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Effect Of Topical 5% Dexpanthenol On Transepidermal Water Loss Values And Skin pH in Patients With A History Of Atopic Dermatitis

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ABSTRACT

Background: What is the latest knowledge on the issue? Some key phrases to use here are: recent studies/although some clinical research has established x, the role of y is not well known. Atopic dermatitis (AD) is a chronic relapsing skin disease with epithelial barrier dysfunction characterized by transepidermal water loss (TEWL) and disruption of the skin acidification process. Use of moisturizers is the main therapy in AD. Petrolatum is proven effective, however its sticky nature may affect patients' adherence. Dexpanthenol is a potential alternative to address this concern.

Objective: To determine the effectiveness of topical 5% dexpanthenol in reducing TEWL and pH values in patients with a history of atopic dermatitis.

Methods: A double-blind, randomized, parallel-group clinical trial enrolled 26 participants. Subjects were assigned to receive either topical 5% Dexpanthenol or 100% Petrolatum twice daily for 4 weeks. TEWL and pH was measured on baseline and week 4.

Results: Thirteen subjects were assigned to each group. Mean change in TEWL from baseline to week 4 was -5.19 ± 0.75 g/m²/h with petrolatum and -7.58 ± 0.37 g/m²/h with dexpanthenol, indicating a significantly greater decrease with dexpanthenol ($p<0.001$). Mean change in skin pH was -0.33 ± 0.03 and -0.68 ± 0.08, respectively, also indicating a significantly greater decrease with dexpanthenol ($p<0.001$). All subjects in the petrolatum group complaints of stickiness and greasiness, whereas all subjects in the dexpanthenol group reported no complaints ($p=0.000$).

Conclusion: Topical 5% dexpanthenol is effective in reducing TEWL and pH values in patients with history of atopic dermatitis compared to topical 100% petrolatum. Dexpanthenol was well accepted with no reported complaints.

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1.Introduction

Atopic dermatitis (AD) is a chronic relapsing skin disease caused by dysregulation of the innate and adaptive immune systems, cytokine imbalance, activation of inflammatory pathways, impaired epithelial barrier function, and microbial imbalance.[1,2] The study found an annual incidence rate of 131 cases of DA visits in dermatology outpatient clinic of Dr. Kariadi Hospital, Semarang.[3] Pathogenesis of AD is strongly related to genetic disorders and environmental triggers, resulting in epithelial barrier dysfunction characterized by transepidermal water loss (TEWL).[4] Mutations of the filaggrin (FLG) gene also disrupt the skin acidification process which plays a role in maintaining normal skin pH.[5]

Management of AD in Indonesia is based on the concept of the Five Pillars of Atopic Dermatitis Management.[1] The use of moisturizers is the mainstay therapy in AD to reduce inflammation and recurrence.[1,6] The ideal function of a moisturizer is to maintain and improve the skin barrier function by delivering lipids and water to the stratum corneum, increasing skin hydration, maintaining skin integrity and appearance, as well as reducing TEWL and facilitating skin barrier repair.[1,7]

Petrolatum is the gold standard of moisturizers in AD. It has an excellent efficacy as occlusive because of its ability to penetrate all layers of the stratum corneum.[8] The role of petrolatum in reducing TEWL in atopic dermatitis patients has been shown in previous studies, but the majority of subjects complained that petrolatum felt "sticky" and "greasy", therefore, even though petrolatum moisturizes and improves the physiological function of the skin, complaints related to its use may reduce patient compliance.[9] The sticky

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nature of petrolatum residue can also absorb dirt and dust, clog sweat glands, and cause a phenomenon known as the petrolatum paradox. Keratin and petrolatum residue stick to the skin, causing the skin to become scalded and flaky when scratched.[10] Despite its effectiveness, continuous use of petrolatum is challenging, and there is a need for alternative moisturizers to address these concerns.

