

Effect of Sunflower Seed Oil Moisturizer Creams on Transepidermal Water Loss in Atopic Dermatitis Pediatric Patients

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Abstract: Atopic dermatitis (AD) is a chronic disease associated with disruption of skin barrier. There is an increase of transepidermal water loss (TEWL) in AD, therefore moisturizers application is essential. Sunflower seed oil (SSO) is one of natural moisturizer contain essential fatty acid that has emollient and occlusive effect. The aim of this study was to ascertain the effect of SSO on TEWL in AD pediatric patients. A hundred and twenty-four pediatric subjects with and without history of AD recruited into one cross-sectional study and three randomize-controlled studies, including the measurement of TEWL on six anatomical sites, the effect of 15% SSO moisturizer cream in healthy skin, comparison of 15% SSO moisturizer cream to controlled, and comparison of 20% SSO moisturizer to 5% urea moisturizer cream in AD patients, respectively. The moisturizer was applied twice daily on forearm or lower leg for two weeks. The TEWL values was measured by Tewameter® 300. The result showed that the highest TEWL values on the extensor part of lower leg (10.72 g/m²/h). The application of 15% SSO moisturizer showed a positive impact on skin barrier by reducing TEWL value in healthy skin (average decrease 9.34 g/m²/h, $p < 0.01$). TEWL decrement value between 15% SSO group compared to controlled group were not significant ($p = 0.283$). While, TEWL decrement value of 20% SSO group had similar results compared to 5% urea group ($p = 0.309$). We concluded that 20% SSO can be used as an alternative and can work as well as urea on AD pediatric patients.

1 INTRODUCTION

Atopic dermatitis (AD) is a common chronic inflammatory skin condition marked by xerosis and highly pruritic skin lesions. (Lyons et al., 2015) Data from the International Study of Asthma and Allergies in Childhood (ISAAC) revealed that the prevalence of AD symptoms in the 6- to 7-year and the 13- to 14-year age groups ranged from 0.7 to 18.4% and 0.8 to 20.5%, respectively. (Williams et al., 1999) Skin barrier function can be assessed by non-invasive measurement of transepidermal water loss (TEWL). In children with a healthy skin, there is a full integrity of the epidermis, presented with minimal TEWL, while in children with AD, the TEWL is increase. (Catherine MacK Correa and Nebus, 2012) Current clinical guidelines recommend skin hydration and the application of moisturizers as nonpharmacologic interventions in AD patients. (Catherine MacK Correa and Nebus, 2012; Lyons et al., 2015) Emollients, is a type of moisturizers which mainly contain lipids and oils that

enhance the skin softness and hydrate the dry skin. (Sethi et al., 2016) There has been increasing interest in using natural ingredients for skin care product including moisturizing creams. It believes to be safe and gentle by health-conscious costumers. (Tobin, 2008) The discovery and development of plant-based ingredients such as inclusion of sunflower seed oil (SSO) in moisturizing cream is become more compelling, because it shown that the essential fatty acid (EFA) contain in the SSO could treated and act as an anti-inflammatory in skin disorders. (Eichenfield et al., 2009; Danby et al., 2013) Hence this study was determined to assess the effect of sunflower seed oil on TEWL in atopic dermatitis pediatric patients.

2 METHODS

Subjects. One cross sectional and three cohorts of subjects were recruited. Subject with inflamed skin on treatment sites, recently having a severe AD based

on SCORAD score, known history of allergy to the moisturizing cream ingredients used in this test, and was using moisturizer 7 days before and during participation were excluded from the study. The subjects were refrained from using any other topical products beside the given moisturizer. Informed consent was obtained from each subject. The studies were approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran-Dr. Hasan Sadikin Hospital Bandung, West Java, Indonesia with ethical clearance. The cross-sectional study consisted of 70 healthy children (forty females and thirty males, ages 6-7 years) were measured for TEWL value on six anatomical sites. The Cohort 1 study consisted of 26 healthy children (thirteen females and thirteen males, ages 6-7 years) were treated with 15% SSO moisturizer cream on lower leg for two weeks. The Cohort 2 study consisted of 16 subjects (eight females and eight males, ages 2-11 years) with previous history of AD, diagnosed by Hanifin-Rajka criteria and recently not in severe condition according to SCORAD score. The Cohort 3 study consisted of 12 subjects (six females and six males, age 2-9 years) with previous history of AD, diagnosed by Hanifin-Rajka criteria and recently not in severe condition according to SCORAD score.

