Comparative efficacy between 5% liquor carbonis detergens cream, 1% hydrocortisone cream and cream base in the treatment of chronic plaque psoriasis: a randomized, single-blind comparison study

Kanawat Kanjanapiboon MD,

Kowit Kampirapap MD,

Bensachee Pattamadilok MD.

ABSTRACT:

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THE INSTITUTE OF DERMATOLOGY, BANGKOK, THAILAND.

Background: Topical therapy is the first line treatment for patients with chronic stable plaque psoriasis affecting a limited body surface area. Topical coal tar is well known and has been effective treatment for psoriasis patients for a long time. However, there are only few clinical trials supporting its clinical efficacy comparing with topical corticosteroid and emollient.

From: Institute of Dermatology, Ministry of Public Health, Bangkok, Thailand.

Corresponding author: Kanawat Kanjanapiboon MD., e-mail: phetpcn29@hotmail.com

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Objective: To evaluate the efficacy and side effects of topical 5% Liquor Carbonis Detergens (LCD) cream comparing with topical 1% hydrocortisone cream and cream base in the treatment of chronic stable plaque psoriasis.

Materials and methods: A randomized, single-blind comparison study consisting of 8-week treatment phase and 4-week post-treatment follow-up phase. Patients with chronic stable plaque psoriasis were randomly recruited at the outpatient department of Institute of Dermatology, Bangkok, Thailand. Each patient was selected three similar psoriatic lesions on the trunk or extremities. The selected lesions were randomized to apply 5% LCD cream or 1% hydrocortisone cream or cream base twice daily. The three selected psoriatic lesions were evaluated using the severity (0-3) scale of erythema, scaling and induration (ESI score) in each visit. Evaluation was carried out at the end of 4^{th} and 8^{th} week during the treatment period and at the end of 12^{th} week during post-treatment follow-up period. Serial photography was taken in every visit. Self-evaluated adverse events by the patients were also recorded during the study period.

Results: Thirty-three of 38 recruited patients completed the study. At the end of 8-week treatment, the mean percentage reduction of the ESI score from baseline was 53.97% in 5% LCD treatment group, 31.98% in 1% hydrocortisone treatment group and 16.88% in cream base treatment group. The mean percentage of the ESI score reduction was statistically significant in all groups ($p < 0.001$) but 5% LCD treatment group was significantly superior to the others ($p < 0.001$). The mean percentage reduction in size of lesions from baseline to up until the end of the 8 weeks was 13.07% in 5% LCD treatment group which was not statistically significant ($p = 0.306$). While the mean percentage extension in size of lesions from baseline to up until the end of the 8 weeks was 37.75% in 1% hydrocortisone treatment group and 73.57% in cream base treatment group which were statistically significant ($p = 0.006$, $p = 0.004$ respectively). The adverse effect was mild local irritation without any systemic side effect in all three groups. The 5% LCD cream was safe and well-tolerated with some complaint about malodor, cloth staining (12.12%) and hyperpigmentation (9.09%).

Conclusion: Our study demonstrated that the 5% LCD cream achieved significantly greater improvement in the ESI score in comparison with 1% hydrocortisone cream and cream base. The 5% LCD cream is a safe and effective corticosteroid-sparing treatment for plaque-type psoriasis patients.

Key words: Plaque type psoriasis**,** Coal tar, Liquor Carbonis Detergens (LCD), Hydrocortisone, Cream base

บทคัดย่อ:

คณวัฒน์ กาญจนพิบูลย์ โกวิท คัมภีรภาพ เบ็ญจ์สชีว์ ปัทมดิลก การศึกษาเปรียบเทียบประสิทธิผลระหว่างครีมทาอนุพันธ์น้ำมันดิน 5% ครีมไฮโดรคอร์ติโซน 1% และครีมเบส ในการรักษาผู้ป่วยโรคผิวหนังสะเก็ดเงินชนิดผื่นหนา วารสารโรคผิวหนัง 2561; 34: 231-244.

