Systemic antibiotic prophylaxis for recurrent infective flares in children and adolescents with atopic dermatitis

Dear Editor,

Atopic dermatitis (AD) is a chronic inflammatory skin disease, affecting approximately 20% of children in Singapore.¹ It is associated with skin barrier defects² and increased skin colonisation with *Staphylococcus aureus*, which can trigger infective flares, especially in more severe disease. Strategies to reduce *S. aureus* colonisation and infection in AD, such as intranasal mupirocin, bleach baths and topical antiseptic agents have shown conflicting results^{3,4} and are not part of standard management of AD in Singapore.^{5,6} Literature on the use of systemic antibiotic prophylaxis in reducing infective flares of AD is lacking.

We performed a retrospective study of children and adolescents less than 18 years of age with moderate-to-severe AD and recurrent infective flares, who were prescribed prophylactic oral cephalexin twice-daily at 16–17mg/kg/dose (maximum 500mg/dose), for at least 1 month. The study was approved by the SingHealth Centralised Institutional Review Board. Cases between September 2017 and April 2020 were included. Our primary outcome was to compare the number of infective flares of AD requiring systemic antibiotic therapy at treatment doses in the 6 months before and after starting cephalexin prophylaxis. Secondary outcomes included number of days of hospitalisation, number of unplanned clinic or emergency room visits for AD flares, number of courses of oral corticosteroid use,

and number of tubes of topical corticosteroids prescribed. We also report on any adverse outcomes of cephalexin prophylaxis.

A total of 13 patients were included. The majority of patients were Chinese (84.6%) and males (61.5%). Most patients (69.2%) had onset of eczema prior to school-going age, with 6 patients (46.2%) before 1 year of age, and 3 patients (23.1%) in their preschool years (between 1 and 6 years of age). The mean age at start of cephalexin prophylaxis was 8.7 years.

Except for 1, all patients had an Investigator Global Assessment (IGA) score of 3 or 4, prior to initiation of cephalexin prophylaxis. Ten patients (76.9%) had positive skin cultures and 3 (23.1%) had negative cultures within 6 months prior to starting cephalexin prophylaxis. Of the 10 patients with positive skin cultures, 5 grew purely methicillin-sensitive *S. aureus* (MSSA) (50%), 4 grew both MSSA and group A *Streptococcus* (40%), and 1 grew methicillin-resistant *S. aureus*, MSSA and *Acinetobacter* (10%). The mean duration of treatment was 152.7 days, with 5 patients (38.5%) treated for more than 6 months. Five patients were on systemic immunosuppressants prior to initiation of cephalexin, and 1 patient was on phototherapy. None of these patients required a change in their systemic treatments during the prophylaxis period. All were continued on the same emollients and cleansers as before starting cephalexin prophylaxis.

Table 1. Comparison of patients' severity in the 6 months before and after cephalexin prophylaxis

	Pre-prophylaxis ^a (n=13)	Post-prophylaxis ^a (n=9 ^b)	Standard deviation	P value
Infective episodes requiring systemic antibiotics	2.8	0.2	1.72	1.00
Unplanned clinic visits	0.6	0	2.00	0.63
Visits to children's emergency	1.3	0.1	1.64	0.70
Hospitalisation days	6.3	0.2	11.50	0.59
Days of systemic corticosteroids (prednisolone)	13.4	3.6	8.08	0.64
Topical corticosteroids prescribed	34.6	13.2	32.00	0.17
Class I	2	0	9/90	0.49
Class II	21	10	8.91	0.57
Class III	12	3	14.35	0.88
Class IV	0	0	9.73	0.81

^a These measurements are means

^b 1 patient was lost to follow-up while on cephalexin prophylaxis, 1 patient is still on cephalexin prophylaxis, and 2 patients have just completed cephalexin prophylaxis. Hence post-prophylaxis data for the 6 months post-cephalexin prophylaxis were not available for these 4 patients.

Table 1 summarises the results of treatment. The mean number of infective flares of AD requiring breakthrough systemic antibiotics at treatment doses as prescribed by any physician was reduced from 2.8 to 0.2 episode in the 6 months before and after starting cephalexin prophylaxis. The mean number of days of hospitalisation and emergency visits were reduced from 6.3 to 0.2 day, and from 1.3 to 0.1 visit, respectively. Systemic corticosteroid use was reduced from 13.4 to 3.6 days, and the mean number of tubes of topical corticosteroids was reduced from 34.6 to 13.2 tubes. However, due to the small number of patients in our cohort, these results were not statistically significant. No adverse events from the use of cephalexin prophylaxis were reported.

The results of our study suggest that cephalexin prophylaxis may be a useful and safe adjunct to reduce the frequency of infective flares in patients with moderate to severe AD. A real potential concern for cephalexin resistance should be considered against the strength of indications and benefit for prescribing it. The limitations of our study included its retrospective nature and presence of confounders such as concomitant use of other treatments, which could not be controlled for. We recommend randomised controlled trials to better evaluate the effectiveness, adverse effects, optimal dosage, and duration of oral antibiotic prophylaxis in the treatment of children and adolescents with moderate-to-severe AD and recurrent infective flares.

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