Gradient Skin Barrier Response Caused by Acute Injury in a Clinical Skin Stripping Model—Implications for Within-Subject Study Design

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Abstract

Transepidermal water loss (TEWL) is an indicator of skin barrier disruption and is routinely used to assess skin response to ostomy barrier formulations: low TEWL readings immediately following barrier removal suggest a barrier formulation is gentle on the skin. Past studies have failed to account for potential interactions between anatomical sites on the abdomen when utilizing TEWL. This study, therefore, aims to determine the equivalency and variability of TEWL response to repeated mechanical stripping at different distances from the abdominal midline and across bilaterally symmetrical sites on the abdomens of healthy volunteers. It was found that proximity to the injury caused by an aggressive barrier formulation influenced nearby TEWL readings, hence, addressing the study's hypothesis of a bilaterally symmetrical injury responses was not possible. This revealed that acute skin stripping injuries cause skin barrier disruption that extends beyond the point of injury. To understand potential correlating demographics for this observation, BMI was investigated. However, this study found no clear correlation between BMI and TEWL, yet being outside the optimal BMI range may increase the likelihood of an abnormal skin barrier function post-injury. Further research is needed identify the cause of this gradient effect and the role of BMI in skin recovery, which has implications for future studies comparing adhesives within an individual.

Methods

Broadly, this study involved the application and subsequent removal of two proprietary barrier formulations— Investigational Product (IP) A, a harsh formulation, and IP B, a gentle barrier formulation—to assess the abdomen's injury response to mechanical skin stripping at different locations across the vertical midline.

Procedure:

Subjects acclimated for 30 minutes in an environmentally controlled room. Baseline TEWL readings were taken.

IP A (harsh barrier formulation) and IP B (gentle barrier formulation) were applied and removed after a 45-minute dwell time, per the site assignments indicated in Figure 1.

IP applications were repeated a total of 7 times, with TEWL readings taken after the 6th and 7th removals.

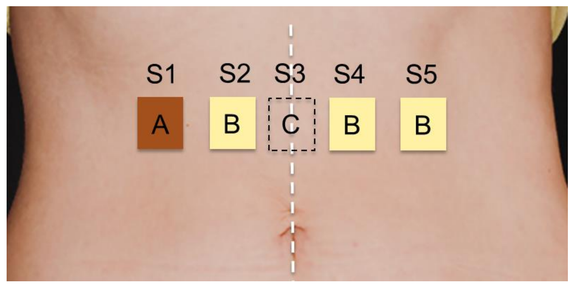

Figure 1. Site Barrier Formulation Assignments

TEWL Differences by Site

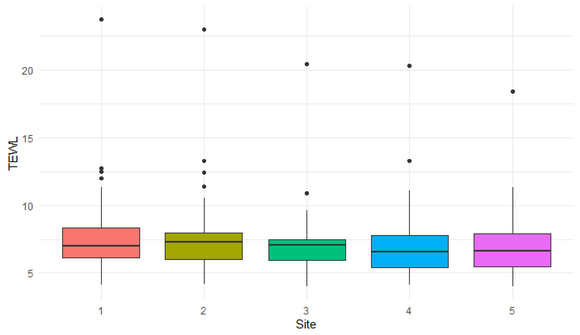

Figure 2. Baseline TEWL by Site. Prior to the application of IPs, all five sites had similar TEWL profiles. The five sites did not have statistically-significant differences in average TEWL values, and the spread of TEWL values at each site was relatively small.

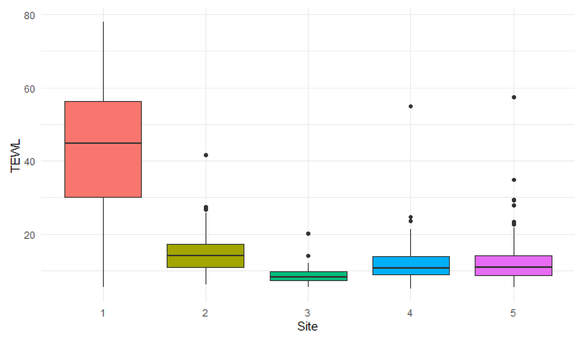

Figure 3. TEWL After 6th IP Removal by Site. By the 6th IP application and removal, TEWL values began to diverge. Site 1, which was the site where the harsh IP was applied, had a significantly higher average TEWL value than the other four sites—as well as a larger spread. Interestingly, sites 4 and 5 had similar average TEWL values and spreads, despite their different distances from the vertical midline. Site 2 appeared to have a slightly elevated TEWL profile compared to site 4, despite their equal distances from the vertical midline.

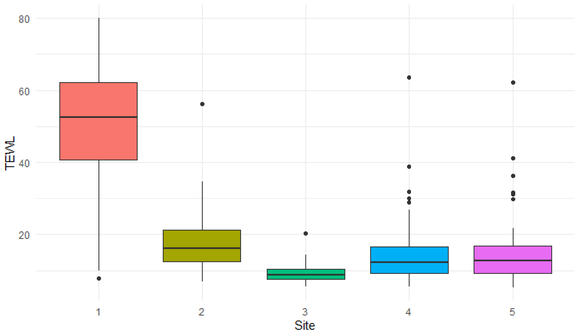

Figure 4. TEWL After 7th IP Removal by Site. After the 7th IP removal, site differences became even more pronounced. Site 1 had a very elevated average TEWL value due to the harsh IP, and site 2 diverged more significantly from site 4.

