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Use of an emollient-containing diaper and pH-buffered wipe regimen restores skin pH and reduces residual enzymatic activity

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Abstract

Background/Objectives: Diaper dermatitis is one of the most frequent skin conditions affecting infants and is associated with elevated skin pH, exposure to urine and feces, and increased fecal protease and lipase activity, resulting in stratum corneum barrier damage and increased risk of infection. The study aim was to determine the impact of two diaper and wipe regimens on newborn infant skin pH and residual enzyme activity after stool cleaning.

Methods: Two diaper and wipe regimens were compared in a randomized, single-blinded crossover study. Regimen A paired an emollient-containing diaper with an acidic, pH-buffered wipe. Regimen B was a non-emollient diaper and wipe with limited buffering capacity. A 3-day washout period preceded each 3-day regimen use period. Skin pH at the perianal/buttocks interface (PBI), genital region, and undiapered chest control were measured at baseline and day 3. Skin swabs were collected for residual enzyme activity after a stool cleaning event.

Results: Diapered skin pH at the PBI was similar to undiapered skin after 3 days of use for Regimen A, while PBI pH for Regimen B was elevated versus control. PBI pH was lower for Regimen A versus Regimen B. After a stool cleaning, PBI skin pH for Regimen A was lower immediately and had lower residual enzyme activity versus Regimen B ($P < .05$), and the pH-lowering effect was sustained up to 60 minutes.

Conclusions: These results suggest that the use of an emollient-containing diaper with a pH-buffered wipe creates conditions favorable to optimum diapered skin health.

KEYWORDS
diaper dermatitis, neonatal, skin barrier

Julie Ogle has retired.

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1 | INTRODUCTION

Neonatal skin provides a barrier to water loss and external irritants, immune surveillance and infection control, acid mantle formation, resilience to mechanical trauma, and thermal regulation.[1] A gradient of pH from neutral at the basal epidermis to acidic at the stratum corneum (SC) is established via several mechanisms including filaggrin proteolysis to produce natural moisturizing factor, generation of free fatty acids from phospholipid hydrolysis, and the activity of the sodium/hydrogen (Na^+/H^+) exchanger, located in the cell membrane.[2] An acidic skin surface is essential for effective function of enzymes forming the SC including lipid synthesis and structure, desquamation of the outermost layers for bacterial homeostasis, SC cell cohesion, inhibition of pathogenic bacteria, and resistance to mechanical trauma,[3,4] and to promote colonization of appropriate, protective resident microflora, and attachment to the skin.[5]

At birth, the skin pH is near neutral, but rapidly decreases as the acid mantle develops. Diapered skin pH was significantly higher than the undiapered control within a few days after birth in full-term newborns.[6] Diapered skin is repeatedly exposed to elevated pH and irritants from urine and feces,[7] including fecal enzymes, bile salts, and bacteria.[8] The method of cleaning diapered skin can also impact skin pH as demonstrated by higher pH when cloth wipes and sterile water were used in hospitalized premature and full-term neonates.[9] Elevated skin pH has increased permeability to exogenous agents and can impair skin barrier repair,[10] thereby increasing the risk of irritation and infection.[1] Fecal enzymes, namely proteases and lipases, damage the skin barrier by direct disruption of proteins and lipids, and the activity of many of these fecal enzymes increases when pH increases.[8,11]

Protection of diapered skin from irritants can be accomplished by application of a topical emollient, absorption of stool by the diaper, and a sufficient skin hygiene routine (eg, cleaning with wipes). This study compared an emollient-containing diaper with an apertured topsheet designed to reduce skin exposure to feces in combination with use of an acidic and pH-buffered wipe versus a standard non–emollient-containing disposable diaper (with a non-apertured topsheet) in combination with use of a wipe with limited buffering capacity. The outcomes measured in a cohort of newborn infants were diapered skin pH after 3 days of regimen use and immediately after a stool cleaning, as well as residual fecal enzyme activity after cleaning.

