

Skin Care in the NICU Patient: Effects of Wipes versus Cloth and Water on Stratum Corneum Integrity

Marty Visscher^a Mauricio Odio^b Teresa Taylor^c Tamina White^c
 Shelly Sargent^c Linda Sluder^c Louise Smith^c Teresa Flower^c Beth Mason^c
 Maureen Rider^c Amy Huebner^c Pattie Bondurant^c

^aSkin Sciences Institute, Cincinnati Children's Hospital Medical Center, ^bProcter & Gamble Company, and

^cRegional Center for Newborn Intensive Care, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

Key Words

Stratum corneum · Skin irritation · Erythema · pH, skin · Transepidermal water loss · Neonatal intensive care unit · Diaper wipe

Abstract

Background: NICU patients are at risk of skin breakdown due to prematurity, irritant exposure, medical status and stress. There is a need to minimize damage, facilitate skin development and reduce infection risk, but the literature on the effects of skin care practices in NICU patients is limited. **Objectives:** To test the hypothesis that baby diaper wipes with emollient cleansers and a soft cloth would minimize skin compromise relative to cloth and water. **Methods:** In 130 NICU infants (gestational age 23–41 weeks, at enrollment 30–51 weeks), measurements of skin condition, i.e., skin erythema, skin rash, transepidermal water loss (TEWL) and surface acidity (pH), within the diaper and at diaper and chest control sites were determined daily for 5–14 days using standardized methods. Treatments were randomly assigned based on gestational age and starting skin irritation score: wipe A, wipe B, and the current cloth and water NICU stan-

dard of care. **Results:** Perineal erythema and TEWL were significantly lower for wipes A and B than cloth and water beginning at day 5 for erythema (scores of 1.11 ± 0.05 , 1.2 ± 0.05 , and 1.4 ± 0.06 , respectively) and day 7 for TEWL (28.2 ± 1.6 , 28.8 ± 1.6 , and 35.2 ± 1.6 g/m²/h, respectively). Wipe B produced a significantly lower skin pH (day 5, 5.47 ± 0.03) than wipe A (5.71 ± 0.03) and cloth and water (5.67 ± 0.04). The starting skin condition, stool total, age and time on current standard impacted the outcomes. **Conclusions:** Both wipes are appropriate for use on medically stable NICU patients, including both full and preterm infants, and provide more normalized skin condition and barrier function versus the cloth and water standard. Wipe B may facilitate acid mantle development and assist in colonization, infection control and barrier repair. Neonatal skin continues to change for up to 8 weeks postnatally, presumably as it adapts to the dry extra-uterine environment.

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Introduction

Skin irritation is associated with diaper wearing. Overhydration, urine, feces, friction, increased skin pH, diet, and age are detrimental to skin integrity via disruption of the stratum corneum (SC) lipids and leading to increased penetration and epidermal inflammation [1, 2]. Fecal enzymes can degrade SC proteins and cause inflammation [3]. Skin compromise triggers processes of SC repair and initially results in hyperproliferation, a defective architecture, aberrant water-binding properties, insufficient hydration and inadequate desquamation, i.e., until the normal homeostasis is restored. In contrast to the full-term newborn, the premature infant has a poor epidermal barrier with few cornified layers [4, 5] and is at risk of increased permeability to exogenous materials (e.g., infectious agents), additional skin compromise, and delayed skin barrier maturation [6]. Clinically, very premature infants frequently exhibit an abnormal pattern of desquamation several weeks after birth, indicative of a hyperproliferative SC. An acidic pH is necessary for the effective functioning of enzymes in SC formation and integrity, i.e., lipid metabolism, bilayer structure, ceramide synthesis, and desquamation [7, 8]. Acidification via free fatty acids is required for SC cell cohesion, while an increased pH may reduce SC integrity and enhance susceptibility to mechanical damage in high-risk infants [9]. An acidic pH contributes to the SC innate immune function by inhibiting colonization of pathogens, e.g., *Staphylococcus aureus* [10].