Assessing the Injury Proximity Effect

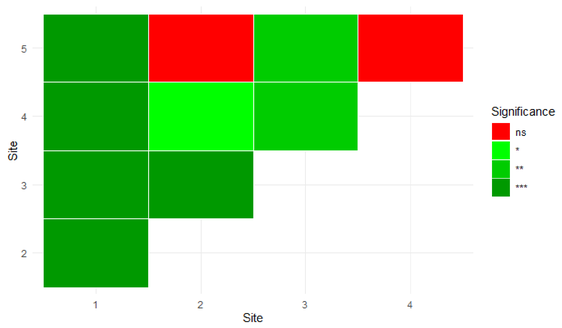

Figure 6. Pairwise Bonferroni-Corrected t-tests Assessing Site Differences in Average TEWL After the 7th IP Removal. Sites 2 and 4, which were bilaterally symmetrical, were found to be significantly different. Sites 4 and 5 were not significantly different.

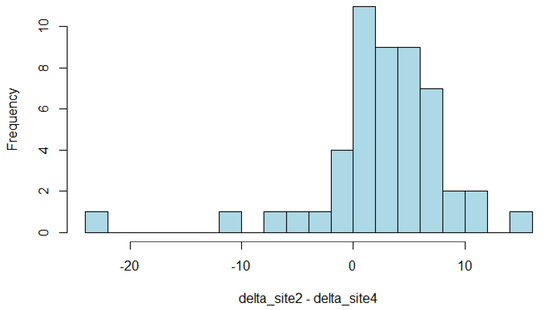

Figure 7. Difference Between the Change in TEWL at Site 2 and the Change in TEWL at Site 4 for Individual Subjects. The majority of subjects had greater TEWL changes (from the baseline reading to the 7th IP removal) at site 2 than at site 4.

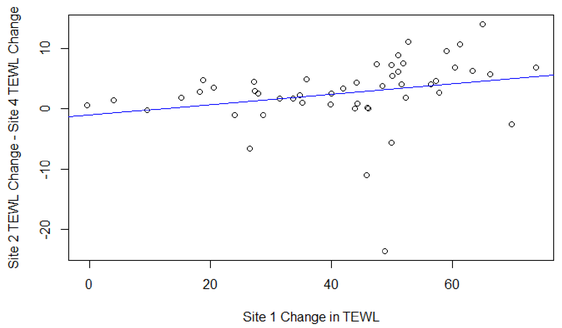

Figure 8. Difference Between the Change in TEWL at Site 2 and the Change in TEWL at Site 4 by the Change in TEWL at Site 2. In addition to most subjects' having greater changes in TEWL at site 2 than at site 4, the difference between the change in TEWL at site 2 and the change in TEWL at site 4 has a positive correlation with the change in TEWL at site 1, suggesting that site 1's proximity to site 2 influences TEWL at site 2.

Discussion

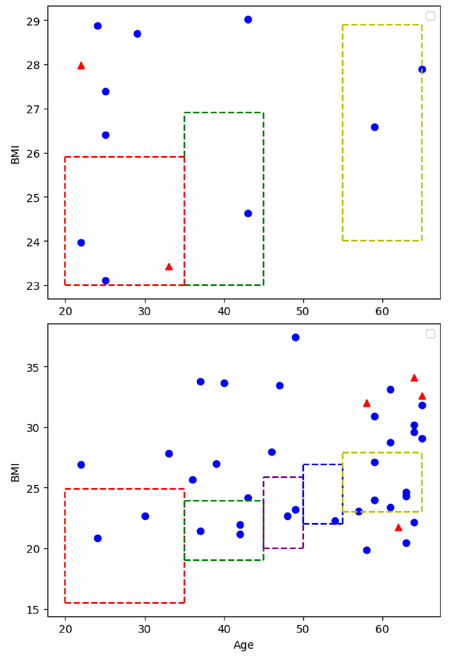

Figure 9. After 7th IP Removal at Site 5- chosen specifically because site 5 is furthest from IP A and thus the confounding effect with the gradient effect is minimized, male (top figure) and female (bottom figure) participants with TEWL value outside of the 1.5 IQR are classified as outliers (red triangles). While not everyone with a BMI outside the optimal BMI ranges (dotted line) showing abnormal TEWL, all the outliers with significantly higher TEWL are either outside of these ranges or close to their edges.

Implications

Despite the gradient effect identified through this study, injury responses to IP A and IP B at each site varied between subjects. Additional research is needed to (1) fully characterize the gradient effect and (2) determine the demographic factors that lead to varying levels of injury severity. A study by Yew et al. (2023) identifies a robust positive correlation between BMI and TEWL in uninjured skin, suggesting that a higher BMI may be causally linked to weaker skin barrier function under normal conditions. However, in the context of our study, where skin barrier disruption is induced through stripping with IP B, we observe that there is not a clear correlation between BMI and TEWL, indicating other factors may have a role in the skin's recovery process. While optimal BMI does not guarantee normal TEWL, being outside the optimal BMI range increases the likelihood of an abnormal skin barrier function post-injury.

Reference: Yew, Yik Weng, et al. "Investigating causal relationships between obesity and skin barrier function in a multi-ethnic Asian general population cohort." *International Journal of Obesity* 47.10 (2023): 963-969.

Acknowledgements

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Hollister