Hope for improved treatment of infants with eczema

New research led by scientists from Trinity College Dublin, and Children’s Health Ireland, Crumlin, offers hope for the improved treatment of infants with eczema. The research showed that corticosteroid treatments reduced disease severity and normalised immune dysregulation.

The scientists, supported by NCRC, have recently published their research in the British Journal of Dermatology.

Eczema, also known as Atopic Dermatitis, is the most common persistent inflammatory disease of early childhood. 60% of cases of eczema begin during the first year of life while 85% begin before a child reaches five years of age. Eczema is caused by a combination of genetic and environmental factors, but the exact mechanisms underlying the development and progression of the disease are not fully understood.

Increased local (within the skin) and systemic (within the peripheral blood circulation) inflammation is evident in infants with eczema but it is not clear what effect standard treatment with topical corticosteroids (creams, gels, ointments containing corticosteroids) has on inflammation within this patient group.

In the recently published study, a team led by Dr Maeve McAleer and Professor Alan Irvine from Trinity’s School of Medicine, set out to investigate responses to first-line corticosteroid treatments in infants with eczema and examine the effect of corticosteroid therapy on skin and blood biomarkers of inflammation.

They recruited 74 treatment-naïve infants (<12 months of age) with moderate to severe eczema, through the Atopic Dermatitis clinic at Children’s Health Ireland, Crumlin. Using minimally invasive skin tape stripping, skin samples were collected before and after a 6-week course of treatment with topical corticosteroids. Blood samples were also collected at both time points.

The scientists found that topical corticosteroid therapy led to an improvement in disease severity, but treatment also normalised systemic immune dysregulation in infants with eczema. Following treatment, altered skin and blood cytokine profiles approached levels seen in children without eczema.

Moreover, the results suggest that local inflammation within the skin is responsible for immune dysregulation in infants with eczema.

Professor Alan Irvine said, “Our study shows that inflammatory signals from the skin of children with eczema leak into the system and are circulating widely. Treating the skin inflammation reduces the levels of these inflammatory signals in the blood. Collectively, these findings help to shape our understanding of the systemic effects of eczema.”

SUMMARY

Background

Atopic dermatitis (AD) is the most common inflammatory skin disease. It is highly heterogeneous in clinical presentation, treatment response, disease trajectory and associated atopic comorbidities. Immune biomarkers are dysregulated in skin and peripheral blood.

Aims

We used noninvasive skin and peripheral biomarkers to observe the effects of real-world topical corticosteroid (TCS) treatment in infants with AD, by measuring skin and blood biomarkers before and after therapy.

Methods

Seventy-four treatment-naïve infants with AD underwent 6 weeks of TCS treatment. Stratum corneum (SC) and plasma blood biomarkers as well as SC natural moisturizing factor (NMF) were measured before and after TCS therapy. Immune markers included innate, T helper (Th)1 and Th2 immunity, angiogenesis, and vascular factors. AD severity was assessed by the Scoring Atopic Dermatitis index, and skin barrier function by transepidermal water loss (TEWL). Twenty healthy infants were recruited as controls.

Results

TCS therapy predictably led to improvement in disease severity. Levels of immune markers in the skin and in the peripheral blood showed significant change from baseline, though most did not reach healthy control levels. The most prominent change from baseline in the SC was in markers of innate immune activation, interleukin (IL)-18, IL-8 and IL-1α, and the Th2 chemokines C-C motif chemokine (CCL)17 and CCL22. In blood, the largest changes were in Th2-skewed biomarkers: CCL17, IL-13, CCL22, IL-5, and CCL26. TEWL decreased after therapy; no significant changes from baseline were found for NMF.

Conclusions

We made three key observations. Firstly, TCS therapies have a profound impact on the SC cytokine profile, with marked normalization across multiple cytokines including those associated with innate immunity, type-2 immunity and vascular cell adhesion and angiogenesis. Given the pluripotency of corticosteroids, this is not a surprising finding. Secondly, we did not detect a difference in NMF, a good proxy of filaggrin expression, after 6 weeks of therapy, showing that expression of this key structural protein is unaffected by the anti-inflammatory effects of TCSs, and NMF deficiency remains following 6 weeks of treatment.27 For patients who have experienced good control of their AD following TCS treatment, this observation implies they have a residual epidermal barrier deficit and susceptibility to future flares, as is seen clinically.

Our third observation is the most novel and surprising: we show that 6 weeks of TCS treatment has a marked effect on the peripheral blood inflammatory cytokine profile. Two potential mechanisms could explain this observation. The first, and we suggest the most likely, is that the aberrant peripheral blood signature in infant AD is largely derived from the skin compartment. This is in agreement with a recent study by Pavel et al.,22 who showed a significant correlation between mRNA and protein expression of various cytokines, indicating local translation into protein in the skin and pinpointing the skin as the primary source for the upregulated proteins. A second potential but less likely explanation is that TCSs are sufficiently absorbed to have a systemic effect on immune profiles. Elucidation of the relative importance of these potential mechanisms is beyond the scope of this observational paper. However, the implications are potentially very important.

The profound impact of topical therapy on systemic biomarkers suggests that the skin compartment generates a major component of dysregulated systemic cytokines in infant AD. There may be long-term beneficial effects of correcting systemic immune dysregulation through topical therapy.