สถาบันโรคผิวหนัง กรมการแพทย์ กระทรวงสาธารณสุข

ยาทาเป็นการรักษาหลักสำหรับผู้ป่วยสะเก็ดเงินชนิดผื่นหนาที่มีระดับความรุนแรงน้อย พบว่ายาทาอนุพันธ์น้ำมันดินเป็นที่รู้จักและถูกใช้ในการรักษาผื่นสะเก็ดเงินมาอย่างยาวนาน แต่ยังมีรายงานการศึกษาเปรียบเทียบประสิทธิผลและผลข้างเคียงของครีมทาอนุพันธ์น้ำมันดินและครีมเบส/ครีมทาสเตียรอยด์ค่อนข้างน้อย

วัตถุประสงค์: เพื่อศึกษาประสิทธิผลและผลข้างเคียงของครีมทาอนุพันธ์น้ำมันดิน 5% ในการรักษาผู้ป่วยโรคสะเก็ดเงินชนิดผื่นหนาโดยเปรียบเทียบกับครีมไฮโดรคอร์ติโซน 1% และครีมเบส

วิธีการรักษา: โครงการวิจัยแบ่งเป็นช่วงการรักษา 8 สัปดาห์และช่วงติดตามหลังการรักษา 4 สัปดาห์ โดยคัดเลือกผู้ป่วยโรคผิวหนังสะเก็ดเงินชนิดผื่นหนาประเภทความรุนแรงน้อยจากแผนกผู้ป่วยนอกสถาบันโรคผิวหนัง ผู้ป่วยแต่ละคนจะได้รับการคัดเลือกผื่น 3 ผื่นบนลำตัวหรือแขน ขาที่มีลักษณะใกล้เคียงกัน โดยแต่ละผื่นจะถูกสุ่มโดยแพทย์ว่าจะใช้ครีมอนุพันธ์น้ำมันดิน 5% ครีมทาไฮโดรคอร์ติโซน 1% หรือครีมเบส วันละ 2 ครั้ง ติดตามผลโดยใช้คะแนนความแดง สะเก็ด และความหนา (ESI score) ของผื่นทุก 4 สัปดาห์ในช่วงการรักษา (สิ้นสุดสัปดาห์ที่ 4 และ 8) และช่วงติดตามการรักษา (สิ้นสุดสัปดาห์ที่ 12) และถ่ายรูปผื่นติดตามทุกครั้ง นอกจากนี้ผู้ป่วยทำการประเมินผลข้างเคียงของยาแต่ละชนิดในช่วงการรักษาและช่วงติดตามการรักษาด้วย

ผลการศึกษา: ผู้ป่วยโรคสะเก็ดเงินชนิดผื่นหนา 33 คน จาก 38 คน เข้าร่วมโครงการวิจัยครบ 12 สัปดาห์ พบว่าหลังการรักษา 8 สัปดาห์ กลุ่มที่ได้รับยาทาอนุพันธ์น้ำมันดิน 5% มีค่าเฉลี่ย ESI score ลดลง 53.97% กลุ่มที่ได้รับครีมทาไฮโดรคอร์ติโซน 1% มีค่าเฉลี่ย ESI score ลดลง 31.98% และกลุ่มที่ได้รับยาทาครีมเบสมีค่าเฉลี่ย ESI score ลดลง 16.88% ทุกกลุ่มมีค่าเฉลี่ย ESI score ลดลงอย่างมีนัยสำคัญทางสถิติ ($p < 0.001$) และกลุ่มยาทาอนุพันธ์น้ำมันดิน 5% มีเฉลี่ยลดลงกว่าอีกสองกลุ่มอย่างมีนัยสำคัญทางสถิติ ($p < 0.001$) นอกจากนี้หลังการรักษา 8 สัปดาห์ พบว่ากลุ่มที่ได้รับยาทาอนุพันธ์น้ำมันดิน 5% มีค่าเฉลี่ยขนาดของผื่นลดลง 13.07% แต่ไม่มีนัยสำคัญทางสถิติ ($p = 0.306$) ในขณะที่กลุ่มที่ได้รับยาทาไฮโดรคอร์ติโซน 1% มีค่าเฉลี่ยขนาดของผื่นเพิ่มขึ้น 37.75% และกลุ่มที่ได้รับยาทาครีมเบสมีค่าเฉลี่ยขนาดของผื่นเพิ่มขึ้น 73.57% ทั้งสองกลุ่มมีค่าเฉลี่ยขนาดของผื่นเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ ($p = 0.006$, $p = 0.004$ ตามลำดับ) ยาทาทั้ง 3 ตัวมีผลข้างเคียงเฉพาะที่คือการคัน ระคายเคืองโดยไม่มีผลต่อระบบภายในร่างกาย ยาทาอนุพันธ์น้ำมันดิน 5% นั้นปลอดภัยแต่มีกลิ่นเหม็น เลอะเสื้อผ้า (12.12%) และอาจทิ้งรอยดำ (9.09%) บริเวณที่ทายาได้

