Early Atopic Dermatitis: Prevention biological data

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Introduction & Objectives

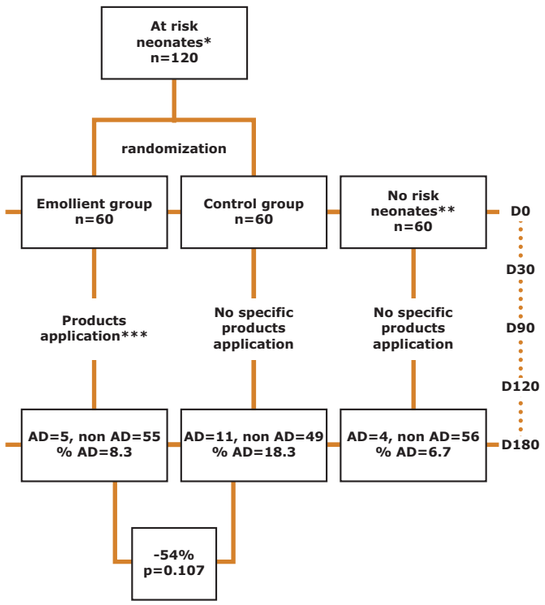
Recent publications reported efficacy of daily applications of emollients from birth to reduce Atopic Dermatitis (AD). Pathophysiology of AD is characterized by low levels of Natural Moisturizing Factors (NMFs) and ceramides. AD is also associated with microbiota dysbiosis; AD lesions are often colonized by Staphylococcus aureus (SA) although likely not in infants as reported in a recent study. While AD is mainly a pediatric disease, little is known about NMF and ceramide levels and staphylococcus colonization before the onset of AD in children at risk of developing AD.

A randomized clinical study has been conducted in infants during the first 6 months of life to evaluate the efficacy of daily applications of a specific emollient to prevent AD in children with a genetic risk of atopy. During this study, we also quantified NMFs, ceramides, SA and Staphylococcus epidermidis (SE) in order to determine whether these biomarkers are predictive of early AD flares. Clinical signs predictive of atopy genetic risk or of AD flare, have also been documented. Lastly, severity and quality of life (IDQOL, DFI) during first AD flare have been scored.

Material & Methods

120 newborns with 2 atopic first-degree relatives (aged 2-3 weeks, classified 'at risk' of developing AD), have been randomly assigned to a prevention group (60 subjects, application of a balm twice a day, cleansing cream and bath oil twice a week) or to a control group (60 subjects) for 6 months. In parallel 60 newborns with no familial history of atopy ('no risk group') have been enrolled. NMF and ceramides, SA and SE have been quantified in skin surface samples collected on forearm, face and AD lesions in 45 children by LC/UV, LC/MS and quantitative PCR respectively.

Figure 1: clinical study flow chart.



*At risk neonates: 2 parental history of atopy
**No risk neonates: non parental history of atopy
***Emollient balm, twice a day + Cleansing cream, twice a week + Bath Oil, twice a week

Results

Frequency of AD during the first 6 months was 8.3% in the prevention group, 18.3% in the control group and 6.7% in the 'no risk group' corresponding to a relative risk reduction of 54% in the prevention group (p=0.11) (table 1).

Table 1: Relative Risk ratio details.

'At risk' infants	Total nb	Had AD (control group)	Had AD (emollient group)	Relative Risk (95% CI)	p-value
Complete	120	n=11/60 (18.3%)	n=5/60 (8.3%)	0.45 [0.17-1.23]	0.11

Association of clinical signs with genetic risk of atopy was observed at birth. Subjects with 2 atopic parents have higher desquamation on body, face, scalp, a higher roughness on body and more erythema of skin folds on body than subjects with no atopic parents (table 2).

Table 2: clinical signs associated with atopy risk at birth.

Clinical signs at birth (2-3 weeks)		Infants with 2 parents having atopy n=120 « At risk »	Infants with no parent having atopy n=60 « No risk »	p-value
Desquamation	Body	60%	36%	<0,1
	Face	46%	30%	<0,05
	Scalp	37%	20%	<0,05
Roughness	Body	51%	28%	<0,05
Erythema of skin folds	Body	14%	0%	<0,05

Predictive clinical signs of AD at birth were also observed. Considering all the subjects, desquamation of the face is higher in subjects developing AD with a relative risk ratio of 3.42 (table 3). When considering 'at risk' subjects, frequency of erythema in neck skin folds was higher in subject developing AD with a relative risk ration of 6.06 (table 4).

Table 3: predictive clinical sign associated with AD onset for all subjects.

