level of health literacy. Sixty- five percent of patients with AMD, 73% of diabetic macular edema patients, and 63% of patients with retinal vein occlusion were shown to have low levels of health literacy.

Consequently, a low level of health literacy also influences the prognosis of the chronic retinal disease considering these conditions require self-monitoring, self-medication and self-care [52]. For example, knowing the importance of taking prescribed medicines at the appropriate dosage and time, monitoring their condition with the assigned home equipment and knowing when it is pertinent to see their provider before their scheduled appointment if new symptoms arise. Health promotion plays a major role in health literacy since these patients will be better equipped to care for their disease if properly educated. Poor health literacy is associated with poorer prognosis such as patients with uncontrolled diabetes who develop diabetic retinopathy with potential damaging effects to the retina and vision [32, 33, 52]. Another example is a patient who continues to eat unhealthy foods causing inflammation in their system, lives a sedentary lifestyle and smokes cigarettes will be more at risk for progressing to advanced AMD which causes irreversible vision loss [52].

Chronic retinal diseases demand self-management from the patient, including self-monitoring and adhering to their providers' recommendations. If this care is not maintained, vision may be negative. In order for health promotion to be effective, it must be delivered in a way the patient can grasp and understand the information. Primary care providers need to be effective communicators, avid listeners and genuinely sympathize with patient concerns. Health promotion is founded on patient-centered care with the idea health involves more than just the illness. The overall health of an individual is influenced by factors outside the health care system [11]. These outside factors include socioeconomic conditions, patterns of food consumption, demographic patterns, learning environments, and family patterns [11]. To maximize patient outcomes, the health care provider should take into consideration and include the outside factors making up the identity of the patient in their management. This approach will ultimately allow the patient to have control of their health and have a sense of responsibility to maintain it.

Health promotion has been effectively implemented with communicable infectious diseases such as sexually transmitted diseases. For example, in targeting vulnerable communities, schools held seminars where they discuss safe sexual practices and the consequences of unprotected sex such as pregnancy and sexually transmitted diseases [11]. With the increasing trend of chronic non-communicable diseases, such as hypertension, type 2 diabetes mellitus and high cholesterol, health promotion has taken a larger role in attempting to combat these conditions. The increasing incidence of these chronic conditions can be due to the increasing availability of jobs where the employees primarily work sitting at a desk in front of a computer. This type of work environment can lead to a sedentary lifestyle which is worsened when coupled with poor eating habits. In a broader view, the economy also suffers due to the widespread sedentary lifestyles that ultimately lead to chronic illnesses [11].

Other factors play a role in this health crisis such as poverty, low education and stress [11]. Consequently, these factors lead to increased risk of high blood pressure, high blood glucose, abnormal serum lipids, high waist-hip ratio, and abnormal lung function. These biological risk factors lead to chronic non-communicable diseases such as heart disease, stroke, cancer, and chronic lung disease. Therefore, health promotion is key to preventing and targeting established illnesses along with medical interventions to attain good health. Health is influenced by social, economic, political forces, cultural identities and discrepancies within communities that are more susceptible to chronic health conditions. These factors ultimately will influence the health of these vulnerable communities and their future. Thus, health promotion is vital in educating communities on the adverse effects of modifiable risk factors and the tools needed to prevent chronic conditions. An important factor of health promotion is that it allows the person to take control of their health by targeting the root of the problem that is exacerbating the illness.

5. The role of lifestyle and nutrition in AMD

AMD is a condition in which modifiable risk factors may play a significant role in its development and progression. These modifiable risk factors can be addressed through health promotion where AMD can be prevented or stabilized. Such risk factors include obesity, unhealthy diet, sedentary lifestyle, smoking, and underlying health conditions including hypertension and cardiovascular disease. A correlation between regular exercise and decreased risk in developing early or late AMD has been shown; however, the effect was stronger with lowering the progression to late AMD [53].

In general, practicing a more active lifestyle allows the person to age with less health complications in contrast to someone who is living a sedentary lifestyle. McGuiness et al. said that an active lifestyle, considered to be 3 h of moderate to intense physical activity per week, was sufficient in decreasing mortality. Regular exercise also increases antioxidant enzyme activity combating oxidative stress, avoiding the acceleration of the aging process systemically and in the eyes [53].

