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# A Randomized, Double-Blind Clinical Trial Comparing the Effects of 1% Ceramide, 10% Lanolin And 10% Urea Cream in Improving Skin Barrier Function of Children with Mild Atopic Dermatitis

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## ABSTRACT

**Objective**: The aim of the study was to compare the effect of 1% ceramide, 10% lanolin and 10% urea cream in improving skin barrier function of mild childhood atopic dermatitis after 14 days of administration.
**Method**: The study was conducted at the Pediatric Dermatology Clinic of the Dermatology and Venereology Department, Dr. Wahidin Sudirohusodo Hospital, and network hospitals in Makassar using a double-blind, randomized clinical trial. There were 16 children with mild atopic dermatitis included in this study, and they were divided into 4 treatment groups. Patients were randomly assigned to receive 1% ceramide cream, 10% lanolin cream, 10% urea cream, or vaseline (control group). Tewameter TM300 was being used to measure transepidermal water loss (TEWL) in the cubital fossa and popliteal fossa before and after 14 days of cream application. The data was analyzed using paired T-test.
**Result**: Decrease in TEWL after 7 days in 1% ceramide, 10% lanolin, 10% urea and vaselin album were 13,71; 12,02; 11,45; and 9,43 consecutively. After 14 days, a more significant TEWL decrease in 1% ceramide, 10% lanolin, 10% urea and vaselin were 24,46; 21,63; 20,73; and 17,33 consecutively, with $p<0,05$.
**Conclusion**: This study showed that 1% ceramide cream is more effective in reducing TEWL compared to 10% lanolin, 10% urea, and vaselin in children with atopic dermatitis after 14 days of application.

***Keywords:*** mild childhood atopic dermatitis, 10% lanolin, 1% ceramide, transepidermal water loss, 10% urea

## INTRODUCTION

Atopic dermatitis (AD) is a common chronic-relapsing, inflammatory skin disease that occurs mainly in young children and baby, although it may happen in any age. AD may decrease patient's quality of life. [1,2] The prevalence of AD has increased globally. The prevalence of this disease in children is quite high, reaching approximately 80% if both parents have a history of atopic dermatitis. [3] In Indonesia, according to the Indonesian Pediatric Dermatology Study Group (KSDAI), atopic dermatitis is one of the 10 most common skin diseases in children. A retrospective study in Outpatient Clinic at Prof. Dr. R. D. Kandou general hospital in Manado, North Sulawesi, Indonesia, from 2010-2012 showed an increase in the number of cases every year. [4] Based on data from Pediatric Subdivision in Outpatient Clinic of Dermatovenereology department, Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia for 5 years (January 2003 - December 2007), there were 184 new cases of atopic dermatitis which most commonly occured in patients aged 5-14 years (30%) followed by 1-4 years old (15%) and 1-11 months old (12%). [5] Atopic dermatitis most commonly occurred at age 2 months and 1 year old (60%), while 30% of AD was seen at 5 years old and only 10% in population ages between 6 to 20 years old. [6]

The etiopathogenesis of atopic dermatitis is still not fully understood. Several studies have revealed that AD is the result of interaction between genetic

susceptibility, skin barrier dysfunction, immunological factor, environmental factor and psychological factor. Genetic susceptibility for DA may cause defect on skin barrier and immune system. [7-9]

Barrier dysfunction in atopic dermatitis skin is mainly attributed to significantly decreased levels of ceramides in the stratum corneum. [10] Ceramide acts as a water modulator and a permeability barrier by forming multi-layered lamellar structures with other lipids between cells in the stratum corneum layers. [11] It is well known that ceramide 1 and 3 level are lower in atopic dermatitis compared to healthy skin. Some studies suggest that adding ceramide into a moisturizer or making lipid-like moisturizers might give a beneficial effect in atopic dermatitis skin. However, a recent study showed that from three different moisturizers, one of which was a ceramide-dominant cream, found no significant difference in disease severity as monotherapy in mild to moderate atopic dermatitis. [12]

The structures of lanolin have a similar chemical composition and properties with lipidic matrix of the stratum corneum. [13] Lanolin is not frequently used due to the potential allergenicity and unpleasant odor. [14]

This study aimed to compare the effect of 1% ceramide cream, 10% lanolin, and 10% urea cream in improving skin barrier function based on TEWL level in children with mild AD.

