International Journal of Women's Dermatology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Women's Dermatology

Noninvasive monitoring of plant-based formulations on skin barrier properties in infants with dry skin and risk for atopic dermatitis☆,☆☆

L. Lünnemann, MD [a], L. Ludriksone [b], M. Schario, ScD [b], S. Sawatzky [b], A. Stroux [b,c], U. Blume-Peytavi, MD [b], N. Garcia Bartels, MD [b,*]

[a] Dermatologic Practice Mahlow, Berlin, Germany
[b] Clinical Research Center for Hair and Skin Science, Department for Dermatology and Allergy, Charité-Universitätsmedizin Berlin, Berlin, Germany
[c] Department of Medical Statistics and Clinical Epidemiology, Charité-Universitätsmedizin Berlin, Berlin, Germany

ARTICLE INFO

Article history:
Received 6 August 2017
Received in revised form 18 October 2017
Accepted 19 October 2017
Available online xxxx

Keywords:
infants
dry skin
atopic dermatitis
skin barrier
emollient
skin potential of hydrogen

ABSTRACT

Background: Dry skin and the associated impaired epidermal barrier function are postulated to constitute a major element in the development of atopic dermatitis.
Objective: The aim of this study was to evaluate the effect of two plant-based formulations on the epidermal barrier function in a defined cohort of infants with a predisposition for atopic dermatitis.
Methods: Over a period of 16 weeks, 25 infants who were ages 3 to 12 months and had an atopic predisposition and dry skin received two emollients that contained pressed juice of the ice plant. The infants received both cream and lotion on the forearm, only cream on the face, and only lotion on the leg. Stratum corneum hydration (SCH), transepidermal water loss (TEWL), skin surface pH, and sebum were assessed on the infants' forehead, leg, and forearm. The Scoring Atopic Dermatitis (SCORAD) index was used for the clinical assessment.
Results: SCH significantly increased in all body regions that were assessed. The forearm and leg revealed stable levels of pH and TEWL, but a decline in pH (week 16) and TEWL (week 4) was noted on the forehead. At week 16, sebum levels were lower on the forehead compared with those at baseline. SCORAD scores improved significantly during the study.
Conclusion: A daily application of both emollients was associated with increased SCH levels and a stable course of TEWL, pH, and sebum on the forehead except for the forehead when compared with the forearm and leg. Clinically, improved SCORAD scores were noted.

Introduction

Daily emollient therapy of the entire body from birth onward may represent a safe and efficacious strategy to prevent atopic dermatitis (AD; Simpson et al., 2010, 2014). In nearly 60% of patients, AD manifests at the age of 3 to 6 months (Irvin and Miller, 2015), and dry skin is often the first morphologically recognizable symptom (Cork et al., 2009). Infants with at least one parent who has AD in particular are at a high risk (Williams et al., 2012). Appropriate emollient therapy during infancy is conjectured to be of particular relevance to delay the onset or even prevent AD (Blume-Peytavi et al., 2009; Cork et al., 2009; Proksch and Lachapelle, 2005; Simpson et al., 2010).

Dry skin is characterized by reduced water content in the stratum corneum (SC) that entails abnormal enzymic and mechanical properties (Rawlings and Matts, 2005). The two pivotal mechanisms that maintain an equilibrium state of SC hydration (SCH) include water retention by the hygroscopic components of the natural moisturizing factor complex and controlled transcutaneous water flux (Fluhr et al., 2012). Both have been shown to be impaired in dry skin conditions (Loden, 2003; Rawlings and Matts, 2005).

