Original Article

The Comparative Study of Efficacy between Cream Containing Spent Grain Wax, Shea Butter, *Argania spinosa* Kernel Oil, Tapioca Starch, and 1% Hydrocortisone Cream in The Treatment of Intertrigo

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Background: Intertrigo is a common skin problem. Although there was no standard treatment due to few clinical studies, topical corticosteroids, and drying agents such as talcum are usually used to treat intertrigo, and the side effects of these agents should be monitoring.

Objective: To compare the efficacy between cream containing spent grain wax, shea butter, *Argania spinosa* kernel oil, Tapioca starch, and 1% hydrocortisone cream for the treatment and prevention of intertrigo.

Materials and Methods: Fifty-eight lesions from 18 intertrigo patients were randomized into two groups, HCC group, which is the 1% hydrocortisone cream and STIMU-TEX AS group, which is the combination cream of spent grain wax, shea butter, *Argania spinosa* kernel oil, and tapioca starch. The evaluations were performed at baseline, the first week, the second week, and the fourth week via scoring of skin redness, pruritus, excoriation, Dermatology Life Quality Index (DLQI), and patient satisfaction. The adverse events were also recorded.

Results: All participants completed the protocol. At the end of the study, 27 of 29 lesions were completely cured in the HCC group, and 25 of 29 lesions cured in the STIMU-TEX AS group. Although the number of complete remissions of the STIMU-TEX AS group was inferior to the HCC group, it was not statistically significant. There was no relapse within two weeks after completing the treatment.

Conclusion: The outcomes showed no statistically significant difference between both groups; thus, the cream may be considered as an alternative treatment and prevention of intertrigo.

Keywords: Intertrigo, Spent grain wax, Shea butter, *Argania spinosa* kernel oil, Tapioca starch

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Intertrigo is an inflammation of the skin at intertriginous areas such as the axilla, groin, cubital fossa, popliteal fossa, neck, and skin folds[1-3]. It is caused by various factors, which are friction, moisture, and warmth in these areas. The risk factors are obesity, warm and humid weather, friction activities, wearing tight outfits, and immobilization. Although intertrigo is not a severe skin disease, it might affect the patient's daily activities, socializing, and quality of life.

Presently, there is no standard treatment for treating intertrigo. Topical corticosteroids are frequently prescribed with a well-responsive result. However, the side effects limit its use[4]. Drying substances are also useful for intertrigo such as zinc oxide, talcum, and starch. However, talcum was proved to increase the risk of ovarian cancer in adults and might cause chronic respiratory problems as well[1,2,5]. As a result, plant powder seems to be a better choice.

There are few studies about treatments of intertrigo comparing topical corticosteroids and topical non-corticosteroids[6]. Accordingly, the

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authors conducted a randomized controlled trial to compare the efficacy of the treatment between topical corticosteroid, which was the 1% hydrocortisone cream and topical non-corticosteroid, which was a combination cream of spent grain wax, shea butter, *Argania spinosa* kernel oil, and tapioca starch.

Materials and Methods

Study design

The present study was an experimental, double-blinded, randomized controlled trial. Trial identification number is TCTR20200719001. A sample size calculation was performed by a PS sample size software (version 3.0) and the information from Hedley et al previous study in 1990[5]. Eventually, 58 sites of the lesion from 18 intertrigo patients were enrolled in the study. All participants were informed about the study background, protocol, risks, benefits, and adverse events. They willingly attended the present study and signed the informed consent form. The demographic data were obtained. The computerizing randomization was performed for dividing participants into two groups, the HCC group, which was the 1% hydrocortisone cream with cream base, and the STIMU-TEX AS group, which was a combination cream of spent grain wax, shea butter, *Argania spinosa* kernel oil, and tapioca starch. The third person concealed the allocation to blind the result to the participants and the evaluators. The authors conducted the present study at Skin center, Srinakharinwirot University, Bangkok, Thailand, between 1 April and 31 June 2019. The protocol was approved by the Human Research Ethics Committee of Srinakharinwirot University (SWUEC/F-442/2561).

Inclusion criteria

Participants must be one month to sixty years old before the time of study recruitment and had one or more erythematous rashes at intertriginous areas. These lesions had to pass the necessary tests or be diagnosed by dermatologists as intertrigo.