สรุปผล: ยาทาอนุพันธ์น้ำมันดิน 5% เป็นทางเลือกหนึ่งที่ปลอดภัยและมีประสิทธิภาพสำหรับรักษาผื่นโรคผิวหนังสะเก็ดเงินชนิดผื่นหนา การศึกษานี้พบว่ายาทาอนุพันธ์น้ำมันดิน 5% ทำให้ผื่นสะเก็ดเงินดีขึ้นกว่ายาทาไฮโดรคอร์ติโซน 1% และครีมเบสอย่างมีนัยสำคัญทางสถิติ

คำสำคัญ: โรคสะเก็ดเงินชนิดผื่นหนา, น้ำมันดิน, อนุพันธ์น้ำมันดิน, ไฮโดรคอร์ติโซน, ครีมเบส

Psoriasis is a common dermatological disease, affecting 1-3% of all races.[1] It is a chronic immune-mediated inflammatory skin disease. Most patients require lifelong treatment to control the disease.[2] The most common form of psoriasis is plaque-type, which is characterized by well-demarcated, scaly, erythematous, hypertrophic plaque. The majority of psoriasis patients have mild to moderate disease course and topical agents represent the first-line therapy for these patients[3]. The topical treatments for psoriasis have included coal tar, corticosteroids, calcipotriol, anthralin, and tazarotene. Topical corticosteroids are common topical treatment for psoriasis but continuous use often causes local and systemic adverse effects as well as tachyphylaxis.[4,5] Coal tar has been a mainstay in the treatment of psoriasis in Thailand for centuries, but despite its widespread use, there is little evidence supporting its clinical efficacy and side effects. There were some studies demonstrated that betamethasone valerate cream (0.1%) was significantly more effective than 10% coal tar cream.[6] Moreover, calcipotriol ointment was also significantly more effective than 15% coal tar solution.[7] Studies revealed that topical coal tar preparations were less effective than other topical treatments[8] but it is still used because it is inexpensive.

There was no study directly comparing the efficacy of topical LCD with mild potency topical corticosteroid and emollient. The purposes of this study were to evaluate the clinical efficacy and adverse effects of 5% LCD cream, the common treatment used in Thailand, compare to 1% hydrocortisone cream and cream base in the treatment of chronic stable plaque-type psoriasis.

Materials and Methods

This study was a prospective, randomized, clinical trial, single-blind comparative study of 5% LCD cream, 1% hydrocortisone cream and cream base. It was carried out at the outpatient department of Institute of Dermatology, Bangkok, Thailand, from March to July 2018.

Selection of study patients

Male and female patients, aged 18-65 years old with diagnosis of mild plaque-typed psoriasis (<10% body surface area involvement, PASI <10) were enrolled in this study. The anatomical distribution of plaque-type psoriasis included the trunk, upper or lower extremities. Patients with only scalp psoriasis, pregnant, breast-feeding patients or drug-induced psoriasis were excluded from the study. Other exclusion criteria were smoking or alcoholic drinking, patients with history of topical coal tar allergy or topical corticosteroid allergy, receiving topical anti-psoriasis treatment during the previous 2 weeks, systemic anti-psoriasis treatment during the previous 4 weeks, immunomodulatory therapy

during the previous 12 weeks or ingestion of medications that were known to influence psoriasis. The study protocol was approved by the Ethics committee of the Institute of Dermatology, and written informed consent was obtained prior to initiating therapy in all patients.

