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## Original Article

## Influence of topical steroids on intraocular pressure in patients with atopic dermatitis

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## ABSTRACT

**Background:** Topical corticosteroids (TCS) can induce adverse effects, such as skin atrophy. Although TCS can cause increases in intraocular pressure (IOP), the effects of daily TCS use on IOP have not been fully elucidated. We evaluated the clinical doses of TCS and the change in the IOP during the daily treatment of atopic dermatitis (AD).

**Methods:** We collected clinical data on a total of 65 patients who were diagnosed with AD and underwent 2 or more IOP measurements at our hospital.

**Results:** Mean monthly facial steroid volumes of  $\leq 11.8$  g and  $\leq 15.0$  g of TCS were applied to 90% of the patients aged 2–12 years and those aged  $\geq 13$  years, respectively. During the treatment, there were no TCS-related increases in IOP in any patient.

**Conclusions:** Our study suggests that TCS might not cause increases in IOP at the abovementioned doses. However, the IOP of steroid responders is known to be highly responsive to steroids. Therefore, patients who have steroids applied to their eyelids had better undergo regular IOP measurements at ophthalmological clinics.

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## Introduction

Atopic dermatitis (AD) is a chronic pruritic inflammatory skin disease, which is associated with skin barrier dysfunction and IgE-mediated sensitization to food and environmental allergens.<sup>1</sup> Due to recurrent skin inflammation, many AD patients need frequent topical corticosteroid (TCS) treatment. TCS is effective against eczematous lesions. However, they can induce adverse reactions, such as telangiectasia and skin atrophy.<sup>2,3</sup> In addition to their effects on the skin, TCS can also induce the increase in intraocular pressure (IOP), leading to the onset of glaucoma.<sup>3</sup> Steroid-induced glaucoma is an iatrogenic disease that can occur after topical or systemic steroid therapy. The administration of steroids can generate an elevated IOP by increasing aqueous outflow resistance, which might be related to morphological and biochemical changes in the trabecular meshwork.<sup>4</sup> The increase in IOP is asymptomatic,

and narrowing of the visual field can progress after the appearance of vision disorders. IOP can be normalized by reducing the dose of the administered steroid or discontinuing it, but long-term chronic treatment can result in irreversible ocular hypertension.

Steroid-induced increases in IOP followed by glaucoma have been reported to be associated with internal steroid use, steroid eye drops, or subconjunctival steroid injections.<sup>5–7</sup> Furthermore, the use of nasal and inhaled corticosteroids has been found to be associated with an increase in IOP.<sup>8,9</sup> With regard to the topical application of steroids to the skin, several case reports have suggested that the frequent application of TCS to the skin can induce glaucoma in patients with AD.<sup>10–17</sup> However, the relationship between the daily use of TCS and ocular hypertension is not fully understood. In this study, we investigated the relationship between the dose of TCS administered and IOP in patients with AD.

## Methods

## Patients

We carried out a retrospective study of 65 patients who were diagnosed with AD by the Department of Dermatology, University Hospital, Kyoto Prefectural University of Medicine and underwent 2

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or more IOP measurements at our hospital's Department of Ophthalmology as part of their outpatient care between January 2008 and December 2014. The patients' data were collected from their charts at our hospital. All of the patients used TCS preparations. The study protocol was approved by the university ethics committee and was conducted in accordance with the Declaration of Helsinki.

#### Cumulative TCS use

The application sites were classified into the head; the face, including the periocular region; and the trunk and extremities. The doses of TCS administered to the periocular region are also estimated for the cases in which the doses were obvious. The ranks of TCS were classified as 'strongest', 'very strong', 'strong', 'medium', and 'weak' in Japan.<sup>18</sup>

#### Duration of TCS use

The duration of the dermatology outpatient care was defined as the duration of the period in which the patient regularly visited the dermatology department of our hospital. Periods during which the patient visited another hospital were excluded.

#### Ophthalmologic examination

An IOP of  $\leq 21$  mmHg was regarded as normal according to the Japanese Ophthalmological Society Guidelines for the Management of Glaucoma (3rd edition).<sup>19</sup>

## Results

#### Patient backgrounds

The 65 patients with AD were divided into two groups according to age. There were 8 childhood (2–12 years old) (mean age  $\pm$  SD,  $8.4 \pm 2.8$  years; 7 males and 1 females) and 57 adolescent and adult ( $>13$  years old) AD cases (mean age  $\pm$  SD,  $35.0 \pm 12.3$  years; 33 males and 24 females) (Table 1). Five (7.7%) of the 65 patients had already been diagnosed glaucoma at the start of the study.