Dexpanthenol is an alcoholic derivative of pantothenic acid (Vitamin B5). Pantothenic acid (C9H17NO5): is chemically known as 3-[(2,4-Dihydroxy-3,3-dimethylbutanoyl)amino] propanoic acid, whereas dexpanthenol (D-panthenol): is chemically known as (+)-2,4-dihydroxy-N-(3-hydroxypropyl)-3,3-dimethylbutyramide.[8] The potential benefits of topical dexpanthenol for skin barrier repair have been proven in various studies. This is related to the hygroscopic nature of dexpanthenol and its ability to increase moisture retention so that it can regenerate the epidermis layer. The hydration effect of dexpanthenol is related to its ability to interact with extracellular lamella lipid segments and protein residues in corneocytes in the stratum corneum, so that it can maintain/increase molecular fluidity. The skin layer that is continuously regenerating requires a skin barrier environment with physiological moisture to maintain the process. Dexpanthenol also plays a role in promoting epidermis regeneration by increasing epidermal differentiation and lipid synthesis.[11,12]

Studies related to the use of topical dexpanthenol on skin barrier repair as measured by TEWL and pH is lacking. Dexpanthenol has various benefits for various dermatological conditions, but its use in atopic dermatitis patients has not been widely studied. This study aims to determine the effectiveness of topical 5% dexpanthenol in reducing TEWL and pH values in patients with a history of atopic dermatitis.

2.Methods

This is a double-blinded randomized clinical trial with two parallel group, pre- and post-test treatment and control design conducted at the Dermatology and Venereology Outpatient Clinic of Dr. Kariadi General Hospital, Semarang in November 2024 to January 2025. Consecutive sampling was applied to include patients with a history of atopic dermatitis, treated at the Dermatology and Venereology Outpatient Clinic of Dr. Kariadi General Hospital during the study period. Study subjects met the following criteria: 1) history of atopic dermatitis based on the criteria of Hanifin and Rajka[13,14] 2) No flare at the measurement site (both volar forearms) 3) Male or female, aged 18 - 45 years [15] and 4) Willing to participate in the study and receive therapy. Exclusion criteria were: 1) history of hypersensitivity to dexpanthenol, 2) active infection at the examination site, and 3) current use of drugs that may dry the skin, including oral retinoids, hormonal therapy, diuretics, chemotherapy, statins, and cimetidine.[16,17]

Subjects were randomly assigned to receive either Dexpanthenol 5% (Group A) or 100% Petrolatum (Group B) using a sequence of sequentially numbered, opaque, sealed envelopes. To ensure allocation concealment, both study preparations were packaged in identical, opaque 30 mL containers with matching spatulas, labeled only as 'A' or 'B'. The allocation sequence was generated and assigned by an independent research assistant not involved in subject observation or outcome assessment, and the randomization key remained sealed until the study was completed.

Subjects were instructed to apply 1 fingertip unit (FTU) to each volar forearm application area (approximately 2% body surface area in total), twice daily immediately after bathing for 4 weeks. The variables assessed were TEWL and pH, measured using TM 300® (Courage & Khazaka, Cologne, Germany). Measurements were taken twice, namely baseline and after 4 weeks of treatment. At each visit, 3 measurements were taken on the volar side of the forearm and the average value was taken. At the beginning of the study, patients were also asked about any complaints of atopic dermatitis, history of skin care product use, and bathing habits including frequency, water temperature, and soap commonly used by the sample. Subjects were considered to have dropped out if an allergic reaction was found during the study.

3.Result

3.1 Subjects' Characteristics

Twenty six subjects met the study criteria and were then included in this study. Subjects were divided into 2 groups. A total of 13 subjects received 5% Dexpanthenol treatment and 13 subjects in the control group received 100% Petrolatum. During the study period, no subjects experienced allergic reactions. All subjects were able to complete the study and no dropouts were recorded (Figure 1).

