Editorial

A Decade of Progress in the Understanding, Prevention and Treatment of Age-related Macular Degeneration in Singapore

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The year 2014 had marked the 10th anniversary of the nationwide Age-related Macular Degeneration (AMD) Awareness Week in Singapore.[1] This public health campaign, organised annually since 2005, aims to generate awareness and understanding of AMD by promoting the importance of education, early detection, and knowledge of treatment and rehabilitation options for the disease. Besides increasing the number of people aged 50 years and older who receive regular eye examinations, the campaign aims to preserve vision and improve the quality of life of individuals affected by AMD and increase the proportion of people with AMD who receive treatment and rehabilitation. At this significant public health milestone, it is timely to review the remarkable decade of progress that has been made in the understanding, prevention and treatment of AMD in Singapore.

AMD is the most important cause of irreversible vision loss among people aged 60 years or older in developed countries and accounts for 8.7% of all causes of blindness worldwide.[2] It is estimated that by 2020, about 196 million individuals could suffer from AMD globally and this number is likely to rise further to 288 million by 2040.[2]

The burden of AMD is enormous. Progressive deterioration of central vision from AMD has devastating implications especially when the disease involves both eyes. AMD adversely affects the quality of life with its impact on common vision-related tasks essential for daily living such as reading, recognising faces and driving. Visual loss in the elderly increases the risk of falls, hip fractures and the need for nursing care. It also has negative psychological implications such as depression associated with the visual limitations. The direct costs of managing AMD such as frequent consultations, investigations, repeated treatments and visual rehabilitation is substantial. The indirect costs to society in the form of loss of productivity, unemployment and caregiver expenses make the financial burden of AMD even higher.

The first area of major advances in Singapore in the last decade is the considerable improvement in our understanding of the epidemiology of AMD and its impact on those suffering from the disease. AMD may be divided into early and late AMD. Based on the Wisconsin age-related maculopathy grading system, early AMD has either soft indistinct or reticular drusen, or both soft, distinct drusen plus retinal pigment epithelial abnormalities while late AMD has either neovascular features or geographic atrophy.[3]

Several key population-based studies published over the past 10 years have shown that AMD, once considered a disease that affects mainly Caucasians, is not rare in Singapore. The age-standardised prevalence of early and late AMD in Singapore is 5.1% and 0.5%, respectively.[3] Interestingly, there is no major racial predilection for AMD in Singapore.[3] Although early AMD is more common in Chinese and Indians compared to Malays, the prevalence of late AMD is similar among the 3 major races in Singapore.[3] It is now known that the prevalence of bilateral AMD is comparable between Singapore Malays and Caucasians.[3]

AMD has several non-modifiable risk factors such as age, female gender and genetic predispositions. Among the known modifiable risk factors for AMD, cigarette smoking is the strongest. Local data have shown that current smokers have a significantly higher risk of developing late AMD (odds ratio (OR) 3.79) compared to non-smokers, especially if they smoke more than 5 packs per day.[4] Another potentially modifiable risk factor, the lack of antioxidant micronutrients in the diet, has been associated with low levels of protective macular pigment (MP) in the eye. Atypical MP profiles have been reported among Singapore Chinese and this may be associated with an increased risk of AMD.[5]

We now better understand the adverse effects of AMD on the quality of life of Singapore patients. Singapore AMD patients are willing to trade off 1.9 years for every 10 years of their remaining life for a hypothetical treatment to restore vision.[6] Also, they are willing to take a 14% risk of death and 10% risk of blindness in both eyes for a hypothetical treatment that can confer perfect vision.[6]

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The second area of advances is the concrete actions taken for primary and secondary prevention of AMD in Singapore. Primary prevention aims at protecting healthy people from developing AMD while secondary prevention refers to preventing the progression of AMD after it has been diagnosed. Although AMD may not be totally preventable, primary prevention by tackling its modifiable risk factors and secondary prevention by encouraging early detection of the disease is vital to reducing its impact. Increasing the awareness of AMD and encouraging certain lifestyle changes such as abstaining from smoking, taking a diet rich in green leafy vegetables and fruits, controlling blood pressure and exercising regularly can potentially help to reduce the prevalence of AMD, especially if begun at an early age. In addition, screening of asymptomatic individuals allows early diagnosis, timely intervention and better outcomes.

The rapidly ageing population and increased longevity in Singapore is likely to result in a gradual rise in the prevalence of AMD.[7,8] However, the awareness of AMD among the community is generally low.

A 2006 telephone survey of 520 Singapore residents, done a year after the first AMD Awareness Week was conducted, showed that only 7.3% respondents were aware of AMD.[9] This puts Singapore among countries with a low awareness of AMD as seen in a global survey which showed AMD awareness levels ranging from 4% to 30%.[10]

The low awareness is part of the reason that prompted Singapore eye care professionals, led initially by the Department of Ophthalmology and Visual Sciences at Alexandra Hospital (and later at Khoo Teck Puat Hospital when the department relocated to its new location) to take concrete actions to tackle the looming public health crisis that the rapidly ageing population in Singapore is likely to face. The annual AMD Awareness Week was thus initiated in collaboration with the AMD Alliance International, a non-profit global alliance of organisations working to raise the awareness of AMD, and the now-defunct Singapore Action Group of Elders (SAGE). The campaign gradually expanded in size and scale over the next 10 years and now involves more than 30 participating organisations including the Health Promotion Board (HPB), patient support groups, educational institutions, hospitals, voluntary organisations, public libraries, community centres, nursing homes, senior citizen homes and religious places of worship.[1] The campaign actively engages ophthalmologists, optometrists and opticians from both the public and private sectors to increase its reach to the community.[1] Activities such as educational health talks on AMD, eye screenings for age-related eye diseases, patient support group meetings, smoking cessation campaigns, educational and art exhibitions on AMD have been organised to raise the awareness of AMD and its modifiable risk factors. Campaign messages have also been broadcasted widely in the media including major newspapers, magazines, radio, television, public transport services (Mass Rapid Transit trains and buses) and the Internet.

