Tolerability and Cosmetic Acceptability of Liquor Carbonis Distillate (Coal Tar) Solution 15% as Topical Therapy for Plaque Psoriasis

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Although generally recognized as an effective therapy for psoriasis, coal tar therapy lost appeal in modern clinical practice due to poor patient acceptability of its aesthetic properties. A new liquor carbonis distillate (LCD) solution 15% (equivalent to coal tar 2.3%) that uses an evaporative and transparent vehicle, fragrance, and a dab-on applicator was developed. Cosmetic acceptability of the LCD solution was compared to calcipotriene cream 0.005% during a randomized, active-controlled, investigator-blinded clinical trial. Participants with moderate plaque psoriasis applied LCD solution or calcipotriene cream twice daily to body lesions for 12 weeks and then were followed for 6 additional weeks without treatment. Participants completed a cosmetic acceptability survey about their medications after starting therapy. Mean ratings for aesthetic and product performance attributes were high in both groups; however, more participants treated with LCD solution versus calcipotriene cream rated their product as more convenient and beneficial compared to prior psoriasis therapies. Ratings of the scent, staining, drying time, and dab-on applicator for the LCD solution were favorable. Participant experience with LCD solution in this study suggests that it is a cosmetically acceptable psoriasis treatment that is comparable to calcipotriene cream.

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Coal tar is one of the oldest-known effective therapies for psoriasis. It is a by-product of the distillation of coal and is composed of roughly 48% hydrocarbon, 42% carbon, and 10% water.[1] The exact mechanism of action of coal tar is not fully understood, but it may suppress DNA synthesis,[2] angiogenesis,[3] and inflammation[4] in psoriatic skin, and help restore the appearance of healthy skin. In clinical trials coal tar preparations were shown to be effective treatments of plaque psoriasis,[5] slower acting than superpotent topical steroids[6] but as effective as calcipotriene[7,8] and tazarotene[9] formulations. Mainly used in hospital settings, coal tar has become a less appealing antipsoriasis agent in modern clinical practice due to the scent, staining, tedious application regimen, and poor patient acceptance and adherence associated with coal tar.[10] However, an easy-to-use, cosmetically acceptable coal tar formulation could be a relevant and valuable option for treating psoriasis today.

A new coal tar solution formulated with liquor carbonis distillate (LCD) 15% equivalent to coal tar 2.3% in an anhydrous transparent vehicle with added fragrance was developed. This LCD solution is dispensed in a 100 mL bottle with a dab-on applicator that allows patients to apply the medication directly to psoriatic plaques at home. Efficacy, cost-effectiveness, patient tolerability, and cosmetic acceptability

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of LCD solution were compared to calcipotriene cream 0.005%, a well-tolerated and cosmetically appealing prescription topical medication,[11] during a randomized, active-controlled, investigator-blinded clinical trial conducted at the Clinical Unit for Research Trials in Skin, Massachusetts General Hospital, Boston, between December 2006 and November 2008. This report presents participant-reported tolerability and cosmetic acceptability findings from the study. The efficacy results will be discussed elsewhere.[12]

Methods

The study consisted of a 12-week treatment phase and a 6-week posttreatment follow-up phase. The study protocol was approved by Partners Human Research Committee, Boston. Informed consent was obtained from all individuals before any study procedures were performed.

Adults 18 years or older with moderate chronic plaque psoriasis (3%–15% body surface area affected) not receiving other therapies were enrolled and randomized to apply either LCD solution 15% or calcipotriene cream 0.005% to areas affected by psoriasis, excluding the head, twice daily at home for up to 12 weeks. The participants received the medication in masked packaging and were instructed not to apply study medications prior to clinical evaluations to avoid unblinding the investigators who were kept unaware of treatment assignment during the study.

After starting therapy, participants completed a comprehensive cosmetic acceptability survey about their medications at weeks 2, 4, 8, 12 (end of treatment), and 18 (6 weeks after stopping treatment). They evaluated tolerability and aesthetic parameters on a 5-grade scale (9=excellent; 7=very good; 5=good; 3=fair; 1=poor) with 1-point increments. Participants compared parameters "easy to use," "gentle to skin," and "works well" to previously used topical psoriasis treatments using a 5-grade scale (6=much better; 4=somewhat better; 2=slightly better; 0=about the same; −2=worse) with 1-point increments. Participants reported application frequency and selected yes or no to indicate if they would want to continue to use the drug product if the study ended that day. Participants using LCD solution also evaluated the product's scent, staining, drying time, and the functionality of the dab-on applicator during the study.

For various parameters of the cosmetic acceptability survey, mean group scores and the proportions/percentages of participants with each score at each study visit were tabulated. Missing scores were filled by the last observation carried forward method for some items that repeated across visits. Proportions of participants with top box scores were compared between groups using the Fisher exact test when appropriate. All statistical tests were 2-tailed, and $P \leq .05$ was considered significant.