Moreover, an association between dry skin and a diminished barrier function has been previously suggested (Loden, 2003). The barrier impairment facilitates the penetration of exogenous irritants through the skin with a subsequent cutaneous inflammatory response (Rawlings and Matts, 2005; Tagami et al., 2006). Furthermore, both mechanisms reportedly undergo a dynamic adaption process throughout infancy, which causes lower natural moisturizing factor amounts

☆ Conflicts of interest: Annette Greco and Professor Florian Stintzing from WALA GmbH commissioned the study and provided the study products but had no influence on the recruiting, reporting, and data analyses.
☆☆ Funding sources: The trial was sponsored by WALA GmbH.
* Corresponding Author.
E-mail address: natalie.garcia-bartels@charite.de (N. Garcia Bartels).

https://doi.org/10.1016/j.ijwd.2017.10.009

and higher transepidermal water loss (TEWL) rates in the SC of infants compared with those of adults with normal skin (Fluhr et al., 2012; Nikolovski et al., 2008). Skin hydration increases during the first 30 days of life in neonates and is significantly higher in infants ages 3 to 12 months compared with adults (Garcia Bartels et al., 2009, 2010, 2011; Lavender et al., 2013)

Adequate skin care may enhance the SC barrier properties and thereby reduce the progression of AD or even prevent AD. Application of oils to the skin of healthy newborns may have different effects on the skin barrier compared with those of newborns with an atopic predisposition (Cooke et al., 2016).

Skin care is common in healthy neonates and infants (Blume-Peytavi et al., 2016; Gao and Simpson, 2014). A trend toward "free-of" cosmetics is widely observed, which means that consumers tend to prefer cosmetics that are free of certain ingredients (e.g., parabens, endocrine disrupters such as phthalates). Moreover, parents tend to prefer products with natural ingredients for their children (Gao and Simpson, 2014). The inclusion of botanical extracts in dermatological skin care products and their usage is increasingly popular especially in patients with AD (Reuter et al., 2010; Stallings and Lupo, 2009). Hence, the scientific evaluation of the effects of botanical extracts on infant skin barrier properties is of particular importance (Kuller, 2016).

Emollients that contain pressed juice of the ice plant, *Mesembryanthemum crystallinum*, have been shown to improve SC hydration in patients with AD (Schario et al., 2014). This plant has been reported to have antioxidant and antibacterial effects and influence the physiology of human keratinocytes (Schario et al., 2014). A previous study suggested that a daily application of moisturizer in neonates without skin disease but at a high risk of developing AD reduced the cumulative incidence of AD significantly (Cowdell et al., 2012). However, a scientific approach to considering the effects of emollients on skin barrier in this risk group as assessed by clinical and biophysical parameters is still lacking (Moncrieff et al., 2013).

The prevention of the manifestation of AD is the focus of the Barrier Enhancement for Eczema Prevention (BEEP) trial that is currently investigating the preventive effect of daily emollient application on infants at risk for AD (Chalmers et al., 2017; Simpson et al., 2012). Our results underline the goals of the BEEP study. We aimed to investigate the impact of a daily application of a plant-based moisturizing lotion and cream with ice plant pressed juice (IPPJ) on the skin barrier function in infants ages 3 to 12 months who are at an increased risk to develop AD and clinically dry skin.

Methods

Study design and participants

This single center, prospective, open-label trial lasted 16 weeks and was conducted between September 2011 and October 2012. Infants ages 3 to 12 months with clinically dry skin, an increased risk of developing AD, and an Erlangen Atopic Score ≥4 points were included in the study. Infants with at least one parent who was afflicted with previously classified atopy (e.g., atopic eczema and/or allergic rhinitis, allergic asthma) were considered at an increased risk of developing AD (Fischer, 1997; Gehring et al., 1991) and those with visible desquamation that was accompanied with a rough tactile sensation were evaluated as having dry skin. Furthermore, parents were required to agree for their child to participate in four swimming sessions. The study exclusion criteria consisted of an acute exacerbation of AD during the last 4 months (defined as the need to apply local or systemic immunosuppressive medication for longer than 3 consecutive days), congenital defects, diabetes, thyroidal diseases, and immunodeficiency and skin disorders of a contagious nature or that affect the investigated biophysical skin parameters.