## METHODS

This study was conducted at the Pediatric Dermatology Clinic of the Dermatovenereology Department, Dr. Wahidin Sudirohusodo Hospital, and hospital networks in Makassar, South Sulawesi, Indonesia, from July to September 2016. Patients were collected with consecutive sampling written informed consent was obtained from each patient. This study was a double-blind randomized clinical trial design and was approved by the Hospital's Institutional Review Board.

Study population was atopic dermatitis patients aged 2-14 years old who met the inclusion and exclusion criteria. Data were collected using a questionnaire which includes history taking and dermatological examination. Photographs were taken at the initial and each visit. Patients were divided into four groups, group 1 was given 1% ceramide cream, group 2 was given 10% lanolin cream, group 3 was given 10% urea cream, and group 4 as control was given vaselin album for 14 days.

The TEWL of each patient skin were examined in the cubital fossa and popliteal fossa using Tewameter® TM 300 on day 7 and day 14. Emollient were used twice daily after bath for 14 days. At each visit, side effects such as itchiness, erythema, pain and stinging sensation were recorded.

The TEWL value interpreted as a normal condition at 0-25 g/h/m2, strained condition at 26-30 g/h/m2, and critical condition at >30 g/h/m2. Collected data were presented in table and graphic. Data collection and analysis were done using paired T-test and p value <0.05 considered as statistically significant.

## RESULTS

A total of 16 patients were included in this study. TEWL examination was done on the cubital fossa and popliteal fossa from all patients. The characteristics of the mild childhood AD patients based on atopy history were listed in table 1. Most patients (31.25%) had more than one characteristic of personal history of atopy, whereas only 2 patients (12.5%) did not have any family history of atopy.

**Table 1. Characteristics of mild childhood AD patients based on atopy history**

| Characteristics | N | % |
|---|---|---|
| History of other atopy | | |
| None | 4 | 25 |
| Bronchial asthma | 4 | 25 |
| Allergic rhinitis | 3 | 18,75 |
| >1 characteristics | 5 | 31,25 |
| History of atopy in the family | | |
| None | 2 | 12,50 |
| Bronchial asthma | 3 | 18,75 |
| Allergic rhinitis | 5 | 31,25 |
| Atopic dermatitis | 3 | 18,75 |
| >1 characteristics | 3 | 18,75 |

Table 2 shows a significant decrease in TEWL value in each group after application of moisturizer for 7 days. There was a decrease in TEWL value from 36.08±5,88 to 22,37±6,94 (13,71) in group 1; 35,25±6,65 to 23,23±8,23 (12,02) in group 2; 34,49±8,30 to 23,04±8,24 (11,45) in group 3; and 31,38±6,70 to 21,95±7,20 (9,43) in group 4. A significant decrease in TEWL value was observed in group 1 compared to control group (vaselin), while the results of group 2 and 3 were not statistically different from control.

**Table 2. Effect of Ceramide cream, Lanolin, urea compared to control on day 0 and 7 after application**

| Intervention | N | TEWL (Mean ± SD) | | Decreased TEWL | Paired T-test |
|---|---|---|---|---|---|
| | | H0 | H7 | | |
| 1% Ceramide | 4 | 36,08±5,88 | 22,37±6,94 | 13,71[c] | p=0,000 |
| 10% Lanolin | 4 | 35,25±6,65 | 23,23±8,23 | 12,02[bc] | p=0,000 |
| 10% Urea | 4 | 34,49±8,30 | 23,04±8,24 | 11,45[ab] | p=0,000 |
| Control | 4 | 31,38±6,70 | 21,95±7,20 | 9,43[a] | p=0,000 |

Paired t-test, [a] and [ab] showed no significant changes (p>0.05), [ab] and [bc] showed no significant changes, [a] and [c] showed significant changes.

Table 3 shows a significant decrease in TEWL value in each group after application of moisturizer for 14 days. There was a decrease in TEWL value of 36.08±5,88 to 11,62±3,58 (24,46) in group 1; 35,25±6,65 to 13,62±5,68 (21,63) in group 2; 34,49±8,30 to 13,76±6,12 (20,73) in group 3; and 31,38±6,70 to 14,05±5,70 (17,33) in group 4. A significant decrease in TEWL was noted in group 1 compared to control group (vaselin), while group 2 and 3 were not statistically different from control.