Results

Participants—Sixty individuals with moderate plaque psoriasis entered the study and were randomized to the LCD group or calcipotriene group. Cosmetic acceptability analyses included data from 54 participants (26 from the LCD group and 28 from the calcipotriene group) who received treatment and completed the cosmetic acceptability survey after baseline. (One participant treated in the LCD group was inadvertently given the wrong survey and was excluded.) Forty-three participants (23 from the LCD group and 20 from the calcipotriene group) completed the study and answered additional questions at week 18. The remaining participants discontinued for various reasons.

Cosmetic Acceptability of LCD Solution vs Calcipotriene Cream—Mean scores for tolerability, aesthetics, and overall impression of the medication in both groups (LCD and calcipotriene) corresponded to very good (Figure 1). Participants using LCD solution were approximately 1.5 times more likely than participants using calcipotriene cream to give the top box score of excellent for "compatible with healing skin," "is a desirable product to treat psoriasis," and "overall opinion of product" at the end of treatment at week 12 (Table), though this difference did not reach statistical significance. In both groups, the majority of participants (25/26 in the LCD group and 26/27 in the calcipotriene group) indicated that they applied the study medication twice daily on most days of the week. Participants treated with LCD solution were as likely as calcipotriene-treated participants to consider the study medication easy to use and to want to continue using the product after the study ended (Figure 2). When participants were asked to compare their study treatment to prior topical therapies, significantly more participants in the LCD group versus the calcipotriene group gave the top box score of much better (than prior topical therapies) for attributes "easy to use" ($P=.0043$) and "works well" ($P=.0096$) during treatment, while ratings for "gentle to skin" were comparable between groups (Figure 3).

Cosmetic Acceptability of LCD Solution—Participants rated LCD solution as quick drying (waiting ≤5 minutes before dressing for 73% [19/26] of participants) and considered its dab-on applicator to be very to extremely easy to use (92% [24/26] of participants), durable (96% [25/26] of participants), and able to dispense an appropriate

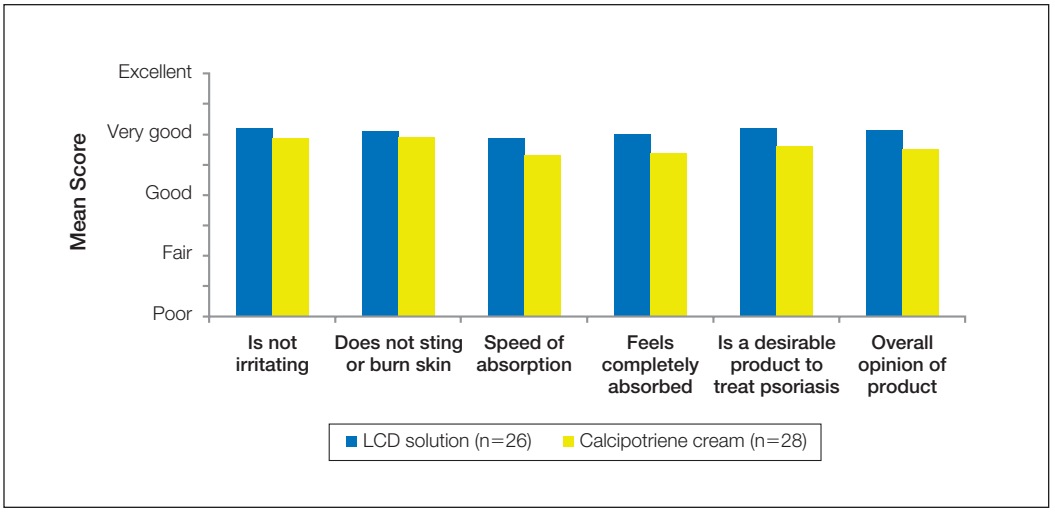

Figure 1. Mean scores for select product attributes of liquor carbonis distillate (LCD) solution 15% and calcipotriene cream 0.005% at the end of treatment (week 12). Participants rated each attribute on a 5-grade scale (9=excellent; 7=very good; 5=good; 3=fair; 1=poor) with 1-point increments.