It is gratifying to note that a 2011 follow-up telephone survey of 559 Singapore residents, 5 years after the initial survey in 2006, showed that the awareness of AMD had increased 4-fold from 7.3% to 28.1%.[11]

Early detection of AMD can be effectively achieved through eye screenings for the elderly. In fact, the Scientific Advisory Board of AMD Alliance International recommends that individuals 55 years or older should have their eyes screened by an eye care professional at least once every 2 years if they have no symptoms.[6] Patients with symptoms of blurring of vision or distorted central vision are recommended to see an eye care professional immediately.[6]

Not surprisingly, the awareness of smoking as a risk factor for AMD was also initially low in Singapore. In the 2006 survey, only 36.7% respondents considered smoking to be a risk factor for AMD.[10] Another local study found that the awareness of the risk of blindness associated with smoking was far lower than that for other more commonly known smoking-related diseases such as lung cancer and heart disease.[12] In fact, only 42.5% of current smokers in the study were aware of the risk of blindness from smoking.[12] To meet this challenge, an anti-smoking campaign has been a major element of the AMD Awareness Week. Eye care professionals warned about the harmful effects of smoking on vision health in the media and scientific publications.[13-15] They also lobbied and worked with the HPB to put a "Smoking causes blindness" graphic health warning on cigarette packs in Singapore to discourage the habit.[16] The results of these efforts was reflected in the fact that a larger proportion of respondents who were familiar with AMD now knew that smoking is a risk factor for AMD (84.1% in 2011 vs 45.9% in 2006).[11]

The AMD Awareness Week also highlights the use of nutritional supplementation to reduce the risk of progression of AMD as a form of secondary prevention.[17] In individuals at high risk of developing advanced AMD, the Age-related Eye Disease Study (AREDS) showed that using high doses of antioxidants (vitamin C 500 mg; vitamin E 400 IU; β-carotene 15 mg) and zinc 80 mg significantly reduced the risk of developing advanced AMD by 25% over 5 years.[18] However, as β-carotene intake was linked to an increased risk of lung cancer in smokers, a subsequent study, the AREDS2, recommended that β-carotene be replaced by lutein and zeaxanthin in the formulation.[18]

The last area of advancement is the huge improvement in treatment outcomes with newer treatment modalities. Slightly more than a decade ago, a diagnosis of AMD meant very few treatment options with little hope for saving sight. Fortunately, there have been great strides made in the

management of AMD in the recent 10 years, with hopes of restoring vision in some patients while stabilising vision in the majority.

Management options for neovascular AMD, which accounts for about 10% of all AMD cases but is responsible for most of the severe vision loss associated with the disease, have rapidly expanded from the dawn of the 21st century.[19] Prior to 2005, only laser photocoagulation and photodynamic therapy (PDT) have been proven modestly beneficial in randomised control trials for treating neovascular AMD.[20] PDT, which uses a special laser wavelength to activate a photosensitive drug verteporfin (Visudyne®, Novartis AG, Basel, Switzerland) in the eye, is better than traditional thermal laser photocoagulation as it achieves ablation of the neovascular tissue in the eye while significantly limiting collateral retinal damage associated with thermal laser treatments.[20] PDT was approved for use by US Food and Drug Administration (FDA) in 2000 and by the Health Sciences Authority (HSA) in Singapore in 2001. PDT was found to be effective especially for a subtype of AMD called predominantly classic subfoveal choroidal neovascularisation (CNV).[20] However, PDT at best stabilises existing vision and is not associated with an improvement in visual acuity.

Recently, agents that effectively block the action of various growth factors such as the vascular endothelial growth factor (VEGF) and placental growth factor (PlGF) responsible for neovascularisation have truly revolutionised the management of neovascular AMD. In the last 10 years, the HSA approved 3 anti-VEGF agents for treating neovascular AMD: pegaptanib sodium (Macugen®, Pfizer, New York, USA) (FDA approval 2004, HSA approval 2006), ranibizumab (Lucentis®, Novartis AG, Basel, Switzerland) (FDA approval 2006, HSA approval 2008), and aflibercept (Eylea®, Bayer HealthCare, Berlin, Germany) (FDA approval 2011, HSA approval 2013).[20] Besides these, another anti-VEGF agent called bevacizumab (Avastin®, Roche, Basel, Switzerland) which is approved for metastatic colorectal cancer, is widely used "off-label" for treating neovascular AMD. Together, these anti-VEGF agents provide, for the first time, a chance of improving vision with up to 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters visual acuity gain in at least one-third of the treated patients while effectively stabilising vision in the remaining majority.[20]

In summary, while Singapore has seen major advances in the understanding, prevention and treatment of AMD over the last decade, there is no room for complacency. AMD remains an emerging public health challenge with Singapore's rapidly ageing population and efforts must be kept up or even stepped up to reduce, if not eradicate, the burden of this sight-threatening condition.

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