Treatment. The cross-sectional study measured the TEWL value of healthy childrens skin without any treatment needed. The cohort 1 study was an experimental analytical prospective study using convenience sampling. According to pediatrics finger tip unit (FTU), the subjects were given 20 g of 15% SSO moisturizing cream per week for two weeks application. Treatments were applied to lower legs twice a day after bath. The cohort 2 study was a double blind controlled study using consecutive sampling. The subjects were given 20 g of 15% SSO moisturizing cream per week for two weeks application for one arm and 20 g of vehicle-controlled moisturizer cream per week for two weeks application for the other arm. Treatments were applied twice a day after bath and leave skin uncovered for at least 30 minutes after each application. Both creams were labelled and blinded to subjects and observer. The cohort 3 study was a double blind controlled study using consecutive sampling. The subjects were given 20 g of 20% SSO moisturizing cream per week for two weeks application for one leg and 20 g of 5% urea moisturizing cream per week for two weeks application for the other leg. Treatments were applied to lower legs after bath and leave skin uncovered for at least 30 minutes after each application. Both creams were labelled and blinded to subjects and

observer. The moisturizer used in this study was allocated in opaque container, labelled and was undergone product testing using animal tests before used with the formula presented in Table 1. While the urea 5% moisturizer was using *Extreme Dry Skin Relief Hand Cream 5% urea*, from Sebamed® (Sebapharma GmbH & Co. KG, Germany).

Table 1. Moisturizer Cream Formula

SSO moisturizer	15%	Vehicle Only moisturizer	SSO 20% moisturizer
R/		R/	R/
Refined Sunflower Oil 15%	Seed	Paraffin 15% Cetostearyl alcohol 10%	Refined Sunflower Seed Oil 20%
Cetostearyl alcohol 10%		Cetomacrogol 2%	Cetostearyl alcohol 10%
Cetomacrogol 10%		Petroleum jelly 5%	Cetomacrogol 10%
Petroleum jelly 5%		Potassium sorbate 0,1%	Potassium sorbate 0,1%
Potassium sorbate 0,1%		Propilen glycol 7,5%	Propilen glycol 7,5%
Propilen glycol 7,5%		Citrus fragrance q.s	Citrus fragrance q.s
Citrus fragrance q.s		<i>Aquadest</i> ad 100 gr	<i>Aquadest</i> ad 100 gr

Biophysical Measurements. Measurements were performed in a room maintained at 20-22°C and 40-60% relative humidity. Subjects were asked to sit in a resting position with their forearm or lower leg exposed for 20 minutes before measurements to acclimatize the test areas. The last application of creams was made 12 to 24 hours before the evaluation to avoid interference of residues with the measurement. TEWL was measured using a Tewameter® 300 (Courage and Khazaka electronic GmbH, Germany).

Statistical Analysis. Results in the cohort 1 study were analyzed using Wilcoxon test. Results in the cohort 2 study were analyzed using Friedman test (before and after treatment) and Mann-Whitney test (comparison between two group). Results in the cohort 3 study were analyzed using Repeated ANOVA and Repeated ANOVA Comparisons (comparison of decrement in TEWL from baseline) and $p < 0.05$ was considered significant.

3 RESULTS

TEWL Value of Various Anatomical Sites in Healthy Pediatric Skin. Seventy healthy children, were having

TEWL measurement on the cheek, forehead, extensor part of lower arm, flexor part of upper leg, extensor part of lower leg, and back, using Tewameter® 300. The mean TEWL value in our study from the highest to the lowest were as follows: the extensor part of lower leg (10.72 g/m²/hour), forehead (8.53 g/m²/hour), extensor part of lower arm (7.56 g/m²/hour), cheek (7.05 g/m²/hour), flexor part of upper leg (6.1 g/m²/hour), and the lowest value obtained from the skin on back (5.46 g/m²/hour).

Effect of 15% SSO Moisturizer in Healthy Pediatric Skin. Twenty-six healthy children applied 15% SSO moisturizer creams to the skin of legs twice a day for 2 weeks. The TEWL measurement was performed at baseline, evaluation week-1, and week-2. Results from the study shown a decrease in TEWL value on application of 15% SSO moisturizer creams from baseline until week-2 evaluation in healthy pediatric skin. The decrement was almost half of the baseline value from 17.66 g/m²/hour to 8.32 g/m²/hour in week-2 evaluation (average decrease 9.34 g/m²/hour) or 47.11% decrease from baseline. This result was statistically significant with $p < 0.01$ ($p = 0.0001$).