Exclusion criteria

Other common intertriginous rashes were excluded, such as erythrasma by clinical and Wood's lamp examination and candidiasis by clinical and potassium hydroxide preparation. Contact dermatitis, atopic dermatitis, inverse psoriasis, and seborrheic dermatitis were also excluded by clinical and history taking[1-3,6-8]. Furthermore, subjects who had a history of allergic to corticosteroid, STIMU-TEX AS, or other ingredients in the study creams should not participate in the study. In terms of safety, pregnant or lactated women also excluded. Topical and systemic anti-inflammatory agents like corticosteroid, NSAIDs, or antihistamine must stop before starting the protocol for two weeks and four weeks, respectively.

Treatment protocol

At the start of the protocol (week 0), participants' general information, previous treatment, and current medication were recorded. The dermatological examination was done by a dermatologist to confirm the diagnosis of intertrigo, including wood lamp examination and potassium hydroxide preparation. Signs and symptoms, skin redness using the visual assessment of erythema (VAE) score, pruritus with numerical rating scale, excoriation, and quality of life using the Dermatology Life Quality Index (DLQI) were also assessed as baseline score[9-12]. Participants were randomly assigned to the HCC group and the STIMU-TEX AS group. An assistant researcher, as a third person, prescribed creams for participants from each group. An HCC group was given a 1% hydrocortisone cream, while A STIMU-TEX AS group received a cream containing STIMU-TEX AS with tapioca starch. Both creams were filled in containers with the same look to blind the evaluator and the participants.

At the second visit (week 1), VAE, numerical rating scale, excoriation, and adverse event reports were evaluated. Then the participants continued using their cream for another week. Their cream would be changed to cream base for HCC group, and cream containing STIMU-TEX AS with tapioca starch for STIMU-TEX AS group when their lesions were completely cured.

For the third visit (week 2), the evaluator assessed the same parameters as the second visit. At this time, most of the lesions were completely gone. In the last visit (week 4), all parameters, including DLQI and patient satisfaction, were evaluated.

Evaluations

The primary outcome, skin redness, was evaluated via VAE by a dermatologist. VAE was modified from the SCORAD score. There were none, slightly, fairly, and extremely redness. The degree of erythematous skin referred to the degree of skin inflammation. Thus, the authors defined score 0 as cured, and score 1 to 3 as uncured. The excoriation score was also modified from the SCORAD score. Besides, the authors used questionnaires to assess

pruritus, DLQI, patient satisfaction, and adverse events. The evaluator would estimate a VAE score of rashes at each visit, including an excoriation using score 0 as absence and score 1 to 3 as presence, a numerical rating scale for pruritus using 0 to 10 scale with 0 as no pruritus and 10 as the most pruritus, and reporting of adverse events. At the last visit, DLQI and patient satisfaction were obtained.

The definition of the disease remission was no erythema (VAE score=0), and the relapse of the disease was 2 or more increasing of the score within two weeks.

Statistical analysis

For baseline characteristics, categorical data were analyzed and reported as frequency and percentage, while continuous data were analyzed and reported as mean ± standard deviation. The Kaplan-Meier method was performed for calculating the median time to remission. In the case of comparing categorical variables between the two groups, a chi-square test was chosen. The Stata, version 13 (StataCorp LP, College Station, TX, USA) was used for statistical analyses. A p-value of 0.05 or less was determined as a statistically significant difference.

Results

Fifty-eight lesions were enrolled in the present study. Twenty-seven lesions were female (46.55%), and thirty-one lesions were male (53.45%). Without having a statistically significant difference, the mean age of the HCC group and STIMU-TEX AS group was 21.21±19.80 and 23.59±20.41, respectively. The range of age was three months to 59 years old. There were 23 child participants of less than 18 years old (39.66%), and 35 adult participants that were 18 years old and older (60.34%). The list of various sites of lesions and demographic data are shown in Table 1. All volunteers participated in the study without discontinuation.

Erythema, pruritus, and excoriation from both groups showed statistically significant improvement in the first week (p<0.001) and continued improving until complete remission in the second week. No relapse of intertrigo was presented at the fourth week. There was no serious adverse event. Subgroup analysis was performed as children and adults. Both children and adults showed similar results, with no statistically significant difference in all parameters.

During the four weeks of therapy, 27 of 29 patients in the HCC group and 25 of 29 patients in the STIMU-TEX AS group achieved remission.

