A Comparative Study of Tar and Betamethasone Valerate in Chronic Plaque Psoriasis: A Study in Thailand

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Objective: *Evaluate and compare the efficacy, safety, and tolerability of coal tar (10% LCD, liquor carbonis detergens), with betamethasone valerate in the therapy of large plaque-type psoriasis.*
Material and Method: *Patients with stable, mild to moderate plaque psoriasis at the Department of Medicine, Lerdsin General Hospital, Bangkok, Thailand were randomized for treatment with either coal tar (10% LCD) cream or betamethasone valerate cream (0.1%). All patients entered a 2 week wash-out period followed by the creams being applied twice daily until completion at 6 weeks. The patient severity of psoriasis was assessed using the modified Psoriasis Area and Severity Index (PASI) score at baseline and after 2, 4, and 6 weeks of treatment.*
Result: *At the end of the trial, the mean reduction of the PASI score from baseline was 38.39% with the coal tar group and 69.36% with the betamethasone valerate group. The mean percentage of the PASI score reduction was statistically significant in both groups but the betamethasone valerate group was significantly superior to the coal tar group. Both drugs' adverse effects were limited to mild irritation localized to the skin without systemic side effects. The Betamethasone valerate cream was safe, effective, and well-tolerated while the coal tar cream was described as messy, malodorous, and with a tendency to staining clothes.*
Conclusion: *The investigator's overall assessment of the treatment response at completion of the trial demonstrated that the betamethasone valerate group achieved significantly greater clearance and marked improvement compared with the coal tar group.*

Keywords: *Coal tar, Betamethasone valerate, Plaque type psoriasis*

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Psoriasis is one of the most common dermatological diseases, affecting 1.4% to 2.9% of population[1]. It is a common, chronic, genetic, and immune-mediated inflammatory skin disease with no cure. Most patients require lifelong treatment to control the condition[2]. The psoriasis patient's quality of life is seriously affected by the disease[3,4]. The significant impact on quality of life includes physical and mental dysfunction similar to those patients with other chronic illnesses such as arthritis, cancer, and diabetes mellitus[5,6]. The most common form of psoriasis is the plaque-type, characterized by well-demarcated, erythematous, hypertrophic plaques with scaling. The topical treatments for psoriasis have included coal tar, corticosteroids, anthralin, calcipotriol, and tazarotene. Topical corticosteroids are the most common application for treatment of psoriasis, especially plaque-type[7]. However, continuous use often leads to tachyphylaxis as well as local and systemic adverse effects[8-10]. In Thailand, one of the standard treatments for chronic plaque psoriasis is the use of 10% coal tar cream (LCD, liquor carbonis detergens). The studies have shown that calcipotriol ointment was as effective as, or superior to, betamethasone 17-valerate[11,12]. Furthermore, calcipotriol ointment was significantly more effective than 15% coal tar solution[13]. Therefore, coal tar should have a lower influence in eradicating psoriasis than betamethasone valerate. Moreover, the present study reveals that topical coal tar preparations are less effective than other

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topical treatments[14]. Coal tar is messy, malodorous, and has a tendency to stain clothing [15] but it is still used because it is inexpensive.

Since there has not been a study directly comparing the treatment of coal tar and betamethasone 17-valerate, the aims of the present study were to evaluate the effectiveness of coal tar, the standard treatment used in Thailand, and betamethasone valerate in the therapy of plaque psoriasis as well as to compare the effectiveness of coal tar with betamethasone valerate.

Material and Method

A prospective, randomized, clinical trial comparison of 10% LCD cream and 0.1% betamethasone valerate cream was carried out at the Department of Medicine, Lerdsin General Hospital, Bangkok, Thailand from 2001 to 2006.

