

ORIGINAL ARTICLE

Topical corticosteroids in atopic dermatitis and the risk of glaucoma and cataracts

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Introduction: There is concern about the development of glaucoma and cataracts associated with topical corticosteroid use in patients with atopic dermatitis (AD).

Objective: We evaluated glaucoma and cataract development in patients with AD to determine whether they are associated with the cumulative dose of topical steroids and the use of topical corticosteroids on the eyelids and periorbital region.

Methods: In all, 88 patients with AD were recruited from the University Medical Centre Utrecht. Patients were interviewed and completed a questionnaire assessing different factors such as AD involvement of eyelids and periorbital skin. The use of corticosteroids in previous years was obtained from pharmacy records. A complete ophthalmologic examination was performed for the presence of glaucoma and cataracts.

Results: Of the 88 patients (41 men and 47 women), with an average age of 37.2 ± 14.3 years (mean $\pm$ SD), one patient had transient ocular hypertension and one patient had optic disc cupping without any glaucomatous defects in his visual field. Seven patients were given the diagnosis of cataracts (one AD-related, two corticosteroid-induced, and 4 age-related). Both patients with corticosteroid-induced cataracts had also used systemic corticosteroids. In all, 37 of the 88 patients had used topical corticosteroids (class III and IV) on the eyelids and periorbital region, with an average frequency of 3.9 days per week and 6.4 months per year for 4.8 years.

Limitations: Small sample size, objectiveness of patient recall about the use of topical corticosteroids on the eyelids/periorbital region, overestimation of topical corticosteroid use from pharmacy records, and lack of information on lifetime corticosteroid use were limitations.

Conclusions: In this retrospective study glaucoma was not seen; two patients with AD had corticosteroid-induced cataracts, which were probably caused by the use of systemic corticosteroids. The application of topical corticosteroids to the eyelids and periorbital region, even over longer periods of time, was not related to the development of glaucoma or cataracts in this study population. (J Am Acad Dermatol 10.1016/j.jaad.2010.01.035.)

Key words: atopic dermatitis; cataract; glaucoma; topical corticosteroids.

Atopic dermatitis (AD) is a relapsing chronic inflammatory disease often affecting large skin areas. Topical corticosteroids are the most important treatment modality for AD. Compliance to therapy with topical corticosteroids is, however, low because of a widespread concern

Abbreviations used:

AD: atopic dermatitis
AS: anterior subcapsular
IOP: intraocular pressure
IQR: interquartile range
PS: posterior subcapsular

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about local and systemic side effects.¹ If eczema is present in the periorbital region and on the eyelids, patients and physicians are even more hesitant to use topical corticosteroids fearing skin atrophy, glaucoma, and cataracts. This often leads to undertreatment of the eczema with a risk of ophthalmologic complications such as keratoconus and abrasion of the cornea caused by chronically rubbing the eyes.

Oral corticosteroids, corticosteroid-containing eye drops, and periocular steroid injections can lead to elevation of intraocular pressure (IOP) and subsequent glaucoma.²⁻⁷ Corticosteroid eye drops bear, however, the greatest risk. The use of nasal or inhaled corticosteroids has not been found to be associated with an increase in IOP, provided that patients have no other risk factors such as a positive family history.⁸⁻¹⁰ Several case reports suggest that frequent application of topical corticosteroids over longer periods of time on the eyelids and periorbital region may induce glaucoma in patients with AD.¹¹⁻²¹

Based on location there are 5 types of cataracts, namely nuclear, cortical, anterior subcapsular (AS), posterior subcapsular (PS), and a combination of these. Age-related cataracts are the nuclear or cortical types, diabetes-related cataracts are cortical or PS types, and cataracts associated with cigarette smoking are nuclear or PS types.²² In 1960 Black et al²³ reported an association between the use of systemic corticosteroids and the development of PS cataract. Of 44 patients with rheumatoid arthritis treated with systemic corticosteroids, 39% had PS cataracts. The use of corticosteroid-containing eye drops and inhaled corticosteroids in asthma have also been associated with PS cataracts.²⁴ AD is associated with AS cataracts, but differentiating AD-associated cataracts from corticosteroid-induced cataracts may be difficult, because PS cataracts or a combination of both types have also been described as associated with AD.²⁵⁻²⁷ Furthermore, it may be difficult to differentiate early lens opacities in the posterior lenticular pole as steroid-induced or other types.²⁸

It is not known by which route topical corticosteroids induce glaucoma or cataract. Direct absorption through the skin of the eyelid has been postulated.