**Table 3. Effect of Ceramide cream, Lanolin, urea compared to control on day 0 and 14 after application**

| Intervention | N | TEWL (Mean ± SD) | | Decreased TEWL | Paired T-test |
|---|---|---|---|---|---|
| | | H0 | H14 | | |
| 1% Ceramide | 4 | 36,08±5,88 | 11,62±3,58 | 24,46[c] | p=0,000 |
| 10% Lanolin | 4 | 35,25±6,65 | 13,62±5,68 | 21,63[bc] | p=0,000 |
| 10% Urea | 4 | 34,49±8,30 | 13,76±6,12 | 20,73[ab] | p=0,000 |
| Control | 4 | 31,38±6,70 | 14,05±5,70 | 17,33[a] | p=0,000 |

Paired t-test, [a] and [ab] showed no significant changes (p>0.05), [ab] and [bc] showed no significant changes, [a] and [c] showed significant changes.

Table 4 shows a significant decrease in TEWL value in each group after application of moisturizer from day 7 to day 14. There was a decrease in TEWL value from 22,37±6,94 to 11,62±3,58 (10,75) in group 1; 23,23±8,23 to 13,62±5,68 (9.61) in group 2; 23,04±8,24 to 13,76±6,12 (9,28) in group 3; and 21,95±7,20 to 14,05±5,70 (7,89) in group 4. A significant decrease in TEWL was noted in group 1 compared to control group (vaselin), while the results of group 2 and 3 were not statistically different from control.

**Table 4. Effect of Ceramide cream, Lanolin, urea compared to control on day 7 and 14 after application**

| Intervention | N | TEWL (Mean ± SD) | | Decreased TEWL | Paired T-test |
|---|---|---|---|---|---|
| | | H7 | H14 | | |
| 1% Ceramide | 4 | 22,37±6,94 | 11,62±3,58 | 10,75[bc] | p=0,000 |
| 10% Lanolin | 4 | 23,23±8,23 | 13,62±5,68 | 9,61[ab] | p=0,000 |
| 10% Urea | 4 | 23,04±8,24 | 13,76±6,12 | 9,28[ab] | p=0,000 |
| Control | 4 | 21,95±7,20 | 14,05±5,70 | 7,89[a] | p=0,000 |

Paired t-test, [a] and [ab] showed no significant changes (p>0.05), [ab] and [bc] showed no significant changes, [a] and [c] showed significant changes.

Table 5 shows decreased TEWL value with application of topical Ceramide, Lanolin, Urea, and vaselin for 7 days. Strained TEWL became normal on day 7 although critical TEWL still can be found. On day 14, 14.

there were no patients with abnormal skin barrier in the 1% ceramide group. However, subjects with strained TEWL were still found on day 7 and day

**Table 5. Effect of Ceramide cream, Lanolin cream, Urea cream on day 7 and 14 based on TEWL**

| Intervention | Initial TEWL Value | | Day 7 | | | Day 14 | |
|---|---|---|---|---|---|---|---|
| | | | Normal | Strained | Critical | Normal | Strained |
| 1% Ceramide | | Strained (n=2) | 2 | 0 | 0 | 2 | 0 |
| | | Critical (n=14) | 8 | 4 | 2 | 14 | 0 |
| 10% Lanolin | | Strained (n=5) | 5 | 0 | 0 | 5 | 0 |
| | | Critical (n=11) | 5 | 2 | 4 | 10 | 1 |
| 10% Urea | | Normal (n=2) | 2 | 0 | 0 | 2 | 0 |
| | | Strained (n=4) | 4 | 0 | 0 | 4 | 0 |
| | | Critical (n=10) | 4 | 3 | 3 | 10 | 0 |
| Control | | Normal (n=3) | 3 | 0 | 0 | 3 | 0 |
| | | Strained (n=4) | 4 | 0 | 0 | 4 | 0 |
| | | Critical (n=9) | 5 | 2 | 2 | 8 | 1 |

## DISCUSSION

Atopic dermatitis is an inflammatory skin disease characterized by intense pruritus with a chronic and relapsing course. It is usually associated with high level of serum immunoglobulin E (IgE) and the presence of atopy history, such as bronchial asthma, allergic rhinitis, and AD found in patients and their families. [15]