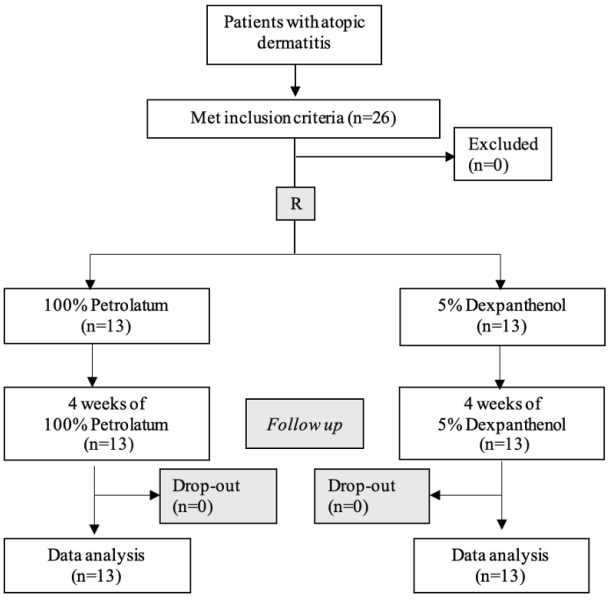


Figure 1. Flow Diagram of Study Subjects. R = Randomization

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Baseline characteristics are summarized in Table 1. Most participants were female: 8 of 13 (61.5%) in the 100% petrolatum group and 9 of 13 (69.2%) in the 5% dexpanthenol group. Mean age was 30.23 ± 3.37 years in the petrolatum group and 31.00 ± 4.51 years in the dexpanthenol group. A bachelor's degree was the most common education level in both groups. Median self-reported duration of AD was 20.0 years (range, 15-35) in the petrolatum group and 20.0 years (range, 15-25) in the dexpanthenol group. The distribution of baseline AD symptoms differed clinically: 5 of 13 participants (38.5%) in the petrolatum group reported no symptoms, whereas 6 of 13 (46.2%) in the dexpanthenol group reported both dry skin and itching. Baseline TEWL and skin pH at the non-flaring forearm sites were numerically similar between groups (17.35 vs 17.54 g/m²/h and 6.27 vs 6.39, respectively).

Table 1. Characteristics of Study Subjects (n=26)

Characteristics	Group		*P*
	100% Petrolatum (n=13)	5% Dexpanthenol (n=13)	
Gender			1.000*
Female	8 (61.5%)	9 (69.2%)	
Male	5 (38.5%)	4 (30.8%)	
Age (years)	30.23 ± 3.37	31.00 ± 4.51	0.627‡
Education			1.0*
Junior High School	1 (7.7%)	1 (7.7%)	
High School	4 (30.8%)	3 (23.1%)	
Bachelor's degree	8 (61.5%)	9 (69.2%)	
Duration of AD (years)	20.0 (15-35)	20.0 (15-25)	0.3‡
Initial AD Symptoms			
None	5 (38.5%)	1 (7.7%)	0.06*
Dry skin	4 (30.8%)	5 (38.5%)	
Itching	3 (23.1%)	1 (7.7%)	
Dry skin and itching	1 (7.7%)	6 (46.2%)	
Bathing frequency			
1x/day	2 (15.4%)	1 (7.7%)	1.0*
2x/day	9 (69.2%)	9 (69.2%)	
>2x/day	2 (15.4%)	3 (23.1%)	
Soap Type			
Moisturising wash	8 (61.5%)	8 (61.5%)	1.0*
Antiseptic	5 (38.5%)	5 (38.5%)	
Use of Warm Water for Bathing			
Yes	8 (61.5%)	10 (76.9%)	0.673*
No	5 (38.5%)	3 (23.1%)	
Post-bath drying method			
Hard rubbing with towel	5 (38.5%)	10 (76.9%)	0.111*
Gentle wiping or patting with towel	8 (61.5%)	3 (23.1%)	
Moisturizer habits			
Never	5 (38.5%)	5 (38.5%)	1.0*
Rarely	4 (30.8%)	5 (38.5%)	
Regularly	4 (30.8%)	3 (23.1%)	
Use of medications related to skin condition			
No	11 (84.6%)	10 (76.9%)	1.0*
Yes	2 (15.4%)	3 (23.1%)	

