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국소 보습제 도포가 정상 영유아 피부에 미치는 영향에 관한 연구

현 무 열 · 이 용 희 · 오 원 종 · 유 광 호 · 박 귀 영 · 김 명 남 · 홍 창 권 · 김 범 준†

중앙대학교 의과대학 피부과학교실

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Effects of Topical Moisturizers on the Skin of Healthy Full-term Infants and Toddlers

Moo Yeol Hyun, Yonghee Lee, Won Jong Oh, Kwang Ho Yoo, Kui Young Park, Myeung Nam Kim, Chang Kwun Hong, and Beom Joon Kim†

Departments of Dermatology, Chung-Ang University College of Medicine, 224-1, Heukseok-dong, Donjak-gu, Seoul 156-755, Korea

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요 약: 보습제는 피부과에서 가장 흔하게 사용하는 제품 중 하나로, 피부장벽을 유지시키고 피부가 촉촉하고 건강하게 보이게 하며, 영유아의 정상적인 피부발달에 매우 중요하게 작용한다. 하지만 보습제 도포가 정상 영유아의 피부에 어떠한 영향을 미치는지에 대한 연구는 제한적이다. 이에 건강한 정상 영유아에서 일반적인 보습제 도포가 피부에 미치는 영향을 알아보고자 본 연구를 진행하였다. 31명의 피부염이 동반되지 않는 건강한 6 – 36개월 연령의 영유아를 대상으로, 하루 2회 목욕 후 눈과 기저귀 착용 부위를 제외한 전신에 존슨즈 베이비 내츄럴 너리싱 로션을 4주간 도포하였다. 임상적 평가는 도포 전후, 1주, 4주에 실시하였다. 매 방문시 피부수분도와 경표피수분손실도, 피부산도 및 거칠기를 측정하였으며 피부표면을 촬영하여 비교하였고 보습제 도포 후 발생한 피부 발진을 포함한 모든 부작용을 기록하였다. 보습제 도포 후 피부수분도는 통계적으로 유의하게 증가하였으며, 경표피수분손실도와 거칠기는 통계적으로 유의하게 감소하였다. 피부산도는 약산성으로 조절되었으며, 육안적으로 피부표면은 매끄럽게 변화한 것이 관찰되었다. 임상 시험 기간 동안 부작용은 관찰되지 않았다. 본 실험을 통해 보습제 도포가 영유아의 피부에 있어 수분을 증가시키고, 피부장벽기능 증강과 약산성의 피부산도 조절 및 거칠기의 호전을 야기하며, 4주간의 보습제 도포가 미치는 영향의 정도를 확인할 수 있었다.

Abstract: Moisturizers are the most prescribed products in dermatology. Treatment with moisturizers aims to maintain skin integrity and overall well-being by providing a healthy appearance. Moisturizers perform very important functions in baby care; however, there are few studies on the effects of moisturizers on the skin of infants. To investigate the effects of moisturizers on the skin of healthy full-term infants and toddlers, thirty-one healthy, full-term, 6- to 36-month-old infants and toddlers without any dermatologic conditions received moisturizer applied to the whole body except the eyes and diaper area after bathing twice daily for 4 weeks. Clinical assessments were conducted before treatment, immediately after the treatment period, and 1 and 4 weeks after treatment. At all visits, skin hydration, transepidermal water loss (TEWL), skin pH, and skin roughness were measured, the skin surface was photographed, and any adverse events were recorded. After using moisturizer, skin hydration significantly increased and TEWL and roughness significantly decreased. The skin pH was modified to mildly acidic and the skin surface was visually smoother than before treatment. There were no statistical significant differences of effects of moisturizers according to age and

† 주 저자 (e-mail: beomjoon74@gmail.com)
call: 02)6299-1544

sex, and adverse events were not observed. The results of moisturizer application on the skin were increased skin hydration, recovery of barrier function, balancing skin pH within a mildly acidic range, and increasing the smoothness of the skin surface for 4 weeks.

Keywords: *baby, moisturizer, skin*

1. Introduction

Moisturizers are the most frequently prescribed products in dermatology. Treatment with moisturizers aims to maintain skin integrity and general well-being of the individual through providing a healthy appearance[1]. The use of moisturizers by mankind has historic roots. The ancient Egyptians frequently anointed their bodies with oils. The Bible describes application of oils to the skin, and ancient Greek and Roman cultures regularly applied oil-containing products. Humans have recognized the value of externally applied lipids for thousands of years, and continue to value them[2].

