SKIN

IN-DEPTH REVIEW

Ocular Disease as a Comorbidity of Atopic Dermatitis

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ABSTRACT

A variety of ocular disorders are commonly encountered in individuals affected by atopic dermatitis (AD). In addition to commonly observed ocular surface disease (OSD), other comorbid eye disorders seen inherently with AD include infections, keratoconjunctivitis, cataracts, and keratoconus. Some ocular diseases are recognized as potential adverse effects of therapies used to treat AD, especially topical and systemic corticosteroids, and biologic agents that inhibit interleukins (IL) 4 and/or 13. The latter includes dupilumab (IL-4/IL-13), tralokinumab (IL-13), and lebrikizumab (IL-13), all of which may be associated with OSD. This article serves to provide a thorough review of ocular diseases that are comorbidities of AD and/or occur in association with therapies used to treat AD.

INTRODUCTION

Atopic dermatitis (AD) is a common chronic inflammatory skin disorder with significant morbidity and adverse impact on quality of life. Pediatric global prevalence varies from 2.7 to 20.1 % with the majority of patients diagnosed prior to five years of age; up to 15% are rated in the severe category of disease severity.[1] Though primarily considered a pediatric disease, a population study noted an adult prevalence of 7.3%, with 60.1% mild, 28.9% moderate, and 11% severe disease.[2]

Comorbidities include allergic and non-allergic rhinitis (40%), asthma (25.7%), food sensitivities (28.6%), and food allergies (20-40%). [3,4] Entities associated with type 2 inflammation, including nasal polyps and eosinophilic esophagitis, have a higher incidence in AD patients; other significant comorbidities include psychiatric (attention deficit hyperactivity disorder, autism, and depression) and autoimmune diseases.[3-5] A large-scale inpatient study in the United States found the prevalence of autoimmune disease to be higher in adults with AD (7.9% vs 5.7%) and children with AD (2.0% vs 1.0%) than in the same populations not affected by AD.[6] AD patients have an increased risk for chronic hand eczema, cardiovascular disease, and bacterial and viral infections (such as molluscum contagiosum).[7] An underappreciated comorbidity of AD by many clinicians is associated ocular disease (**Table 1**). With the recognized association of ocular surface diseases (OSD) noted with biologic therapies used to treat AD that inhibit interleukin-4 (IL-4) and/or IL-13, there has been an increased awareness of this comorbidity with greater focus on recognition and management.

Table 1. Ocular Surface Disease Comorbidities and Atopic Dermatitis

Disease	Prevalence in Atopic Dermatitis	Common Symptoms	Complications/Increased risk	Therapies
Dry Eye	2/3 of patients [3]	Red eyes, minimal pain, gritty eye discomfort, light sensitivity, excessive tearing, normal to intermittent blurring, most often bilateral but can be unilateral [13]	Conjunctivitis, keratitis, corneal ulceration	Hydration, artificial tears and other eye lubricants, anti-inflammatory drops, punctal plugs, contact lens
Blepharitis	22-71.4% [9, 12]	Erythematous and pruritic eyelids, red, irritated eyes, crusting or matted eyelids in morning and without visual changes or pain	Dry eyes, chalazions, styes, corneal ulceration, meibomian gland dysfunction	Warm compresses, lid massage and washing, artificial tears If not responsive, consider antibiotic ointments and possibly oral antibiotics
Conjunctivitis	31.1% - 81.4%[12, 14]	Significant pruritus, diffuse redness, watery discharge, normal vision usually bilateral (allergic) Normal vision, diffuse injection, gritty sensation, clear or serous discharge, frequently unilateral with subsequent involvement of second eye (viral) Purulent discharge, affected eyelids stuck together in the morning (bacterial)	Dry eye, infection, Atopic Keratoconjunctivitis, Vernal Keratoconjunctivitis	Antihistamine eye drops, mast cell stabilizing eye drops, corticosteroid eye drops
Atopic Keratoconjunctivitis	25-42% [19, 20] (71% in more recent study)	Intense ocular pruritus, burning, tearing, ropy, sticky mucous discharge, often foreign body sensation	Cataracts, corneal ulceration and scarring, vision loss	Avoiding rubbing eyes, artificial tears, cold compresses For mild disease: Antihistamine eye drops, mast cell