Our study showed that most of the patients included in this study had more than one atopy manifestations. Fourteen patients had other history of atopy in the family. Bronchial asthma was the most common atopy history found in this study. It is similar with study by Anastasia et al that found bronchial asthma was the most common atopy history found in atopic dermatitis patient. Atopic dermatitis usually is accompanied with history of atopy in the family. [16] Tay et al found 52% of atopic dermatitis patients had no history of other atopy. [17]

This study showed that changes in TEWL value were significant in the cubital fossa area or popliteal fossa area. TEWL value was consistently decreased in all groups for 7 days and became normal after 14 days of application. Two subjects showed an increase in TEWL value in the cubital fossa after 14 days of intervention. It may be caused by environmental factor or intense exposure to air conditioner. [18]

A significant decrease in TEWL value was found 7 days and 14 days after the application of 1% ceramide. Ceramide may improve permeability of damaged skin barrier. [13] Byeong et al found a significant decrease of TEWL value in AD patients after 14 days application of ceramide. [14] Simpson et al also found a significant clinical improvement in terms of decrease in TEWL value after application of ceramide for 4 weeks. Skin barrier function was improved as shown by reduced TEWL value. [19]

This study showed a statistically significant decrease in TEWL value ($p<0.05$) before and after application of 10% urea, but it was not significantly differ compared to control group. Study by Setyaningrum and Hutomo in patients with atopic dermatitis found ceramide level increased by 30% and clinical improvement in terms of xerosis, pruritus, and erythema with topical application of 10% urea. [20] Bissonnette et al found decrease in SCORAD index of patients with atopic dermatitis using 5% urea and 10% urea. [21] Study by Grether-Beck et al aimed to evaluate urea application on cutaneous barrier function in 21 healthy human volunteers. After 4 weeks of once daily 10% urea application, there was no significant decrease in TEWL, while 20% urea significantly improved skin barrier function, shown as a 31% decrease in TEWL levels. [22]

Significant decrease in TEWL value was also found on day 7 and day 14 in control group. It is well known that petrolatum has occlusive properties on skin surface and may prevent or decrease water loss from the skin.

Statistical analysis was done using paired T-test. It was found that 1% Ceramide cream have a higher decrease in TEWL value compared to other moisturizers, followed by 10% lanolin, 10% urea, and vaselin album. A decrease in

TEWL value was higher after 7 days of application compared to 14 days of application, but it was not statistically different.

Mixture of 3 main fat ingredients of stratum corneum consist of ceramide, cholesterol, and fatty acids with a proportion of 3:1:1 and concentration around 1-2% can accelerate skin barrier regeneration. [23] All subjects showed significant decreased in TEWL value compared to initial TEWL measurement. In the TEWL strained category, skin barrier begin to normal after 7 days, while in critical category, abnormal skin barrier may still be found. There were no patients had abnormal skin barrier after application for 14 days, except 1 subject using lanolin and vaselin with strained TEWL. In strained TEWL, ceramide and urea may increase speed of TEWL repair in 7 days, compared to lanolin and vaselin which require more than 14 days.

We recommend a further study with a larger sample size and compare the effectiveness of these moisturizers with different concentrations as an alternative moisturizer to overcome skin dryness in AD patients. A longer period of study is also recommended to further evaluate TEWL value after stopping the administration of the moisturizers.

## CONCLUSION

Application of 1% ceramide cream, 10% lanolin, 10% urea, and vaselin album for 14 days in children with mild atopic dermatitis may reduce TEWL value. 1% ceramide cream give a significant difference and a better effect compared to other emollients applied until day-14. Application of 1% ceramide cream and 10% urea for 7 days resulted in a rapid decrease in TEWL value compared to 10% lanolin, and vaselin album based on categorical TEWL.