An excellent discussion of moisturizers has been provided by Draelos, who defines moisturizers as externally applied compounds comprising multiple components, including occlusive ingredients and humectants[3]. Moreover, moisturizers perform multiple functions executed by a great variety of ingredients. Apart from the moistening the skin, they affect the structure and barrier function of diseased and healthy looking skin[4]. Application of moisturizers to the skin induces changes in both superficial and deep layers. The chemical and physical characteristics of the individual ingredients determine the overall performance of the formulation[4].

Moisturizers also perform very important functions in babies. Immediately after birth the skin barrier of healthy full-term neonates is competent, yet skin-barrier function continues to develop throughout at least the first year of life[5]. Special care procedures are required to ensure healthy development and protect the skin from irritation and inflammation, as well as to create a sense of well-being[6]. Although there are a lot of products that claim to promote the moistening effect, provide protection, and enhance development of baby skin, studies on the actual effects of moisturizer on baby skin are limited.

In this study, we aimed to evaluate the effects of moisturizers on the skin of healthy full-term infants and toddlers. In addition, we figure out any dependencies of effects on the differences of age or sex.

2. Material and Methods

A single-center, single-agent, subject and evaluator-opened clinical study was undertaken to investigate the effects of moisturizer on infants and toddlers after 4 weeks of normal use. This study was performed in accordance with the principles of the Declaration of Helsinki and Korean Good Clinical Practice, and local regulatory requirements. The study was reviewed and approved by the Institutional Review Board. Parents/guardians of all subjects provided written informed consent prior to study participation.

2.1. Trial subjects

The trial subjects were healthy full-term Korean male and female children aged 6- to 36- months without any dermatologic conditions (e.g., atopic dermatitis, eczema, psoriasis, rosacea, diaper rash, or seborrheic dermatitis) and the parent or legal guardian who regularly cared for them. Parents and legal guardians aged at least 18 years were eligible to enroll their child in the study. The parents and guardians were instructed to apply the provided test lotion twice a day for 4 weeks and not to apply other body moisturizer to the infant throughout the study. Subjects with clinically determined moderate to severe dryness, erythema, rash, or an overall skin condition which, in the Investigator's judgment, made the subject ineligible or placed the subject at risk were excluded from the study.

Table 1. Ingredients of the Test Product,, Johnson's Baby Natural Nourishing Lotion

Purified water	Phenoxyethanol
Glycerine	Carbomer
Cetyl alcohol	Potassium cetyl phosphate
Soybean oil	Hydrogenated palm glycerides citrate
Hydrogenated stearyl olive esters	Methylparaben
Olive leaf extract	Tetrasodium EDTA
Cornstarch	Ethylparaben
Mauritia flexuosa fruit oil	Sodium hydroxide
Chamomilla recutita flower extract	Propylparaben
Aloe barbadenisis leaf juice	Sodium cocoyl amino acid
Tocopherol	Sarcosine
Tocopheryl acetate	Potassium aspartate
Dimethicone	Magnesium aspartate

Table 2. Parent's Guide to the Use of Topical Treatment

	Face & Neck	Arm & Hand	Leg & Foot	Trunk (Front)	Trunk (Back) inc. Buttocks
Age	Number of Fingertip Unit				
<1 yrs	1	1	$1^1/_2$	1	$1^1/_2$
1 ~ 2 yrs	$1^1/_2$	$1^1/_2$	2	2	3
3 ~ 5 yrs	$1^1/_2$	2	3	3	$3^1/_2$

2.2. Materials

The test product was a commercially available moisturizer, Johnson's Baby Natural Nourishing Lotion (Johnson and Johnson Korean, Inc., Korea), containing purified water, glycerol, potassium phosphate, extraction of olive leaf, palm oil, vitamin E, and essential minerals (Table 1).

The pH of this product was near 5.5, mild acidic. The adults had to apply the test product on the whole body of the infant excluding eyes and diaper area twice daily after bathing for 4 weeks. They continued to use their regular brand of baby-wash and shampoo provided they had been using the product for at least 1 month prior to the start of the test. All participating parents or legal guardians were instructed to apply a thin layer of the trial lotion by the adult fingertip unit method (Table 2).