‡ Levene Test, *Chi-Square Test

In terms of bathing habits, most subjects bath twice daily, reported by 69.2% of participants in both groups. Moisturizing body wash was the most commonly used soap type, used by 61.5% of participants in each group. Majority of subjects reported using warm water, reported by 61.5% in the Petrolatum group and 76.9% in the Dexpanthenol group. Post-bath drying method in most participants in the Petrolatum group (61.5%) reported gently patting or wiping with a towel, while 76.9% in the Dexpanthenol group reported hard rubbing using towel. Moisturizing habit was also assessed, with most participants in the Petrolatum group (38.5%) reported never using moisturizer. Similar number was observed in dexpanthenol group, with 38.5% participants either rarely or never use moisturizer. Finally, most participants in both groups reported no history of prior treatment, observed in 84.6% subjects of the Petrolatum group and 76.9% of the Dexpanthenol group.

3.2 TEWL

TEWL decreased significantly from baseline to week 4 in the 100% petrolatum group (17.35 ± 2.10 to 12.16 ± 2.18 g/m²/h; p<0.001) and in the 5% dexpanthenol group (17.54 ± 2.35 to 9.96 ± 2.20 g/m²/h; p<0.001). The mean change from baseline (week 4 minus baseline) was -5.19 ± 0.75 g/m²/h with petrolatum and -7.58 ± 0.37 g/m²/h with dexpanthenol. Decrease in TEWL is therefore greater in dexpanthenol group and statistically significant (p<0.001). TEWL results are shown in Table 2 and Figure 2.

Table 2. TEWL value of 100% petrolatum and 5% dexpanthenol groups

	Mean TEWL		p
	100% Petrolatum	5% Dexpanthenol	
Baseline	17.35 ± 2.10	17.54 ± 2.35	<0.001‡
Week 4	12.16 ± 2.18	9.96 ± 2.20	<0.001‡
Change from baseline	-5.19 ± 0.75	-7.58 ± 0.37	<0.001*

‡ Paired t-test, *Independent t-test

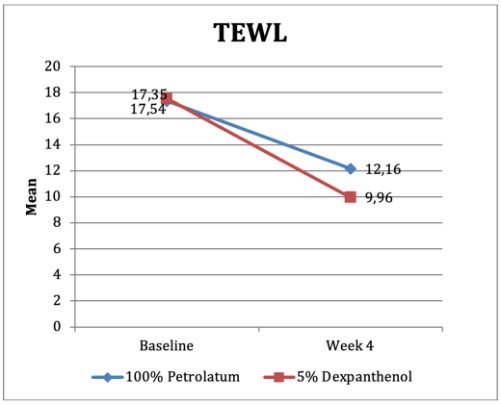


Figure 2. Decrease in TEWL between 100% Petrolatum and 5% Dexpanthenol

3.3 pH

Skin pH decreased significantly from baseline to week 4 in the 100% petrolatum group (6.27 ± 0.36 to 5.94 ± 0.36; p<0.001) and in the 5% dexpanthenol group (6.39 ± 0.27 to 5.70 ± 0.27; p<0.001). The mean change from baseline (week 4 minus baseline) was -0.33 ± 0.03 with petrolatum and -0.68 ± 0.08 with dexpanthenol. Decrease in skin pH is therefore greater in the dexpanthenol group and statistically significant (p<0.001).

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Measurement of pH values are shown in Table 3 and Figure 3.

