



DO YOU KNOW THE OCULAR EFFECTS OF HRT?



This review of potential harms and benefits associated with hormone replacement therapy will help you provide the best possible eye care to all patients.

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As eye care physicians, we are well aware of how systemic medications and conditions can affect ocular health. Although hormone replacement therapy (HRT) is becoming increasingly common, discussions about these treatments and their potential ocular effects have been minimal. HRT may be prescribed to patients for a multitude of reasons, including hormone imbalance, menopause, gender-affirming care, and prostate cancer. The Tear Film

& Ocular Surface Society Dry Eye Workshop II Report has suggested that sex hormones play a part in multifactorial ocular surface disease.¹ What effects does HRT have on the eyes? Are all side effects negative? This article addresses these questions.

HORMONES AND OCULAR HEALTH **Androgen**

Androgen plays a role in ocular surface health by supporting the development and function of the meibomian glands, lacrimal glands,

the cornea, and the conjunctiva. Deficiency in androgen can lead to poor corneal wound healing, damage to conjunctival and corneal cells, increased signs of dry eye disease (DED), and limbal stem cell dysfunction.¹ This may result in worsening of patients' dry eye symptoms or even neurotrophic keratoconjunctivitis. Androgen also has a pilosebaceous effect, meaning that it helps to maintain a proper function of the sebaceous glands and hair follicles, resulting in a balance of moisture in the eyes and skin.

The lacrimal gland is an androgen target; therefore, dysregulation of androgen can lead to gland dysfunction and aqueous tear deficiency.¹ At the same time, the meibomian glands utilize androgen to help suppress keratinization and stimulate lipid and fatty acid production, which is integral to the functionality of the meibomian glands.¹

Decreased androgen is commonly found in patients with Sjögren syndrome and also occurs during menopause, pregnancy, and lactation. Patients taking estrogen-containing oral contraceptives and those on feminizing HRT may also experience a reduction in androgen production.¹

Estrogen and Progesterone

These hormones are found in human tears, with receptors in the meibomian glands, lacrimal glands, cornea, and conjunctiva.¹ Patients on estrogen and/or anti-androgen therapy may experience an improve-

IT IS COMMON FOR PATIENTS WITH BREAST CANCER WHO ARE ON ANTI-ESTROGEN THERAPY, SUCH AS TAMOXIFEN, TO EXPERIENCE OCULAR SIDE EFFECTS, INCLUDING SEVERE CHRONIC EVAPORATIVE DED.

ment in acne, in part because of the blocking of the androgens, which are responsible for sebum and lipid production.² This has shown to lead to improvements in meibomian gland dysfunction and ocular rosacea.²

On the flip side, both estrogen and androgen influence the production of all components of the tear film; therefore, a reduction or imbalance in these hormones could lead to worsening DED.³ This change in hormone balance is the underlying reason why peri- and postmenopausal women have a higher incidence of DED.³

Ongoing studies have shown improved signs and symptoms of menopause-associated DED in patients on HRT.^{3,4}

Research suggests that estrogen also has a neuroprotective effect on the retina and the optic nerve.⁵ Yet another study investigated the potentially beneficial effect of estrogen on vasodilation, which reduces vascular resistance and increases blood flow within the central retinal artery and ophthalmic artery.⁶

This was in stark contrast to both androgen and progesterone, which were found to reduce retinal blood flow.⁶

It is common for patients with breast cancer who are on anti-estrogen therapy, such as tamoxifen, to experience ocular side effects, including severe chronic evaporative DED.⁷ These patients should be monitored for tamoxifen toxicity within the retina and cornea, as well as worsening DED. For patients who experience worsening DED, the eye care physician should treat the side effects rather than stop potential life-saving medication, as we would in the scenario of retinal toxicity.

Testosterone

Testosterone and dihydrotestosterone bind to androgen receptors on sebaceous cells, causing an increase in gland size and in sebum production, which stimulates increased keratinization and formation of microcomedones.^{2,8} These changes can lead to an increase in acne development and ocular rosacea.^{2,8}

Guidelines suggest that patients receiving testosterone should be evaluated every 3 months for adverse

AT A GLANCE

- ▶ Androgen supports the development and function of the meibomian glands, lacrimal glands, the cornea, and the conjunctiva.
- ▶ Estrogen and androgen influence the production of all components of the tear film; therefore, a reduction in these hormones could lead to worsening DED.
- ▶ Worsening meibomian gland dysfunction, DED symptoms, and *Demodex* blepharitis are all potential side effects of HRT with testosterone.

LET'S TALK PRONOUNS

If you're not accustomed to asking your patients about their pronouns, below are some quick pointers to help make the conversation smoother.

- You cannot tell just by looking at someone whether they are gender nonconforming or what their gender identity and pronouns are.¹
- Some transgender patients will use she/her or he/him pronouns, while others may use different pronouns. Some common nonbinary (ie, gender identities that are not solely male or female) pronouns you may encounter include:¹
 - They/Them/Theirs
 - Ze/hir/hirs
 - No pronouns
- If you or your staff members make a mistake, simply apologize, correct yourself, and move on. Patients will generally be understanding when you handle the situation appropriately.²
- You can help patients feel more at ease by introducing yourself with your own pronouns. There are subtle ways to do this, such as wearing a button or pin with your pronouns displayed or including them in your professional email signature.²

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effects.² Worsening meibomian gland dysfunction, DED symptoms, and *Demodex* blepharitis are all potential side effects of HRT with testosterone.

GENDER-AFFIRMING CARE

It is important to understand what our gender-nonconforming patients may be experiencing and to treat any ocular or visual side effects caused by HRT, regardless of our individual beliefs or feelings. Patients who are undergoing these therapies may be doing so to reduce gender dysphoria and accompanying psychological and emotional distress. These patients often have already undergone significant evaluation and psychological assessment and

may be anxious about seeking care. It is up to us as their provider to make them feel safe.

Patients undergoing feminizing HRT typically are prescribed spironolactone (Aldactone, Pfizer) to block male sex hormone (ie, androgen) receptors and suppress testosterone production.⁹ Estrogen is typically added to this regimen after 4 to 8 weeks.⁹ Progesterone may also be added to help with mood, libido, and breast development.⁹

Patients undergoing masculinizing HRT are usually prescribed only testosterone.¹⁰ Neither oral methyl-testosterone nor androgen are typically used because of side effects, but rather progesterone-only birth

control until amenorrhea is achieved as testosterone levels increase.⁹

Younger patients may be on medication for puberty hormone suppression, or "puberty blockers."⁸ These will most likely be gonadotropin-releasing hormone analogues, which help to decrease the development of both primary and secondary sex characteristics.⁹

Remember, part of taking care of our patients is knowing who they are. Ask their preferred pronouns and chosen name. This is an easy way to make the patient feel you are there for them. For tips on how to start this conversation with patients, see *Let's Talk Pronouns*.

KNOW YOUR PATIENTS

The side effects of HRT are manageable, and some are even potentially beneficial to ocular health. Always make sure to really look at what medications your patients are taking so you can be prepared to meet their needs. ■

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