Table 1. Demographic data

Demographic data	HCC group[1] (n=29); n (%)	STIMU-TEX AS group[2] (n=29); n (%)	p-value
Sex			0.188
Female	11 (37.93)	16 (55.17)	
Male	18 (62.07)	13 (44.83)	
Age (year)			0.653
Median (IQR)	22.47 (0.61, 33.44)	22.47 (0.61, 43.59)	
<18	12 (20.69)	11 (18.97)	
18 to 60	17 (29.31)	18 (31.03)	
Site of lesion			
Axilla	7 (24.14)	5 (17.24)	
Groin	4 (13.79)	4 (13.79)	
Inframammary fold	3 (10.34)	3 (10.34)	
Interdigital area	1 (3.45)	1 (3.45)	
Neck	1 (3.45)	1 (3.45)	
Cubital fossa	6 (20.69)	8 (27.59)	
Popliteal fossa	4 (13.79)	4 (13.79)	
Umbilicus	0 (0.00)	0 (0.00)	
Others			
• Skin fold at thighs	1 (3.45)	1 (3.45)	
• Skin fold at wrists	1 (3.45)	1 (3.45)	
• Skin fold at forearms	1 (3.45)	1 (3.45)	

IQR=interquartile range

[1] HCC group: 1% hydrocortisone cream; [2] STIMU-TEX AS group: a combination cream of spent grain wax, shea butter, Argania spinosa kernel oil, and tapioca starch

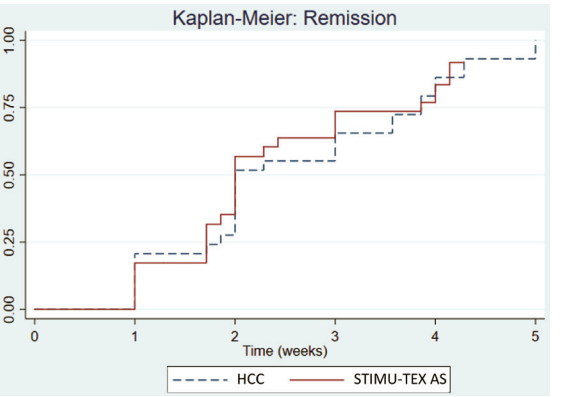

Figure 1. Kaplan-Meier curve showed the cumulative incidence of remission of both groups.

The remission incidence rate in the HCC group was about 93/100 per month and 86/100 per month in STIMUTEX AS group, respectively (p=0.752). The median time to remission in the HCC group was not significantly different from the STIMUTEX AS group at two versus two weeks. The cumulative incidence

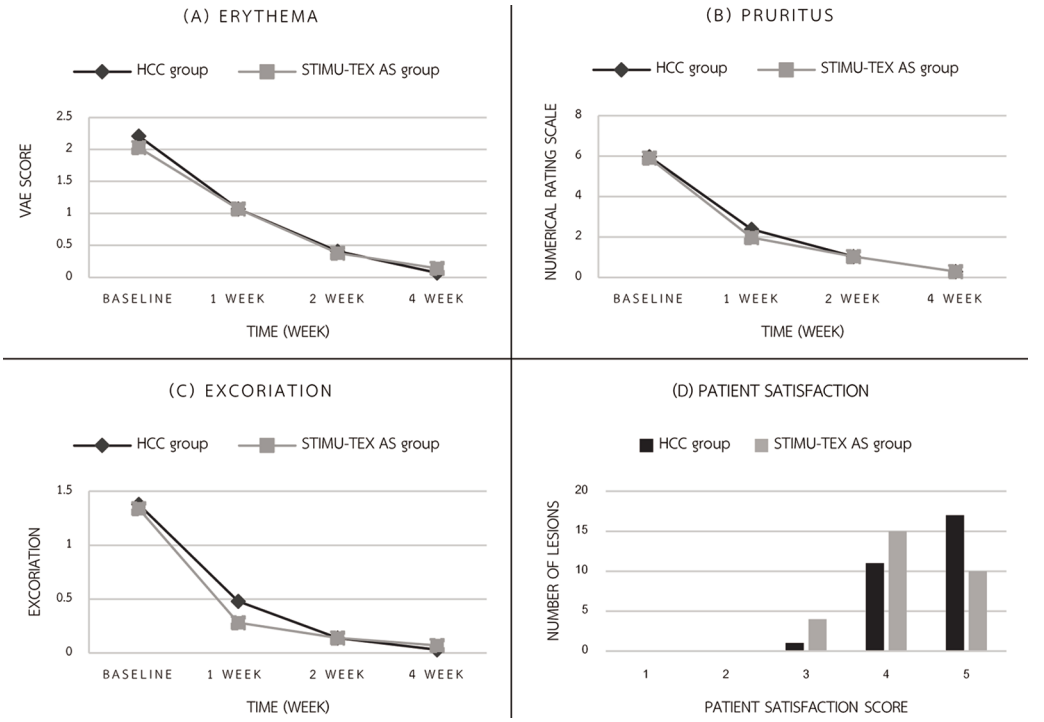

Figure 2. (A) Erythema, (B) Pruritus, (C) Excoriation, (D) Patient satisfaction.

of remission of both groups is shown in Figure 1. Patients in the HCC group had a similar probability of remission when compared with STIMUTEX AS group.