Selection of study patients

The present study population included adult patients of either sex with a clinical diagnosis of stable, mild to moderate psoriasis, who had had plaque psoriasis on the body for at least 6 months. The anatomical distribution of plaque-type psoriasis included the trunk, upper or lower limbs. Pregnant patients, patients with only scalp psoriasis or drug-induced psoriasis were excluded. Other exclusion criteria were severe psoriasis (more than 50% skin involvement), systemic anti-psoriasis treatment, or ultraviolet irradiation treatment during the previous 8 weeks and ingestion of medications that were known to influence psoriasis.

Study design and treatment regimens

There were two phases to the present study: the wash-out phase and a randomized treatment phase.

Wash out phase

During the 2-week wash-out period, patients used only 10% urea cream applied twice daily.

Randomized treatment phase

After the 2-week wash out period, the patients were randomized to receive treatment with either 10% LCD cream or 0.1% betamethasone valerate cream, applied twice daily for 6 weeks. The lesions treated were distributed on the upper and lower extremities and trunk. No facial or flexural lesions were treated. The patients were assessed at the beginning of the present study and were followed-up every 2 weeks for 6 weeks of treatment. They were evaluated by the same physician on the severity of clinical signs, namely erythema, induration, infiltration, and desquamation using the modified Psoriasis Area and Severity Index (PASI)[16]. Each of the clinical signs was graded 0-4. The patients were assessed on both the extent and the severity of psoriasis and it was compared with previous visits. At the end of the present study, the overall assessment of the treatment response from the beginning of treatment was made by the same physician using a six-point scale, -1 = worse, 0 = no change, 1 = slight improvement, 2 = moderate improvement, 3 = marked improvement, 4 = cleared. Compliance was assessed by weighing the cream.

Statistical analysis

The efficacy of treatment was calculated by comparing the change of the PASI score from baseline values within each patient. The mean PASI score change from start of the present study and the score at 2, 4, and 6 weeks were made by paired t-test. The mean PASI score change between 10% LCD cream and 0.1% betamethasone valerate cream at 2, 4 and 6 weeks was compared by using an independent t test.

A comparison of the physician's overall assessment of response to 10% LCD cream and 0.1% betamethasone valerate cream was performed using the Pearson Chi-Square test. A p-value of less than 0.05 was considered significant.

Results

Fifty-eight patients entered the washout phase of the present study and were randomized to either treatment with 10% LCD cream (28 patients) or 0.1% betamethasone valerate cream (30 patients). The two treatment groups were well matched at baseline with respect to age, sex, and severity of psoriasis as scored by modified PASI (Table1). The compliance of both groups was excellent. Patients who withdrew from the study had been excluded from the data and most of them, treated with coal tar cream, complained of dirty staining of clothes and an unacceptable treatment response.

Efficacy

The mean percentage reduction in PASI from baseline up until the end of the trial was 38.39% with the 10% LCD treatment group and 69.36% with the betamethasone group (Table 2). The change of mean percentage of PASI from the baseline to the end of the 6 weeks was statistically significant in both the 10% LCD treatment group and the betamethasone group ($p < 0.001$). The mean difference between the coal tar

Table 1. Demographic data at baseline

	Coal tar (n = 28)	Betamethasone (n = 30)
Age (year)		
Mean (SD)	40.3 (13.4)	42.4 (12.8)
Range	19-68	16-69
Sex		
Male (%)	60.7	63.3
Female (%)	39.3	36.7
Total sign score (PASI at first visit)		
Mean (SD)	17.1 (2.9)	17.7 (3.8)
Range	10.8-21.6	9.2-21.8

Table 2. PASI score during the 6 weeks of the randomized treatment phase

	Coal tar (n = 28)	Betamethasone (n = 30)	p-value#
Baseline	17.11±2.9	17.74±3.8	>0.48
2 weeks	14.83±3.0	12.95±3.4	
% change from base line	13.56±8.5	27.23±10.6	<0.001
Probability*	<0.001	<0.001	
4 weeks	12.31±3.6	8.68±3.8	
% change from base line	28.18±16.5	51.41±18.2	<0.001
Probability*	<0.001	<0.001	
6 weeks	10.60±4.1	5.52±4.5	
% change from base line	38.39±21.1	69.36±23.3	<0.001
Probability*	<0.001	<0.001	

Data are presented as mean ± 1 SD
* p-value for within-group change
# p-value for between-groups change

treatment group and the betamethasone group in the percentage change in PASI from baseline to the end of 6 weeks was 30.97% which was statistically significant ($p < 0.001$).The mean percentage decrease in PASI in the betamethasone group was also significantly greater than the coal tar group.

