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ABSTRACT

postnatal changes in the skin, despite the clinical importance of this issue. *Aim:* To assess temporal changes in skin water content in preterm infants. *Study design:* A prospective observational study. *Subjects:* Infants admitted to the neonatal intensive care unit were included in this study. *Outcome measures:* Skin water content was measured at five different skin regions using dielectric methods at a depth of 1.5 mm. Skin water content was measured on postnatal day 1 in 101 infants, and the correlation between skin water content and gestational week was analyzed. Measurements were also made on postnatal days 2, 3, and 7, and every 7 days thereafter until the corrected age of 37 weeks in 87 of the 101 infants. Temporal changes were statistically analyzed after dividing participants into seven groups by gestational age. *Results:* On postnatal day 1, skin water content correlated inversely with gestational age at all skin regions. Skin water content decreased significantly over time, converging to the level of term infants by the corrected age of 32–35 weeks. *Conclusions:* Skin water content at a depth of 1.5 mm was related to corrected age and reached the level of term infants by the corrected age of approximately 32–35 weeks.

Background: Preterm infants have immature skin, which contributes to skin problems. Very little is known about

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1. Introduction

Skin care for preterm infants is an issue of major concern in neonatal intensive care units (NICUs), and skin problems sometimes become the primary cause of life-threatening events. Preterm infants have immature skin at birth, and changes begin soon after delivery due to maturation and the change from the intra-uterine to extra-uterine environments. The skin consists of the epidermis, with the uppermost layer of the stratum corneum (SC), the dermis, and subcutaneous tissue. Several studies have reported immaturity and maturation of the epidermis in preterm infants; the immature epidermis has a thin or unformed SC [1], allowing excessive transepidermal water loss (TEWL) [2-4]. Appropriate water balance can thus be difficult to maintain in preterm infants because the epidermis is immature. Compared with research on the epidermis, few reports have described immaturity of the dermis and subcutaneous tissue. Less collagen and fewer elastic fibers in the dermis result in a relatively high dermal water content (dermal edema) in preterm infants [5], which can lead to pressure/ischemic injury to the immature skin [6]. Evaluation of temporal changes in skin water content may thus provide important information for skin care in preterm infants. For this purpose, quantitative methods for evaluating skin water content in preterm infants might prove useful.

The present study evaluated temporal changes in skin water content using quantitative methods in term and preterm infants managed in the NICU.

2. Material and methods

Written informed consent for participation in this prospective observational study was obtained from the parents of potential participants immediately on admission to the NICU. All study protocols were approved by the ethics committee of Saitama Medical Center, Saitama, Japan.

2.1. Subjects

Infants born in the period between October 1, 2010, and September 30, 2012, who stayed in the NICU of Saitama Medical Center were eligible for inclusion in this study. To avoid interobserver errors, the study was initiated when one specific investigator (A.I.) was available. Of the 101 eligible infants, 14 were excluded from analysis of developmental changes of skin water content because of a lack of data from more than three data points.

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2.2. Skin water content measurement

Skin water content was measured using a MoistureMeterD (Delfin Technologies, Kuopio, Finland). The principle of measurement for this device has been well-described in previous studies [7,8]. Briefly, the device comprises a probe and a control unit. The depth of measurement (0.5, 1.5, 2.5, or 5 mm) is selectable by changing probes with different dimensions. The control unit generates 300-MHz electromagnetic waves, which are transmitted to the tissue to the abovementioned depth via an open-ended coaxial probe placed onto the skin. When reaching the tissue, the proportion of the electromagnetic wave that is reflected depends on the tissue dielectric constant (TDC), which itself depends on the amount of free and bound water in the tissue volume through which the wave passes [9]. Reflected wave information is sent to a control unit via the same probe used for wave transmission, and the TDC is displayed on the control unit. Theoretically, tissue with no water has a TDC value of 1, and pure water has a TDC value of about 78.5. TDC is directly proportional to tissue water content, and skin water content was calculated using the following formula: skin water content (%) = $100 \times (\text{TDC value} - 1)/77.5 [10,11]$.

This study aimed to evaluate water content, particularly in skin layers deeper than the epidermis. Given that thickness of the SC reportedly, ranges from 5.6 μ m to 35.4 μ m for infants [12], and the epidermis of preterm infants at postnatal day 1 has only 2.9 \pm 0.5 cell layers [1], we selected a probe that could measure water content to a depth of 1.5 mm, so that the majority of the value comes from the layers of skin deep to the epidermis. The 2.5- and 5-mm probes were not chosen because placement of these probes in close contact with the skin of very preterm infants was too difficult. Measurements were made on postnatal days 1, 2, 3, and 7, and every 7 days thereafter until a corrected age of 37 weeks. For all infants at all time points, measurements were made at the forehead, chest, thigh, abdomen, and dorsal aspect of the foot. Each measurement was made three times to obtain a mean value for TDC. Skin water content was then calculated using the abovementioned formula.