				stabilizing eye drops. For more severe disease: topical corticosteroids and calcineurin inhibitors
Vernal Keratoconjunctivitis	Seen with greater frequency in patients with atopic disease[22]	Significant ocular pruritus, photophobia, foreign body sensation, mucous discharge, ocular pain (with corneal involvement), usually bilateral but can be unilateral especially in younger patients	Corneal shield ulcers, vision loss	Avoidance of known allergies and rubbing of eyes, artificial tears, cold compresses For mild disease: Antihistamine eye drops, mast cell stabilizing eye drops For more severe disease: topical steroids and calcineurin inhibitors
Keratoconus	0.5-39% [30]	Asymmetric visual complaints, blurry or distorted vision, frequent and difficult vision correction, photophobia, increasing glare [30]	Corneal hydrops (sudden corneal swelling and opacification), corneal scarring, vision loss	Eyeglasses or contact lens, corneal collagen cross-linking, surgery (intrastromal corneal ring segments, cornea transplant)
Cataracts	1-25% [29]	Blurry or clouded vision, decreased night vision, photophobia, myopia, or asymptomatic	Vision loss	Surgery
Glaucoma open angle	Primarily associated with corticosteroid use[34]	Can be asymptomatic until significant disease develops	Peripheral vision then central vision loss, optic nerve damage, blindness	Topical beta blockers, other indicated eye drops, prostaglandins, surgery
Retinal Detachment	4-8% [36]	Chronic history of eye rubbing, facial involvement, sudden onset or increase of “floaters,” or flashes of light (photopsia), a curtain or shadow over a part of the visual field, blurred or distorted vision;	Vision loss	Surgery

		with progression, loss of peripheral or central vision[21, 23]		
Bacterial Blepharitis	Also see blepharitis above – primarily associated with *Staphylococcus aureus* (colonization in up to 86% in AD versus non-AD 25%)[27]	Associated with increased rubbing of the eyes, similar symptoms to blepharitis noted above, though may have mucopurulent discharge and more prominent erythema	Dry eyes, chalazions, styes, corneal ulceration, meibomian gland dysfunction	Warm compresses, lid massage and washing, artificial tears, antibiotic therapy
Herpes simplex keratitis	3.9-fold increase versus non-AD[39]	Blurry vision, acute pain, watery discharge, photophobia, red eye	Uveitis, post-infectious epithelial disease, keratopathy, visual loss	Topical antivirals, oral antivirals. avoidance of topical corticosteroid monotherapy, surgery (rarely)

In the past, ocular disease in AD patients was reported at 25-50%, though more recent data supports a prevalence between 85-91.3%.[8–11] This historic underestimation is compounded by a study finding that 63% of patients with OSD were asymptomatic on initial evaluation.[10] Achten et al noted that 25% of AD patients with moderate to severe OSD did not report any ocular symptoms.[9] The assessment of OSD in AD is compounded by differences in study design, sample groups, and evaluators (self vs. dermatologist vs. allergist vs. ophthalmologist). In general, studies done by ophthalmologists demonstrated a significantly higher prevalence of OSD. OSD noted with AD includes eyelid eczema, blepharitis, dry eye, conjunctivitis, atopic and vernal keratoconjunctivitis, keratoconus, cataracts, glaucoma, retinal detachment, and increase in ocular infections. In this review, ocular comorbidities in AD patients and an evaluation of the effects of AD medications on associated ocular disease will be reviewed.

DISCUSSION

Blepharitis

Blepharitis is inflammation of the eyelids and can be anterior (outer lid affecting the lash margin) or posterior (inner lid associated with the meibomian glands). Blepharitis was reported in 22-71.4% of AD patients, with lid eczema noted in 65.7% of patients with AD in Japan.[9, 12] Signs and symptoms include erythematous and pruritic eyelids; red, irritated-appearing eyes; and crusting or matted eyelids in the morning that are usually not associated with visual changes or pain.

Dry Eye

Dry eye has been defined as “a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film.”[13] It

may be accompanied by ocular symptoms, secondary to tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities.[13] Dry eye has been identified as one of the most common OSD in AD patients, affecting up to two thirds of patients.[3] The typical presentation of dry eye includes bilateral involvement, red eyes due to increase in visible scleral and conjunctival vascularity, "gritty" eye discomfort, excessive tearing, light sensitivity, normal to intermittent blurred vision.