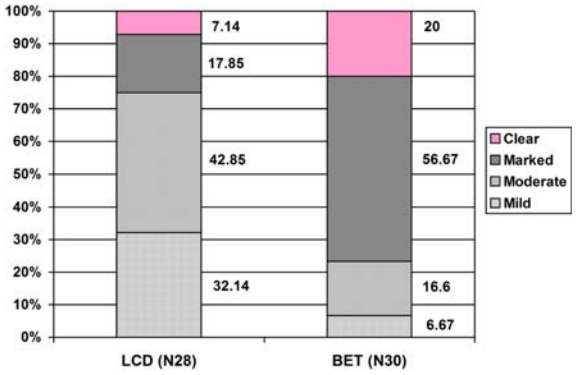
The mean percentage change in PASI from baseline to up until the end of the 4 weeks was 28.18% in the 10% LCD treatment group and 51.41% in the betamethasone group. These mean percentage reductions of PASI were statistically significant in both the coal tar treatment group and the betamethasone group ($p < 0.001$). The mean difference in the percentage change in PASI from baseline up until the end of the 4 weeks between the two treatment groups was 23.23% where the betametasone treated group was statistically significantly superior to the coal tar treated group ($p < 0.001$).

The mean percentage decrease in PASI from baseline to up until the end of the 2 weeks was13.56% in the coal tar treatment group and 27.23% in the betamethasone group. Both treatment groups had a statistically significant reduction in the mean percentage in PASI from the baseline to up the end of the 2 weeks ($p < 0.001$). The mean percentage reduction of PASI was statistically significantly higher in the betamethasone treated group than in the coal tar treated group at the end of the 2 weeks ($p < 0.001$).

Both treatments showed a statistically significant reduction in the PASI score at end of 2, 4 and 6 week of treatment ($p < 0.001$). The rate of decrease was greater during the first 2 weeks up until the end of 4 weeks treatment but slightly declined during next 4 weeks up until the end of 6 weeks. The means reduction in the total sign score from baseline to the end of treatment at 2, 4 and 6 weeks were statistically significantly greater in the betamethasone group than the coal tar group ($p < 0.001$).

The patients in both groups assessed the aesthetic features of both creams. The greasiness of both creams was similar however, the coal tar group complained more about malodorous, dirty staining and irritation of their cream. The adverse events reported during the present study showed only irritation, which was typically a slightly burning or itching sensation with no reaction visible on the skin. These reactions were found more commonly in the coal tar group than the betamethasone group but were not statistically significant. Two patients in the coal tar group had an unsatisfactory treatment response that caused withdrawal from the trial. There was no withdrawal of patients from the trial in the betamethasone group.

The percentage of patients in each category of the investigators' global assessment of disease severity at the end of trial is shown in Fig. 1. The overall assessment of treatment response at the end of 6 weeks showed 24.99% of patients treated with the coal tar cream cleared or achieved marked improvement as compared with 76.67% in the betamethasone group ($p < 0.001$ (Pearson Chi-Square value 15.826 df 3)). The difference between the coal tar cream and betamethasone cream was statistically significant ($p < 0.001$), showing superior efficacy in the betamethasone group.