The infants were not allowed to shower, bathe, or swim for at least 5 hours after application of the test product.

Subjects were evaluated in the clinic at baseline (before using product), immediately after using the product, and after 1 and 4 weeks. Parents or legal guardians were instructed not to apply any product to the subjects for 24 h before each visit to the clinic. After washing the test areas, the subjects rested in an area maintained at 20 ~ 25 ℃ and 40 ~ 60% humidity for 30 min to accommodate to this atmosphere. A single researcher performed all measurements for objective analysis and the same skin area was evaluated at every visit.

Table 3. Subject Characteristics

	Subjects
Sex	
Male	12 (38.7)
Female	19 (61.3)
Age	
month, mean ± SD	21.5 ±10.1
6 ~ 12 mth	8 (25.8)
13 ~ 24 mth	8 (25.8)
25 ~ 36 mth	15 (48.4)

2.3. Measurement of skin hydration, TEWL and pH

Skin hydration was measured using a Corneometer CM 825 (Courage-Khazaka electronic GmbH, Germany) to determine the moisture content of the stratum corneum (SC) using an electrical capacitance method. This measurement is given in arbitrary units (AU) that are proportional to the dielectric constant of the surface layer of the skin and increase as the skin becomes more hydrated. Transepidermal water loss (TEWL), which reflects the amount of water escaping through the SC, was measured using Vapometer (Delfin Technologies, Inc., USA) on the subjects' forearms. Skin pH was measured using a skin-pH-meter PH905 (Courage-Khazaka electronic GmbH, Germany). Triplicate measurements were taken on one dorsal forearm (selected by the clinician) of each cooperative subject at each test visit.

2.4. Skin surface and texture analysis

The skin surface was photographed with Folliscope and the skin texture was imaged and measured using Visioscan VC98 (Courage-Khazaka electronic GmbH, Germany) and Primos premium (GFM, Teltow, Germany) on one dorsal forearm at each test visit. The average roughness (R3 and Ra) value was analyzed using the photographed images.

2.5. Adverse event

Adverse events were assessed during the time of test. On every visit, the investigator-evaluator was responsible for documenting all reported and observed adverse events such as erythema, dead skin cells, rashes, and swelling.

2.6. Data and statistical analysis

To investigate the influence of age and sex, we analyzed all data with grouping by age and sex: three groups by age (6 ~ 12 months, 13 ~ 24 months and 25 ~ 36 months), and two groups by sex (male and female).

The statistical analysis package SPSS 19.0 was used to evaluate the efficacy of the test product for skin hydration, TEWL, skin texture, and skin pH. The results of skin improvements were calculated and evaluated as percentages. Parametric test, c, and non-parametric Wilcoxon signed ranks test were used. The data are given as averages and standard deviation. Pearson correlation coefficient was used to analyze relationship between age and biophysical parameters and impaired t-test was done for finding correlation between sex and biophysical parameters. The significance level was set as 5% (i.e., a p value < 0.05 is statistically significant).

3. Results

3.1. Subject's characteristics

Thirty-one subjects (12 males and 19 females) were initially invited and all subjects completed the entire treatment protocol and returned for follow-up visits. Subjects ranged in age from 6 to 36 months (6 ~ 12 months [n=8], 13 ~ 24 months [n=8], and 25 ~ 36 months [n=15]) with an average age of 21.5 ± 10.1 months (Table 3).

3.2. Biophysical measurements

Skin hydration values measured by Corneometer were 36.81 ± 7.98 AU before treatment, 53.37 ± 8.38 AU immediately after treatment, 43.80 ± 7.49 AU at 1 week after, and 49.15 ± 6.82 AU at 4 weeks after product use. There was a statistically significant increase ($p < 0.05$) in AU immediately after, 1 week after, and 4 weeks after product use (Figure 1).

An increase in TEWL indicates impairment to the skin

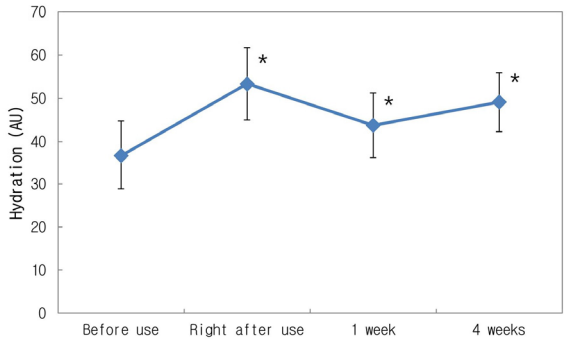

Figure 1. Changes in corneometer measurements during the trial period. The AU value increases as the skin becomes more hydrated. The mean value of corneometer measurements increased significantly after application of moisturizer (*p < 0.05 versus baseline).

