

Hormonal Effect on Dry Eye in Menopausal Women—A Review Article

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Abstract

Review Article

Various researches have been done to understand dry eye in the recent years, which have included the dry eye state and hormonal effect on dry eye. The term Dry eye syndrome or disease (DES/DED) is a multifactorial ocular surface disease that refers to a condition those results in inadequate lubrication of the ocular surface. DES causes symptoms of ocular pain, discomfort and decreased visual acuity and tears film instability with potential damage to the ocular surface and ultimately affects quality of life of patients. It is more prevalent in females specifically in the menopausal and postmenopausal age group. This is probably due to imbalance of sex hormones. Various studies reported potential role of hormones replacement therapy in menopause associated dry eye. This review article will help to understand the influence of sex hormones in dry eye in menopausal women.

Keywords: Dry eye, menopause, sex hormones.

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INTRODUCTION

Dry eye disease (DED) is defined as “A multifactorial disease of the tears and ocular surface that result in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface [1]”. The symptoms of dry eye vary considerably from patient to patient. Dry eye can cause debilitating symptoms including ocular discomfort, burning, foreign body sensation, grittiness, photophobia and decreased vision thus affecting the quality of life. DED is one of the main reasons that patients visit ophthalmologists.

The prevalence of DES/DED may vary because of the lack of a gold standard for diagnosis; moreover, each study seems to use different criteria. Depending on how it is defined and the population studied, the prevalence of DES is anywhere from 6.7 percent to 28.7 percent [2, 3]. Women are 1.5 to three times more likely than men to have the condition [4, 5]. Most cases are seen after menopause, but women with premature ovarian failure also have a higher risk of dry eye [6]. Researchers believed that low estrogen levels after menopause must be responsible for higher rates of DES in older women. But more recent research has explored the role of androgens. Androgen has been proven to have an effect on tear production and function [7]. Androgens are sex hormones that are present in

both men and women and with age their levels decrease. As normally women have lower level of androgens, age-related decreases may push levels below the amount needed for optimum eye health. However, the correlation between systemic estrogen and testosterone and DED is less clear.

Hormonal effect on dry eye

Both androgen and estrogen have known effects on the synthesis and components of the tear film. The tear film has three components- the aqueous layer secreted by the lacrimal gland, the lipid layer secreted by the meibomian glands, and mucin layer secreted by the conjunctival goblet cells. Sex steroids receptors are present on the meibomian glands responsible for producing the oil component of tears that prevent evaporation [8].

Recent studies have suggested that androgen deficiency may be the main cause of the meibomian gland dysfunction, tear film instability and evaporative dry eye that are characteristic of Sjogren's syndrome, which occurs mostly in women [9]. Androgens regulate the meibomian glands, which maintain tear film stability and prevent tear film evaporation. [10]. Androgen binding result in synthesis and secretion of lipids from these glands while estrogens cause a decrease in lipid production [11]. Thus increased levels of estradiol are believed to be a risk factor for dry eye.

The influence of hormone replacement therapy (HRT) in menopausal women remains unclear. When some authors believe that HRT improves the quality and volume of the tear film, others have shown that it increases the risk of dry eye. It is possible that HRT may alleviate postmenopausal dry-eye symptoms by increasing goblet cell density [12], however studies show that HRT worsens dry-eye symptoms in some cases and estrogen only HRT seems to be worse than a combined estrogen and progesterone therapy. Data from the Women's Health Study suggests a 69 percent increased risk of dry eye associated with postmenopausal estrogen therapy and a 29 percent higher risk for women taking estrogen plus progesterone therapy [13].

Androgen replacement therapy can have significant side effects when administered systemically. For this reason, androgen eye drops are an alternative route to limit the systemic absorption. 30% of dry eye patients receiving a testosterone eye drop became asymptomatic compared to 8% in the control group after 6 months of treatment [14]. A study reported that transdermal preparation when applied to the eye lids resulted in a 51% decrease in dry eye symptoms [15]. These transdermal preparations and newer conjugated androgen eye drops decrease the symptoms and are tolerable to most patients [16].

Benefits of androgen therapy remain controversial. A recent study revealed that testosterone treatment in dry eye syndrome did not find any additional benefit in symptoms and signs from placebo for topical testosterone or systemic testosterone and estrogen [17]. But the limitation of this study was a very small size and also a short follow-up period.

Treatment

Treatment of dry eye includes simple measures like lubrication and in severe cases anti-inflammatory, immunomodulatory, and surgical interventions.

Hormonal treatment of dry eye disease is critical. It is really challenging to identify which patients will benefit most from hormonal treatment. Patient selection depends on factors like age and endogenous hormonal level.

The study done by Connor *et al.* showed that younger the patients more the benefit from androgen eye drop therapy is limited to peri and post-menopausal women. But this therapy did not lead to the same degree of symptom relief in premenopausal women [15]. Another study done by Feng *et al.* found that HRT improved tear production in patients > 50 years of age with dry eye [18].

In addition to age, patient's endogenous androgen level is also important. It has been reported that women with low testosterone levels experienced

complete symptomatic relief from androgen eye drops and systemic testosterone therapy. [19] Men on androgen blockers and patients with complete androgen insensitivity syndrome are also good candidates for androgen therapy [20].

CONCLUSION

Imbalance in sex hormones plays an important role in the pathophysiology dry eye disease in menopausal age group. Hormones in general and androgens in particular, represent an important trophic factor for the ocular surface, and that their deficiency leads to inflammation. It is becoming increasingly essential to know the interactions between hormones and the lacrimal and meibomian glands. Further study on this relationship may result in new and improved treatment.

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