* The difference between LCD vs BET was significant ($p < 0.001$)

Fig. 1 Investigator's overall assessment of treatment response at the end of treatment

Discussion

The present study confirmed the effectiveness of coal tar in the treatment of mild to moderate psoriasis vulgaris. The patients treated with coal tar slowly improved from baseline until the end of 2, 4, and 6 weeks treatment and the rate of improvement was the same for each period. Moreover, the investigator's overall assessment reported that over 67.8% of patients who applied coal tar could achieve at least moderate improvement by the end of 6 weeks. However, it was statistically significantly less effective than patients treated with the betamethasone valerate cream. Furthermore, it was less tolerated than betamethasone valerate since it was more commonly malodorous, stained clothing, caused local irritation, and showed slow improvement.

In addition, the reduction of psoriasis treated by 10% LCD cream was the same as in a previous study[13] which used 15% coal tar solution, as well as a study by Williams[17] where the treatment was 5% crude coal tar. Moreover, Ellis[18] reported effective reduction in clinical psoriasis by tar. In another study, Lowe[19] showed clinical superiority of 5% crude coal tar in combination with UVB, compared with emollients plus UVB. The study in 1993 by Kanzler and Gorsulowsky[20] demonstrated that a 5% LCD therapy produced a mean PASI score improvement of 48.7% at the end of week 4, which was similar to the present study, and a 10% LCD therapy reduced the mean PASI score by 28.18%. Both studies showed greater statistically significant improvement of psoriasis at the end of 4 weeks.

The results demonstrated that betamethasone valerate cream therapy led to highly significant improvements in mild to moderate psoriasis vulgaris. Moreover, patients receiving betamethasone valerate showed rapid onset of improvement from baseline at the end of 2 weeks and 4 weeks and slow improvement after 4 weeks up until the end of 6 weeks. Furthermore, the investigators' overall assessment showed over 76.6% of patients treated with betamethasone valerate achieved marked improvement and clearance at the end of 6 weeks, which showed the high efficacy of this treatment. In addition, in patients treated by betamethasone valerate, it was well tolerated with only mild local irritation as a side effect.

The results of betamethasone valerate treatment in the present study are in agreement with other researches[11,21] which demonstrated a markedly significant reduction in mean clinical signs of psoriasis at end of 2, 4, and 6 weeks. In another study, Kragballe[12] reported that betamethasone valerate treatment could achieve a reduction of mean PASI score by 61.4% at end of the 6-week study, which was the same results as the present study where betamethasone valerate reduced the mean PASI score by 69.36% at end of trial. Furthermore, the investigators' overall assessment of the treatment response in a study by Molin[22] showed that 56% of patients treated with betamethasone valerate cream cleared or achieved marked improvement which was similar to results of betamethasone valerate therapy in the present study demonstrated where 76.67% achieved clearance or marked improvement. In addition, the comparative flow cytometric study of keratinocytes by Glade[23] reported that reduction of the percentage of basal keratinocytes in S- and G_2M-phase by calcipotriol and by calcipotriol with betamethasone 17-valerate was 24% and 47% respectively at the end of 8 weeks. The flow cytometric study showed calcipotriol with betamethasone 17-valerate was more effective than calcipotriol alone, which demonstrated that betamethasone 17-valerate was statistically significant in the treatment of psoriasis at keratinocytes level as shown with results of betamethasone 17-valerate therapy in this study. It should be noted that this study demonstrated results from short-term treatment with betamethasone valerate and coal tar, however with similar long-term therapy of both drugs may lead to unwanted adverse effects[9,24,25].

In conclusion, the present study has shown that betamethasone valerate (0.1%) and coal tar (10% LCD) were effective for the treatment of mild to moderate psoriasis vulgaris however, betamethasone valerate was significantly superior to coal tar, and had the advantages of being odorless as well as non-staining of

clothes. Both treatments were generally well tolerated and adverse events included only local irritation, found more commonly in the coal tar group, with mild itching or burning sensations without skin signs or systemic events. The results of the present study conclude that betamethasone valerate (0.1%) should be chosen as standard treatment for psoriasis in preference to coal tar (10% LCD) in view of its lower efficacy. However for patients with financial constraints coal tar is better than no therapy at all, as sometimes occurs in Thailand.