In the design of research on neonatal skin, the changes related to SC barrier adaptation and maturation must be considered. Healthy full-term newborn skin undergoes progressive changes in epidermal barrier properties, e.g., increased hydration and water binding, during the first month of life as it adapts to the dry extra-uterine environment [11]. Newborn skin was significantly drier than the skin of older infants (1, 2 and 6 months) and their mothers [12]. Water-handling behavior and levels of SC water-binding amino acids continue to develop throughout the first year of life [13]. For premature infants, SC formation is rapid with exposure to a dry environment [14, 15] and NICU practices, e.g., incubator humidity, have evolved to optimize it [16]. Estimates of the time to complete barrier maturation vary from 2 to 9 weeks postnatal age [14, 17–19]. Decreases in skin pH immediately after birth have been reported for healthy full-term neonates [11, 20, 21]. Skin pH decreased for 4 weeks postnatally in VLBW infants, varied with gestational age (GA), and was higher for a longer time (i.e., infants

<1,000 g) [22]. Evaluation of multiple skin parameters, including measures of irritation, SC barrier integrity (transepidermal water loss, TEWL), and surface acidity, is required to fully characterize the response to topical treatments.

For NICU patients, routine care, e.g., diaper skin care/ changing, bathing, can provoke physiological responses including increased heart rate, increased oxygen saturation, and behavioral disruption (increased motor cues, etc.) [23, 24]. Nurses commonly report even greater responses for NICU infants who have diaper skin damage (breakdown), although the magnitude has not been reported. These disturbances cause stress for parents and healthcare staff as they work to calm the infant. Diaper skin breakdown is common in hospitalized patients [25]. The relationship between skin damage and pain has not been quantified but nurses and parents know it is painful. Skin compromise may also delay the start of enteral feeds, i.e., until the condition improves.

The literature on common skin care practices in NICU populations is limited. Cloth and water is widely used for diaper skin cleansing, but water alone is often insufficient for soil removal [26]. Evidence-based practice guidelines recommend a soft cloth or wipes free of alcohol and detergents, but lack data among neonates [27]. We hypothesized that the use of baby diaper wipes based on emollient cleansers and a cloth substrate to minimize friction would maintain normal skin condition (i.e., better) relative to water-soaked 4 × 4 cloths, the current standard of care for NICU infants. The aims of the present study were to evaluate diaper skin condition longitudinally with assigned treatments as part of the infant's routine care by bedside caregivers and to compare the effects of wipes with cloth and water.

Subjects and Methods

Infants from the Regional Center for Newborn Intensive Care (RCNIC; level III NICU) of the Cincinnati Children's Hospital Medical Center (CCHMC) were recruited from November 2006 to January 2008. The majority of RCNIC patients were admitted for surgical procedures, comprehensive diagnoses, or from outlying areas. The research was approved by the CCHMC Institute Review Board. Parents/guardians provided written informed consent. Exclusions were: medically unstable; greater than 12 weeks of age (adjusted GA for infants <38 weeks); expected stay <5 days; epidermal defects, and receiving phototherapy. GA was confirmed by examination upon admission. Evaluations were conducted daily except when the infant could not tolerate the procedures. Diaper skin breakdown was treated with a standard cream (petrolatum, zinc oxide or combinations) until resolution.

Randomization

At enrollment, randomization was stratified into two GA categories (23–37 and ≥ 38 weeks) and two initial skin condition categories (skin erythema or rash ≤ 0.5 score, and skin erythema or rash ≥ 1.0 score for any diaper skin region [perineal, genital, intertriginous, buttocks]). Eligible subjects were assigned to one of three treatment groups (wipe A, wipe B, cloth and water) after the initial skin evaluation. Subject treatment assignments were recorded and sealed in individual opaque envelopes to prevent unblinding of the entire population.

Outcomes

The primary outcome was perineal skin condition and measured as skin irritation (erythema) and SC barrier integrity (TEWL in $\text{g/m}^2/\text{h}$). Within the diaper area, the perineum is the region of the most severe skin compromise. Secondary outcomes were diaper skin pH, skin condition in the genital, buttocks and intertriginous regions, and changes in skin adaptation (measured as SC barrier integrity and surface pH) over the study period. Factors that could impact diaper skin condition, e.g., stool frequency, stool total, number of diaper changes, were recorded for inclusion in the analysis.