Written informed consent for each infant was obtained from the infant's legal guardians after the nature of the study had been fully explained and before the initiation of any study-related activity. After enrollment, baseline data were collected during follow-up visits at weeks 4 (W4), 12 (W12), and 16 (W16). Parents were instructed to visit the study site in addition to regularly scheduled visits if their infant showed any type of rash. The trial was approved by the local ethics committee and conducted in compliance with the Declaration of Helsinki.

Intervention

All children received daily skin care with two emollients. Both interventional products contained IPPJ, and both the body care lotion and intensive cream were manufactured and labelled by Dr. Hauschka Med (WALA Heilmittel GmbH, Bad Boll, Germany; Greco and Lindequist, 2010). The ice plant body care lotion consisted of aqua, *Mesembryanthemum crystallinum* extract, alcohol, *Simmondsia chinensis* oil, *Persea gratissima* oil, *Prunus amygdalus dulcis* oil, *Manihot utilissima* starch, cera alba, lanolin, lysolecithin, *Mangifera indica* seed butter, *Butyrospermum parkii* butter, *Daucus carota* extract, sucrose stearate, sucrose distearate, *Chondrus crispus* extract, glyceryl stearate, hectorite, xanthan gum, stearic acid, *Amyris balsamifera* oil, *Rosmarinus officinalis* extract, and sodium stearoyl lactylate. Ingredients of the Intensive Ice Plant cream are aqua, *Mesembryanthemum crystallinum* extract, *Persea gratissima* oil, glycerin, *Mangifera indica* seed butter, alcohol, tricaprylin, *Prunus amygdalus dulcis* oil, *Simmondsia chinensis* oil, *Sesamum indicum* oil, lanolin, cetearyl alcohol, bentonite, *Butyrospermum parkii* butter, *Daucus carota* extract, *Rosmarinus officinalis* extract, *Amyris balsamifera* oil, lysolecithin, gleceryl oleate, and xanthan gum. The cream had a higher concentration of natural lipids than the lotion.

Parents were instructed on the dosage and application mode at the time of inclusion in the study (Table 1). The lotion and cream were applied only on the forearms. The forehead served as a control area for the cream formulation and the leg for the lotion. No other emollients were allowed except for sunscreen lotion; however, parents were instructed to use physical sunscreen. Parents were advised to retain their routine bathing procedures with the usual cleansing products.

Outcome variables and clinical evaluations

The primary outcome variable was SCH on the forearm. The secondary outcome variables were TEWL, pH, sebum content, and

Table 1
Baseline characteristics of participants

Characteristic	Participants (n = 26)
Infant sex	
Female, n (%)	14 (53.8)
Male, n (%)	12 (46.2)
Premature birth, n (%)	7 (26.9)
Age (month) MW ± SD	7.27 ± 2.7
(Median) [Range]	(8.0) [3-12]
Age of gestation (SSW) MW ± SD	37.27 ± 3.4
(Median) [Range]	(39.0) [29-42]
Body length at V0 (m) MW ± SD	0.70 ± 0.05
(Median) [Range]	(0.71) [0.6-0.8]
Weight (kg) MW ± SD	7.8 ± 1.6
(Median) [Range]	(7.6) [5.0-11.5]
Breast fed, n (%)	25 (96.1)
Atopic dermatitis infant n (%)	4 (15.4)
Last vaccination time 4 month before inclusion, n (%)	17 (65.4)
Medication, n (%)	17 (65.4)
Regular skin care performed prior to inclusion, n (%)	25 (96.2)

MW, XXX; SD, standard deviation; SSW, XXX.

Please cite this article as: Lünnemann L, et al, Noninvasive monitoring of plant-based formulations on skin barrier properties in infants with dry skin and risk for atopic dermati..., International Journal of Women's Dermatology (2017), https://doi.org/10.1016/j.ijwd.2017.10.009