Conjunctivitis

Conjunctivitis is defined as inflammation of the conjunctiva and can be bulbar, involving the surface of the globe to the limbus, or tarsal, which involves the lining of the eyelids. Conjunctivitis can be due to allergic, non-allergic (irritant triggered), or infectious etiologies. Variable occurrence rates of conjunctivitis have been reported, with a recent meta-analysis noting an overall prevalence of 31.1% in AD patients; allergic conjunctivitis was stated to be the most common etiology.[12] Achten et al noted tarsal conjunctivitis in 81.4% of all patients and 100% of severe AD patients evaluated.[14] Additionally, the range of conjunctivitis incidence noted in the placebo groups in dupilumab trials that included subject with moderate-to-severe AD was 2.1 -11%. [15]

Allergic conjunctivitis (AC) commonly presents bilaterally with pruritus, diffuse redness, and watery discharge and can be seasonal or perennial. Bielory documented a 42% incidence of allergic conjunctivitis in AD patients.[12] Viral conjunctivitis has a typical presentation of unilateral involvement with diffuse injection, a gritty sensation, and clear or serous discharge; subsequent involvement of the second eye may occur. Bacterial conjunctivitis has a similar presentation to viral conjunctivitis, though the discharge is more often purulent and the affected eyelids are usually matted together in the morning.

Atopic Keratoconjunctivitis

Atopic keratoconjunctivitis (AKC) is a chronic, noninfectious inflammatory condition associated with a familial history of atopy, with over 95% with concomitant AD and 87% with asthma.[16] The prevalence of AKC in AD has been reported to range between 25% to 42%, with a more recent study noting a prevalence of 71%.[17, 18] AKC classically presents in the late teenage years to early adulthood, with a peak incidence between 30-50 years of age. AKC is usually bilateral with symptoms including intense ocular pruritus; burning; tearing; a ropy, sticky mucous discharge; and often a foreign body sensation. On examination, upper and/or lower eyelid conjunctivitis can progress to exhibit giant papillary conjunctivitis. AKC can be associated with chronic blepharitis, meibomian gland dysfunction, infections (staphylococcal or herpetic), cicatricial conjunctivitis, subepithelial fibrosis, symblepharon, cataracts and keratoconus.[19, 20] With recurrent corneal involvement, neovascularization, punctate or macroepithelial erosion, and ulcerations can occur and lead to corneal scarring and visual impairment.[21]

Vernal Keratoconjunctivitis

Vernal Keratoconjunctivitis (VKC) is an uncommon seasonal OSD, which similar to AKC, may progress to exhibit corneal scarring and permanent visual changes.[22] Most children present with symptoms between 3 to 6 years of age, as 80% present prior to age 10 years and boys are 3-4 times more likely to be affected.[23] There is an increased incidence in subtropical, warm, and dry climates. VKC is usually bilateral, except in younger patients who may present with unilateral disease. Characteristic

symptoms of VKC include marked ocular pruritus, photophobia, foreign body sensation, mucous discharge, and ocular pain with corneal involvement. Classic signs of VKC include bilateral, giant "cobblestoned" papillae (present more often in the upper eyelid), conjunctival hyperemia, superficial keratopathy, and corneal shield ulcers. VKC has been classified into three forms based on location:

1. Palpebral VKC which involves the upper palpebral or tarsal conjunctiva and has potential for associated corneal involvement.
2. Limbal VKC which involves the limbus of the eye and has been reported more commonly in Asian and Black populations.[24]
3. Mixed VKC which has features of both the palpebral and limbal forms.[24]

Though usually self-limited with resolution by adolescence, persistence into adulthood my occur; complications can include shield ulcers, infectious keratitis, corneal opacities, limbal stem cell deficiency, keratoconus, and visual impairment.[25] Ali et al noted that as many as 12% of VKC patients are adults and up to 82% develop post puberty.[26] The post pubescent VKC disease is notable since patients usually do not have any signs of AD with lower incidence of corneal ulceration.[19]

Keratoconus

Keratoconus (KC) is a progressive corneal disease characterized by a progressive thinning of the corneal stroma and increased, asymmetric corneal curvature. KC can potentially cause visual impairment. Patients with AKC and VKC are at risk for development of KC. Incidence of KC in AD patients has been noted between 0.5% to 39%.[27] Symptoms include asymmetric visual complaints, blurry or distorted vision, frequent and difficult visual correction (glasses and contact lens), photophobia and increasing glare. In severe cases, there is the Munson's sign, a V-shaped outward indentation in the lower eyelid caused by the enlarged protruding cone while the patient has a downward gaze. Complications can include corneal hydrops, which can lead to stromal edema, severe pain and vision loss. Chronic eye rubbing associated with facial AD is reported to be a significant risk factor for development of KC.[28]

Cataracts

Cataracts have been observed in 5-38% of AD patients.[29, 30] They can be seen in the pediatric population and most commonly are anterior or posterior subcapsular cataracts.[21] Anterior cataracts are classically associated with AD while the posterior variety is commonly associated with corticosteroid use. Beck et al noted that the etiology of cataracts in AD has not been clearly delineated and suggested cataract formation may be related to facial distribution of AD, disease severity, eye rubbing, chronic inflammation, genetic predisposition, and corticosteroid use.[31] Symptoms may include blurry or cloudy vision, decreased night vision, photophobia, and or myopia.