Regular exercise alone does not reduce the odds of developing AMD. The person must practice living a healthy lifestyle with a diet low in unhealthy foods, smoking avoidance, consuming alcohol in moderation, regular exercise and regular visits with their primary eye care and health care providers. Chronic illnesses stemming from unhealthy lifestyles have many complications and associations that include. Leading a healthy lifestyle decreases the risk of the development of chronic illnesses such as hypertension, diabetes, cardiovascular disease, and AMD [45].

Proper nutrition plays a significant role in reducing the risk of AMD. Dietary xanthophyll carotenoids play a major role in maintaining the integrity of the macula [38, 54, 55]. Seddon found that people who have a high intake of dietary carotenoids had a 43% lower risk of AMD [45]. Higher consumption of lutein and zeaxanthin correlated with a reduction in the risk of AMD. These carotenoids can be found in brightly colored vegetables as well as green leafy vegetables such as spinach, kale, turnip greens, and collard greens. Seddon's results showed that those who reported consuming a one-half cup serving of green leafy vegetables 5 times a week had an 88% reduction in the risk of AMD [45].

Another study by Seddon et al. showed evidence indicating high intake of dietary fats contributes to the progression of advanced AMD. In particular, vegetable fat was shown to increase the risk of progression of AMD. Animal fat was also shown to increase risk, but to a lesser extent [56]. The study also find that saturated, monounsaturated, polyunsaturated, and trans-unsaturated fats were remarkable

for aiding the progression of AMD [56]. The results also proved dietary fat intake was independent in increasing the risk of AMD without the influence of obesity, since the participants' body mass index was controlled in the study.

Both obesity and dietary fat intake promote inflammatory markers in the body which increase the risk of cardiovascular disease and, potentially, AMD [56]. Interestingly, nuts have been shown to have a significant role in reducing the risk of cardiovascular disease, type 2 diabetes mellitus, and AMD. The Physician's Health Study showed men who consumed nuts at least twice a week had a reduction rate of 50% for the risk of sudden cardiac death and a 30% reduction rate in coronary heart disease [56]. The Nurses' Health Study revealed women who consumed nuts 5 or more times a week had a 35% reduction rate of coronary heart disease and a 27% reduction in the risk of type 2 diabetes mellitus [56]. Nuts are also said to aid in maintaining the integrity of the macula because of its beneficial properties [56]. Nuts contain resveratrol, a compound that has antioxidant, antithrombotic, and anti-inflammatory properties, which have a positive effect on the integrity of the macula [56]. Nuts also contain vitamin E, copper, magnesium, and dietary fiber which can help prevent coronary heart disease, atherosclerosis and decrease total cholesterol levels [56].

Antioxidants, vitamins and minerals have been shown to aid in reducing the risk of AMD. These micronutrients have been compounded into dietary supplements to help prevent AMD and its progression [57]. Anthocyanins, red-purple pigments, are shown to have antioxidants and anti-inflammatory properties with the potential in maintaining macular wellness [57]. Anthocyanins are found in red to purple-colored flowers, fruits and vegetables. Examples are blueberry, bilberry, strawberry, currant and grapes. Notably, bilberry has been extracted to be included in supplementation for its antioxidant properties [57]. Anthocyanins are also believed to promote the synthesis and regeneration of rhodopsin, along with promoting an increase in blood flow in the retina.

The xanthophylls lutein and zeaxanthin are carotenoids that are only obtained through the diet since the body is unable to synthesize them. Lutein and zeaxanthin are found in green leafy vegetables, such as spinach and kale, along with fruits avocado and maize [45, 57]. Lutein and zeaxanthin are most concentrated within the macula. The retinal isomerases convert lutein into meso-zeaxanthin in the retina which is also found in macula [58]. The MPOD value directly correlates with the integrity of the macula. The macular carotenoids begin to degenerate when an individual lives an unhealthy lifestyle, consequently increasing inflammatory markers. Individuals at risk for AMD or with signs of the disease may benefit from foods with lutein and zeaxanthin or supplementation with these to increase their serum and macular carotenoid levels. An increase in lutein and zeaxanthin serum levels secondary to supplementation has been shown to increase MPOD and improve visual function measures such as contrast sensitivity, glare tolerance and photo stress recovery [40–42, 57, 59, 60].