Skin Measurements

Each diaper region, perineal, genital, buttocks, and intertriginous, was evaluated for irritation (erythema and rash) using standardized scales (7-point 0–3, 0.5 grade increments). Numerical scores were based on surface area of coverage and intensity of the compromise [28]. The perineal region was the rectangular area from the edge of the scrotum or vulva, beyond the anus and laterally to the outer edge of the gluteal muscles. SC integrity was measured as TEWL ($\text{g/m}^2/\text{h}$) with a closed chamber device (VapoMeter, Delfin Technologies, Ltd, Finland) using standardized protocols [29–31]. The measurement diameter of the VapoMeter is 12 mm, corresponding to an area of $\sim 120 \text{ mm}^2$ and constituting a localized (versus regional) value. Within the perineal region, the localized area of the most severe compromise was selected for TEWL measurement. Typically, it was to the left or right of the anus. For subjects without skin damage, an area to the left or right was randomly selected for daily evaluation. In order to correlate skin compromise with TEWL values, the local site was also evaluated for erythema (0–4) and dryness (0–6) using standardized scales [32, 33]. For clarity, ‘perineal site’ is the full perineal region and ‘local site-perineal’ is within the perineum where instrumental measures were taken. Similar localized skin sites ($\sim 120 \text{ mm}^2$) on the chest (midline, nipple) and within the diaper (suprapubic) were controls for all measurements. The pH of diaper and chest controls was measured with a flat electrode (Skincheck™, Hanna Instruments, UK) calibrated daily to pH 4 and 7 [34].

Study Procedures

The study was a single blind design wherein research personnel (judges) were unaware of the subject’s treatment. Prior to enrollment, cloth and sterile water was used for cleansing with a liquid cleanser as needed for substantive soils (Johnson’s® Baby Shampoo). All infants used the same products for routine skin care (diapers, bathing). Treatments were applied about 8 times per 24 h by multiple caregivers (2–4 different nursing staff, parents, family members) over the course of the study. Nine neonatal nurses from the RCNIC and the investigator (M.O.V.) conducted the once dai-

ly evaluations 15–20 min after a skin cleansing/diaper change. The research staff did not apply treatments. To minimize disruption, the evaluations were conducted as part of the infant’s routine clustered care (typically performed every 3 or 4 h). Variability due to soils (feces, urine, creams) was minimized by assessing the skin 15–20 min after cleansing/diaper changes. The 15- to 20-min interval between diaper change and skin evaluation was used as a means to allow skin equilibration to similar conditions for each subject, since typical approaches, e.g., skin exposure to open air, were not practical in this population. Previous work on water equilibration within the diaper (data not included) showed that 15 min was sufficient for skin surface water to evaporate thereby avoiding artifacts due to the cleaning process itself. Erythema and rash were scored visually followed by TEWL and pH. Developmentally supportive infant care was used to minimize disruption. The bedside nurse recorded skin breakdown and diaper cream use twice per 12-hour shift. Stool and urine totals, stool frequency, and number of diaper changes for the preceding 24 h were recorded.

Skin Cleansing Treatments

The diaper wipes were selected from available products that could be purchased by healthcare institutions in the event that the current cloth and water standard was found to be less than optimal. The selection criteria included: absence of a volatile alcohol (e.g., ethyl alcohol, isopropyl alcohol); absence of fragrance; lack of known skin irritants (e.g., anionic surfactants such as ammonium lauryl sulfate); absence of formaldehyde-releasing preservatives; presence of a soft cloth, and availability of published trials among infants [35–37]. Wipe A (Pampers® Sensitive Wipes, Procter & Gamble, Ohio, USA) was a nonwoven substrate impregnated with water, aloe barbadensis leaf juice, disodium EDTA, xanthan gum, bis-PEG/PPG-16/16 PEG/PPG-16/16 dimethicone, caprylic/capric triglyceride, PEG-40 hydrogenated castor oil, sodium phosphate, sodium hydroxymethylglycinate, benzyl alcohol, iodopropynyl butylcarbamate, citric acid, bisabolol, and chamomilla recutita (matricaria) flower extract for a product pH of 5.2. The benzyl alcohol is a nonvolatile ingredient used as a product preservative and present at very low levels. Wipe B (Pampers® Sensitive Wipes) was a nonwoven substrate impregnated with water, glycerin, citric acid, PEG-40 hydrogenated castor oil, sodium citrate, benzyl alcohol, phenoxyethanol, xanthan gum, sodium benzoate, disodium EDTA, bis-PEG/PPG-16/16 PEG/PPG-16/16 dimethicone, ethylhexylglycerin, caprylic/capric triglyceride, aloe barbadensis gel, bisabolol, and chamomilla recutita extract. Wipe B was formulated with acids as the preservative system for a product pH of 4.0. Treatment C was 4 × 4 inch 4-ply rayon/polyester nonwoven formed fabric (Allegiance® General-Use Sponges, Cardinal Health, Ill., USA) and water (Similac Water, Sterilized, Ross Pediatrics, Ohio, USA; system pH of 5.2).