Glaucoma

Though open angle glaucoma has been noted with increased frequency in AD patients versus the general population, it has primarily been attributed to corticosteroid induced increased intraocular pressure (IOP).[32] A recent study concluded that there was no causal association between AD and open angle glaucoma.[33] However, for at risk AD patients with chronic steroid use, especially on the face, periodic IOP screening is advisable as glaucoma can be asymptomatic until significant disease develops.

Retinal Detachment

The incidence of retinal detachment (RD) in AD has been observed to be between 4-8%.[34] Patients with RD consistently have facial involvement and a chronic history of eye rubbing which emphasizes the optimization of facial dermatitis.[21] In a Japanese study comparing patients with AD and RD, those who had better AD control, were less likely to have bilateral detachment and unilateral detachment.[34] In a study by Lee et al, RD in AD patients occurred at a younger age (average age 23 years old), had a poorer prognosis, more likely to bilateral, and had a marked increased risk of RD within 1 year of cataract surgery.[35]

Infections

AD patients are more prone to skin infections secondary to skin barrier defects, immune dysregulation, dysbiosis of skin flora, and staphylococcal aureus colonization.[36] The bacterial colonization in the eyelid margins and conjunctival sacs in AD patients was 86% versus 25% in non-AD patients.[27] As previously mentioned, blepharitis is markedly increased in AD. Herpetic ocular disease occurs at an increased frequency in AD patients with more reoccurrences and prolonged healing times.[37, 38] Patients with herpes simplex keratitis can present with blurry vision, acute pain, watery discharge, photophobia, and red eye.

Treatment-Associated Ocular Disease

Although ocular disease is a common comorbidity of AD, therapies used to treat AD can induce ocular adverse effects (**Table 2**).

Corticosteroids

Prolonged use of systemic corticosteroids increases the risk of cataracts, glaucoma, and central serous chorioretinopathy (CSC); increased IOP is more likely to occur with facial/periocular application of topical corticosteroid therapy for AD.[40]

Biologic Agents

Dupilumab. Dupilumab, is the first biologic agent approved in 2017 by the United States Food and Drug Administration (US FDA); it is currently FDA-approved for moderate-to-severe AD in patients 6 months of age and older, inhibiting both IL-4 and IL-13 activity via binding to the IL-4 alpha chain. A literature review of publications discussing dupilumab-associated ocular surface disease (DAOSD) reported through July 29, 2020, included 77 studies and more than 11,000 patients; the incidence rates of DAOSD in real-world prospective studies and real-world retrospective studies were 25.1% and 20.6%, respectively, versus 10.9% in the pivotal randomized, controlled trials (RCTs).[41] The specific DAOSD observed in case reports and case series were conjunctivitis (96.5%), keratitis (4.5%), blepharitis (24.4%), dry eyes (5.8%), watery eyes (4.6%), and severe conjunctivitis (23.2%).[41] The mean latency period to the onset of conjunctivitis was 14.75 weeks.[41] Only 4.5% of patients with DAOSD stopped therapy, and permanent sequelae, such as cicatricial changes, were rare.[41] Since this review, Achten et al published studies displaying a 91% incidence of OSD in moderate to severe AD patients prior to dupilumab therapy. Surprisingly, only half of the patients with DASOD reported ocular complaints before or during dupilumab therapy. The studies noted DAOSD in approximately one-third of the patients, although this percentage may have been affected by the increased percentage of patients with early diagnosis and treatment by these researchers. Achten et al noted that OSD severity was associated with AD severity, facial and/or eyelid involvement, and increased tear fluid biomarkers (periostin, IL-22, and thymus and activation-regulated chemokine [TARC]).[14]

IL-13 Inhibitors

Table 2. Ocular Disease Associations with Medications Used to Treat Atopic Dermatitis

