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Review article

Age-related eye disease and gender

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ABSTRACT

Worldwide, the prevalence of moderate to severe visual impairment and blindness is 285 millions, with 65% of visually impaired and 82% of all blind people being 50 years and older. Meta-analyses have shown that two out of three blind people are women, a gender discrepancy that holds true for both developed and developing countries. Cataract accounts for more than half of all blindness globally and gender inequity in access to cataract surgery is the major cause of the higher prevalence of blindness in women. In addition to gender differences in cataract surgical coverage, population-based studies on the prevalence of lens opacities indicate that women have a higher risk of developing cataract. Laboratory as well as epidemiologic studies suggest that estrogen may confer antioxidative protection against cataractogenesis, but the withdrawal effect of estrogen in menopause leads to increased risk of cataract in women. For the other major age-related eye diseases; glaucoma, age-related macular degeneration (AMD) and diabetic retinopathy, data are inconclusive. Due to anatomic factors, angle closure glaucoma is more common in women, whereas the dominating glaucoma type; primary open-angle glaucoma (POAG), is more prevalent in men. Diabetic retinopathy also has a male predominance and vascular/circulatory factors have been implied both in diabetic retinopathy and in POAG. For AMD, data on gender differences are conflicting although some studies indicate increased prevalence of drusen and neovascular AMD in women. To conclude, both biologic and socioeconomic factors must be considered when investigating causes of gender differences in the prevalence of age-related eye disease.

Contents

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1. Introduction

In the aging population, age-related cataract, age-related macular degeneration (AMD), glaucoma, and diabetic retinopathy (DR) are prevalent in high numbers, with about 37%, 10%, 3%, and 2% of people 70–74 years old suffering from these conditions [1]. Even though the female to male ratio varies among these eye diseases, women are in majority among the blind and the visually impaired; about two of three blind people are women [2]. This gender difference may in part be explained by the longevity of women. Other causes however, such as differences in requirement for good vision in daily life activities, in the propensity to seek health care or gender inequity in access to health care, may also contribute to this discrepancy. In addition, life-style related factors, such as smoking and sun exposure, may differ between genders and thus influence the risk of eye diseases and its distribution between sexes. Lastly, there are sex-dependent biologic differences, which may affect the disease-causing pathogenic mechanisms.

In all parts of the world and at all time periods for which data exist, the longevity pattern is the same; women live longer than men. In average, life expectancy for women is 5 years longer than for men [3]. Even though this difference is smaller in countries with high pediatric mortality and more pronounced in countries with a high overall longevity, women outlive men everywhere regardless of educational, economic, political and health critera [3]. Men have higher mortality rates than women for all the common death causes, including accidents, cardio- and cerebrovascular disorders, cancers, infections and chronic pulmonary disease [4]. Possible biologic explanations for gender-related differences in mortality and morbidity basically fall into two categories; genetical or hormonal. Genetic factors that favor female longevity are 1. the heterogametic sex hypothesis; 2. telomere attrition; and 3. mitochondrial inheritance. The importance of sexual hormones in aging is central in the reproductive theory of aging, according to which a dysfunctional hypothalmic-pituitary-gonodal (HPG) axis is associated with increased mortality in both sexes [5]. The longer life-span in women, which is even more pronounced in those entering menopause at higher age, and the fact that castrated men have the same life expectancy as women suggest that estrogens are beneficial in the aging process [6]. It is known that the risk of cardiovascular disease increases with high androgen levels and low estrogen levels both in men and in postmenopausal women [7]. Compared to premenopausal women, men have a higher prevalence of hypertension and a higher risk of cardiovascular disease. However, after menopause there is no gender difference in risk of cardiovascular disease and women even have a higher prevalence of hypertension than men of the same age [8]. A summary of genetical and hormonal effects that may promote female longevity and health is shown in Table 1. For details on the listed mechanisms, see reviews by Austad and Zetterberg [4,9].

This review will focus on the four most common eye diseases in elderly people; age-related cataract, age-related macular degeneration, glaucoma and diabetic retinopathy. Gender-specific prevalences and possible mechanisms for any gender differences, as well as the effect of endogenous and/or exogenous estrogen, will be presented. Knowledge on sex-related effects on pathogenic mechanisms is important to understand the basis of disease and thus provide means for new therapies. Also, finding socioeconomic explanations to gender differences in disease prevalence, such as gender inequity in access to cataract surgery, is crucial for equal allocation of health care resources (Table 2).

Table 1
Biologic factors that may promote female longevity and health.

A. Genetic factors
1. The heterogametic sex hypothesis
2. Telomere attrition
3. Mitochondrial inheritance
B. Estrogen-mediated protection
1. Favorable distribution of body fat and beneficial lipid metabolization
2. Neuroprotective effects
3. Activation of immune system
4. Improved stress response
5. Anti-oxidative properties
- ROS scavenging
- Generation of NO which can neutralize ROS
- Activation of the thioredoxin pathway
- Upregulation/activation of Mn-SOD and GPx

GPx: Glutathione peroxidase; Mn-SOD: Manganese superoxide dismutase; NO: nitric oxide; ROS: radical oxygen species.

2. Methods

Data was identified through search in PubMed (http://www.ncbi.nlm.nih.gov/pubmed) using the terms “age-related macular degeneration”, “aging”, “blindness”, “cataract”, “diabetic retinopathy”, “estrogen”, “eye disease”, “gender”, “glaucoma” and “visual impairment”. Bibliographies from identified articles were used to further augment the search. By design, both summaries of previous reviews, older original articles and newer studies were included. Only articles written in English were included. There was no time limit for inclusion of the studies.

3. Gender-based differences in visual impairment and blindness

The estimated number of people suffering from blindness globally is 32.4 millions [2]. For people with moderate and severe visual impairment (MSVI; decimal visual acuity of <0.3 but ≥0.05) the number is 191 millions [2]. The major cause of blindness globally is cataract, accounting for 51% of all blind people, whereas uncorrected refractive errors is the major cause of MSVI (43%) followed by cataract (33%) [10]. There are huge inequalities in the proportion of blind and visually impaired people between different regions of the world; for people older than 50 years, the prevalence of blindness and MSVI in African and Asian regions is in the range of 4–6% and 16–24% respectively with corresponding numbers in high-income regions of ≤0.4% and <5% [2].

In all regions of the world, the prevalence of blindness and MSVI after adjusting for age is higher for women than for men [2]. Globally, in 2010 women accounted for 60% of all blindness and 57% of all MSVI [2]. A bit surprisingly, two independent studies report a higher gender inequality in industrialized countries than in Africa [2,11]. In the Sub-Saharan African region, the ratio of blindness in women as compared to men was lowest; 1.11 to 1.13, as compared to high-income countries where the difference was more than 1.5 in favor of men [2]. One possible explanation is that the longer life-expectancy in women will result in a larger discrepancy in blindness and visual impairment between genders in high-income countries, where the difference in lifespan between men and women is bigger.

4. Gender differences in specific age-related eye diseases

4.1. Lens opacities and cataract

When reporting the prevalence of cataract, a variety of definitions and study designs are used; either population-based studies

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