Effect of 15% SSO Moisturizer Compared to Vehicle Controlled in AD Pediatric Skin. Sixteen subjects with history of AD and currently in mild condition based on SCORAD score applied 15% SSO moisturizer creams twice a day to one arm and vehicle-controlled moisturizer creams to the other arm. In 15% SSO group after two weeks of moisturizer application the average decrement of

TEWL was 6.16 g/m²/hour \pm 1.51 g/m²/hour. While in vehicle-controlled group after two weeks of moisturizer application the average decrement of TEWL was 6.18 g/m²/hour \pm 1.59 g/m²/hour. Statistically using Friedman test, TEWL decrement value on both group were significant with $p < 0,001$. In 15% SSO group, after two weeks of moisturizer application, TEWL decrement value was raised from 1.6 g/m²/hour (19.22%) to 2.26 g/m²/hour (26.78%). While in vehicle-controlled group, after two weeks of moisturizer application, TEWL decrement value was also raised from 1.38 g/m²/hour (17.21%) to 1.75 g/m²/hour (21.43%). According to Mann-Whitney analytical test with Confidence Interval 95%, the total TEWL decrement value between 15% SSO group and vehicle-controlled group was not statistically significant ($p = 0.283$).

Effect of 20% SSO Moisturizer Compared to 5% Urea Moisturizer in AD Pediatric Skin. Twelve subjects with history of AD and currently in mild to moderate condition based on SCORAD score applied 20% SSO moisturizer creams twice a day to one leg and 5% urea moisturizer creams to the other leg. The TEWL values between 20% SSO group and 5% urea group were presented in Table 2. TEWL decrease in both group from baseline to week-2 evaluation was significant ($p < 0.001$). The decrease of TEWL in 20% SSO group (49.80%) was superior to 5% urea group (42.75%). This result was not statistically significant when compared 20% SSO group to 5% urea group from baseline to week-2 evaluation ($p = 0.309$).

Table 2. TEWL Values between 20% SSO Group and 5% Urea Group

Cream	Time	Average TEWL (g/m ² /hour)	TEWL decrease (%)	<i>p</i> value	TEWL decrement Baseline-week-2	<i>p</i> value
20% SSO	Baseline	15.20 \pm 3.498				
	Week-1	10.93 \pm 2.56	49.80	<0.001	7.57 \pm 3.33	
	Week-2	7.63 \pm 2.43				0.309
5% Urea	Baseline	14.55 \pm 1.945				
	Week-1	11.18 \pm 1.947	42.75	<0.001	6.22 \pm 3.00	
	Week-2	8.33 \pm 2.65				

4 DISCUSSION

Measurement of TEWL is useful to evaluate the physical barrier function of stratum corneum. The TEWL value differs, depends on anatomical location

and affected by the environment, as well as the size and amount of corneocyte.(Machado et al., 2010) A study by Rougier et al. concluded that the larger corneocytes size correlated with the longer route for the permeation, which presented in lower TEWL value.(Rougier et al., 1988) Our study found the

highest mean TEWL value were from the skin on extensor part of lower leg (10.72 g/m²/hour) and the lowest mean TEWL value were from the skin on back (5.46 g/m²/hour). Comparative assessment of TEWL by Fluhr et al. showed a difference in the baseline values, with the highest TEWL value from the skin on forehead (22.4 g/m²/h) and the lowest TEWL values from the skin on the lower leg (7.7 g/m²/h). (Fluhr et al., 2002) The difference of these studies results maybe due to the subject of our study included children aged 6-7 years only, with presumably high contact and friction of the lower legs from trauma and their daily activity. It is supported with one study showed that the reciprocating sliding and contact between skin and working implements, sports appliances, improper footwear, and textile materials, etc. may lead to skin damage. (Chen et al., 2015)

Linoleic acid was the major essential free fatty acid (EFA) content found on SSO. Linoleic acid contain in SSO can converts to arachidonic acid, a precursor to prostaglandin E₂ (PGE₂), which was a known modulator of cutaneous inflammation. (Eichenfield et al., 2009) One study in Bangladesh, using topical SSO on preterm infants showed that SSO reduced the passage of pathogens from the skin surface into the bloodstream compared with untreated controlled group. (Darmstadt et al., 2007) Our study supported the theory that topical use of 15% SSO inclusion in moisturizing cream has the positive impact on healthy pediatric skin, with reducing the total TEWL value compare to baseline.

Pediatric skin with history of atopy and presented with AD showed a different physical barrier compare to the healthy pediatric skin. In human keratinocytes, PPAR- α activators, including linoleic acid, showed a regulatory effect by increasing involucrin, transglutaminase protein and mRNA levels. (Hanley et al., 1998; Eichenfield et al., 2009; Danby et al., 2013) Our study revealed that 15% SSO moisturizer significantly reduce the TEWL value in AD pediatric skin, and similar results to vehicle-controlled group. This results maybe due to the moisturizing effect of the vehicle-controlled moisturizer used in this test, contain paraffin and petroleum jelly which were occlusive type of moisturizer. (Sethi et al., 2016) While propilen glycol which was also add in the vehicle is the mixture of emollient, humectant, and occlusive moisturizer. (Sethi et al., 2016) According to this result we consider a higher concentration of SSO to have the better effect compared to controlled moisturizer.