Vitamins A, C and E are micronutrients that have been shown to reduce the risk of AMD [57]. Fruits and vegetables rich in vitamin A have shown a strong association with a decreased risk of AMD due to vitamins A's close relationship to carotenoids. Vitamin C is a potent antioxidant that protects the body from free radicals causing oxidative stress. Deprived levels of vitamin C can cause an accumulation of lipofuscin and loss of photoreceptors [57]. Vitamin E is also a potent antioxidant and serves as an important micronutrient in regulating retinal health. Zinc is a mineral that serves as a co-factor for metabolically active enzymes which has many vital roles in maintaining immunity, reproduction and neuronal development. Zinc is also found in the retina where it serves a vital role in maintaining macular health [57].

Bioavailability is an important factor to consider, since the absorption of micronutrients is affected by multiple factors such as stress, alcohol consumption, caffeine, drug intake, and exercise [57]. Fats and oils have been shown to assist in the absorption of these micronutrients. With that in mind, obtaining these micronutrients from animal sources rather than plant-based sources can increase their absorption. For example, egg yolk is an excellent source of zeaxanthin and has shown to be more bioavailable than comparable amounts from oral supplements or from plant sources [57].

5.1 AREDS-1, AREDS-2 and the Rotterdam study

Before the age-related eye disease study (AREDS), supplements containing zinc and antioxidants for AMD prevention and treatment were available for consumer consumption despite little evidence of its effects on risk reduction [61]. Therefore, the National Eye Institute (NEI) developed a randomized clinical trial where high doses of zinc and antioxidant vitamins (vitamins C, E and beta carotene) were investigated. AREDS was an 11-center double-masked clinical trial. The subjects were divided into 4 groups and had to have vision of 20/32 or better in one eye [61]. The first group was randomized to take a formula consisting of 500 mg of vitamin C, 400 IU of vitamin E, and 15 mg of beta carotene. The second was assigned to take mineral supplements of 80 mg of zinc, as zinc oxide and 2 mg of copper as cupric oxide. The third group was placed on a combination of both antioxidants and zinc while the fourth group took a placebo [61].

The results of AREDS showed that the group taking antioxidants plus zinc had the highest odds reduction, odds ratio (OR) of 0.66, along with a 25% risk reduction in AMD [47]. The AREDS study concluded that people aged 55 years or older with moderate AMD (defined as the presence of one or more of the following: extensive intermediate size drusen, at least 1 large druse, or non-central geographic atrophy in 1 or both eyes) or advanced AMD or vision loss due to AMD in 1 eye (but not the other), and without contraindications such as smoking, should consider taking a supplement of antioxidants plus zinc. In contrast to eyes with early AMD, which did not benefit from supplementation, people with intermediate to advanced AMD showed a greater effect in reducing the risk of progressing while taking antioxidants and zinc supplements [47].

AREDS 2 was a multicenter, randomized, double-masked, placebo-controlled phase 3 study that investigated whether the carotenoids lutein and zeaxanthin, and/or omega-3 long-chain polyunsaturated fatty acids (ω-3 LCPUFAs) docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) could further reduce the risk of AMD progression. AREDS 2 was also designed to investigate if eliminating beta carotene and/or lowering the dosage of zinc could be effective in preventing AMD progression [62].

All participants were randomly assigned to: (1) placebo (n = 1012); (2) L + Z (10 mg/2 mg, n = 1044); (3) ω-3 LCPUFAs (eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) [650gmg/350 mg] n = 1069); or (4) the combination of $L + Z$ and ω−3 LCPUFAs (n = 1078). All participants were offered a secondary randomization to 1 of 4 variations of the original AREDS formulation keeping vitamins C (500 mg), E (400 IU), and copper (2 mg) unchanged while varying zinc and beta-carotene as follows: zinc remains at the original level (80 mg), lower only zinc to 25 mg, omit beta-carotene only, or lower zinc to 25 mg and omit beta-carotene [62].