Absorption from spills of corticosteroid ointment over the lid margin seems more likely, because bits of cosmetics can be observed in women's tear film. Furthermore, it has been shown that topical corticosteroids present in sweat running down the eyelids contaminate the conjunctival sac. A third possibility is systemic absorption of topical corticosteroids with distribution to the eye.²⁹

The aim of this retrospective study was to evaluate whether topical corticosteroids, both cumulative use and use on the eyelids and periorbital region, are associated with the development of glaucoma and cataracts in patients with AD.

METHODS

Patients

In all, 88 patients with AD (41 men and 47 women), average age 37.2 ± 14.3 years (mean $\pm$ SD), were recruited from the outpatient clinic and clinical department of the University Medical Centre Utrecht. The diagnosis of AD was made

according to the criteria of Hanifin and Rajka.³⁰ All patients included had moderate to severe AD. Patients were given the diagnosis for allergic asthma and allergic rhinitis on the basis of their personal history and medication use for these diseases. The local ethical committee approved this study. Patient characteristics are shown in Table I.

Questionnaire

Data on lifestyle parameters, such as alcohol use and smoking, presence of additional diseases, hypertension, and diabetes mellitus,³¹⁻³⁵ were obtained by the use of a questionnaire.

Cumulative topical corticosteroid use

Cumulative amount of topical corticosteroids used during the 2 years before inclusion of the 88 patients was calculated using individual patient pharmacy prescription records. In addition, of 73 patients, the cumulative use of topical corticosteroids during 5 years before inclusion was calculated. The pharmacy records were also used to evaluate the additional use of oral (cumulative dose expressed in milligrams of prednisone), inhaled, and nasal corticosteroids during the same time period. In The Netherlands there is not one unified pharmacy

CAPSULE SUMMARY

- Frequent application of class III and IV topical corticosteroids to the eyelids in patients with atopic dermatitis is not associated with the development of glaucoma or cataracts.
- The cumulative dose of topical corticosteroids in patients with atopic dermatitis is not related to the development of glaucoma or cataracts.
- Regular screening for glaucoma and cataracts in patients with atopic dermatitis using high cumulative amounts of potent topical corticosteroids is recommended, especially if additional risk factors are present.

Table I. Atopic dermatitis patient characteristics (n = 88)

	Patients, median; IQR
Age, y, mean $\pm$ SD	37.2 $\pm$ 14.3
Sex, M/F*	41/47
Total IgE, kU/L	2483; 625-8005
TARC, pg/mL	1233; 640-3504
Eczema on eyelids and periorbital region*	58
Other atopic diseases*	
Asthma	27
Allergic rhinitis	18
2-y Topical corticosteroid use, g (n = 88)	735; 395-1670
5-y Topical corticosteroid use, g (n = 73)	1630; 815-3175
5-y Systemic corticosteroid use, mg (n = 73)	310; 0-1741

F, Female; IQR, interquartile range; M, male; TARC, thymus and activation-regulated chemokine.

*Expressed as number of patients.

record system, however, individual patient pharmacy prescription records were checked to encompass the retrospective study period. Topical corticosteroids are not obtainable without a prescription in The Netherlands, therefore it is not necessary to account for nonprescription use. Data pertaining to the use and frequency of topical corticosteroids on eyelids and periorbital region were obtained by the use of a questionnaire. The use of topical immunomodulating agents (eg, pimecrolimus and tacrolimus) was not captured. The classification of potency of topical corticosteroids was according to the US classification of classes I to VII (class I being the most potent).

Ophthalmologic examination

A complete ophthalmologic examination of the patients was performed. The signs of early lens opacification were observed biomicroscopically. IOP was measured by Goldmann Tonometry (Haag-Streit, Koeniz, Switzerland). Signs of early glaucoma were investigated using both the tonometry and the cup/disc ratio of the optic disc seen during ophthalmoscopy.