Study design and treatment regimens

There were two phases of the study: 8-week treatment phase and 4-week post-treatment follow-up phase. After recruitment according to inclusion and exclusion criteria, each patient was selected three similar psoriatic lesions on the trunk or extremities and labeled number "1", "2", or "3". Each lesion was at least 5 cm apart, involved an area not more than 100 cm^2 and had total ESI score at least 6. Three different medications including 5% LCD cream, 1% hydrocortisone cream and cream base were provided in identical containers and randomized by the drug dispenser to labeled "A", "B" and "C" respectively. A physician who selected the lesions was blinded. The "A", "B", and "C" cream were indicated for applying lesions number "1", "2" and "3" respectively. The patients were instructed to apply each lesions with cream "A", "B", or "C" for 8 weeks and then discontinued for another 4 weeks of post-treatment period. The other topical medications were prohibited to apply on the treatment sites while enrolled in this study. The remaining psoriasis lesions (at least 5 cm apart from study sites) were prescribed standard topical treatments. The assessment was done at 4, 8, and 12 weeks after the first visit. The severity of the selected lesions were evaluated by the same physician using erythema, scaling, induration (ESI) scoring (0-3) in each visit. The size of the lesions was also calculated in square centimeter (cm^2) to determine clinical responsiveness. For each visit, the patients underwent serial photography using digital camera and the same photographer. Self-assessment by the patients regarding side effects on a three-point scale (0=none, 1=mild, 2=moderate, 3=severe) was also recorded. Compliance was assessed by weighing the cream in gram (g) in every visit.

Statistical analysis

SPSS for Microsoft Windows was used for statistical analysis. The efficacy of treatment was evaluated by comparing the change of the ESI score and size of the lesions from baseline values within each patient. The change in mean ESI score and lesion size at baseline, 4, 8 and 12 weeks in each group were analyzed using the paired t-test. The repeated measurement ANOVA was used to compare the mean ESI score and the size change between 5% LCD cream, 1% hydrocortisone cream and cream base group at 4, 8 and 12 weeks. Post hoc test by Bonferroni was used to compare the mean ESI score and the size change between any two groups. P-

value <0.05 was considered statistically significant.

Results

Thirty-three out of 38 patients with mild chronic stable plaque-typed psoriasis completed this study. Five patients were excluded from the study due to pregnancy (1 person), unacceptable treatment response (2 persons) and moving to distant workplaces (2 persons). The patients' demographic data are shown in Table 1. All patients were considered excellent compliance.

Table 1 Demographic characteristics of all psoriasis patient (N=33)

	N (%) or mean ± SD	Median [min, max]
Gender		
Female	10 (30.3)	
Male	23 (69.7)	
Age (year)	45.09 ± 12.37	43 [20, 65]
Body weight (kg)	72.36 ± 15.04	70 [49, 112]
Height (cm)	165.42 ± 11.49	168 [145, 188]
BMI	26.35 ± 4.06	26.3 [19.92, 36.57]
BMI >25	21 (63.6)	
Underlying disease		
Allergic rhinitis	1 (3)	
HIV infection	1 (3)	
Old CVA	1 (3)	
Thyroid disease	1 (3)	
Hypertension	4 (12.1)	
DM type II	2 (6.1)	
None	24 (72.7)	
Duration of psoriasis (months)	153.36 ± 145.75	84 [9, 516]
PASI at baseline	6.25 ± 2.27	

The ESI score and size of each lesion were recorded at baseline, 4 weeks, 8 weeks and 12 weeks. The mean ESI score and size of lesions in each treatment group at the various periods

were calculated and illustrated in Table 2, Figure 1 and Figure 2. The mean percentage change in the ESI scores and size of lesions are given in Table 3. The mean percentage reduction in ESI score from baseline up until the end of 8-week treatment phase was 53.97% with 5% LCD treatment group, 31.98% with 1% hydrocortisone treatment group and 16.88% with cream base treatment group (Table 3). The change of mean percentage of ESI score from the baseline to the end of 8-week treatment phase was statistically significant in all three groups ($p < 0.001$). The mean difference between the 5% LCD group and 1% hydrocortisone group in the percentage change in ESI score from baseline to the end of 8 weeks was 21.99%, the mean difference between 5% LCD group and cream base group was 37.09%, while the mean difference between 1% hydrocortisone group and cream base group was 15.1%. The mean percentage decrease in ESI score of 5% LCD group was significantly greater than the 1% hydrocortisone group and cream base group ($p < 0.001$). While comparing the mean percentage reduction in ESI score between the controls, 1% hydrocortisone group was also significantly greater than cream base group ($p = 0.015$). The mean percentage reduction in size of lesions from baseline to up until the end of the 8 weeks was 13.07% in 5% LCD treatment group which was not statistically significant ($p = 0.306$). While the mean percentage extension in size of lesions from baseline to up until the end of the 8 weeks was 37.75% in 1% hydrocortisone treatment group and 73.57% in cream base treatment group which were statistically significant ($p = 0.006$, $p = 0.004$ respectively).