Medication	Mechanism of Action	Common Ocular Associated Disease	Less Common Ocular Associated Disease
Antihistamines	H1 receptor blocker	Dry Eye (if necessary, preference for newer non-sedating antihistamines that have less anticholinergic, drying effects)	Those associated with dry eye
Corticosteroids	Anti-inflammatory	Anterior and posterior cataracts, glaucoma, opportunistic infections of the eye, and delayed corneal healing[40]	Systemic: Increased intraocular pressure, cataracts, central serous chorioretinopathy, hypertensive retinopathy, exophthalmos, ocular muscle palsy, blue sclera in children, refractive changes, pseudotumor cerebri[46] Topical: Increased intraocular pressure, cataracts, periocular/eyelid cutaneous atrophy
Dupilumab	IL-4/IL-13 antagonist	DAOSD including conjunctivitis seen in 10.9% of RCTs and up to 45% in prospective studies.[47] 85% of DAOSD: Dry eye, meibomian gland dysfunction, blepharitis, kerato- conjunctivitis (including vernal, atopic, follicular, and papillary) keratitis[48]	12.5% of DAOSD: limbitis, conjunctivitis[48] Rare (2.5% of DAOSD); punctal stenosis, limbal epithelial stem cell deficiency, corneal ulceration, posterior scleritis, anterior and intermediate uveitis, cystoid macular edema, chorioretinitis[48]
Tralokinumab	IL-13 antagonist	Dry eye, conjunctivitis/ keratoconjunctivitis (2-6%)[43]	Peripheral ulcerative keratitis
Lebrikizumab	IL-13 antagonist	Dry eye, conjunctivitis/ keratoconjunctivitis (6-13%)[42]	Keratitis
JAK Inhibitors	Janus kinase inhibiton	No recognized risk versus placebo[44]	Not significant versus placebo[44]

Lebrikizumab, Tralokinumab. Both IL-13 inhibitors, lebrikizumab and tralokinumab, are US FDA-approved for moderate-to severe AD in adolescents and adults, and have been associated with conjunctivitis (7.5% and 6%, respectively, in RCTs) and keratitis.[42, 43] These percentages are lower than those noted with dupilumab, however, a recent systematic review and network meta-analysis of RCTs showed that odds ratios (ORs) for conjunctivitis were 2.88 for dupilumab, 2.58 for lebrikizumab, and 2.46 for tralokinumab.[44] With increased use of IL-13 inhibitors, further information will likely be forthcoming regarding the potential for associated ocular disease with these agents.

Janus Kinase (JAK) Inhibitors.
OSD has not been identified as a recognized adverse effect directly Associated with use of JAK inhibitors. A Canadian expert panel concluded that there was no evidence that JAK inhibitors increased the incidence of OSD in patients with AD.[45]

Identification of Ocular Disease

Ocular surface diseases (OSDs) are common yet underdiagnosed comorbidities in AD, affecting up to 91% of AD patients; as many as a quarter of the patients with moderate to severe OSD can be asymptomatic.[11] If not recognized and/or left untreated, OSD can potentially lead to significant morbidity including reduced quality of life and visual impairment.

Thyssen et al concluded that dermatologists should be aware of the following ocular conditions associated with AD: allergic conjunctivitis, blepharitis, eyelid eczema, keratoconjunctivitis, keratoconus, ocular surface infections (bacterial or viral), cataracts, and increased intraocular pressure (glaucoma) secondary to corticosteroid treatment.[49] These authors noted that it is prudent for dermatologists to be vigilant for "red flag" signs and symptoms: moderate and severe ocular redness, severe blepharitis, ongoing viral ocular infections, such as herpes simplex, worsening or persistent eye pain, eye symptoms that continue despite topical therapies, light sensitivity, or vision changes.[49] An approach assessing OSD via a review of "red flag" symptoms and documentation of eye disease, eye rubbing behavior, and use of ophthalmic medications should be considered in each visit.[40]

Standardized assessment tools for OSD in AD patients include the Utrecht Ophthalmic Inflammatory and Allergic disease (UTOPIA) evaluation from Achten, and systems created by Shim and a recent British consensus meeting (**Table 3**).[14,50] The UTOPIA scoring requires a slit lamp and is best suited for completion by an ophthalmologist. The Shim scoring system is based on DAOSD risk factors including older age, history of conjunctivitis, and a baseline Eczema Area and Severity Index (EASI) score ≥ 28; the predicted risks for AD patients rated with 0, 1, 2, 3, 4, and 5 points were 5.8%, 14.2%, 30.7%, 54.3%, 76.2%, and 89.6%.[50] A collaboration between the British Association of Dermatologists (BAD) and the Royal College of Ophthalmologists resulted in a consensus statement for the management of biologic associated ocular disease that included the creation of a succinct scoring system (RAPID): Redness plus any one of the following symptoms: acuity loss; pain; intolerance of light; and damaged cornea.[48] If a patient has redness plus at least one other symptom, immediate referral to an ophthalmologist is strongly recommended. The expert consensus amended their recommendation for children under 7 years of age (secondary to an increased tolerance of ocular surface inflammation) that if any ocular symptoms are present, immediate referral to the ophthalmologist is indicated.[48] This last