Statistical Analysis

Regional erythema and rash scores were computed as the difference from the within diaper control site (suprapubic). Baseline measures and group characteristics were evaluated using ANOVA and the appropriate pair-wise procedures (SigmaStat, SPSS, Inc.) with significance at $p \leq 0.05$. Treatment effects were assessed for days 5, 7, 10 and 14 using linear mixed models repeated measures procedures with day of treatment as the repeat (F statistic, $p \leq 0.05$; SPSS, SPSS, Inc.). The linear mixed models procedure permits analysis of subjects measured at different times (i.e., through-

Table 1. Demographic characteristics (mean \pm SD for ages; mean \pm SE for all others) for the total population and each treatment group

Parameter	Total	Wipe A	Wipe B	Cloth and water
Number	130	45	45	40
Gestational age at birth, weeks	33.8 \pm 4.3	34.3 \pm 4.4	33.3 \pm 4.8	34.0 \pm 3.8
Weight at birth, kg	2.28 \pm 0.09	2.33 \pm 0.15	2.21 \pm 0.16	2.29 \pm 0.16
Age at start, weeks	38.4 \pm 4.1	38.2 \pm 4.2	39.4 \pm 0.7	37.5 \pm 0.4
Weight at start, kg	2.86 \pm 0.08	2.86 \pm 0.14	3.08 \pm 0.15	2.64 \pm 0.12
Adaptation time, weeks (birth to enrollment)	4.6 \pm 0.4	4.0 \pm 0.6	6.1 \pm 0.7	3.5 \pm 0.5
Time on cloth and water, weeks	3.1 \pm 0.3	2.6 \pm 0.4	3.8 \pm 0.5	2.8 \pm 0.4
Gender				
Female	48	15	17	16
Male	82	30	28	24
Mixed stool/urine, g (previous 24 h)	151.1 \pm 11.8	140.1 \pm 20.3	145.5 \pm 20.1	169.8 \pm 21.2
Stool frequency (previous 24 h)	4.0 \pm 0.2	3.6 \pm 0.4	3.8 \pm 0.4	4.7 \pm 0.4

out the 14-month enrollment period) and inclusion of incomplete cases (e.g., cases where measurements could not be performed due to patient factors). Repeated measures procedures are used for time course data, i.e., where the effects on any given day are influenced by previous treatments. The covariance type was diagonal. Covariates examined during analysis included initial (baseline) skin condition, age at study start (postnatal age), GA, stool total, and time on cloth and water. The randomization stratum for a GA of 23–37 weeks was broad and subjects varied in the length of time from birth to study start. Since neonatal skin changes during the immediate newborn period, GA and time from birth were included as covariates to insure that differences in treatment outcomes were not biased by these factors [11]. Treatment comparisons were made with the method of Bonferroni. Analysis of variance (univariate GLM) was used for subgroup analyses.

Results

Subjects

A total of 131 infants were enrolled. Ninety-seven infants were <38 weeks GA and 33 were ≥ 38 weeks GA (table 1). One subject withdrew on study day 2. One infant (25 weeks GA) died due to complications unrelated to the study, after completion of study participation and a period of medical instability. In general, infants were admitted to the RCNIC for surgery or specialized diagnostics/consultation. Primary diagnoses among study subjects included respiratory, gastrointestinal, genetic, cardiac, congenital, neurological, and craniofacial conditions. There are ~ 750 admissions to the RCNIC per year (~ 875 for the study period). Patients were evaluated for eligibility by the principal investigator (M.O.V.) as determined by the judgment of the clinical staff regarding the

medical status (stable, unstable), progress in recovery from medical condition, and anticipated length of stay. The enrollment rate was about 33% of eligible infants and lower than expected, given the minimal risk of the procedures. The trauma of having an ill newborn and of being in an ICU setting may have discouraged participation. The mean participation was 10.4 days and 56 infants completed 14 days. The adaptation time (birth to enrollment) was 0.4–16.4 weeks. The time on cloth and water before study start was 0.1–13.4 weeks.

Initial Skin Condition

Initial (baseline) erythema was highest for the perineal (1.2 \pm 0.1) and intertriginous (1.3 \pm 0.1) regions. Rash was highest in the perineum (0.5 \pm 0.1). TEWL ($\text{g}/\text{m}^2/\text{h}$) differed significantly among the three 'localized' sites that were evaluated: perineal (36.9 \pm 3.3); within diaper (14.0 \pm 0.7), and chest (11.0 \pm 0.5). Skin pH was higher for the diaper area (5.74 \pm 0.05) than the chest (5.33 \pm 0.03; $p < 0.05$). The 3 treatment groups did not differ significantly in demographic characteristics (GA, age at start, adaptation, time on cloth and water; table 1) or skin measures at baseline (skin grades, TEWL, pH; ANOVA, Dunn's method for multiple comparisons, $p \leq 0.05$; data not shown). The demographic characteristics were incorporated into the statistical model in order to account for nonsignificant differences among the 3 treatment groups.