Five percent urea cream was often used as moisturizer in AD, which act as humectant by

attracting water from the environment and retains it within the cells. On one study comparing 5% and 10% urea moisturizer, both improved atopic dermatitis skin lesion using scoring atopic dermatitis severity index (SCORAD). (Bissonnette et al., 2010) The 5% urea moisturizer was preferred by subjects over the 10% urea lotion using the cosmetic acceptability questionnaire. (Bissonnette et al., 2010) In this cohort study we compare the 20% SSO moisturizer with 5% urea moisturizer in AD pediatric skin. To our knowledge there were no study comparing urea and SSO in AD pediatric skin before. The result showed that both 20% SSO moisturizer and 5% urea moisturizer significantly reduce the TEWL value on week-2 application compare to baseline. Comparison analysis of the 20% SSO moisturizer to 5% urea moisturizer was not significant, but the TEWL decrement value in 20% SSO group (49.80%) was superior to 5% urea group (42.75%).

5 CONCLUSIONS

From this result, we concluded that 20% SSO can be use as an alternative and can work as well as urea on AD pediatric patients.

REFERENCES

- Bissonnette, R., Maari, C., Provost, N., Bolduc, C., Nigen, S., Rougier, A., Seite, S., 2010. A double-blind study of tolerance and efficacy of a new urea-containing moisturizer in patients with atopic dermatitis. *Journal of Cosmetic Dermatology* 9, 16–21.
- Catherine MacK Correa, M., Nebus, J., 2012. Management of patients with atopic dermatitis: The role of emollient therapy. *Dermatology Research and Practice*.
- Chen, C.-Y., Yu, C.-A., Hong, T.-F., Chung, Y.-L., Li, W.-L., 2015. Contact and frictional properties of stratum corneum of human skin. *Biosurface and Biotechnology* 1, 62–70.
- Danby, S.G., Alenezi, T., Sultan, A., Lavender, T., Chittock, J., Brown, K., Cork, M.J., 2013. Effect of olive and sunflower seed oil on the adult skin barrier: Implications for neonatal skin care. *Pediatric Dermatology* 30, 42–50.
- Darmstadt, G.L., Saha, S.K., Ahmed, A.S.M.N.U., Choi, Y., Chowdhury, M.A.K.A., Islam, M., Law, P.A., Ahmed, S., 2007. Effect of Topical Emollient Treatment of Preterm Neonates in Bangladesh on Invasion of Pathogens Into the Bloodstream. *Pediatric Research* 61, 588–593.
- Eichenfield, L.F., McCollum, A., Msika, P., 2009. The benefits of sunflower oleodistillate (SOD) in pediatric

- dermatology. *Pediatric Dermatology*.
- Fluhr, J.W., Dickel, H., Kuss, O., Weyher, I., Diepgen, T.L., Berardesca, E., 2002. Impact of anatomical location on barrier recovery, surface pH and stratum corneum hydration after acute barrier disruption. *British Journal of Dermatology* 146, 770–776.
- Hanley, K., Jiang, Y., He, S.S., Friedman, M., Elias, P.M., Bikle, D.D., Williams, M.L., Feingold, K.R., 1998. Keratinocyte differentiation is stimulated by activators of the nuclear hormone receptor PPARalpha. *The Journal of investigative dermatology* 110, 368–375.
- Lyons, J.J., Milner, J.D., Stone, K.D., 2015. Atopic Dermatitis in Children: Clinical Features, Pathophysiology, and Treatment. *Immunology and Allergy Clinics of North America*.
- Machado, M., Salgado, T.M., Hadgraft, J., Lane, M.E., 2010. The relationship between transepidermal water loss and skin permeability. *International Journal of Pharmaceutics* 384, 73–77.
- Rougier, A., Lotte, C., Corcuff, P., Maibach, H.I., 1988. Relationship between skin permeability and corneocyte size according to anatomic site, age, and sex in man. *J Soc Cosmet Chem* 39, 15–26.
- Sethi, A., Kaur, T., Malhotra, S., Gambhir, M., 2016. Moisturizers: The slippery road. *Indian Journal of Dermatology* 61, 279.
- Tobin, D.J., 2008. Human hair pigmentation--biological aspects. *International journal of cosmetic science* 30, 233–57.
- Williams, H., Robertson, C., Stewart, A., Ait-Khaled, N., Anabwani, G., Anderson, R., Asher, I., Beasley, R., Bjorksten, B., Burr, M., Clayton, T., Crane, J., Ellwood, P., Keil, U., Lai, C., Mallol, J., Martinez, F., Mitchell, E., Montefort, S., Pearce, N., Shah, J., Sibbald, B., Strachan, D., von Mutius, E., Weiland, S.K., 1999. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 103, 125–138.