Table 3. pH value of 100% petrolatum and 5% dexpanthenol groups

	Mean pH		p
	100% Petrolatum	5% Dexpanthenol	
Baseline	6.27 ± 0.36	6.39 ± 0.27	<0.001‡
Week 4	5.94 ± 0.36	5.70 ± 0.27	<0.001‡
Change from baseline	-0.33 ± 0.03	-0.68 ± 0.08	<0.001*

‡ Paired t-test, *Independent t-test

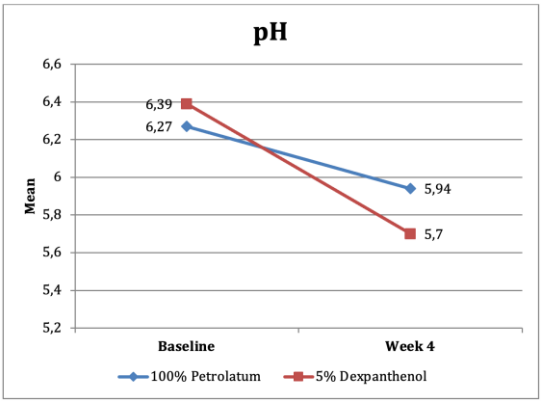


Figure 3. Decrease in pH between 100% Petrolatum and 5% Dexpanthenol

3.4 Related Complaints

Self-reported complaints related to application of either 100% petrolatum or 5% dexpanthenol is also recorded and summarized in Table 4.

Table 4. Self-reported application-related complaints of 100% petrolatum and 5% dexpanthenol

Related Complaints	Group		p
	100% Petrolatum	5% Dexpanthenol	
None	0 (0%)	13 (100%)	0.00*
Sticky and greasy	13 (100%)	0 (0%)	

*Chi-square test

All subjects in the petrolatum group complaints of stickiness and greasiness, whereas all subjects in the dexpanthenol group reported no complaints. This difference was found to be statistically significant with p = 0.0000

4.Discussion

4.1 Subjects' Characteristics

Most of the subjects in each group were female and the mean age was 30.23 ± 3.37 years in the 100% petrolatum group and 31.00 ± 4.51 years in the 5% dexpanthenol group. Median duration of AD was 20 years in both groups [20.0 (15-35) and 20.0 (15-25)]. Duration of AD was self-reported as the elapsed time from the participant's recalled first onset or diagnosis of AD to study enrollment; it did not represent uninterrupted active disease. In adults with a mean age of approximately 30 years, this duration broadly corresponds to onset during childhood or adolescence. However, because onset was recalled retrospectively, measurement error is possible. Atopic dermatitis is a lifelong condition, and genetic studies have shown that there are many genes involved in the development and maintenance of the skin barrier and immune function in the heritability of AD. The duration of symptom-free periods among patients with AD is still not understood, and the frequency of assessment needed to monitor patients with intermittent disease is still unknown.[18]

The highest frequency of bathing in the subjects of both groups was twice a day, which was observed in 69.2% of the subjects in the 100% Petrolatum group and comparable to the subjects in the 5% Dexpanthenol group. Use of warm bath was common, found in 61.5% of the Petrolatum group and 76.9% of Dexpanthenol group. The main purpose of skin cleansing is to remove dirt from the skin surface and control its odor, without removing the surface proteins and lipids of the stratum corneum barrier. Products containing surfactants are able to break down and emulsify most of the dirt and skin contaminants into finer particles and allow their subsequent release and removal from the skin surface.19 However, continuous water exposure may damage the skin barrier, as it disrupts the intercellular lipid lamella of the stratum corneum, causing swelling of the corneocytes, resulting in water accumulation in the intercellular space. Bathing with hot temperatures may also cause an increase in TEWL compared to cold temperatures, hence it is recommended to use cold or warm water and avoid hot water.[20]

Post-bath drying method is also a part of the skin cleansing habit. Most subjects in the Petrolatum group gently wipe or pat their body with a towel, which was observed in 61.5% whereas hard-rubbing using a towel was the most common method in 76.9% of subjects in Dexpanthenol group. Mechanical friction duet o the use of towels can affect the integrity of the skin barrier. It may be a mild stimulus with little effect on healthy skin, however AD patients are sensitive to exogenous stimuli and have lower skin barrier function, which may potentially cause irritation and further disruption of the skin barrier.[21]