Outcome Measures: Treatment Effects

The primary outcome measure of skin erythema (both perineal region and the localized perineal site) was significantly lower for both wipes compared to cloth and wa-

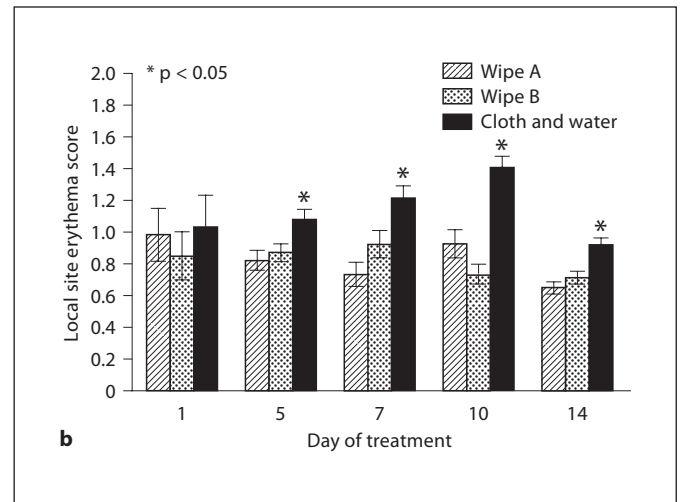
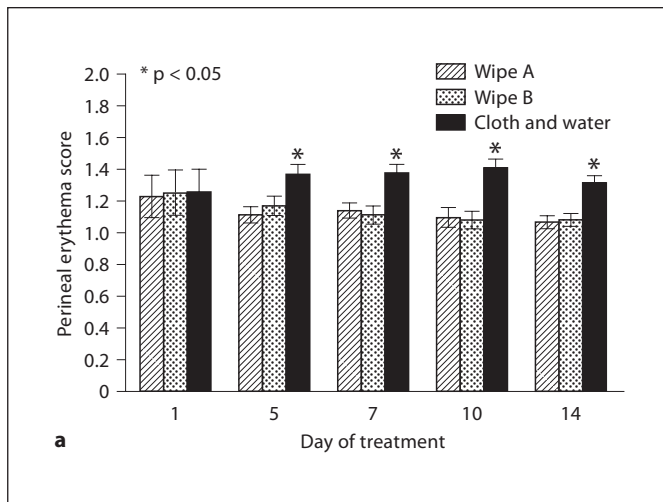
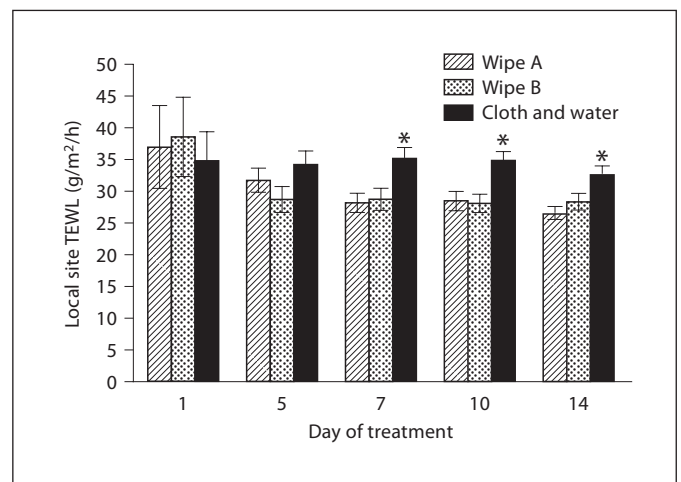


Fig. 1. Skin erythema. **a** Mean perineal erythema (estimated marginal means \pm SE) was significantly lower for both wipes than for cloth and water on days 5, 7, 10, and 14 ($* p = 0.03\text{--}0.000$). **b** Localized perineal site erythema (estimated marginal means \pm SE) was significantly lower for each wipe than for cloth and water on days 5, 7, 10, and 14 ($* p = 0.04\text{--}0.000$).