The mean percentage reduction in ESI score from baseline to up until the end of the 4 weeks was 32.27% in the 5% LCD treatment group, 19.34% in the 1% hydrocortisone treatment group and 8.86% in the cream base treatment group. These mean percentage reductions of ESI score were statistically significant in 5% LCD group, 1% hydrocortisone group and cream base group ($p < 0.001$, <0.001, 0.001 respectively). The mean difference between the 5% LCD group and 1% hydrocortisone group in the percentage change in ESI score from baseline to the end of 4 weeks was 12.93%, the mean difference between 5% LCD group and cream base group was 23.41%, while the mean difference between 1% hydrocortisone group and cream base group was 10.48%. The mean percentage decrease in ESI score of 5% LCD group was significantly greater than the 1% hydrocortisone group and cream base group at the end of 4 weeks ($p = 0.004$, $p < 0.001$ respectively). While the mean percentage decrease in ESI score of 1% hydrocortisone group was also significantly greater than the cream base group at the end of 4 weeks ($p = 0.024$). The mean percentage

reduction in size of lesions from baseline to up until the end of the 4 weeks was 1.44% in 5% LCD treatment group which was statistically significant (p = 0.034). While the mean percentage extension in size of lesions from baseline to up until the end of the 4 weeks was 17.48% in 1% hydrocortisone treatment group and 27.47% in cream base treatment group which were statistically significant (p = 0.040, p = 0.027 respectively).

During the post-treatment follow-up period from 8 weeks to up until the end of 12 weeks, the mean percentage increase in ESI score was 50.51% in the 5% LCD treatment group, 26.31% in the 1% hydrocortisone treatment group and 16.94% in the cream base treatment group. These mean percentage increase of ESI score were statistically significant in 5% LCD group, 1% hydrocortisone group and cream base group (p < 0.001). The mean difference between the 5% LCD group and 1% hydrocortisone group in the percentage change in ESI score from 8 weeks to the end of 12 weeks was 24.2%, the mean difference between 5% LCD group and cream base group was 33.57%, while the mean difference between 1% hydrocortisone group and cream base group was 9.37%. The mean percentage increase in ESI score of 5% LCD group was not statistically greater than the 1% hydrocortisone group and cream base group at the end of 12 weeks (p = 1, p = 0.348 respectively). The mean percentage extension in size of lesions from 8 weeks to up until the end of the 12 weeks was 28.84% in 5% LCD treatment group which was not statistically significant (p = 0.087). While the mean percentage extension in size of lesions from 8 weeks to up until the end of the 12 weeks was 17.49% in 1% hydrocortisone treatment group and 16.25% in cream base treatment group which were statistically significant (p < 0.001, p = 0.017 respectively).

Table 2 The mean ESI score and size of the lesions at baseline, 4 weeks, 8 weeks and 12 weeks

	Group (n = 33)			*p*-value
	5% LCD cream	1% hydrocortisone	Cream base	
Baseline	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**ANOVA**
ESI	6.67 ± 0.74	6.7 ± 0.73	6.67 ± 0.82	0.983
Area (cm^2)	15.51 ± 18.46	11.58 ± 13.51	9.83 ± 11.64	0.285
4 weeks				
ESI	4.48 ± 1.23	5.39 ± 1.09	6.09 ± 1.26	<0.001
Area (cm^2)	14.18 ± 17.6	12.56 ± 14.32	11.14 ± 12.5	0.711
8 weeks				

Table 2 The mean ESI score and size of the lesions at baseline, 4 weeks, 8 weeks and 12 weeks (Cont.)