2 | METHODS

2.1 | Study design

This was a single-blind, randomized, 3-day in-use, 2-test product crossover study including a washout period. The study was reviewed and approved by an Institutional Review Board (Advarra, Inc), and parents/caregivers provided written informed consent for their child. The study was conducted by Comprehensive Research Group. Sixty-one subjects were enrolled, and 38 infants completed the necessary pre-stooling and post-stooling procedures while using both product regimens and were included in the analyses. Infants were between the ages of >7 days and <2 months, willing to refrain from topical skin products, and willing to use the specified diapers and wipes for the study period. Infants were excluded if they were taking oral or topical medications for a skin condition or antibiotics or had a serious skin condition or a skin condition that the investigator concluded would prohibit the infant from fully participating. Compliance with product use was confirmed at each visit. Caregivers were provided compensation for their time and travel cost to/from the clinical site.

Regimen A consisted of a diaper with an apertured topsheet containing a petrolatum-based emollient (Pampers® Swaddlers™; emollient listed (on product label)) and an acidic, sodium citrate and citric acid pH-buffered wipe (Pampers® Sensitive™ Wipes).[9] Regimen B was a non-emollient diaper[12] and a wipe with limited buffering capacity, as determined by acid-base titration.[12] A "washout period" to acclimate the skin was completed 3 days prior to each regimen, using a non-emollient diaper[13] and non-buffered wipe as determined by acid-base titration.[14]

2.2 | Skin measurements

Skin pH was measured with a Hanna Instruments™ Model 99181 pH meter, calibrated daily at pH 4 and 7, before (after the infant's morning diaper change) and after stool cleaning. Skin pH, skin swabs, and stool samples were also collected by study staff post–stool cleaning after 3 days of regimen use. Skin pH was measured on the infants' chest, perianal/buttock interface (PBI), and suprapubic site of the genital area. After a stooling event, the caregiver cleaned the infant as they normally would, and pH measurements were taken at the PBI and genital areas at time 0 (immediately after cleaning), 15, 30, and 60 minutes post–stool cleaning.

2.3 | Enzyme assessment

Skin swabs from the PBI were taken by study staff using a flocked swab (Puritan HydraFlock®), dipped in sterile saline, immediately after a stooling event, using a template to standardize collection area. Swabs and stool samples were stored at −80°C. Skin swabs and stool samples (20mg) were extracted in 1mL trypsin assay buffer (pH 8.3) and analyzed to determine total protease activity using the Pierce™ Fluorescent Protease Assay Kit. The values represent the total protease activity expressed in "ng/swab" or "ng/mg stool" trypsin equivalent units.

2.4 | Statistics

Skin pH and total protease activity were analyzed using a repeated-measures model for crossover data that included fixed effects for treatment, visit, and treatment-by-visit interaction along with a random subject effect. All testing was 2-sided at $\alpha = .05$.

3 | RESULTS

3.1 | Demographics

Thirty-eight infants had a stool event while on Regimens A and B, allowing comparison of post–stool cleaning pH and protease activity. Infants were, on average, 39.1 weeks' gestational age at birth and 2.6 weeks old, and weighed 3.89 kg (8.55 lb) at enrollment (Table 1).

TABLE 1 Demographics

Demographics	
Measures	**Result**
Sex	
Girls	16 (42.1%)
Boys	22 (57.9%)
Ethnicity	
Hispanic/Latino	2 (5.3%)
Non-Hispanic/non-Latino	36 (94.7%)
Race	
Asian	2 (5.3%)
Black or African American	5 (13.2%)
Multiracial	8 (21.1%)
White/Caucasian	23 (60.5%)
Diet at enrollment	
Breast milk only	25 (65.8%)
Formula only	4 (10.5%)
Mostly breast milk (50% or more)	9 (23.7%)
Gestational age (weeks)	
Number of subjects	38
Mean	39.1
Median	39.0
Min-max	36.0-41.0
Age (weeks)	
Number of subjects	38
Mean	2.6
Median	3.0
Min-max	1.0-5.0
Weight at enrollment (lbs)	
Number of subjects	38
Mean	8.55
Median	8.52
Min-max	6.64-9.90