2.3. Standard practice in our NICU

Very preterm infants (less than 28 weeks) are commonly placed under high environmental humidity (more than 70–80%) as the initial setting on admission to the NICU, to prevent excessive TEWL. Humidity

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Clinical characteristic by gestational age.

is subsequently intermittently decreased within a few weeks. In our NICU in this study, initial settings for environmental humidity in the incubator on postnatal day 1 were approximately 90%, 80%, and 70% for infants in the 22–24, 25–27, and 28–30 week groups, respectively, and intermittently decreased according to infant body temperature, taking care not to induce hypothermia. Humidity was kept under 70% until postnatal days 35, 14, and 3 in the 22–24, 25–27, and 28–30 week groups, respectively, and under 60% until postnatal days 70, 42, and 28 in these groups, respectively. In the older age groups, humidity was kept within approximately 45–60% during the study period.

2.4. Data analysis and statistics

Infants were divided into 22–24, 25–27, 28–30, 31–33, 34–36, and ≥ 37 week groups.

Correlations between gestational age and skin water content on postnatal day 1 were analyzed using Pearson's correlation test. Skin water content was then collected in each group at each time point and temporal changes were statistically analyzed using one-way repeated analysis of variance. Correlations between changes in skin water content and changes in humidity and total fluid intake during the first 7 days as well as changes in body weight from birth to 28 postnatal days were also analyzed using Pearson's correlation test. Two-tailed *P* values less than 0.05 were considered significant. StatFlex (Artec, Osaka, Japan) was used for all statistical analyses.

3. Results

Clinical characteristics of groups by gestational age are shown in Table 1. In the analysis of developmental changes, 3, 1, 1, 4, 4, and 1 infant from the 22–24, 25–27, 28–30, 31–33, 34–36, and \geq 37 week groups were excluded, respectively, because of a lack of data.

3.1. Correlations between skin water content and gestational age

At postnatal day 1, skin water content correlated inversely with gestational age at all skin regions (forehead, r = -0.74, P < 0.001; chest, r = -0.83, P < 0001; thigh, r = -0.88, P < 0.001; abdomen, r = -0.91, P < 0.001; foot, r = -0.78, P < 0.001) (Fig. 1).

	22-24 weeks	25-27 weeks	28-30 weeks	31-33 weeks	34-36 weeks	≥37 weeks
n	10	15	15	22	33	6
Gestational age (weeks)	23.8 (0.8)	26.9 (0.9)	28.7 (0.8)	33.3 (0.9)	35.3 (0.9)	37.3 (1.8)
Birth weight (g)	572 (100)	790 (180)	1038 (221)	1524 (296)	2073 (471)	2451 (828)
Male sex	7 (70%)	6 (40%)	8 (53%)	9 (41%)	22 (67%)	2 (33%)
Cesarean delivery	10 (100%)	9 (60%)	11 (73%)	22 (100%)	29 (88%)	4 (67%)
1-min Apgar score	4 (1-8)	5 (1-8)	6 (1-8)	8 (1-8)	8 (1-9)	8 (8-9)
5-min Apgar score	6.5 (1-9)	8 (4-9)	8 (5-9)	9 (5-9)	9 (1-10)	9 (9-10)
Mechanical ventilation at birth	10 (100%)	13 (87%)	11 (73%)	2 (9%)	2 (6%)	0 (0%)
Days of ventilation	61.5 (38-172)	34 (0-110)	4 (0-52)	0 (0-6)	0 (0-4)	0
CPAP at birth	0 (0%)	1 (7%)	3 (20%)	7 (32%)	8 (24%)	2 (33%)
Sepsis	2 (20%)	1 (7%)	1 (7%)	0 (0%)	0 (0%)	0 (0%)
RDS	9 (90%)	11 (73%)	8 (53%)	0 (0%)	1 (3%)	0 (0%)
ROP requiring laser	8 (80%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
NEC	2 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
PDA requiring ligation	4 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
BPD	9 (90%)	7 (47%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IVH, grade III or IV	1 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Days of fluid intake >120 ml/kg/day	8.5 (6–16)	10 (6–19)	11 (4–24)	6 (5–12)	5 (3-8)	4.5 (3-25)
Days of enteral feeding >100 ml/kg/day	25 (15–59)	12 (8–31)	16 (7–19)	6 (2-14)	5 (2-10)	4 (2–24)

BPD, bronchopulmonary dysplasia; CPAP, continuous positive airway pressure; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity.

Values are expressed as median (range) or number (%) (male sex), with the exception of gestational age and body weight (mean [standard deviation]).

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