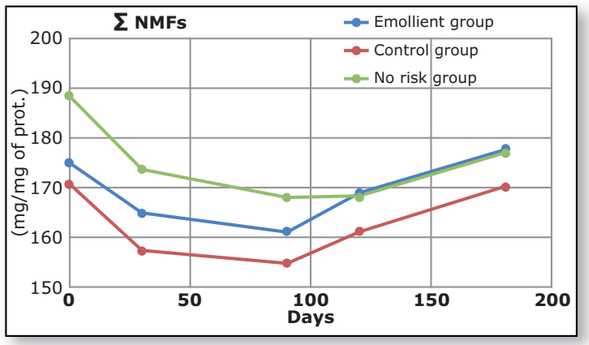
Clinical sign at birth (2-3weeks): all groups (n=180)	Had AD (n=20)	No AD (n=160)	Relative Risk (95% CI)	p-value
Face desquamation	14/20 (70%)	59/160 (36.8%)	3.42 [1.38-8.49]	0.004

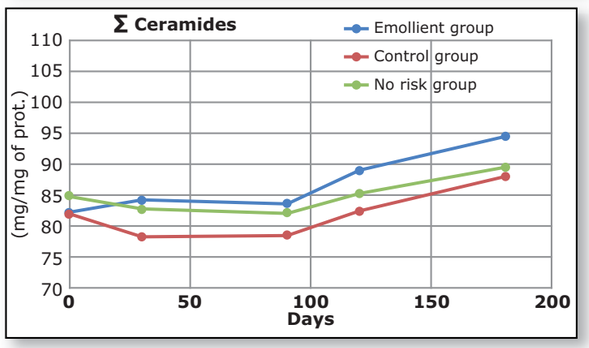
Table 4: predictive clinical signs associated with AD for 'at risk' subjects.

Clinical sign at birth (2-3weeks): infants 'at risk' (n=120)	Had AD (n=16)	No AD (n=104)	Relative Risk (95% CI)	p-value
Erythema in the neck folds	8/16	9/104	6.06 [2,63-13,96]	p<0,001

Mean SCORAD of the first AD flare was similar in the 3 groups: 24.1 in the 'at risk' prevention group, 23.3 in the 'at risk' control group and 26.3 in the 'no risk' group. A concomitant alteration of the quality of life evaluated by IDQOL and DFIQ has been observed during first AD flare in 'at risk' children: (IDQOL: emollient group 10.75, control group 10.62. DFIQ: emollient group 6.75, control group: 6.37).
Depletion of NMFs was noticed in 'at risk' children vs 'no risk' children at birth. At 6 months of age, control 'at risk' subjects still presented a lower level of NMF than in the 'no risk' group. Interestingly NMFs levels were restored following daily applications of emollients. Evolution of ceramides levels paralleled that of NMFs, ceramide quantities were lower in 'at risk' subjects and increased following product application (figure 2).
No significant difference in NMFs and ceramides levels has been observed between AD and non-AD children.

Figure 2: NMFs and Ceramides quantification on forearm for each group at each time point.





Infants were poorly colonized with SA from D0 (2-3 weeks of life) to D180: only 6 children among 45 presented SA on forearms and 15 on the face. In contrast, infants were largely colonized with SE: 42 infants on the forearm and 35 on the face. Only 2 AD lesions out of 11 were found positive for SA and 9 for SE. Levels of SA and SE colonization were not modified by emollients (table 5).

Table 5: Frequency of SA and SE colonization in subjects.

	TOTAL	At risk				No risk
	45	Emollient		Control		
S aureus						
Forearm	6/45 (13.3%)	1	1	1	1	2
Face	15/41 (36.6%)	1	3	2	2	7
AD lesion	2/11 (18.1%)	0/4		2/7		
S Epidermidis						
Forearm	42/45 (93.3%)	4	10	10	10	8
Face	35/41 (85.4%)	3	10	5	10	7
AD lesion	9/11 (81.8%)	3/4		6/7		

Conclusion

A new skin care prevention program in AD, from birth on and for 6 months decreased AD occurrence in children with a familial history of AD (-54%), which is in good agreement with recently published data (1,2). This clinical trial showed that product application restored NMFs and ceramide levels: these data provide new insights in the comprehension of their efficacy in the prevention of AD. Furthermore, emollient application did not alter staphylococcus early colonization. Interestingly, there were clinical signs at birth that were associated both with atopic risk and with AD onset. Detecting these signs may help the clinician to identify critical subjects that should enter AD prevention program.

References

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