RESULTS

Figure 3: Mean distribution of corneodesmosomal adhesion proteins. Desmoglein 1 distribution was more uniform in AD and more peripheral in soap-induced xerosis (right). Significance was identified using non-parametric unpaired (AD) and paired (xerosis) t-tests.

Figure 4: Skin-surface-pH was elevated in both AD and soap-induced xerosis.

Figure 5: Caspase activity was elevated in AD but there was no significant change in soap-induced xerosis. Chymotrypsin-like activity was elevated in soap-induced xerosis but there was no significant change in AD. Finally, trypsin-like activity was elevated in AD. Significance was identified using non-parametric unpaired (AD) and paired (xerosis) t-tests.

Evidence for premature SC shedding was observed in AD.

CONCLUSIONS

- In AD, broadly elevated protease activity leads to increased corneodesmosome degradation, resulting in a defective barrier with SC thinning and immature corneocytes exposed at the SC surface.
- In soap-induced xerosis, elevation of chymotrypsin-like protease activity (but not broad-spectrum/caseinolytic activity) leads to increased degradation of all but the peripheral corneodesmosomes, leaving loosely adhered corneocytes in the upper SC, resulting in a defective barrier exhibiting the flaky characteristics of xerotic skin.

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Corneocytes had reduced cohesion at the SC surface in soap-induced xerosis.

Figure 6: Transepidermal water loss (TEWL), a measure of skin barrier function, was elevated in both AD and soap-induced xerosis, suggesting an impaired barrier in both conditions. Significance was identified using parametric unpaired (AD) and paired (xerosis) t-tests.

Figure 7: Corneocyte size at the SC surface (left) and estimated SC thickness (right) were reduced in AD, but there was no significant change in soap-induced xerosis. Significance was identified using parametric unpaired (AD) and paired (xerosis) t-tests.

REFERENCES


ABNORMAL CORNEODESMOSOME DISTRIBUTION IN ATOPIC DERMATITIS AND SOAP-INDUCED XEROSIS

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INTRODUCTION

- Serine proteases play a role in stratum corneum (SC) desquamation through the proteolysis of corneodesmosomes.
- Two key corneodesmosomal adhesion proteins, desmoglein 1 and desmocollin 1, are degraded by trypsin-like and chymotrypsin-like serine proteases to facilitate corneocyte sloughing.
- In the lower SC, the stratum compactum, corneodesmosomes cover the SC surface uniformly. As corneocytes mature and progress upwards through the SC, the corneodesmosomes become degraded. In the uppermost layers of the SC, the stratum disjunctum, only the peripheral corneodesmosomes remain.
- SC pH is an important regulator of skin barrier homeostasis, and when elevated increases the activity of serine proteases, which in turn accelerates corneodesmosome proteolysis, resulting in barrier breakdown.
- We aimed to investigate the consequences of elevated SC protease activity in atopic dermatitis (AD) and soap-induced xerosis at the SC surface.

METHODS

- 2 cohorts were recruited. One cohort received a non-alkyl control group (n=12) and an active AD group (n=12). Cohort 2 was non-atopic and underwent an exfoliation washing regimen to induce xerosis on one forearm using an alkyl carboxylate soap, leaving the other forearm untreated (n=5).
- Desmoglein 1 and desmocollin 1 distribution was determined for samples of SC removed by tape stripping. Samples were stained with anti-DSG1 (Progen Biotechnik) or anti-DSCL (Santa Cruz Biotechnology) and Alexa Fluor 488 (Life Technologies). Samples were determined for samples of SC removed by tape stripping.
- Skin-surface-pH was measured using a Skin-pH-meter Fluka GmbH, Germany).
- Skin barrier function was determined using an Aquapix TEWA machine (Bioks, UK).
- Corneocyte size was determined by measuring the surface area of fluorescently stained corneocytes using ImageJ.
- SC thickness and cohesion was determined by removing the SC by tape stripping and measuring protein content.
- Statistical significance was determined using GraphPad Prism 6 (GraphPad Software, San Diego, CA, USA) for non-parametric tests and IBM SPSS Statistics 20 (IBM, Armonk, NY, USA) for parametric tests. **p ≤ 0.01, *** p ≤ 0.001. Error bars on figures indicate SEM.