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## REFERENCES

1. Leung D, Eichenfield L, Boguniewicz M. Atopic Dermatitis. In: Wolff K, al e, editors. Fitzpatrick's Dermatology in General Medicine. 7th ed. New York: McGraw-Hill; 2008.
2. Thomsen SF. Atopic dermatitis: natural history, diagnosis, and treatment. ISRN allergy. 2014;2014:354250-.
3. Bieber T. Atopic dermatitis. The New England journal of medicine. 2008;358 (14):1483-94.
4. Keles F, Pandealeke H, Mawu F. Profil Dermatitis Atopik pada anak di Poliklinik Kulit dan Kelamin di RSUP Prof. Dr. R.D. Kandou Manado pada Januari 2013-Desember 2015. Jurnal e-Clinic. 2016;4(27).
5. Departemen Dermatologi dan Venereologi Rumah Sakit Dr. Wahidin Sudirohusodo. Data jumlah kunjungan pasien kulit anak di RS Dr Wahidin Sudirohusodo 2003-2008. 2008.
6. Motala C. Atopic dermatitis and food hypersensitivity. Current Allergy & Clinical Immunology. 2003;16(3):89-95.
7. Leung DY, Soter NA. Cellular and immunologic mechanisms in atopic dermatitis. J Am Acad Dermatol. 2001;44(1 Suppl):S1-s12.
8. Friedmann P, Holden C. Atopic dermatitis. In: Bums T, Breathnach S, Cox N, Griffiths C, editors. Rook's texbook of dermatology. 7th ed. Victoria: Blackwell Science; 2004.
9. Wulansari D, Pohan S. Imunopatogenesis Dermatitis Atopi. Berkala Ilmu Kesehatan Kulit dan Kelamin. 2007;19(2):154-61.
10. Imokawa G, Abe A, Jin K, Higaki Y, Kawashima M, Hidano A. Decreased level of ceramides in stratum corneum of atopic dermatitis: an etiologic factor in atopic dry skin? The Journal of investigative dermatology. 1991;96(4):523-6.
11. Imokawa G, Kuno H, Kawai M. Stratum corneum lipids serve as a bound-water modulator. The Journal of investigative dermatology. 1991;96(6):845-51.
12. Miller DW, Koch SB, Yentzer BA, Clark AR, O'Neill JR, Fountain J, et al. An over-the-counter moisturizer is as clinically effective as, and more cost-effective than, prescription barrier creams in the treatment

of children with mild-to-moderate atopic dermatitis: a randomized, controlled trial. Journal of drugs in dermatology: JDD. 2011;10(5):531-7.
13. Boncheva M, Damien F, Normand V. Molecular organization of the lipid matrix in intact Stratum corneum using ATR-FTIR spectroscopy. Biochimica et biophysica acta. 2008;1778(5):1344-55.
14. Flynn TC, Petros J, Clark RE, Viehman GE. Dry skin and moisturizers. Clinics in dermatology. 2001;19(4):387-92.
15. Leung DY. Atopic dermatitis: new insights and opportunities for therapeutic intervention. The Journal of allergy and clinical immunology. 2000;105(5):860-76.
16. Anastasia A, Djuanda A. Pengaruh Lanolin 10% dalam vaselin album terhadap pH kulit pasien dermatitis atopik anak. Media Dermato Venerelogica Indonesiana. 2003; 31:65-9.
17. Tay YK, Kong KH, Khoo L, Goh CL, Giam YC. The prevalence and descriptive epidemiology of atopic dermatitis in Singapore school children. British Journal of Dermatology. 2003;146(1):101-6.
18. Proksch E, Elias P. Epidermal Barier in Atopic Dermatitis. In: Bieber T, Leung D, editors. Atopic Dermatitis. New York: Marcel-Dekker; 2002.
19. Simpson E, Böhling A, Bielfeldt S, Bosc C, Kerrouche N. Improvement of skin barrier function in atopic dermatitis patients with a new moisturizer containing a ceramide precursor. Journal of Dermatological Treatment. 2013;24(2):122-5.
20. Setyaningrum T, Hutomo M. Penggunaan Pelembab pada Dermatitis Atopi. Berkala Ilmu Kesehatan Kulit dan Kelamin. 2003;15(3):200-7.
21. Bissonnette R, Maari C, Provost N, Bolduc C, Nigen S, Rougier A, et al. A double-blind study of tolerance and efficacy of a new urea-containing moisturizer in patients with atopic dermatitis. Journal of cosmetic dermatology. 2010;9(1):16-21.
22. Grether-Beck S, Felsner I, Brenden H, Kohne Z, Majora M, Marini A, et al. Urea uptake enhances barrier function and antimicrobial defense in humans by regulating epidermal gene expression. The Journal of investigative dermatology. 2012; 132(6):1561-72.
23. Chamlin SL, Kao J, Frieden IJ, Sheu MY, Fowler AJ, Fluhr JW, et al. Ceramide-dominant barrier repair lipids alleviate childhood atopic dermatitis: changes in barrier function provide a sensitive indicator of disease activity. J Am Acad Dermatol. 2002;47(2):198-208.

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