	Group (n = 33)			*p*-value
	5% LCD cream	1% hydrocortisone	Cream base	
ESI	3.03 ± 1.51	4.55 ± 1.42	5.52 ± 1.09	<0.001
Area (cm2)	14.03 ± 20.06	14.6 ± 16.25	14.21 ± 16.83	0.991
12 weeks				
ESI	4.42 ± 2.08	5.67 ± 1.98	6.42 ± 1.71	<0.001
Area (cm^2)	15.44 ± 21.75	16.14 ± 17.49	16.66 ± 20.14	0.969

Data are presented as mean ± 1 SD

p-value by ANOVA test

Table 3 Mean reduction in the ESI scores and size of lesions at each timepoints.

	Group (n = 33)			*p*-value# (Repeated ANOVA)	Post hoc test by Bonferroni◊		
Baseline to 4 weeks	**5% LCD cream Mean diff ± SD.**	**1% HC Mean diff ± SD.**	**Cream base Mean diff ± SD.**		**5% LCD vs 1% HC**	**5% LCD vs cream base**	**1% HC vs cream base**
ESI	-2.18 ± 1.33	-1.3 ± 0.98	-0.58 ± 0.9	<0.001	0.004	<0.001	0.024
Percentage change (%)	(-32.27 ± 18.39)	(-19.34 ± 14.9)	(-8.86 ± 14.59)				
Probability*	<0.001	<0.001	0.001				
Area (cm^2)	-1.33 ± 3.44	0.99 ± 2.65	1.31 ± 3.24	0.001	0.010	0.003	1
Percentage change (%)	(-1.44 ± 47.9)	(17.48 ± 81.86)	(27.47 ± 75.8)				
Probability*	0.034	0.040	0.027				
Baseline to 8 weeks							
ESI	-3.64 ± 1.71	-2.15 ± 1.39	-1.15 ± 1.06	<0.001	<0.001	<0.001	0.015
Percentage change (%)	(-53.97 ± 22.15)	(-31.98 ± 21.09)	(-16.88 ± 15.43)				
Probability*	<0.001	<0.001	<0.001				
Area (cm^2)	-1.48 ± 8.2	3.02 ± 5.85	4.38 ± 8.02	0.005	0.047	0.005	1
Percentage change (%)	(-13.07 ± 81.62)	(37.75 ± 118.89)	(73.57 ± 153.35)				
Probability*	0.306	0.006	0.004				

Table 3 Mean reduction in the ESI scores and size of lesions at each timepoints. (Cont.)

	Group (n = 33)			*p*-value# (Repeated ANOVA)	Post hoc test by Bonferroni◊		
	5% LCD cream Mean diff ± SD.	1% HC Mean diff ± SD.	Cream base Mean diff ± SD.		5% LCD vs 1% HC	5% LCD vs cream base	1% HC vs cream base
Baseline to 12 weeks							
ESI	-2.24 ± 2.31	-1.03 ± 2.04	-0.24 ± 1.9	0.001	0.061	0.001	0.387
Percentage change (%)	(-32.49 ± 32.42)	(-14.75 ± 31.77)	(-2.31 ± 27.62)				
Probability*	<0.001	0.007	0.470				
Area (cm^2)	-0.07 ± 10.63	4.56 ± 7.21	6.83 ± 12.45	0.025	0.214	0.024	1
Percentage change (%)	(4.67 ± 158.07)	(58.48 ± 146.99)	(114.44 ± 254.59)				
Probability*	0.969	0.001	0.003				
8 weeks to 12 weeks							
ESI	1.39 ± 1.2	1.12 ± 1.22	0.91 ± 1.31	0.287	1	0.348	1
Percentage change (%)	(50.51 ± 73.71)	(26.31 ± 45.09)	(16.94 ± 24.98)				
Probability*	<0.001	<0.001	<0.001				
Area (cm^2)	1.41 ± 4.6	1.54 ± 2.16	2.45 ± 5.59	0.576	1	1	1
Percentage change (%)	(28.84 ± 129.2)	(17.49 ± 37.72)	(16.25 ± 34.05)				
Probability*	0.087	<0.001	0.017				

Data are presented as mean ± 1 SD

HC = hydrocortisone

* *p*-value for within-group change (pair t-test)

p-value for between-groups change (repeated ANOVA test)

◊ *p*-value for two-group comparison (post hoc test by Bonferroni)

The patients assessed the aesthetic features and side effects of three creams, grading as 0-3 scale (0=none, 1=mild, 2=moderate, 3=severe). The adverse event reported during this study showed only local irritation, which was typically a slightly burning or itching sensation with no

visible reaction on the skin. This reaction was found in 5% LCD treatment group, 1% hydrocortisone treatment group and cream base treatment group but were not statistically significant both within-group and between-groups. No systemic adverse effect was observed. In 5% LCD treatment group, 12.12% of the patients complained slightly more about malodor and cloth staining but was not statistically significant. Three (9.09%) patients from the 5% LCD treatment group complained that the area applied 5% LCD cream got improved but leaving with hyperpigmentation.

