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Ocular Surface Disease during dupilumab treatment in patients with atopic dermatitis, is it possible to prevent it?

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Dear Editor,

Atopic dermatitis (AD) is the most common inflammatory skin disease that affects up to 20% of children and 2-5% of the adult population. This disorder can have a dramatic impact on the quality of life, in fact, negatively affects sleep, productivity, mood, and quality of life. Recently, encouraging results have been obtained with the use of dupilumab. This drug is a human monoclonal antibody directed against the shared α sub-unit of the interleukin (IL)-4 and IL-13 receptor approved for adult patients affected by moderate-to-severe AD.¹⁻²

Clinical trials and real-life data have demonstrated efficacy and safety of this treatment, however, trials have also shown an increased incidence of conjunctivitis.³ Indeed, it would be more correct to use the term of Ocular Surface Disease (OSD), an umbrella term that includes all types of dupilumab-induced ocular inflammation including dry eye, conjunctivitis, and keratitis. Interestingly, the incidence of OSD is not observed in patients with asthma, chronic sinusitis, and eosinophilic esophagitis treated with Dupilumab.⁴ It was hypothesized that dupilumab may have different effects on AD, or that this may be due to properties specific to the eye, periocular dermatitis has also been attributed to contact allergen hypersensitivity due to dupilumab induced increased of T helper 1 response. Another observation, consider the possibility that Demodex mites may prosper due to the decreased IL-4 and IL-13 levels of ocular cytokines,⁵ leading to IL-17-mediated inflammation and a disease similar to ocular rosacea. However, IL-17 is decreased in dupilumab-treated patients and the disease course of conjunctivitis is too short in comparison with

ocular rosacea. Moreover, blocking α sub-unit of the IL-4 receptor causes increased systemic bioavailability of free IL-4 and IL-13. This maybe causes inflammatory symptoms whether by stimulating the CD40-dependent IgE production via B cells or by activating the IL-13 R alpha 2 receptor that has not been blocked by dupilumab or both.⁶ Why OSD occurs exclusively in patients with AD remains unclear; however, some authors have found, through conjunctival biopsies, the decreased density of intraepithelial goblet cells suggesting that OSD occurs secondary to tear film alteration and subsequent conjunctival irritation.⁷ Based on these observations, we hypothesized that the use of artificial tears could prevent the occurrence of ocular complications.

Since February 2019, we have observed 30 adult patients with severe AD undergoing dupilumab treatment. These patients received the drug as recommended dosage, an initial dose of 600 mg followed by 300 mg injected every other week. During the first administration of the monoclonal antibody, patients were instructed to instill artificial tears, one drop per eye two times a day, and they were advised to avoid too dry environments and abuse of smartphones or similar devices. After six months of treatment, nobody of the patients examined reported ocular symptoms or the appearance of conjunctivitis and keratitis. It should be noted that among the patients they were not present visual display terminal workers and contact lens users.

Conjunctivitis and other ocular complications that develop after the administration of dupilumab for AD may be severe enough to necessitate stopping the therapy, indicating the importance of early prevention. Surely our experience is limited due to the small number of patients examined, but it would be advisable to try to gather everyone's experiences, and create an ad hoc protocol, possibly in collaboration with ophthalmologist specialists, to prevent the onset of this worrying complication.

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