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การศึกษาเปรียบเทียบระหว่างทาร์และเบตาเมทาโซนวาเลอเรตในการรักษาโรคสะเก็ดเงินเรื้อรังชนิดแผ่น การศึกษาในประเทศไทย

ประสูตร ถาวรชัยสิทธิ์, กิติพงษ์ หาญเจริญ

การศึกษาประสิทธิภาพ ความปลอดภัยและความทนทานของทาร์ครีม (10% LCD, liquor carbonis detergens) เพื่อเปรียบเทียบกับเบตาเมทาโซนวาเลอเรตครีมในการรักษาโรคสะเก็ดเงินเรื้อรังชนิดแผ่นใหญ่ที่กลุ่มงานอายุรกรรม โรงพยาบาลเลิดสิน กรุงเทพมหานคร ประเทศไทย โดยใช้วิธีการสุ่มผู้ป่วยที่มีโรคสะเก็ดเงินเรื้อรังชนิดแผ่นที่มีเสถียรภาพขนาดน้อยและปานกลางเพื่อรักษาด้วยทาร์ครีม (10% LCD)หรือเบตาเมทาโซนวาเลอเรตครีม (0.1%) โดยให้ผู้ป่วยทุกคนเข้าสู่ภาวะปลอดการรักษา 2 สัปดาห์ และหลังจากนั้นให้การรักษาด้วยครีม วันละ 2 ครั้ง นาน 6 สัปดาห์ การประเมินภาวะความรุนแรงของโรคสะเก็ดเงิน โดยใช้เครื่องชี้วัดการเปลี่ยนแปลงของพื้นที่และความรุนแรงของสะเก็ดเงิน (PASI) ในวันแรกของการรักษา สัปดาห์ที่ 2, 4, และ 6

ผลการศึกษาพบว่า ค่าเฉลี่ยการลดลงของค่า score เครื่องชี้วัดการเปลี่ยนแปลงของพื้นที่และความรุนแรงของสะเก็ดเงินจากวันแรกของการรักษาเท่ากับ 38.39% ของกลุ่มผู้ป่วยที่รักษาด้วยทาร์ครีม และเท่ากับ 69.36% ของกลุ่มผู้ป่วยที่รักษาด้วยเบตาเมทาโซนวาเลอเรตครีม การลดลงของเปอร์เซ็นต์ของค่าเฉลี่ยของค่า score เครื่องชี้วัดการเปลี่ยนแปลงของพื้นที่และความรุนแรงของสะเก็ดเงินมีนัยสำคัญทางสถิติทั้งสองกลุ่ม แต่การลดลงของกลุ่มผู้ป่วยที่รักษาด้วยเบตาเมทาโซนวาเลอเรตครีมมีนัยสำคัญสูงกว่าของกลุ่มผู้ป่วยที่รักษาด้วยทาร์ครีม

สรุปผลการรักษาพบว่ากลุ่มผู้ป่วยที่รักษาด้วยเบตาเมทาโซนวาเลอเรตครีมสามารถหายทั้งหมดและดีขึ้นมาก มีนัยสำคัญมากกว่าของกลุ่มผู้ป่วยที่รักษาด้วยทาร์ครีม ภาวะแทรกซ้อนของยาทั้งสองจำกัดที่การระคายเคืองเล็กน้อยของผิวหนังโดยปราศจากภาวะแทรกซ้อนของระบบอื่นทั้งหมด เบตาเมทาโซนวาเลอเรตครีมมีความปลอดภัย ประสิทธิภาพความทนทานที่ดี และมีประสิทธิภาพดีกว่าทาร์ครีมซึ่งมีความสกปรก กลิ่นเหม็น และมีโอกาสเปื้อนเสื้อผ้า