Statistical analysis

Statistical analysis was performed using software (SPSS for Windows, Version 12, SPSS Inc, Chicago, IL). When skewed distributions in outcome parameters were observed, median and interquartile ranges (IQRs) were described. No further statistical analysis was performed because of the small number of patients in this study.

RESULTS

Topical corticosteroid use

The patients used mainly class III (fluticasone propionate and betamethasone valerate) topical corticosteroids on the body and both class III and IV (triamcinolone acetonide) topical corticosteroids on the eyelids and periorbital region. The median use of topical corticosteroids of all patients in the 2 and 5 years before investigation was 735 g (395-1670 IQR) and 1630 g (815-3175 IQR), respectively. The median use of systemic corticosteroids 5 years before inclusion was 310 mg (0-1741 IQR). In all, 58 of the 88 patients had eczema on the eyelids and in the periorbital region. In all, 37 patients regularly used topical corticosteroids on the eyelids and periorbital region. The average frequency of application of topical corticosteroids on the eyelids and periorbital region was 3.9 days per week, 6.4 months per year for 4.8 years. One of 37 patients using topical corticosteroids on the eyelids and periorbital region was given the diagnosis of corticosteroid-induced cataracts. This patient had a history of long-term systemic corticosteroid therapy, smoked, and had a high alcohol intake (75 U/wk) (Tables I and II).

IOP and glaucoma

Only one patient showed ocular hypertension at initial examination, with a pressure of 32 mm Hg in the right eye and 31 mm Hg in the left eye, without symptoms of vision loss. Subsequent investigation did not reveal any glaucomatous defects in visual field or any cupping or atrophy of the optic disc. The patient did not receive treatment for her ocular hypertension, and repeated eye pressure measurements 1 month and 5 months later were near normal (pressure right eye 23 and 22 mm Hg, respectively, and left eye 23 and 21 mm Hg, respectively). This patient had used a cumulative dose of 890 g and 1750 g of topical corticosteroids in the 2 and 5 years, respectively, before investigation. In addition she had used two corticosteroid preparations of class III potency (fluticasone propionate and betamethasone valerate) on her eyelids daily during a few months before and 4 to 5 times per week after the initial examination. A second patient had cupping of his optic disc without ocular hypertension or symptoms of vision loss. Further investigation did not reveal any glaucomatous defects in his visual field. None of the 88 patients had a positive family history for ocular hypertension or glaucoma.

Cataracts

Seven patients were found to have cataracts, as shown in Table III. One patient was given the

Table II. Topical corticosteroid use on eyelids and periorbital region in patients with atopic dermatitis

	All topical corticosteroids n = 37 (mean $\pm$ SD)	Class III topical corticosteroids n = 14 (mean $\pm$ SD)	Class IV topical corticosteroids n = 23 (mean $\pm$ SD)
Days per week	3.9 $\pm$ 2.6	3.9 $\pm$ 2.8	3.9 $\pm$ 2.5
Months per year	6.4 $\pm$ 3.9	6.7 $\pm$ 3.9	6.3 $\pm$ 3.9
Years	4.8 $\pm$ 5.6	5.7 $\pm$ 7.3	4.3 $\pm$ 4.5

Table III. Characteristics of patients given diagnosis of cataracts (n = 7)

Sex	Age, y	Smoking, cigarettes/d	Alcohol, U/wk	Diagnosis of ophthalmologist	AD on eyelids	Total topical corticosteroid use, g*	Topical corticosteroids on eyelids	Frequency of use on eyelids	Use of systemic corticosteroids, mg [†]
M	23	0	1	AD-related unilateral cataract	Yes	240	None	na	None
M	46	10	75	Corticosteroid-induced bilateral cataracts	Yes	2780	Class IV	7 d/wk, 12 m/y during 6 y	2110
F	60	0	0	Corticosteroid-induced bilateral cataracts	Yes	410	None	na	6570
F	78	0	4	Age-related bilateral cataracts	No	2480	na	na	2381
M	48	0	0	Age-related unilateral cataract	Yes	1930	None	na	2840
M	53	0	8	Age-related bilateral cataracts	No	1070	na	na	5200 [‡]
M	74	0	14	Age-related bilateral cataracts	No	1760	na	na	475

AD, Atopic dermatitis; F, female; M, male; na, not applicable.

