Incidence, prevalence, and risk of selected ocular disease in adults with atopic dermatitis

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Background: Ocular comorbidities are common in atopic dermatitis (AD) as the result of the disease itself or the use of medication. No large-scale epidemiologic data exist on the prevalence of ocular comorbidities in adults with AD.

Objectives: We sought to examine the prevalence and risk of selected ocular comorbidities in adult patients with AD.

Methods: All Danish individuals ≥18 years of age were linked in nationwide registries. Adjusted hazard ratios (HRs) were estimated by means of Cox regression.

Results: A total of 5766 and 4272 adults were categorized as having mild and severe AD, respectively. At least 1 prescription of anti-inflammatory ocular agents was claimed in 12.0% and 18.9% of patients with mild and severe AD, respectively. In adjusted analysis, the HR of conjunctivitis was 1.48 (95% confidence interval [CI], 1.15-1.90) for mild AD and 1.95 (95% CI, 1.51-2.51) for severe AD. The HR of keratitis was 1.66 (95% CI, 1.15-2.40) for mild AD and 3.17 (95% CI, 2.31-4.35) for severe AD. For adults with severe AD, the HR for keratoconus was 10.01 (95% CI, 5.02-19.96). AD was associated with "cataract only" in individuals <50 years of age.

Limitations: A limitation of the study is that observational studies cannot establish causality.

Conclusions: Adults with AD had a significant and disease severity–dependent increased risk of development of conjunctivitis, keratitis, and keratoconus compared with that of the general population. (J Am Acad Dermatol 2017;77:280-6.)

Key words: atopic dermatitis; conjunctivitis; epidemiology; ocular; prevalence; risk.

Atopic dermatitis (AD) is a prevalent inflammatory skin condition. Ocular comorbidities are common and are included in the widely acknowledged Hanifin and Rajka criteria, which contain most factors that encompass AD as a syndrome. These describe recurrent conjunctivitis, predisposition to keratoconus, and anterior subcapsular cataracts as minor criteria.[1-3] Whereas atopic

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glaucoma has been suggested as its own entity, glaucoma as well as infectious keratoconjunctivitis and cataract may occur as complications of corticosteroid therapy.

Recently, dupilumab, a human monoclonal antibody against interleukin (IL)-4 receptor-α, was successfully used in a trial against AD in adults.[4] However, conjunctivitis without specified cause occurred significantly more frequently in the dupilumab-treated groups than in the placebo group (SOLO 1, 2% vs 7-11%; SOLO 2, 1% vs 9%),[4] and 1 patient left the trial because of conjunctivitis. Moreover, the recent phase 2 trial with the IL-13 inhibitor lebrikizumab, used for adult AD (the TREBLE study), showed a weak trend for more cases of conjunctivitis in the active group (oral presentation at the 2016 European Academy of Dermatology and Venereology congress).

CAPSULE SUMMARY

- Patients with atopic dermatitis have an increased risk of ocular comorbidities.
- Epidemiologic data from nationwide Danish registries confirm that adults with atopic dermatitis have an increased risk of conjunctivitis, keratitis, and keratoconus compared with that of the general population.
- Introduction of biologic agents to treat adults with atopic dermatitis may further increase the risk.

The previous observations have led to emerging concern about the incidence of conjunctivitis during near-future biologic AD therapy and the possible long-term consequences thereof. Because there currently are no large-scale epidemiologic data on the prevalence or incidence of conjunctivitis and related ocular comorbidities in adults with AD, we examined these in adult patients with AD on the basis of the nationwide Danish registry data.

METHODS

Data sources

We used Danish nationwide registries, which enable cross-linkage of data on medication use, diagnoses, vital statistics, and socioeconomic data at an individual level.[5-7]

Study population

The study comprised all Danish adults ≥18 years of age on January 1, 1997. Study commencement was the latter of either January 1, 1997, or an adult diagnosis of AD, if appropriate. Patients were classified as having adult AD if, after their 18th birthday, they had received a diagnosis (inpatient or ambulatory) of AD by a dermatologist (International Classification of Diseases [ICD]-8 691 and ICD-10 L20) recorded in the Danish National Patient Registry. Control subjects and patients were followed from study commencement until December 31, 2012, death, migration, or the occurrence of an endpoint, whichever came first. Patients were classified as having severe AD if they received or had received systemic therapy consistent with severe disease (methotrexate, azathioprine, mycophenolate mofetil, systemic corticosteroids, psoralen plus ultraviolet A, or cyclosporine). Patients who did not receive such therapy were classified as having mild AD. Information on tax-reported household income was obtained from Statistics Denmark.

Outcomes

The primary endpoints were a diagnosis of conjunctivitis (ICD-10 H10, B30), keratitis (ICD-10 H16), keratoconus (ICD-10 H18.6), cataract (ICD-10 H25, H26, H28), and glaucoma (ICD-10 H40, H41, H42), respectively, as well as a claimed prescription for ocular anti-infective agents (anatomic therapeutic chemical S01A), ocular anti-inflammatory agents (anatomic therapeutic chemical S01B), and ocular combination products, that is, those containing both anti-infective and anti-inflammatory agents (anatomic therapeutic chemical S01C), respectively.

Statistical analysis

We described baseline characteristics with means and standard deviations for continuous variables and frequencies and percentages for categorical variables. The baseline prevalence was determined as the percentage of individuals who had received one of the prespecified diagnoses or claimed a prescription, as appropriate, within the past 5 years before study commencement. SAS v9.4 (SAS Institute Inc, Cary, NC) and STATA v13.0 (StataCorp, College Station, TX) were used to summarize incidence rates per 1000 person-years, and Cox regression models were performed to obtain hazard ratios (HRs). Incidence during follow-up was calculated for all individuals who had not received such diagnosis or prescriptions before the study. Sensitivity analyses were performed in which those with prevalent disease were not excluded. HRs were calculated as age- and sex-adjusted and fully adjusted (in which age, sex, socioeconomic status, and health care consumption were considered). Socioeconomic status was calculated as an age-standardized index