Fig. 2. Instrumental evaluation of stratum corneum barrier integrity (transepidermal water loss) and skin surface pH. Mean TEWL values ($\text{g}/\text{m}^2/\text{h}$, estimated marginal means \pm SE) for infants treated with wipe A, wipe B, and cloth and water over the treatment period. TEWL for the local perineal site was significantly lower for both wipes than cloth and water on days 7 ($* p \leq 0.01$), 10 ($* p \leq 0.002$), and 14 ($* p \leq 0.03$).

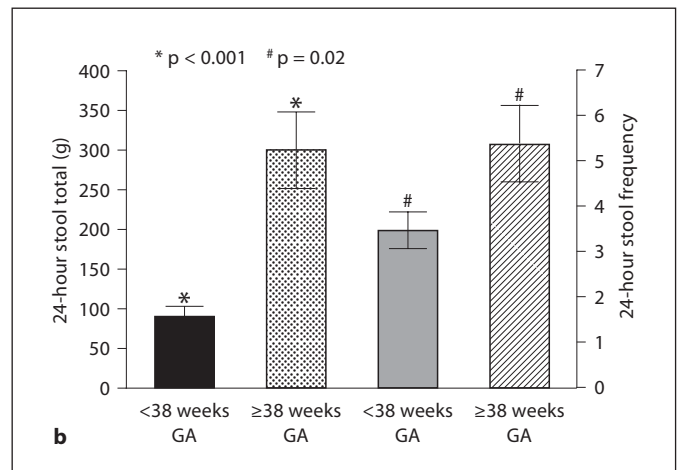
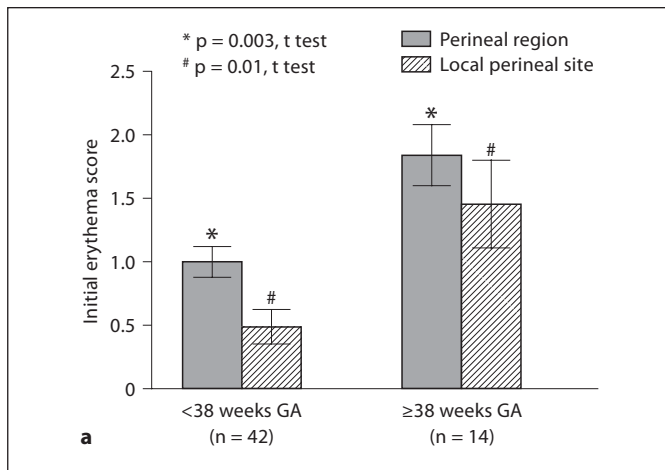


ter beginning on day 5 (fig. 1). Measures of SC barrier integrity (TEWL of localized perineal site) were lower for both wipes than cloth and water on days 7 ($p = 0.01$) and 14 ($p = 0.002$; fig. 2). For the secondary outcomes, scores for skin treated with wipes were lower than cloth and water ($p < 0.05$) as follows: perineal rash (days 5, 7, 10, 14, wipe B, and day 14, wipe A); genital erythema (days 5, 7, and 14, wipe B); buttocks erythema (day 14, wipe B), and buttocks rash (day 14, both wipes). The skin pH for wipe B (range 5.44–5.48, SE \pm 0.03) was lower than wipe A (range 5.67–5.73, SE \pm 0.02) and cloth and water (range 5.63–5.67, SE \pm 0.02–0.04) at every time ($p \leq 0.002$). None of the subjects exhibited intolerance to either wipe.

Factors Influencing Skin Condition

The initial skin measurements (baseline) were analyzed to determine the impact of patient characteristics

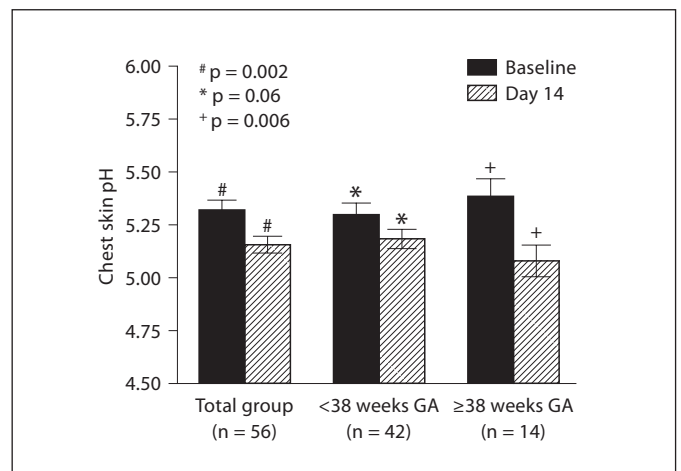
on skin condition. Initial perineal erythema was correlated with stool frequency (correlation coefficient 0.64, $p = 0.000$) and stool total (0.54, $p = 0.000$) but not with GA at birth. The lack of an association between skin compromise and GA was surprising, given the vulnerability of premature skin [4–6, 17, 18, 38]. A subgroup analysis was conducted for the 56 infants who completed 14 days to examine the influence of GA on perineal erythema. The demographic characteristics between this subset and the total population were similar. The group was subdivided by GA at birth <38 weeks ($n = 42$) or ≥ 38 weeks ($n = 14$). Demographic characteristics are shown in table 2. GA group was significant for initial perineal erythema, localized site perineal erythema, perineal rash, stool frequency and stool total (g). The group <38 weeks GA had lower baseline perineal erythema, perineal rash, local site erythema, stool frequency and stool total, high-