Most subjects in the Petrolatum group never used moisturizer, which was found in 38.5% of subjects while in the Dexpanthenol group 38.5% never or rarely use moisturizer. Regular moisturizer is the mainstay therapy of AD to reduce inflammation, maintain remission, and reduce relapses, which lowers the need for topical corticosteroid use. The ideal function of moisturizer is to maintain and improve skin barrier function by delivering lipids and water to the stratum corneum, increasing skin hydration, maintaining skin integrity and appearance, and reducing transepidermal water loss (TEWL) and facilitating skin barrier repair.[1,6,22]

4.2 Effects of 100% Petrolatum on TEWL and pH

Petrolatum is one of the main occlusive moisturizers for AD management. Petrolatum is able to create a protective

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barrier and help maintain skin acidity through “acid mantle” protection.23 Administration of petrolatum increases the expression of barrier proteins, filaggrin, and loricrin as well as an increase in antimicrobial peptides, including human □□-defensin 2 and LL-37. This causes petrolatum to be able to inhibit water evaporation.24,25

Murakami et al. investigates the role of petrolatum in reducing TEWL in patients with atopic dermatitis, with a significant decrease from 19.2 ± 12.2 g/h/m2 to 15.6 ± 7.8 g/h/m2.9 Topical petrolatum significantly reduce pH compared to baseline (ΔpH 0.58 ± 0.28) in patients with history of atopic dermatitis. Petrolatum as an occlusive is able to create a protective barrier and help maintain skin acidity through healthy acid mantle protection and lower skin pH in atopic dermatitis patients.[23]

Despite its benefit in moisturizing and improving the physiological function of the skin, petrolatum is related to stickiness and greasiness, which may affect patient compliance.9 Its sticky nature can also absorb dirt and dust, clog sweat glands, and cause a phenomenon known as the petrolatum paradox. When keratin and petrolatum residue stick to the skin, the skin will become scaly and flaky when scratched.10 This makes continued use of petrolatum a challenge despite its effectiveness, and there is a need for alternative moisturizers to address these concerns

4.3 Effects of 5% Dexpanthenol on TEWL and pH

Dexpanthenol is an alcohol derivative of pantothenic acid, a component of coenzyme A which functions as a cofactor for various reactions catalyzed by enzymes, including the transfer of acetyl groups of fragments of various lengths reacting with sulfhydryl groups of coenzyme A. These reactions are important in carbohydrate metabolism, gluconeogenesis, fatty acid degradation, and in the synthesis of sterols, steroid hormones, or porphyrins. Coenzyme A also plays a role in protein modification, such as N-terminal acetylation, internal amino acid acetylation, and fatty acid acylation, thereby affecting protein localization, stability, or activity.[8,26,27]

Topical 5% dexpanthenol has advantages over petrolatum because in addition to being able to improve skin barrier function, it has a higher compliance rate for the use of dexpanthenol is higher than petrolatum, because its consistency is lighter and more comfortable for use by atopic dermatitis patients. It also has additional properties, including anti-inflammatory, antioxidant, and supports wound healing.[8,26,27]

The role of dexpanthenol in skin hydration and reducing TEWL is related to its ability to interact with extracellular lamella lipid segments and protein residues in corneocytes in the stratum corneum, thereby maintaining/increasing molecular fluidity. Dexpanthenol promotes epidermal regeneration by increasing epidermal differentiation and lipid synthesis, thereby maintaining the integrity of the skin barrier.[11,12]