*Use during 2 y before investigation.

[†]Prednisone use 5 y before investigation.

[‡]Use during 4 y before investigation.

diagnosis of an AD-induced cataract (unilaterally), because of the AS location of the cataract and young age at time of diagnosis. In the 2 years before examination (the use during 5 years could not be calculated) he cumulatively used 240 g of topical corticosteroids; he did not apply topical corticosteroids on the eyelids and periorbital region and he had not used systemic corticosteroids. Two patients were given the diagnosis of corticosteroid-induced PS cataracts (both bilateral). Both patients had a history of long-term systemic corticosteroid therapy. As mentioned previously, one of these patients used topical corticosteroids on eyelids and periorbital region and had additional risk factors, namely smoking and alcohol use. Four patients were given the diagnosis of age-related cataracts, 3 men and one woman with ages ranging from 48 to 78 years. None of the patients with cataracts had hypertension or diabetes mellitus. There was no difference in the amount of inhaled or nasal corticosteroids between patients with and without cataracts (data not shown).

DISCUSSION

Only one of 88 patients with AD had a transient increase in IOP. The IOP normalized despite continued use of class III topical corticosteroids on her eyelids, suggesting that there was no relation between the high IOP and the use of corticosteroids. In our study 37 of 58 patients with AD and eczema in the eyelids and the periorbital area applied corticosteroids on a regular basis on this region and even in the 23 patients using class III corticosteroids with a mean frequency of 4 days per week, for several months, no glaucoma was found. These data suggest that regular application of class III and IV topical corticosteroids does not induce an increase in IOP and glaucoma.

There are no data on the prevalence of glaucoma or ocular hypertension in patients using topical corticosteroids on the eyelids and in the periorbital area. Thus far, only case reports have been published. Cubey¹¹ described a patient with AD who developed glaucoma after using fluocinolone acetate 0.1% ointment on his face and eyelids every

night for 7 years. In our patient population there were 4 patients who had used topical corticosteroids (class III and IV) daily, 12 months per year for a varying number of years. None of these patients developed glaucoma. Sahni et al¹⁷ described a patient with AD who developed glaucoma after having used 100 g of betamethasone dipropionate 0.05% every 2 weeks for 16 months (cumulative amount 3200 g) including frequent application of topical corticosteroids in the periorbital region. In this patient glaucoma was probably caused by systemic absorption of large amounts of potent topical corticosteroids. There was one patient in the current study who used almost 3200 g of mainly class III topical corticosteroids for 16 weeks; however, he did not develop glaucoma or cataracts. All other patients had used less than 2200 g in 16 months. The patient with glaucoma reported by Zugerman et al,¹² had contact allergy and had used both triamcinolone acetonide 0.1% on his eyelids for a few months and had corticosteroid injections in the periorbital region. The development of glaucoma in this patient may be ascribed to the periorbital steroid injections. The patient who was reported by Ross et al²¹ had therapy-resistant glaucoma and retrospectively it emerged that he had used hydrocortisone and betamethasone on his face and periorbital eczema approximately twice a week during the previous 2 years, but not regularly in the 3 months before his first visit. Michaeli-Cohen et al²⁰ reported two patients with AD with glaucoma. A 45-year-old man given the diagnosis of cataracts and glaucoma had treated his facial AD with class III topical corticosteroids for a number of years. The second patient was a 35-year-old woman with AD who developed glaucoma after applying betamethasone cream to her face and to her eyelids since her early teens. She had myopia and her mother also had glaucoma.