The results did not show a significant risk reduction with the addition of lutein and zeaxanthin or DHA and EPA. There was also no significant effect of the elimination of beta carotene or lowering the zinc dosage. Thus, it was determined that lutein and zeaxanthin could be an effective and safe substitute for beta

carotene considering the higher association of lung cancer in current smokers or former smokers taking beta carotene. There is no reported association of lutein and zeaxanthin with lung cancer. It was determined the dosage of zinc could be lowered without any harmful adverse effects [62]. In conclusion, it is now recommended that patients with intermediate AMD or advanced disease in one eye (but not the other) should consider taking an AREDS 2-based supplement along with a broad-spectrum multivitamin to prevent the progression to advanced AMD.

The Rotterdam Study, a prospective, population-based study, investigated whether dietary nutrients and antioxidants reduce the incidence of developing early AMD in people aged 55 or older who are at a high genetic risk [63]. The study investigated the CFH Y402H and LOC387715 A69S gene variants which have been said to increase the risk of developing AMD if present. In the presence of the CFH Y402H gene and the LOC387715 A69S gene, the risk of AMD increases by 11 and 15 times, respectively [63]. This study sought to demonstrate any synergistic effects of CFH Y402H and LOC387715 A69S with nutrients [63].

The results showed a positive interaction of CFH Y402H with zinc, beta carotene, lutein, zeaxanthin, EPA, and DHA. In addition, there was a positive interaction of LOC387715 A69S with zinc, EPA, and DHA. The study determined that zinc, beta carotene, lutein, zeaxanthin, EPA, and DHA reduce the risk of developing early AMD in individuals who are considered to be at high genetic risk [63]. The authors recommended for this high genetic risk group to a diet rich in these nutrients. Foods rich in zinc include fortified cereals, meats, dairy products, nuts, and seeds. Foods rich in beta carotene, lutein and zeaxanthin include dark green leafy vegetables such as spinach and kale, egg yolk, and orange vegetables including carrots, peppers, and pumpkin. Foods rich in EPA and DHA include oily fish such as herring, salmon, sardines, trout, and tuna [63].

6. Discussion

Health promotion is a daunting concept due to the wide range of elements under its umbrella. One goal of health promotion is to empower the patient, giving them responsibility so that they are in charge of their own health care. Giving them the responsibility for their health will allow patients to set expectations and understand the consequences if not followed. The patient empowerment model ensures that health promotion is applied in the exam rather than occurring after the visit. Managing risks mirrors health promotion's overall goal. Patients at high risk for health complications need to be managed more closely and provided with the appropriate education to maximize their outcomes.

Patient-centered care is the foundation of health promotion, where the patient's treatment and management are actively tailored to best fit them, considering outside factors specific to the patient [11]. Communication is essential in maximizing the patient's outcome; however, it must be delivered effectively. Communicating with the patient should not be rushed or insensitive, especially when the patient's health is not optimal at that moment. Patients can become discouraged if they sense their health care provider is not invested in their care.

Communication can vary to include written, verbal or role modeling forms, depending on the case and patient. Up-to-date knowledge and skills are enforced in the field of nursing to give the patient the most appropriate treatments while upholding the health promotion model. Coordinated care is where multiple disciplines and/or professions can communicate with one another and keep each other updated on the current status of their patient. Patients with chronic illnesses typically have more than one provider for their care. By coordinating care with an

inter-professional model, the patient's health care providers will be updated on the recent findings from the other providers caring for the patient. This communication is key to optimizing the flow, experience and care of the patient.

Health promotion can play a large role in educating patients on ways to reduce their risk of AMD, considering the modifiable risk factors involved in the disease. Getting the message across to the targeted audience depends largely on the accessibility of information. Health promotion can occur in schools, clinics, workplaces, residential areas and local community centers where people may gather and learn about how to take control of their health. Effective promotion addresses health while also taking into consideration the full spectrum of influences affecting health. For example, it considers cultural and social behaviors that are most prevalent in that particular setting. To properly deliver the information, there needs to be a strategic approach on how to convey the message for each specific population. Any disease can be addressed for each population if divided into the following four categories: healthy population, population with risk factors, population with symptoms, and population with the disease. Kumar et al., developed a flow chart that shows the categories and what topics need to be covered to effectively communicate the message [11].