Table 3. Scoring Systems for Ocular Surface Disease

Name	Scoring System Details	Advantages	Disadvantages
Utrecht Ophthalmic Inflammatory and Allergic disease (UTOPIA)	Each of the following characteristics of ocular surface disease, blepharitis, meibomian gland dysfunction, tarsal conjunctivitis, bulbar conjunctivitis, limbitis, limbal vascularization, punctate corneal epitheliopathy, and hurricane corneal epitheliopathy (altered staining pattern) is assessed by severity: none (0), mild (1), moderate (2), severe (3) Overall score of 0 - no disease, 1-4 - mild disease, 5-8 - moderate disease, 9 or greater - severe disease[51]	Accurate and reproducible	Requires slit lamp, best if performed by an ophthalmologist; not realistic for the non-ophthalmologist due to insufficient training and lack of slit lamp availability
Shim scoring system	Points were calculated by: age less than 25 years. (0); age 25-39 years (1), age greater than 39 years (2); baseline EASI score greater than 27 (1) Risk of DAOSD for 0,1,2,3,4, and 5 points were 5.8%, 14.2%, 30.7%, 54.3%, 76,2%, and 89.6% respectively.[50]	Easily assessed and helpful for determination of patient risk	Formulated for risk of OCD in dupilumab patients, newer scoring system
RAPID	For ocular surface disease, the RAPID acronym (R: redness, A: acuity, P: pain, I: intolerance to light, D: damage to cornea Immediate referral to an ophthalmologist is indicated for redness (mild, moderate, or severe bulbar redness-conjunctival) plus any one of the following symptoms: acuity worsening or loss (no requirement of a Snellen chart), pain (more than a foreign body sensation or irritation), intolerance of light (photophobia/sensitivity), and/or damage to cornea (visual, opacity, or purulent discharge) If the patient is under 7 years of age (secondary to an increased tolerance of ocular surface inflammation), if any ocular symptoms are observed, an immediate ophthalmology referral should be made[48]	Helps to standardize process of accessing ocular disease; a positive RAPID assessment will easily determine the necessity for an ophthalmology assessment	Could be inconsistency in scoring due to differences in clinician assessments though less likely secondary to simplicity

scoring system could be a consideration for all AD patients.

It is important to recommend ophthalmologic evaluation early in the course of AD as initial and sequential periodic evaluations are significant due to the frequency of ocular disease in AD patients. Patients utilizing topical corticosteroids, especially on the face, may require more frequent evaluation, especially for IOP and cataracts. The availability of newer nonsteroidal topical agents for AD, including for children, reduces the dependence on topical corticosteroid therapy on the face which will help reduce the ocular adverse effects associated with topical corticosteroid therapy. During office visits, clinicians and their staff are encouraged to ask patients about ocular symptoms to reduce the risk of dry eye and other OSD.

To help prevent DAOSD, regular use of lubricating, preservative free eye drops may be beneficial.[52] Other guidance prior to initiation of dupilumab and anti-IL-13 medications include: avoidance of excessive hand-to-eye contact, eye rubbing, decreasing aeroallergen exposure, warm compresses for inflamed eyelids, cleansing with a preservative-free eye wash, humidifier use, and staying well-hydrated.[22] Educating AD patients on the increased prevalence of OSD both in AD and with associated therapies is paramount, especially when defining the “red flag” symptoms. Despite a prevalence of DAOSD of up to 45% in a study that followed patients up to 4 years, the discontinuation of dupilumab occurred in only 0.5% of patients with most OSD noted early in therapy and with an 87% resolution rate.[53] For patients who experience inadequate response and/or adverse effects with dupilumab, including conjunctivitis, there have been case reports with successful switches to tralokinumab [54]and JAK inhibitors (abrocitinib).[55]

CONCLUSION

There is a need for research further delineating the relationship between AD, OSD, and biologic therapies, as well as studies assessing time-efficient screening protocols that will continue close collaboration with dermatologists and ophthalmologists.

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