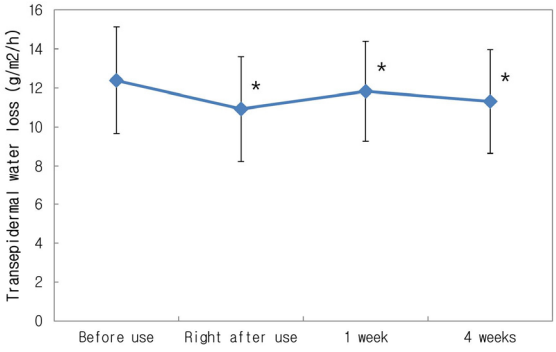

Figure 2. Changes in corneometer measurements during the trial period. The AU value increases as the skin becomes more hydrated. The mean value of corneometer measurements increased significantly after application of moisturizer (*p < 0.05 versus baseline).

barrier, whereas a decrease in TEWL means repair of the skin barrier. As shown in Figure 2, skin TEWL values were 12.39 ± 2.73 (before treatment), 10.92 ± 2.69 (immediately after treatment), 11.83 ± 2.55 (1 week after treatment), and 11.31 ± 2.65 (4 weeks after treatment). Compared with baseline, there were statistically significant decreases in TEWL immediately after, 1 week after, and 4 weeks after product use.

Skin pH values were 4.81 ± 0.36 before treatment, 5.10 ± 0.32 immediately after use, 5.48 ± 0.57 at 1 week after, and 5.48 ± 0.74 at 4 weeks after product use. Therefore, a small but significant increase in pH values

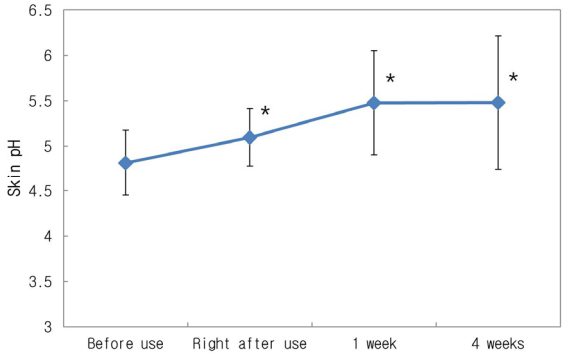

Figure 3. Changes in skin pH during the trial period. Skin pH increased significantly and then stabilized near a value of pH 5.5 (*p < 0.05 versus baseline).

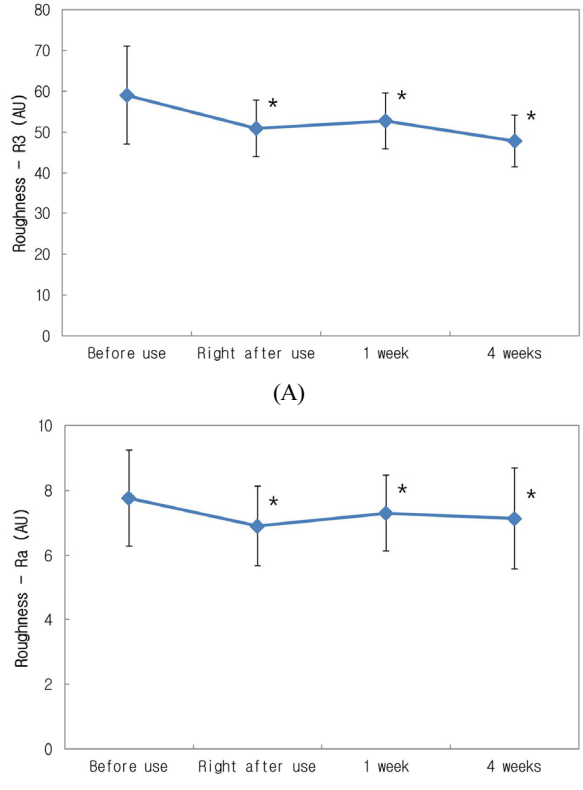

Figure 4. Changes in skin roughness during the trial period. (A) Roughness measured by Visioscan (B)Roughness measured by Primos premium (*p < 0.05 versus baseline).

was observed in at all time points after product use (Figure 3).