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Fig. 3. Initial skin erythema (a) and stool characteristics (b) by strata of GA at birth. The group <38 weeks GA had lower baseline perineal erythema (* $p = 0.003$, t test), local site erythema (# $p = 0.01$), stool frequency (# $p = 0.01$) and stool total (* $p < 0.001$) than the ≥ 38 weeks GA cohort.

Fig. 4. Chest skin pH measurements at baseline and on day 14 for the infants who completed 14 days of evaluation. The stratum corneum pH decreased significantly from baseline to day 14 ($p = 0.002$, paired t test). The pH decrease was significant for infants ≥ 38 weeks GA ($p = 0.006$) and directional for the infants <38 weeks GA ($p = 0.06$).



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er chest TEWL ($p = 0.02$), and longer adaptation time (defined as the number of weeks from birth to the baseline assessments at study start) than the ≥ 38 weeks GA cohort ($p = 0.02$; (fig. 3; table 2).

Skin Changes over Time and Adaptation

The effects of maturation on skin barrier properties were determined from the chest skin barrier integrity (TEWL) and surface acidity measures since the site was not affected by study treatments. The 56 infants who completed 14 days of assessment were used for this analysis by comparing days 1 and 14 (paired t test). TEWL was not different from baseline (12.1 ± 0.8) to day 14 (12.0 ± 0.7). However, the SC pH decreased from 5.33 ± 0.04 at baseline to 5.17 ± 0.04 on day 14 ($p = 0.002$, paired t test; fig. 4). Since the mean time from birth to enrollment was 5.1 ± 0.6 weeks, the pH decrease suggests that neonatal

Table 2. Demographic characteristics and instrumental measures of TEWL and skin pH for the subjects with 14 days of evaluation segmented by GA strata (mean \pm SD for ages; mean \pm SE for all other values)

Parameter	<38 weeks GA (n = 42)	≥ 38 weeks GA (n = 14)	p value groups
GA birth, weeks	32.1 \pm 3.6	38.9 \pm 0.9	<0.001
Age start, weeks	36.8 \pm 3.4	41.8 \pm 3.1	<0.001
Adaptation, weeks	5.6 \pm 4.4	2.9 \pm 2.9	0.02
TEWL, g/m ² /h			
Perineal	29.3 \pm 2.4	49.4 \pm 13.0	0.08
Diaper	15.0 \pm 1.3	14.7 \pm 3.3	0.4
Chest	13.4 \pm 1.0	8.7 \pm 1.1	0.02
Skin pH			
Diaper	5.65 \pm 0.08	5.88 \pm 0.16	0.2
Chest	5.31 \pm 0.05	5.39 \pm 0.08	0.4

skin continues to change well after birth, presumably as it adapts to the dry environment. The pH decrease was significant for infants ≥ 38 weeks GA ($p = 0.006$) and directional for the infants < 38 weeks GA ($p = 0.06$). The younger infants had a longer time from birth to study start (adaptation time) and the smaller difference in skin pH between days 1 and 14 may indicate that the reduction in skin surface acidity is greater immediately following birth.