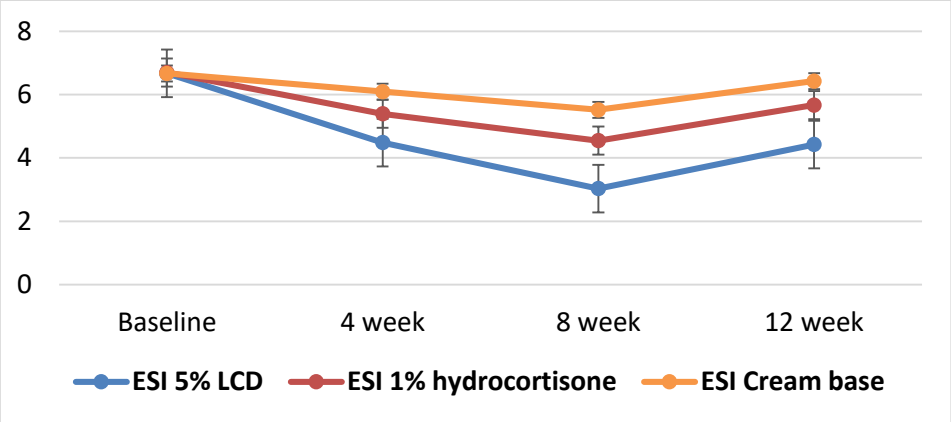

Figure 1 Mean ESI scores during each timepoints

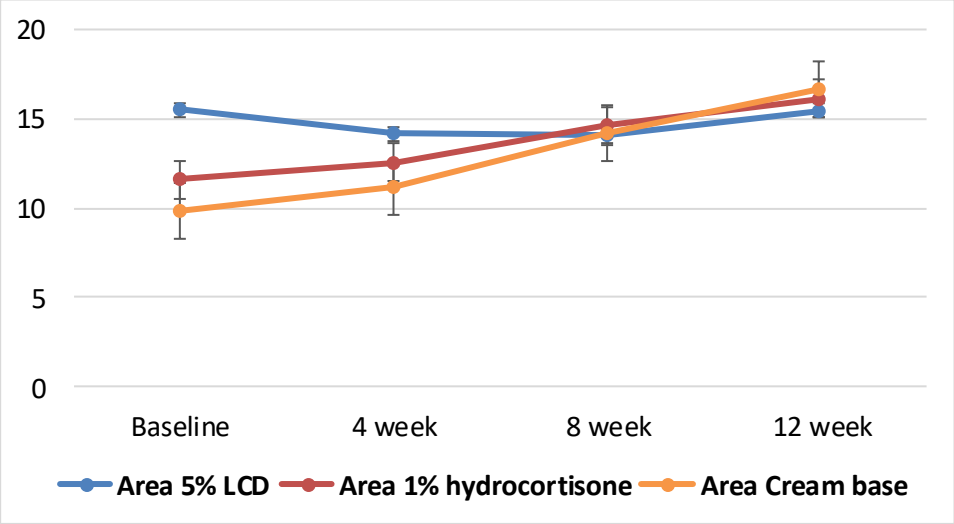

Figure 2 Mean size (cm^2) of lesions during each timepoints

Discussion

All three treatments showed a statistically significant reduction in the ESI score at the end of 4 and 8 weeks of treatment ($p < 0.001$). The mean reduction in the ESI score from baseline to the end of treatment at 4 and 8 weeks were statistically significantly greater in the 5% LCD treatment group than 1% hydrocortisone group and cream base group ($p < 0.005$). While the mean reduction in the ESI score from baseline to the end of treatment at 4 and 8 weeks was also statistically significantly greater in the 1% hydrocortisone group than cream base group ($p = 0.024$, $p = 0.015$ respectively). The present study confirmed the effectiveness of 5% LCD cream in the treatment of mild plaque-typed psoriasis. The patients treated with 5% LCD cream showed rapid onset of improvement from baseline until the end of 4 weeks (32.27%) and slightly slower improvement after 4 weeks until the end of 8 weeks (21.7%).