Stettler et al. has proven the superiority of dexpanthenol in restoring the skin barrier as measured by TEWL. Subjects in the study were given dexpanthenol for 24 days, and a decrease in the average area under the curve (AUC) of TEWL was found compared to baseline (168.36 vs. 123.38 g/h/m2, p = 0.023).28 Another study by Gehring et al. on 20 healthy subjects who were exposed to repeated SLS showed that topical application of 5% dexpanthenol applied twice daily for 7 days could significantly reduce TEWL, with a greater reduction with 5% dexpanthenol emulsion.[29]

The role of dexpanthenol in improving skin pH is demonstrated by Peltier et al. who found improvements in skin pH levels in atopic subjects who were given a cleansing agent containing dexpanthenol on skin prone to atopy. In this study, improvements were found in skin pH levels after 28 days of administration (5.21 ± 0.50 to 5.18 ± 0.45 pH, ΔpH 0.03 ± 0.05).[30]

Both 100% petrolatum and 5% dexpanthenol significantly reduced TEWL and skin pH after 4 weeks. However, the decrease was greater with dexpanthenol. Change was defined as week 4 minus baseline, therefore more negative mean change in TEWL (-7.58 ± 0.37 vs -5.19 ± 0.75 g/m²/h; $p<0.001$) and skin pH (-0.68 ± 0.08 vs -0.33 ± 0.03; $p<0.001$) indicates a greater reduction with dexpanthenol than with petrolatum. Based on the findings above, administration of 5% dexpanthenol for 4 weeks is superior to 100% petrolatum in reducing TEWL and pH.

To the best of the author's knowledge, this is the first study to compare the role of petrolatum and dexpanthenol on skin barrier. The study focuses on adults patients with a history of atopic dermatitis, suggesting the superiority of dexpanthenol to decrease TEWL and pH compared to petrolatum. All subjects completed the study with no reports of allergic reaction, indicating the safety of both petrolatum and dexpanthenol. Subjects’ characteristics and habits, including bathing practices, were also considered, as these factors may influence outcomes particularly in humid environments such as Southeast Asia. The study further highlights participants’ adherence to the prescribed topical agents, with complaints of stickiness in petrolatum whereas dexpanthenol was well accepted with no reported complaints.

Despite its strengths, several limitations should be considered. First, the small sample size resulted in a clinically relevant imbalance in self-reported baseline symptoms. Although baseline TEWL and skin pH at the non-flaring measurement sites were numerically similar, residual confounding cannot be excluded. Second, AD duration was self-reported and may be affected by recall bias. Third, application-related complaints were assessed using a non-validated self-report. Petrolatum has recognizable sticky and greasy nature, therefore participant blinding may have been compromised for this subjective outcome, creating a high risk of reporting or detection bias. These complaint data should therefore be regarded as exploratory and do not establish superior adherence or tolerability. Fourth, skin-barrier improvement was assessed only with TEWL and pH; additional measures such as corneometry could strengthen the evidence. Fourth, skin-barrier improvement was assessed only with TEWL and pH; additional measures such as corneometry could strengthen the evidence. Subjects were recruited from a single geographical and environmental

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setting, which limits generalizability. Lack of long-term follow up causes inability to assess its role to maintain skin barrier, therefore further studies with a longer period of time are encouraged to assess the sustainability and effectiveness of dexpanthenol to maintain skin barrier.

5.Conclusion

This study demonstrated that topical 5% dexpanthenol is effective in reducing TEWL and pH values in patients with history of atopic dermatitis compared to topical 100% petrolatum. Use of Dexpanthenol was well accepted with no reported complaints

Ethical Approval

This study was approved by ethical committee of Kariadi Central General Hospital Semarang and Faculty of Medicine of Diponegoro University with number 16322/EC/KEPK-RSDK/2024

Conflicts of Interest

The authors declare no conflict of interest.

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Author Contributions

Dr. Muslimin, Sp.DVE, Subsp. OBK, FINSDV, FAADV and and DR. dr. Radityastuti, Sp.DVE, Subsp.DA, FINSDV, FAADV contributed for conceptualization, methodology and validation. Dr. Izzah Basyir contributed for medical writing and editing.

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