Additional factors such as a family history of glaucoma, pronounced myopia, anterior segment trauma, history of diabetes mellitus, or a connective tissue disorder may increase the risk of steroid-induced glaucoma.⁴ Glaucoma caused by frequent application of topical corticosteroids during the short term may remit after stopping topical therapy³; this may have biased our results. However, it also has been reported that IOP may not return to normal upon cessation of the topical corticosteroid, especially in those patients with long duration of use.³⁶

Patients with increased ocular pressure experience few symptoms and therefore visual impairment may be advanced when symptoms do arise. For that reason patients at risk and those using high cumulative amounts of potent topical corticosteroids should be screened for glaucoma on a regular basis.

Observational studies in patients with eczema and psoriasis on maintenance therapy with class III topical corticosteroids (0.1% betamethasone valerate) show that prolonged application (varying from months to years) in quantities of less than 20 g per week had no significant effect on adrenal gland function in the majority of patients.³⁷⁻⁴⁰ This suggests that these amounts may not induce systemic side effects; however, prospective studies to confirm this have not been performed. The mean cumulative amount in our study population (735 g in 2 years and 1630 g in 5 years) is much lower than the above-mentioned amount.

In our study population the prevalence of AD-related cataracts, corticosteroid-induced cataracts, and age-related cataracts was 1.1%, 2.3%, and 4.5%, respectively. The prevalence of cataracts in patients with AD is increased compared with the general population and varies between 8% and 17%.^{25,41-44} Distinguishing corticosteroid-induced cataracts from AD-related cataracts may be a source of bias in cataract studies in patients with AD. Amemiya et al⁴⁵ found cataracts in 16 eyes of 11 of 44 patients (25%): AS cataracts in 4 eyes, PS cataracts in 8 eyes, intermediate type cataracts in two eyes, and mature type cataracts in two eyes. Katsushima et al⁴⁴ found cataracts in 22 eyes of 13 of 75 patients with AD (17.3%): AS cataracts in 3 eyes, PS cataracts in 8 eyes, a combination of AS and PS cataracts in 9 eyes, and mature cataracts in two eyes. The use of topical corticosteroids on facial skin was not significantly associated with cataract formation in these patients with AD. Taniguchi et al⁴⁶ reported cataracts in 34 eyes in 20 of 79 patients with AD (25%): AS cataract in one eye, PS cataracts in 18 eyes, a combination of AS and PS cataracts in 7 eyes, mature cataracts in 4 eyes, and early cataracts in 4 eyes. This study did not show a relation between cataracts and the duration of topical corticosteroid use on the face. However, neither study reported the potency and frequency of application of topical corticosteroids.

In our study both patients with corticosteroid-induced cataracts had regularly used systemic corticosteroids. One patient also had applied topical corticosteroids to the eyelids on an almost daily basis. In this patient the presence of cataracts was probably caused by the use of systemic corticosteroids. The results of our study and the findings of Katsushima et al⁴⁴ and Taniguchi et al⁴⁶ suggest that the use of topical corticosteroids on the eyelids and periorbital region is safe with respect to the induction of cataracts. Patients using systemic corticosteroids have an increased risk for developing cataracts and should be regularly screened by an ophthalmologist.

To our knowledge this is the first report that evaluates the occurrence of glaucoma and cataracts in relation to days, months, and years of topical corticosteroid use on the eyelids and periorbital region, and that evaluates the effect of cumulative use of topical corticosteroids. Limitations of our data are the small sample size, objectiveness of patient recall about the use of topical corticosteroids on the eyelids/periorbital region, overestimation of topical corticosteroid use by pharmacy records, and lack of lifetime corticosteroid use.

In conclusion, in our study two patients with AD had corticosteroid-induced cataracts, one an AD-related cataract, and 4 age-related cataracts. The patients with AD and corticosteroid-induced cataracts had regularly used systemic corticosteroids. There were no patients with glaucoma. In our study population the frequent application of topical corticosteroids (class III and IV) on the eyelids and periorbital region, even over longer periods of time, was not related to the development of glaucoma or cataracts. Also, the reported 2- and 5-year cumulative amount of topical corticosteroids was not associated with the development of glaucoma or cataracts. Still, patients with AD using high cumulative amounts of potent topical corticosteroids or using oral corticosteroids should be regularly screened for glaucoma and cataracts, especially if additional ophthalmologic or systemic risk factors are present.

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