To investigate skin roughness, R3 was measured using Visioscan and Ra was measured using Primos premium;

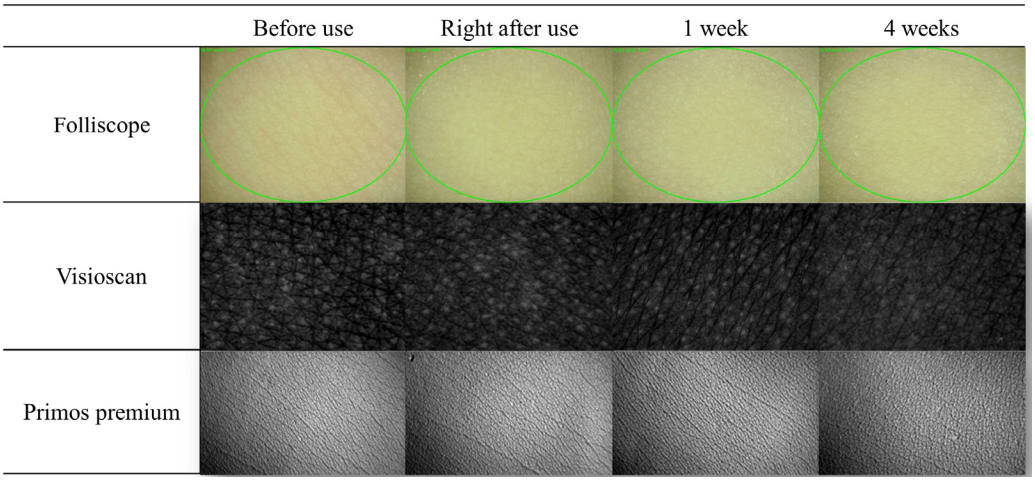

Figure 5. Visual changes in the skin surface photographed by Folliscope, Visioscan, and Primos premium during the trial period. Application of moisturizers to the skin induced a visible improvement of skin roughness.

Table 4. Correlation between Age, Sex and Biophysical Parameters

	Age		Sex
	(Pearson correlation coefficient)	(*p*-value)	(*p*-value)
Corneometer	0.205	0.268	0.276
TEWL	0.058	0.758	0.097
pH	0.176	0.342	0.374
R3	-0.118	0.527	0.880
Ra	0.094	0.615	0.462

a high value for R3 and Ra indicates that the skin surface is rough, whereas low values mean that the skin surface is smooth. There were statistically significant decreases in R3 and Ra ($p < 0.05$) immediately after, 1 week after, and 4 weeks after product use, compared with baseline (Figure 4).

As shown in Figure 5, the skin surface images using Folliscope, Visioscan, and Primos premium became smoother during the trial period.

3.3. Correlation between age, sex and biophysical parameters

The three groups divided by age and the results of these subgroups distributed similarly to average data. And there were no statistically significant correlation between age and all of the biophysical parameters in Pearson correlation coefficient. Alike age, there were no significant correlation between sex and biophysical parameters in impaired *t*-test (Table 4). These results reflected a consistent effect of moisturizer on the infant skin irrespective of differences by sex and age.

3.4. Adverse events

No significant adverse effects such as skin irritation or allergic reactions were observed.

4. Discussion

Moisturizers have multiple functions apart from moistening the skin. Immediately after application of a moisturizer the surface becomes smoother as a result of filling

of spaces between partially desquamated skin flakes[7,8]. The visual appearance of the skin changes, the surface becomes softer, and the friction is changed[9].

There is an immediate increase in the degree of hydration of the SC as a result of absorption of water from the product, whereas build-up of water in the SC due to the occlusive effect from lipids is delayed[10]. In addition, there is a growing recognition of the function of lipids in the skin as modulators of inflammation and the immune response. Some moisturizers have a pH of 5.5 because mild acidity prevents SC dehydration whereas neutral or alkaline preparations lead to swelling of the SC and subsequent SC dehydration[11]. Moreover, at a pH of 5.5 there is no interference with the cutaneous microflora.

