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Quantitation of baby wipes lotion transfer to premature and neonatal skin

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ABSTRACT

Exposure to topically applied substances occurs routinely in premature and hospitalized infant care. Safety determinations are most accurate when exposures are based on appropriately designed studies to capture variations in practice patterns and population heterogeneity. Current safety assessments may not reflect actual practice resulting in overly conservative or understated default assumptions for toxicological determinations. We quantified the amount of baby wipes lotion transferred to premature and term neonatal skin as grams/kg body weight/day. We observed the soil type and number of wipes used for skin cleansing and measured lotion transfer from one wipe applied to freshly clean, dry skin. A Bayesian imputation approach was applied to compute lotion exposure and produce summary statistics. Model covariates were age and weight at evaluation, gender, soil type, soil amount, and number of diaper changes per day.

Lotion transfer was measured for 66 premature and 55 term neonates with 449 and 254 evaluations, respectively. The wipes per day was 12.52 overall (all infants and soils), 12.78 for premature and 12.21 for term neonates. Lotion transfer was 0.20 g/kg/day (95th percentile) overall, 0.21 for premature and 0.19 for term neonates. The statistical and experimental methodology represents an effective strategy for determining exposure and assessing risk.

1. Introduction

Exposure to topical agents occurs routinely in neonates including premature and hospitalized infants who have tapes, adhesives, monitor leads, diapers, antiseptics (e.g., chlorhexidine gluconate), cleansers, wipes, and diaper rash cream applied during their care. Safety determinations are most accurate when experimental measurements of exposure are in the context of end user demographics and reported as grams per body weight or per surface area per day (Kosemund et al., 2009). When experimentally based safety data are not available, hospitals and the health care institutions often decide the appropriateness for neonatal use from a review of published information on the fully formulated product, ingredients, frequency of use and a risk/benefit analysis. Product usage instructions may indicate a minimum age, e.g., older than one month, and/or suggest that the decision to use be left to the physician. For example, the Centers for Disease Control guideline recommends skin disinfection with 2% chlorhexidine gluconate (preferred), tincture of iodine, an iodophor or 70% alcohol for adults and older pediatric patients for prevention of intravascular catheter related infections (Lewis-Byers and Thayer, 2002). Recommendations cannot be made for infants <2 months due to limited evidence or lack of consensus (Garland et al., 2002; Lewis-Byers and Thayer, 2002), leaving health care institutions to decide the specifics of practice (Tamma et al., 2010) without any empirical supports. In

Abbreviations: CCHMC, Cincinnati Children's Hospital Medical Center; gestational age, GA; g, grams; kg, kilograms; LN, log-normal; MCMC, Markov chain Monte Carlo; NB, negative binomial; NICU, Neonatal Intensive Care Unit; WHO, World Health Organization.

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another example, medication excipients have not been tested sufficiently in neonates to determine safety and, procedures for selection and evaluation of excipients have been proposed to minimize risks (Turner et al., 2014).

The complexities of evaluating premature and hospitalized infants have thus far precluded generation of technical exposure data for this population. Consequently, safety assessments may be based on data for older or healthy term infants and they may not reflect actual practice for other infants. This strategy may result in default assumptions that may over or under predict actual exposure used for toxicological exposure based risk assessments by product manufacturers and regulatory authorities. Once accurate data from hospital use conditions are generated, the assumptions can be modified to reflect actual exposure and applied to safety assessments. To our knowledge, there are no reports of exposure levels for topically applied products among either premature or hospitalized neonates.

We conducted a study among hospitalized infants to determine the amount of lotion transferred in grams/kilograms body weight/day at the 95th percentile during diaper skin cleansing. Secondary outcomes were number of wipes per cleaning, number of cleaning events per day, and diaper soil load, frequency and type. The number of wipes used to clean the skin and the soil type were observed at one diaper change per infant in 24 h. Lotion transfer was then measured after cleansing was complete using one wipe on clean, dry skin. It was not feasible to measure lotion transfer at every diaper change during 24 h in a Neonatal Intensive Care Unit. Therefore, a statistical model based on the assumption of missing at random data was applied to determine the number of wipes used and the amount of lotion transfer per diaper change, i.e., at the times when the diaper changes were not observed. Model covariates were age at evaluation, weight at evaluation, gender, soil type, soil amount, and number of diaper changes per day. This information was extracted from infant's medical record. We report exposures for the total population, the premature infants (<37 weeks) and the full term infants (≥37 weeks − one month). The lotion transferred is also reported for premature infants further classified as early premature infants (24 < 32 weeks gestational age) and mid/late premature infants (32 < 37 weeks gestational age) following the World Health Organization (WHO) convention (Blencowe et al., 2012).

