SHORT COMMUNICATION

Are Infants and Toddlers with Moderate-to-severe Atopic Dermatitis Undertreated? Experiences of a Finnish Tertiary Care Hospital

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There is substantial need for effective treatments in pediatric AD (1). Mild topical corticosteroids and basic emollients are used as first-line. In non-responsive cases and frequent relapses, topical calcineurin inhibitors are recommended (2). For children under 2 years of age, 0.03% tacrolimus ointment and 1% pimecrolimus cream have been approved (3). 0.1% tacrolimus ointment has been used off-label in pediatric AD (4), but there is still limited data regarding long-term treatment in children under 2 years of age (5). We analysed the use and safety data of topical tacrolimus in small children with AD and compared the usage with topical corticosteroids.

MATERIALS, METHODS AND RESULTS

Interim analysis of a three-year follow-up study (4) was conducted, comparing 2 treatment modalities; tacrolimus ointment (both 0.03% and 0.1%) and topical corticosteroids (mild and mid-potency), in a cohort of 1 to 3 year old children. This was a randomized non-blinded follow up study with a one week wash-out period.

A total of 152 children with moderate to severe AD (Rajka and Langeland Eczema Severity Score) (4) were randomized for topical corticosteroids (hydrocortisone 1% and if needed hydrocortisone-17-butyrate cream) or topical tacrolimus (0.03% and if needed 0.1% ointment). There was a drop out of 15 patients during the first year due to nonadherence. Patients were advised to use topical corticosteroids twice per day for courses of 3-5 days or topical tacrolimus twice daily until the skin has cleared and thereafter twice per week if needed. Clinical assessment (including use of topical treatment) and assessment of severity were performed after the first week, at months 1, 3, 6, 9 and 12 and thereafter every 6 months.

At baseline, blood eosinophil count, total serum IgE, specific IgE antibodies (aeroallergens and food allergens) and skin prick tests were measured to investigate if early signs of atopy predict response to treatments. The cohort is characterized in detail in a former publication (4).

Fifty-one patients (85.0%) in the corticosteroid group (n=60) and 50 (78.1%) in the tacrolimus group (n=64) needed to switch to a more potent treatment. There were no significant differences between groups (p=0.325, χ²-test; Fig. 1). Disease severity and high Eczema Area and Severity Index (EASI) score predicted the need for more potent treatment (p=0.009, Mann–Whitney U-test). Switch to more potent treatment was due to poor treatment response in localized body sites (limbs, trunk, lichenified areas) or to frequent relapses. The switch to a more potent treatment was mostly needed on the extremities. If the patients needed a more potent treatment they usually needed it during the first follow-up year. Here, the treatment was switched to either hydrocortisone-17-butyrate cream (corticosteroid group) or tacrolimus 0.1% ointment (tacrolimus group). Characteristics of the treatment groups are shown in Table SI1. Comparisons of the treatment groups are shown in Table SI1

Switch to more potent treatment (p=0.779, Fisher’s exact test). No sex differences were observed. Only the clinical disease severity (EASI) correlated with the need for a more potent treatment, i.e. physician observed non-responsiveness or frequent relapses after withdrawal of milder topical treatment.

Tacrolimus blood concentrations were measured in the tacrolimus group (0.03% and 0.1%) at 1-week and 1-year visits. Five patients at week 1 had a tacrolimus concentration slightly above normal, but the values normalized (<1.5 µg/l) in control samples taken the following week (data shown previously) (4).

DISCUSSION

In our experience many small infants and toddlers with moderate to severe AD need an off-label use of more po-

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from the switch to a more potent topical treatment, i.e. mid-potency corticosteroids or 0.1% tacrolimus.

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REFERENCES

1. LePoidevin LM, Lee DE, Shi VV. A comparison of international management guidelines for atopic dermatitis. Pediatr Dermatol 2019; 36: 36–45.
2. Wollenberg A, Barbarot S, Bieger T, Christen-Zaech S, Deleuran M, Fink-Wagner A, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. J Eur Acad Dermatol Venereol 2018; 32: 657–682.
3. Siegfried EC, Jaworski JC, Kaiser JD, Hebert AA. Systematic review of published trials: long-term safety of topical corticosteroids and topical calcineurin inhibitors in pediatric patients with atopic dermatitis. BMC Pediatr 2016; 16: 75.
4. Perälä M, Ahola M, Mikkola T, Pelkonen AS, Remitz A, Mäkelä MJ. Young children with moderate-to-severe atopic dermatitis can be treated safely and effectively with either topical tacrolimus or mild corticosteroids. Acta Paediatr 2020; 109: 550–556.
5. Mandelin JM, Rubins A, Remitz A, Cirule K, Dickinson J, Ho V, et al. Long-term efficacy and tolerability of tacrolimus 0.03% ointment in infants: a two-year open-label study. Int J Dermatol 2012; 51: 104–110.
6. van Halemijn KF, Bohnen AM, van den Berg PJ, Pasmans SGMA, Bindels PJE, Elshout G. Different potencies of topical corticosteroids for a better treatment strategy in children with atopic dermatitis (the Rotterdam Eczema study): protocol for an observational cohort study with an embedded randomised
open-label controlled trial. BMJ Open 2019; 9: e027239.
7. Morley KW, Dinulos JG. Update on topical glucocorticoid use in children. Curr Opin Pediatr 2012; 24: 121–128.
8. Dharmage SC, Lowe AJ, Matheson MC, Burgess JA, Allen KJ, Abramson MJ. Atopic dermatitis and the atopic march revisited. Allergy 2014; 69: 17–27.
9. Moawad S, Mahé E, Aubert-Wastiaux H, Phan A, Maruani A, Chiaverini C, et al. Topical corticosteroid concerns among parents of children with psoriasis versus atopic dermatitis: a French multicenter cross-sectional study. Am J Clin Dermatol 2018; 19: 261–265.
10. Li AW, Yin ES, Antaya RJ. Topical corticosteroid phobia in atopic dermatitis: a systematic review. JAMA Dermatol 2017; 153: 1036–1042.
11. Bridgman AC, Eshtiaghi P, Cresswell-Melville A, Ramien M, Drucker AM. The burden of moderate to severe atopic dermatitis in Canadian children: a cross-sectional survey. J Cutan Med Surg 2018; 22: 443–444.
12. Yang EJ, Beck KM, Sekhon S, Bhutani T, Koo J. The impact of pediatric atopic dermatitis on families: a review. Pediatr Dermatol 2019; 36: 66–71.
13. Castellsague J, Kuiper JG, Pottegård A, Anveden Berglind I, Dedman D, Gutierrez L, et al. A cohort study on the risk of lymphoma and skin cancer in users of topical tacrolimus, pimecrolimus, and corticosteroids. Clin Epidemiol 2018; 10: 299–310.
14. Remitz A, Harper J, Rustin M, Goldschmidt WF, Palatsi R, van der Valk PG, et al. Long-term safety and efficacy of tacrolimus ointment for the treatment of atopic dermatitis in children. Acta Derm Venereol 2007; 87: 54–61.
15. Lynde CW, Bergman J, Fiorillo L, Guenther L, Keddy-Grant J, Landells I, et al. Clinical insights about topical treatment of mild-to-moderate pediatric and adult atopic dermatitis. J Cutan Med Surg 2019; 23: 35–135.
16. Eichenfield LF, Totri C. Optimizing outcomes for paediatric atopic dermatitis. Br J Dermatol 2014; 170: 31–37.