Discussion

In this study, skin cleansing with diaper wipes composed of a soft nonwoven substrate with water and emollient cleansers led to decreased skin irritation compared to use of the current standard of cloth and water among hospitalized premature and full-term neonates. Significantly lower TEWL indicated a more normalized SC barrier for wipes than for cloth and water. Skin treated with wipe B was more acidic (lower pH) than with wipe A or cloth and water. This assessment provides the first report of the skin effects of wipes and the cloth and water standard in high-risk neonates. The question of clinical significance associated with the magnitude difference in skin erythema that we observed with use of wipes compared to cloth and water must be considered. This question, we believe, is best addressed in the context of the relation between skin barrier integrity and susceptibility to irritant damage. Diaper area skin exists in an environment of persistent threat to its integrity due to exposure to over-hydration, friction, fecal irritants, etc. [39]. There is a linear relationship between the severity of erythema and percutaneous irritant penetration [40]. A positive correlation between increased TEWL (as an indicator of skin barrier disruption) and percutaneous penetration of irritants has been demonstrated [41–43]. Considering this evidence, the higher erythema scores observed in the group assigned to cloth and water predict that the diaper area skin of these children is at a higher risk for more severe irritant responses than that of children assigned to use of wipes. Thus, regardless of the quantitative erythema scores observed on any given child, at any given point in time, a risk-based benefit analysis favors the use of wipes over cloth and water for diaper area care in the NICU.

The results extend and are consistent with previous reports in older, healthy infants that found: (a) diaper wipe treatment resulted in significantly lower perineal erythema and roughness versus a cotton washcloth and

water ($n = 41$, 15 ± 1.0 months) [37]; (b) intertriginous erythema was lower with wipes than with water and an implement ($n = 102$, 6–24 months) [35]; (c) atopic infants ($n = 57$, 11.7 ± 4.1 months) had no adverse effects during 4 weeks on wipes [35], and (d) no differences in periurethral skin colonization with Gram-negative bacteria (*Escherichia coli*, *Klebsiella* spp., *Proteus* spp.) or *Staphylococci* were found in healthy infants (1–24 months) on wipes ($n = 96$) or cloth and water ($n = 77$) [44]. One of four wipes ($n = 302$, 4–12 months) decreased diaper skin pH from 5.6 to 5.0 ($p < 0.01$) but no differences in erythema or rash were seen [45].

We investigated the treatment effects on skin surface pH as a secondary outcome, given previous reports on the important role of acidity in skin barrier function. The rate of barrier recovery after tape stripping was increased with a pH 5.5 buffer [46]. Topical treatment of the SC with PPAR α activators was shown to increase the rate of skin pH lowering immediately following birth in neonatal animals, thereby demonstrating that the adaptive mechanisms can be influenced with exogenous materials [47]. Therefore, we speculate that the provision of an acidic skin pH, as demonstrated for wipe B, may offer an additional approach to facilitate barrier repair and acid mantle development in neonates at risk for skin compromise. The importance of an acidic SC for barrier development and repair coupled with our observation of continued postnatal acidification suggest that skin surface pH may be an important marker of SC maturation and adaptation.

A relevant study limitation is that treatment could not be evaluated on infants aged 23–29 weeks, primarily due to the infants' medical conditions and the reluctance for parents to provide informed consent prior to improvement in their infant's status. The lower erythema in the preterm population was somewhat unexpected and attributed to the significantly lower stool exposure. While the variables of GA and adaptation time cannot be delineated, the combination appears to result in reduced stool exposure. Infants with high stool exposure in the immediate postnatal period seem to be at greatest risk for skin breakdown. However, additional investigation on the skin effects of diaper wipes on infants of 23–29 weeks GA immediately following birth is warranted. Similarly, the study population was limited to medically stable infants and did not include those with high acuity even though diaper skin cleansing is part of their routine care. In clinical practice, information on the excluded subsets could be obtained by ongoing monitoring and quality control measures of skin condition within this population.

The present study was further limited in that it did not elucidate the effects of individual formulation ingredients or of the cloth to determine the specific factors that were responsible for the observed measures of skin condition. For example, the effect of the substrate alone could be determined by preparing a 'water only' wipe. Additional studies are required to identify the ingredient effects and/or to evaluate materials that could further improve skin condition or mitigate the effects of irritants.

Overall, both diaper wipes are appropriate and effective for diaper skin care among similar NICU infants. This was confirmed by primary outcome measures of perineal skin condition, i.e., both visual scores (erythema) and measures of SC integrity (TEWL), which convincingly showed improved diaper area skin condition for wipes compared to cloth and water. The skin pH-lowering property of wipe B may have important implica-

tions for acid mantle development, skin colonization, infection control, and have an influence on alkaline irritants (e.g., stool, enzymes). The SC of this cohort of high-risk neonates continues to change long after birth. Elucidation of factors that impact skin condition provides the basis for treatment strategies and interventions in the high risk population. Studies to examine the effects of pH-lowering diaper creams and the influence of stool pH, enzyme levels, consistency, and nutritional source are warranted.

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