For healthy populations, topics such as lifestyle and prevention of risk factors with primordial prevention need to be addressed. Primordial prevention is used to lessen the incidence of a disease by educating the individual before they become symptomatic. In this model, they are given the necessary knowledge and tools to reduce their risk considering their environmental, socioeconomic, behavioral conditions, and cultural practices [11]. For a population at risk, there must be active health promotion including how to overcome modifiable risk factors and attending regular appointments with members of the health care team. The population with symptoms specifically needs access to medical care for early detection, treatment and management, promotion of a healthy lifestyle.

If there is a disability resulting from the condition, rehabilitation will have an important role. The population with the known disorder must be offered treatment and care, healthy lifestyle reinforcement and any disability and rehabilitation services needed. Chronic diseases have grown to be a main factor in global mortality. Health promotion can be used for individuals with non-communicable diseases where an intervention can be initiated to avoid further progression. For example, health promotion alone can prevent heart disease and stroke by 80%, diabetes by 80% and 40% of cancers by reducing major risk factors that exacerbate their development [11].

AMD is a multifactorial disease where nutrition and diet play a significant role in potentially reducing the risk of its development and progression. With age, there is an increase in the production of free radicals, causing oxidative stress exacerbating the aging of tissues. A growing body of evidence suggests a key pathogenetic factor involves chronic inflammation and immunosenescence, which may be brought on by sustained oxidative stress paired with reduced antioxidant capacity [25, 32, 33, 40]. Given that systemic low-grade inflammation may be strongly influenced by the gut microbiota, particularly among older adults [64], sufficient absorption of these protective micronutrients is essential for promoting redox balance [65–67]. Antioxidants and other nutrients decrease the oxidative stress occurring in the eyes. Examples include vitamins (C, D, and E), zinc, and carotenoids (lutein and zeaxanthin) [40, 68]. Interestingly, these antioxidants work together by a protective chain where they assist each other when one is in the process of neutralizing free radicals. Vitamins C and E, along with lutein and zeaxanthin, arguably share a significant role in that antioxidant network.

The Mediterranean diet has been studied and recommended for its healthy foods which have shown show an association to lower mortality and cancer rates, and reduced risk of AMD [69]. Consequently, this type of diet decreases the amount of inflammation and oxidative stress in the body and ultimately in the retina.

The Mediterranean diet is rich in fruits, legumes, vegetables, bread, cereals, potatoes, beans, nuts, seeds, olive oil [69]. The diet includes low to moderate amounts of dairy products and alcohol with even lower quantities of red meats. This diet is in contrast to the typical pro-inflammatory Western diet. A report in The American Journal of Nutrition showed a 26% reduction in the progression to advanced AMD in participants who strictly adhered to a Mediterranean diet alone [69]. The study also showed that the addition of AREDS supplementation did not further decrease the risk when coupled with the Mediterranean diet. Overall, the study proved following this diet rich in fruits, vegetables and lean protein can aid in slowing the progression to advanced AMD [69].

In understanding the association of AMD, nutrition, and systemic factors, can motivate their patients to take control of their ocular health. Primary care physicians should recommend regular eye examinations including a dilated retinal examination to assess for AMD and other conditions. In addition, encourage patients to visit their eye care provider whenever the patient experiences a change in their vision. This gives the eye care providers a better chance to detect and manage early disease before extensive damage has occurred. Dry AMD is most associated with complaints of gradual decrease in vision while rapid vision loss is more closely associated with wet AMD.

All health care providers can educate their patients that unhealthy habits such as smoking can cause damage to their retina and ultimately their vision. At times, patients tend to not take their chronic illness seriously because they may not see any obvious physical signs. To emphasize the importance of controlling their chronic illness, the primary care provider can warn the patient that their unhealthy choices can consequently lead to irreversible vision loss. It is possible the patient may become more concerned when it is brought to their attention that their vision could be irreversibly damaged.

If health promotion is effectively initiated and maintained, the patient may be more willing to take control of their condition, improve their adherence to treatments, maintain their follow-up appointments, and self-monitor their illnesses.

Conflict of interest

Alexander Martinez None Joseph Pizzimenti None Drake W. Lem none. Dr. Pinakin Gunvant Davey none.

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