3.2 | Skin pH

Skin pH at the PBI was significantly lower for babies using Regimen A vs. Regimen B after 3 days of use ($P < .05$). The skin pH at the PBI was significantly higher for Regimen B compared to the undiapered control site ($P < .05$), while no significant difference was found between Regimen A and undiapered skin ($P = .34$; Figure 1). Genital skin pH measurements were similar to the results at the PBI (Regimen A, skin pH: 5.35 ± 0.08; Regimen B, genital skin pH: 5.57 ± 0.09; $P < .05$). PBI and genital skin pH were similar for the 2 washout periods (data not shown).

Immediately after a stooling event and cleaning, the PBI skin pH was lower for infants on Regimen A vs. Regimen B ($P < .05$), and this effect was maintained at 15, 30, and 60 minutes after cleaning (Figure 2; $P < .05$). After 3 days of Regimen A, PBI skin pH values at all post–stool cleaning time points were significantly lower compared to skin pH after 3 days of Regimen B use ($P < .05$). Similar results were found at the genital area immediately after stool cleaning (Regimen A, skin pH: 5.04 ± 0.90; Regimen B, skin pH: 5.57 ± 0.91; $P < .05$) and were maintained for up to 60 minutes ($P < .05$).

3.3 | Residual enzyme activity

Swabs taken immediately after caregiver cleaning of the PBI demonstrated a 40% reduction in the total protease activity when collected from the skin of infants using Regimen A versus Regimen B ($P < .05$; Figure 3). There were no differences in the enzyme activity in the stool itself between regimens or as a result of the number of wipes used.

3.4 | Adverse events

There were no treatment-related AEs during the study. There were 6 instances of diaper dermatitis in the crossover population with no discernible pattern of occurrence across products.

4 | DISCUSSION

The results of this study demonstrate that an advanced diaper skincare regimen including an emollient-containing diaper and an acidic, pH-buffered wipe (Regimen A) reduced the pH in the diapered area to a level similar to normal, undiapered skin. In addition, the skin pH at the PBI and genitals was significantly lower than when using a non–emollient-containing diaper and wipe with limited pH-buffering capacity (Regimen B). This pH-lowering effect occurred after only 3 days of product use, suggesting that the skin benefits of Regimen A are rapid and are likely attributed to the absorption of stool and urine, the protection of skin via transfer of the emollient to skin, and lasting pH effects of the acidic, pH-buffered wipe. Given the previous association between higher skin pH and diaper dermatitis,[15] this finding may be clinically significant based on previous work demonstrating a skin pH-lowering effect of diapers containing absorbent gelling materials and lower diaper dermatitis scores.[16] Lower skin pH for Regimen A occurred immediately after cleaning and was maintained for at least 60 minutes between diaper changes. The finding

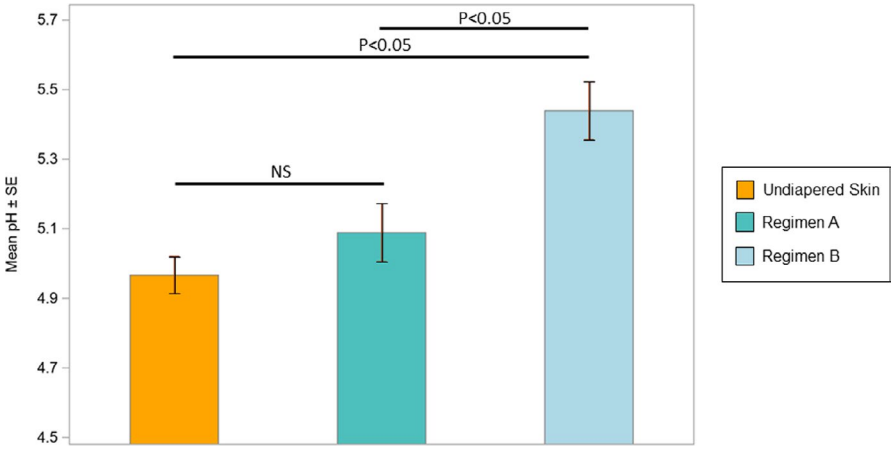

FIGURE 1 Skin pH at an undiapered skin site (Chest; yellow bar) and the perianal/buttock interface after 3 days of use of either Regimen A (green bar) or Regimen B (blue bar). Statistical significance is indicated by the connected bars. NS, not significant