2. Methods

2.1. Subjects

Infants from the 59-bed Level IV Newborn Intensive Care Unit (NICU) of Cincinnati Children's Hospital Medical Center (CCHMC) participated. Patients were admitted for surgical procedures, comprehensive diagnosis or from birth hospitals without intensive care units. The Institutional Review Board of CCHMC approved the protocol and granted a waiver of written informed consent. Infants with any condition that interfered with diaper area skin cleansing (e.g., surgical incision, wound) or a diagnosis of epidermolysis bullosa were excluded. Infants ≥37 weeks gestational age (GA) who were older than one month at the time of this study were excluded. Infants in critical condition, e.g., on high frequency oscillatory ventilation, on extracorporeal membrane oxygenation, were excluded at the investigator's discretion to minimize potential disruptions.

2.2. Experimental design

Diaper wipes (Pampers® Sensitive Wipes, The Procter & Gamble Company, Cincinnati, OH, USA) were routinely used for all NICU patients. The lotion transfer experiments were conducted under actual end user conditions at the infant's bedside during a scheduled nursing assessment. The skin area covered by the diaper is cleansed and diapers are weighed at these times for measuring the soil amount. Nursing assessments occurred at every 3–4 h depending upon the infant's care plan. The number of wipes per skin cleansing was expected to depend on infant age, size, gender, within diaper excrement type (urine, feces, mixed urine/feces) and soil quantity (Visscher et al., 2009, 2012). Within subject variability was addressed by conducting multiple evaluations on the same infant, over several days and multiple caregivers, i.e., nurse or parents. Potential caregiver effects were technique for holding and wiping, number per task and area of skin to be cleansed.

2.3. Lotion transfer measurement

The number of wipes per diaper change was determined from direct observation of one skin cleansing procedure per day. Next, the lotion transferred to clean dry skin from one additional wipe was measured gravimetrically with an analytical balance (model MS303S, capacity 320 g, readability 0.001 g, repeatability (sd) 0.001 g, linearity 0.002 g, stabilization time 1.5 s, Mettler-Toledo, Inc. Columbus, OH, USA). A package of Pampers® Sensitive Wipes (same production lot) was provided per infant and used only for transfer experiments. The procedure was as follows: (1) caregiver cleaned the diapered skin area with wipes per standard NICU practice, placed a dry diaper around the infant, blotted the skin and removed his/her gloves. (2) Caregiver donned new pre-weighed gloves. (3) Caregiver removed a single wipe, placed it on the balance, removed it and wiped the skin using the same soiled skin cleansing procedure. (4) Time from wipe removal from the package to completion of cleansing was recorded. (5) Caregiver placed the used wipe on the balance for weight determination. (6) Caregiver immediately removed the gloves and placed them on the balance.

The lotion transferred was the difference in wipe weight before and after wiping and corrected for loss on gloves and from evaporation as follows:

$$\begin{aligned}\text{Lotion transfer}(g) = &(\text{Wipe weight before}\\ &-\text{wipe weight after wiping})\\ &-(\text{glove weight after}\\ &-\text{glove weight before})\\ &-\text{amount lost to evaporation during wiping}.\end{aligned}$$

NICU temperature and humidity were well controlled. Infants in open beds were exposed to the environmental conditions of the room. Evaporation curves were generated for each of three NICU ward conditions and used to calculate evaporative loss (Table 1). Equations were generated for 14 incubator temperature and humidity settings encountered for the subjects and used to calculate evaporative loss (Table 2). Evaporative loss from wipes was found to be linear over the first 5 min of exposure to environmental conditions, to encompass the time taken by the study nurses to complete the diaper skin wiping. The time was recorded and used in the

Table 1
Evaporation correction equations for NICU locations and radiant warmers.

Condition	Evaporation correction (y) grams[a]
Location 1	$y = 0.0003x + 0.0008$
Location 2	$y = 0.0003x + 0.0008$
Location 3	$y = 0.0003x + 0.0023$
Radiant Warmer	$y = 0.001x + 0.0112$

[a] x = time (sec) required for process of wiping clean dry skin.