There are many studies on the effects of moisturizer on human skin in the literature, however research targeted at children, and specifically neonates, infants, and toddlers, is very limited. Simpson *et al*.[12] reported a study evaluating the safety and tolerability of a body wash and moisturizer regimen for infants and toddlers with atopic dermatitis. This study involved 6- to 36-month old infants and toddlers with a history of atopic dermatitis who used body wash and moisturizer twice daily for 4 weeks. The results showed that TEWL decreased from 7.84 $g/m^2/h$ to 6.25 $g/m^2/h$ and corneometer readings increased from 34.65 AU to 42.99 AU at the forearm after 4 weeks. Compared with the study of Simpson *et al*., our results showed similar changes in TEWL and corneometer values, although the AU values by corneometer increased more in our study (from 36.81 AU to 49.15 AU). We presume that the higher score in our study reflects the subjects were healthy full-term infants without atopic dermatitis, which is characterized by an impaired ability to bind and hold water within corneocytes.

In general, human skin pH is more acidic than the skin of other mammalian species[13]. The average reported skin pH is 4.8 and a range of 4.0 ~ 4.9 is most common[14]. The skin of neonates is less acidic than that of adults (range of 6.7 ~ 7.5) and between the ages of 1 month to 12 years the cutaneous pH changes to become more similar to that of adults (range of 4.0 ~ 6.0)[15]. The skin pH then appears to remain constant until approximately 80 years of age. Regarding gender, a few reports have indicated gender associations[16-18], but these are not supported by other studies[12,19,20]. In our study, the initial skin pH before using the product was 4.8, the same as the average reported skin pH in humans. There were no statistical significances in skin pH between the groups divided by age or sex in our study, concordant with previous reports. After 1 and 4 weeks of test product use theskin pH increased to 5.48, which is very close to the value of pH 5.5, same as pH of product.

It is well known that moisturizers improve the dryness and roughness of skin. Moisturizers can make the skin feel smoother, a property known as emolliation. Cracks and gaps between desquamating corneocytes are filled by the moisturizer, decreasing the roughness of the skin[2]. Therefore, application of moisturizers to the skin induces tactile and visual changes of the skin surface. We measured skin roughness by two modalities, Visioscan and Primos premium. Both results showed a statistically significant decrease in R3 and Ra value during the trial period, indicating that the use of moisturizer improved skin roughness. In addition, as shown in Figure 5, the skin surfaces gradually became smoother and cracks or minor fissures were decreased.

Although no adverse effects were observed in our study, any topical substance can irritate the skin and cause adverse reactions. Although moisturizers are considered to be very safe, the most common adverse reactions are sensory or subjective sensations such as smarting, burning, and stinging. Allergic reactions also can be induced by moisturizers and the potential allergens in moisturizers are mainly fragrances and preservatives. More than 2,000 substances are used in fragrances and over 100 of these have been identified as allergens[21]. Cosmetic acne and folliculitis resulting from blockage of the follicular orifices are rarely encountered side effects of moisturizers, although teenagers are

particularly prone to this reaction. Photosensitivity dermatitis and systemic side effects are extremely rare[21]. Parents should keep in mind the possibility of these side effects when they apply moisturizers on their children.

This study has some limitations. First, it does not have a control group without application of moisturizers for comparison of efficacy. However, it would be unethical that subjects in control group should not apply moisturizer during the study period and besides, the subjects were infants and toddlers. Therefore, we designed a single active agent study without a control. In addition, the checkable biophysical parameters are very limited, because the subjects could not be cooperative to us. Second, the body washes, used in bathing before using the moisturizer, were not the same among participants. We overcame this limitation by mandating that the subjects had to keep using the body washes that they used before participating in our study to minimize the influence of using non-unified products.

In conclusion, our results showed that the effects of moisturizer application on the skin were increased skin hydration, recovery of barrier function, balancing skin pH within a mild acidic value, and making the skin surface smooth. These changes are very helpful to maintaining the healthy skin of baby, and emphasize the importance of using moisturizer once again. Demographic differences are not affected to efficacy of application of moisturizers in infants and toddlers. Because there are few studies on the effects of moisturizers on physiologic properties of healthy, full-term infants and toddlers without atopic dermatitis, our results can also applicable to basic data for further moisturizer efficacy researches.

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