Only 5% LCD treatment group showed a statistically reduction in the size of lesions at the end of 4 weeks of treatment ($p = 0.034$) but not at 8 weeks of treatment ($p = 0.306$). Both 1% hydrocortisone treatment group and cream base treatment group showed a statistically extension in the size of lesions at the end of 4 weeks and 8 weeks of treatment. These might be explained by only 5% LCD cream could control the disease progression but 1% hydrocortisone and cream base could not.

During the post-treatment follow-up period from 8 weeks to up until the end of 12 weeks, the mean percentage increase of ESI score were statistically significant in all groups ($p < 0.001$) but not statistically significant when comparing between groups ($p = 0.287$). There was no statistically significant difference in the relapse rates between the three modalities. The mean percentage extension in size of lesions from 8 weeks to up until the end of the 12 weeks in 5% LCD treatment group was not statistically significant ($p = 0.087$). While the mean percentage extension in size of lesions from 8 weeks to up until the end of the 12 weeks in 1% hydrocortisone treatment group and cream base treatment group were statistically significant ($p < 0.001$, $p = 0.017$ respectively). These showed that 5% LCD cream could control the size of lesions during the 4-week post-treatment period but could not control the disease severity as the mean ESI score was increased. While the 1% hydrocortisone group and cream base group could not control both the disease severity and the size of the lesions during the 4-week post-treatment period.

Side-effect in all modalities of treatment was local irritation, which was typically a slightly burning or itching sensation on the skin, without systemic side effect. The 5% LCD cream was safe

and well-tolerated with some complaint (12.12%) about malodor and cloth staining. Mild lesional pigmentation observed in three patients (9.09%) on 5% LCD cream but faded in a few weeks after stopping therapy.

The result of the present study was similar to the previous studies. The study in 1993 by Kanzler and Gorsulowsky showed that 5% LCD therapy produced a mean ESI score reduction of 48.7%, statistically superior to treatment with only emollient, at the end of week 4.[9] In another study, Lowe demonstrated clinical superiority of 5% crude coal tar in combination with suberythemogenic UVB, compared to emollients with suberythemogenic UVB.[10] As well as a study by Williams where clinical efficacy of 5% crude coal tar was demonstrated.[11]

Coal tar is one of the oldest and an effective treatment for psoriasis. The main active antipsoriatic component of coal tar is carbazole which has antiangiogenic activity. Carbazole inhibits the production of inflammatory IL-15 by human mononuclear cells. IL-15 is elevated in psoriasis and contributes to psoriatic inflammation. Carbazole also reduces the activity of inducible nitric oxide synthase (iNOS), which is proinflammatory and elevated in psoriasis. Moreover, carbazole inhibits signal transducer and activator of transcription (stat) 3-mediated transcription, which is relevant in the pathogenesis of human psoriasis. In brief, the actions are suppression of DNA synthesis, reduction of mitotic activity in the basal layer and anti-inflammatory activity.[12]

The limitations of the present study are its small sample size, male predominance and multiple topical creams in a single patient. In the future, clinical studies could be designed on a large clinical size, enrolled more female patients and less comparative modalities of treatment. Lastly, the amount of sun exposure was not controlled in the treatment protocol that might affect the results. As sun exposure are known to have an additive effect not only in tar-based regimens.[13, 14]

In conclusion, the present study has shown that 5% LCD cream, 1% hydrocortisone cream and cream base were effective for the treatment of mild plaque-type psoriasis. However, 5% LCD cream was significantly superior to 1% hydrocortisone group and cream base group in view of both ESI score and size reductions. 5% LCD cream had some adverse effects such as malodor, cloth staining and hyperpigmentation but were not statistically significant. All three treatments were generally well tolerated and adverse events included only local irritation. 5% LCD cream should be chosen as standard treatment for mild plaque-type psoriasis in view of its efficacy, few side effects and low cost.

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