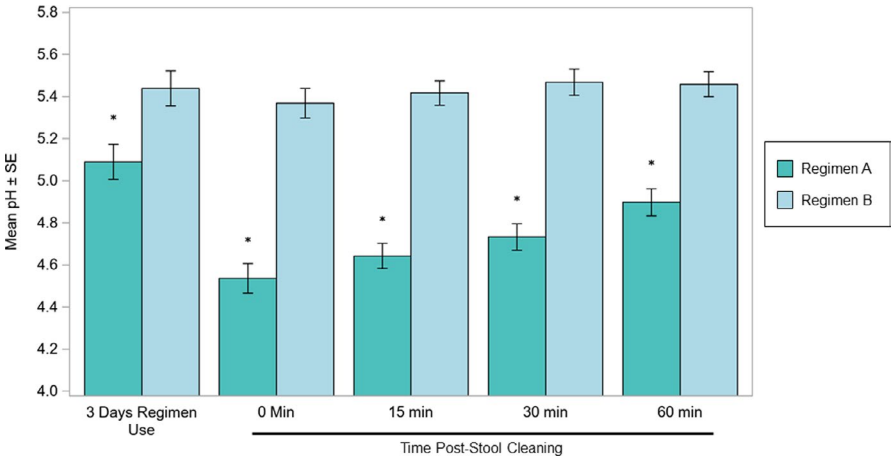

FIGURE 2 Perianal/buttock interface skin pH after 3 days of use and 0-60 minutes post–stool cleaning (Regimen A, green bars; Regimen B, blue bars). There were no differences between product regimens for stool pH (Regimen A: 5.7 ± 0.11; Regimen B: 5.6 ± 0.11) or number of wipes used post–stool cleaning (Regimen A: 2.49 ± 0.20; Regimen B: 2.66 ± 0.20). * $P < .05$ vs. Regimen B

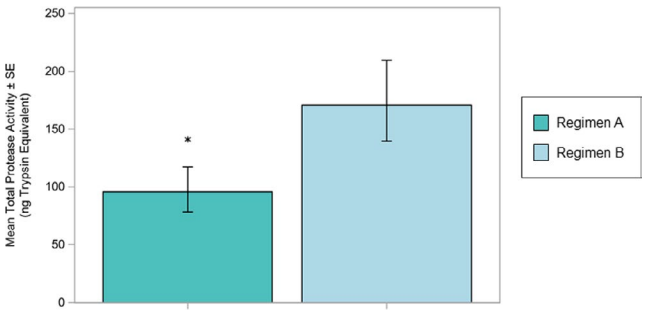

FIGURE 3 Babies on Regimen A (green bar) had 40% less enzyme activity remaining on skin post–stool cleaning vs. Regimen B (blue bar). There were no differences between product regimens for stool enzyme activity (Regimen A: 1819 ± 167; Regimen B: 2041 ± 187 ng/mg stool) or number of wipes used post–stool cleaning (Regimen A: 2.52 ± 0.25; Regimen B: 2.57 ± 0.25). * $P < .05$ vs. Regimen B

of 40% less protease activity post–stool cleaning on Regimen A is significant and may cumulatively have impacts on skin during regular use. The protease activity could be further reduced considering that these enzymes are less active at the lower skin pH experienced by babies on Regimen A (>95% reduction vs. Regimen B; data not shown). The skin pH results are consistent with previous reports in which use of an acidic, pH-buffered wipe significantly reduced diaper skin pH compared to an unbuffered wipe and to a cloth and sterile water among hospitalized premature and full-term infants.[9] They are also congruent with previous work by Adam et al in which infant skin pH was significantly reduced immediately after cleaning from a stooling event. However, the previous work followed pH for only 6 minutes, whereas we demonstrated a pH-lowering effect for 60 minutes in this study.[17] Thus, protection of the skin via use of superabsorbent, emollient-containing diapers and acidic, pH-buffered wipes may be a factor in the promotion of skin health and reduction in the risk of DD caused by enzyme-containing stool.