DLQI showed improvement in both groups. In the HCC group, the DLQI score reduction was 9.69±6.01, while the STIMU-TEX AS group was 8.31±6.26. There was no statistically significant difference (p=0.396). Regarding patient satisfaction, it was found that the score in the HCC group was non-significantly higher than the STIMU-TEX AS group. (Figure 2).

Discussion

The comparison of the present study was an efficacy between a cream containing STIMU-TEX AS with Tapioca starch and a 1% hydrocortisone cream in the treatment and prevention of intertrigo. From the previous study, Hedley et al in 1990[6] showed corticosteroids being effective in intertrigo significantly, and STIMU-TEX AS has been shown in Jirabundansuk et al[13] study that having an anti-inflammatory property equivalent to 1% hydrocortisone cream without any side effects for the treatment of atopic dermatitis. Accordingly, the study was conducted and showed that the cream could also treat other inflammatory skin diseases like intertrigo.

The present study results showed that the efficacy between a cream containing STIMU-TEX AS with Tapioca starch, and a 1% hydrocortisone cream was equivalent. Statistically, there were no significantly different results between these two groups. Their lesions were improved significantly within the first week ($p<0.001$) in both groups, and the Kaplan-Meier method showed the time to complete remission of intertrigo in two weeks. In the prevention aspect, there was no relapse of the lesion within two weeks. Tapioca starch, having a water-absorption property, might have a significant role in this part. It helps to dry skin and reduces friction, so it decreases the risk of new lesion development. Because of the cream preparation of this product, this cream has less risk of inhalation and safer than the powder preparation.

STIMU-TEX AS has a main component called linoleic acid, an unsaturated fatty acid, which has anti-inflammatory effects[14-19]. From the previous study in 2008, Senapati et al found the evening primrose oil, which contains linoleic acid, has an anti-inflammatory property, and helps to repair skin barrier function in atopic dermatitis treatment[20]. Therefore, intertrigo lesion improvement in STIMU-TEX AS group might result from this unsaturated fatty acid.

The results emphasized the anti-inflammatory property of STIMU-TEX AS from the previous study.

Jirabundansuk et al conducted the study in mild to moderate atopic dermatitis[13], which is one of the inflammatory skin diseases similar to intertrigo. It may also be helpful in other inflammatory skin diseases; thus, further study should be performed.

The present study also had a limitation. The follow-up period for prevention, two weeks, maybe too short for the relapse of intertrigo. For further study, tapioca starch might be studied with other plant starch such as rice starch or corn starch to compare the cost-effectiveness. Moreover, an objective measurement like Mexameter® might be beneficial to get rid of human error caused by the evaluator.

In conclusion, a cream containing spent grain wax, shea butter, *Argania spinosa* kernel oil, and tapioca starch has not differed from the 1% hydrocortisone cream for intertrigo treatment. Consequently, this cream may be considered as an alternative treatment. Furthermore, it can be used as a preventive measured as well.

What is already known on this topic?

The previous study of Hedley et al in 1990 showed corticosteroids being effective in intertrigo. The prior research of Jirabundansuk et al study showed that a cream containing STIMU-TEX AS has an anti-inflammatory property is as useful as 1% hydrocortisone cream in mild to moderate atopic dermatitis, which is an inflammatory skin disease as intertrigo is. Furthermore, powders and starches have a water absorption property and are widely used for the treatment and prevention of intertrigo. However, there is no standard treatment for intertrigo.

What this study adds?

The results of this study showed no significant difference of efficacy between a cream containing STIMU-TEX AS with Tapioca starch, and a 1% hydrocortisone cream for treatment and prevention of intertrigo. No serious adverse event occurred. Thereby, this cream may be recommended as an alternative treatment for intertrigo.

Conflict of interest

Zuellig Pharma Co., Ltd. funded this study. However, the authors declare that the company has not involved in any steps of the study.

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