#### Duration of TCS use

Concerning the patients in whom medium-class TCS were applied to the face, the duration of steroid use was  $\leq 8.5$  months in

**Table 1**  
Patient characteristics in each age group.

	Childhood patients (2–12 years), median; range	Adolescent and adult patients ( $\geq 13$ years), median; range
Sex, M/F	7/1	33/24
Age, y, mean $\pm$ SD	$8.4 \pm 2.8$	$35.0 \pm 12.3$
Serum total IgE (IU/L)	1968; 38–4107 (n = 6)	10,403; 652–72,700 (n = 35)
Serum TARC (pg/mL)	699; 153–2297 (n = 5)	2168; 152–18,290 (n = 27)
Blood eosinophils (%)	9.4; 1.0–17.2 (n = 5)	7.8; 0.3–30.5 (n = 40)
Blood eosinophils ( $\mu$ L)	730; 69–1230 (n = 5)	630; 30–2940 (n = 40)
Serum LDH (IU/L)	288; 236–320 (n = 6)	280; 173–762 (n = 44)
Duration of dermatological therapy (month)	20; 0.5–119 (n = 8)	31; 0.5–163.5 (n = 57)
Other atopic diseases		
Asthma	4	22
Allergic rhinitis	2	18

M, male; F, female; TARC, thymus and activation-regulated chemokine; LDH, lactate dehydrogenase.

90% of those aged 2–12 years and  $\leq 28$  months in 90% of those aged  $\geq 13$  years (Table 2). The duration of weak or medium-class TCS applied to the periorbital region was  $\leq 0.5$  months in 90% of both AD patients aged 2–12 years and those aged  $\geq 13$  years.

#### Doses of TCS

The total doses of TCS administered are presented as the median and the 75th and 90th percentile doses applied to the face, scalp, trunk, and extremities (Table 3). Concerning the patients in whom medium-class TCS were applied to the face, the monthly dose was  $\leq 11.8$  g in 90% of the patients aged 2–12 years and  $\leq 15$  g in 90% of those aged  $\geq 13$  years. With regard to the most doses of systemic TCS use among the patients, a non-glaucomatous patient was administered 5647 g of steroids in 41 months, and a glaucomatous patient was administered 855 g of steroids in 13.5 months.

#### Measurement of the IOP

No significant increase in IOP associated with the topical application of steroids was observed (Supplementary Figs. 1–3). Increases in IOP due to inflammation after eye surgery were noted in 2 patients (3.1%). A slight increase in IOP was observed in 1 (1.5%) during the period of the use of steroid eye drops for conjunctivitis and steroid ointments for the eczematous lesion on the whole body. The IOP was 17.3 mmHg in the right and 17.0 mmHg in the left at the beginning of treatment, and changed slightly to 24.2 and 15.7 mmHg 4 weeks later and 22.0 and 21.2 mmHg 7 weeks later, respectively. The patient had continued to use steroid eye drops and steroid ointments for 2 years. At 2 year after starting treatment, IOP measurements were performed again and showed 14.0 mmHg in the right and 13.7 mmHg in the left.

#### Glaucoma patients' data

Detailed data for 5 glaucoma patients are shown in Table 4. The patients consisted of 1 patient with open-angle glaucoma (No. 1), 3 with steroid-induced glaucoma (Nos. 2, 3, and 5), and 1 whose disease was unclassified (No. 4). In the patients with steroid-induced glaucoma, the route of application of corticosteroid for inducing glaucoma was unknown (Nos. 2, 3, and 5). Medium-class

**Table 2**  
Duration of TCS use in AD patients (month).

		2–12 years (n = 8)			13 years $\leq$ (n = 57)		
		Median	75th	90th	Median	75th	90th
Scalp	Weak (n = 0)	0	0	0	0	0	0
	Medium (n = 25)	0	4.5	10.5	0	3.0	20.0
	Strong (n = 10)	0	0	0	0	0	2.5
	Very strong (n = 14)	0	0	0	0	0	8.0
	Strongest (n = 1)	0	0	0	0	0	0
Face	Weak (n = 0)	0	0	0	0	0	0
	Medium (n = 53)	2.0	5.5	8.5	3.5	10.0	28.0
	Strong (n = 10)	0	0	0	0	0	0.5
	Very strong (n = 0)	0	0	0	0	0	0
	Strongest (n = 0)	0	0	0	0	0	0
Periorbital region	Weak (n = 11)	0	0	0.5	0	0	0.5
	Medium (n = 9)	0	0	0	0	0	0.5
	Strong (n = 0)	0	0	0	0	0	0
	Very strong (n = 0)	0	0	0	0	0	0
	Strongest (n = 0)	0	0	0	0	0	0
Trunk and extremities	Weak (n = 2)	0	0	0	0	0	0
	Medium (n = 27)	7.0	9.5	23.5	0	2.5	29.5
	Strong (n = 23)	0	14.5	19.0	0	0.5	8.0
	Very strong (n = 54)	0	0	0.5	7.5	20.5	37.0
	Strongest (n = 11)	0	0	0	0	0	4.5

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