This study is novel in terms of considering the impact of two unique diapered skincare regimens (ie, diaper and wipe) on the skin properties of newborn infants. While the current study examined regimen use short-term, given the repeated exposure to irritants (eg, feces) and the increased risk of diaper skin damage, these results may have implications on skin health longer term. Further work is needed in this regard. Since an acidic skin pH is required for SC cell cohesion, an increased pH may reduce its integrity and increase susceptibility to mechanical damage.[10,18,19] Further, an acidic skin pH is necessary to promote colonization of appropriate, commensal resident microflora and attachment to the skin.[5] Higher skin pH can alter the normal skin flora and increase the risk of infection by common skin species including Staphylococcus, Streptococcus, and Candida.[20]

Given the central role of fecal enzyme activity in diaper dermatitis, it is of particular interest that Regimen A reduced residual protease activity post–stool cleaning. This effect was not due to the number of wipes used and is unlikely to reflect differences in caregiver behavior as the same infant and caregiver used both product regimens. These results are consistent with previous literature showing a disposable diaper with an apertured topsheet was more effective at absorbing stool in the diaper and left less stool on the skin surface.[21] The diaper used in Regimen A contained an emollient on the topsheet, and previous investigations demonstrated such products transferred the emollient to skin[22] and reduced average erythema scores on diapered skin.[23] The acidic, pH-buffered wipe is expected to reduce activity of residual enzymes remaining on skin.[24]

While the goal of the current study was to demonstrate the acute impact of a diaper and wipe regimen on infant skin pH and reduced enzymatic activity on the skin, additional studies to examine the long-term impacts of the regimen are needed, including examination of skin integrity or impact on diaper dermatitis incidence and severity. This should be investigated in a future study. The impact of diet on residual enzyme activity was not possible given the predominance of breastfed infants in this newborn population, but could be investigated in a future study. Further, the lower skin pH at the PBI in Regimen A vs. B was persistent across Fitzpatrick skin types, but requires further investigation given the limited number of infants across all skin types (eg, <10% of Fitzpatrick types V and VI). An improvement in skin barrier properties is supported by previous findings demonstrating accelerated barrier recovery in the presence of acidic pH conditions (pH = 5.5) compared to a neutral pH (pH = 7.4).[10,25] Previous publications have demonstrated the ability of a diaper[26] and wipe[9,17] to impact skin pH, and this study shows an impact of the 2 common diapering products when used together; however, a limitation of the design is that it makes it impossible to ascribe the overall effect to any one product attribute. The study reflects how the products are actually used—that is, frequently the same brand of diapers and wipes is purchased—and the resulting skin condition parents may achieve. Removal of fecal material is a property of both the absorbent diaper and the liquid containing wipe during cleaning, and the specific contribution should be investigated in future studies.

Skincare in the diaper area, especially in newborns, is of concern to parents[7] as it is a source of anxiety and increased health care use, so solutions to prevent or reduce DD remain a priority.[27] Professionals are in a position to advise parents of best practices by dispelling any misconceptions that skin pH is neutral (ie, that of water; ~7) and to share the benefits of skincare products with an acidic profile as supportive of skin health.

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CONFLICT OF INTEREST

Jennifer Gustin, Lisa Bohman, Julie Ogle, Tanuja Chaudhary, Lijuan Li, Gina Fadayel, Maria C. Mitchell, and Andrew Carr are employees of The Procter and Gamble Company.

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