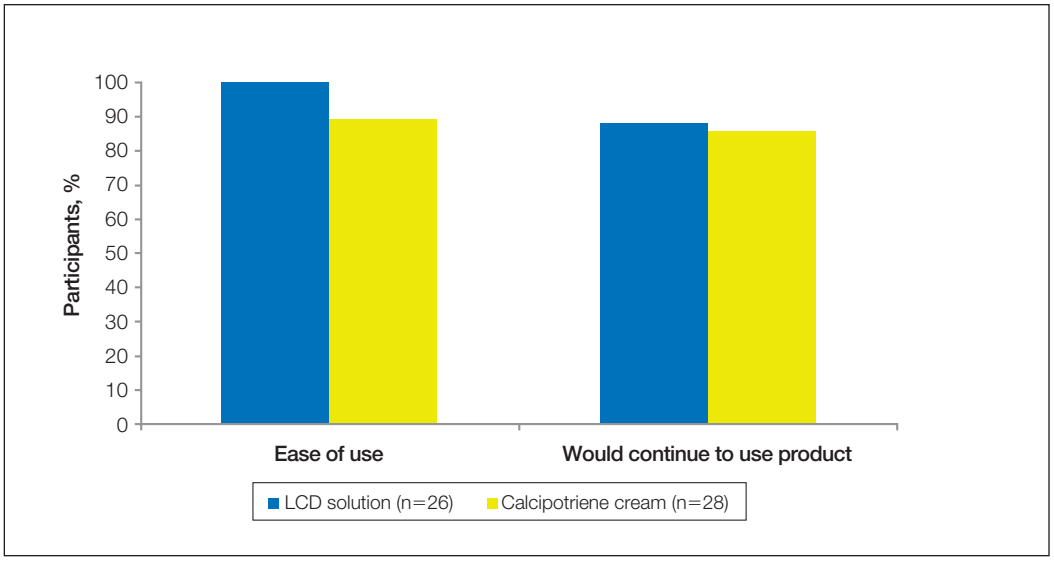

Figure 2. Participants with positive impressions of liquor carbonis distillate (LCD) solution 15% and calcipotriene cream 0.005% at the end of treatment (week 12).

amount of solution (96% [25/26] of participants). Participants were aware that LCD solution had a fragrance, and the majority of participants found the scent profile of LCD solution to be acceptable and not disruptive to the therapeutic regimen (Figure 4). Forty-six percent (12/26) of participants treated with LCD solution noted some mild staining on their clothes, bedsheets, or skin that faded within a week of stopping therapy. No staining was visually apparent during clinical evaluations or in clinical photographs (Figure 5). None of the participants treated with LCD solution stopped treatment because of aesthetic issues and 81% (21/26) reported that the benefits of LCD solution outweighed any negatives.

Comment

A formulation's irritation potential, aesthetics, and ease of application can substantially impact patient adherence to therapy[13] and clinical efficacy of topical antipsoriatic agents.[14,15] Coal tar preparations have proven efficacy in hospital or psoriasis day care–type settings[10] but have not made a successful transition to modern outpatient dermatology practice due to the scent, staining, messiness, and inconvenient application regimen associated with coal tar. In this

Participant Responses for Various Product Attributes at the End of Treatment (Week 12; N=54)[a]

Product Attribute	Treatment Group	Participant Response, n (%)				
		Excellent	Very Good	Good	Fair	Poor
Speed of absorption	LCD	5 (19.2)	13 (50.0)	5 (19.2)	3 (11.5)	0 (0)
	Calcipotriene	4 (14.3)	14 (50.0)	6 (21.4)	2 (7.1)	2 (7.1)
Feels completely absorbed	LCD	6 (23.1)	13 (50.0)	4 (15.4)	3 (11.5)	0 (0)
	Calcipotriene	5 (17.9)	12 (42.9)	7 (25.0)	2 (7.1)	2 (7.1)
Ability to dry quickly	LCD	5 (19.2)	13 (50.0)	3 (11.5)	4 (15.4)	1 (3.8)
	Calcipotriene	5 (17.9)	12 (42.9)	7 (25.0)	2 (7.1)	2 (7.1)
Is not irritating	LCD	11 (42.3)	8 (30.8)	4 (15.4)	3 (11.5)	0 (0)
	Calcipotriene	10 (35.7)	9 (32.1)	5 (17.9)	3 (10.7)	1 (3.6)
Feels comfortable on skin	LCD	9 (34.6)	9 (34.6)	6 (23.1)	2 (7.7)	0 (0)
	Calcipotriene	8 (28.6)	9 (32.1)	8 (28.6)	1 (3.6)	2 (7.1)
Does not sting or burn skin	LCD	12 (46.2)	7 (26.9)	4 (15.4)	1 (3.8)	2 (7.7)
	Calcipotriene	11 (39.3)	8 (28.6)	5 (17.9)	2 (7.1)	2 (7.1)
Compatible with healing skin	LCD	11 (42.3)	8 (30.8)	3 (11.5)	3 (11.5)	1 (3.8)
	Calcipotriene	8 (28.6)	8 (28.6)	8 (28.6)	3 (10.7)	1 (3.6)
Is a desirable product to treat psoriasis	LCD	13 (50.0)	5 (19.2)	5 (19.2)	2 (7.7)	1 (3.8)
	Calcipotriene	9 (32.1)	9 (32.1)	4 (14.3)	3 (10.7)	3 (10.7)
Overall opinion of product	LCD	12 (46.2)	6 (23.1)	4 (15.4)	3 (11.5)	1 (3.8)
	Calcipotriene	8 (28.6)	9 (32.1)	7 (25.0)	0 (0)	4 (14.3)

Abbreviations: LCD, liquor carbonis distillate solution 15%; calcipotriene, calcipotriene cream 0.005%.

[a]Participants who received treatment and completed the cosmetic acceptability survey after baseline: LCD group (n=26) and calcipotriene group (n=28).

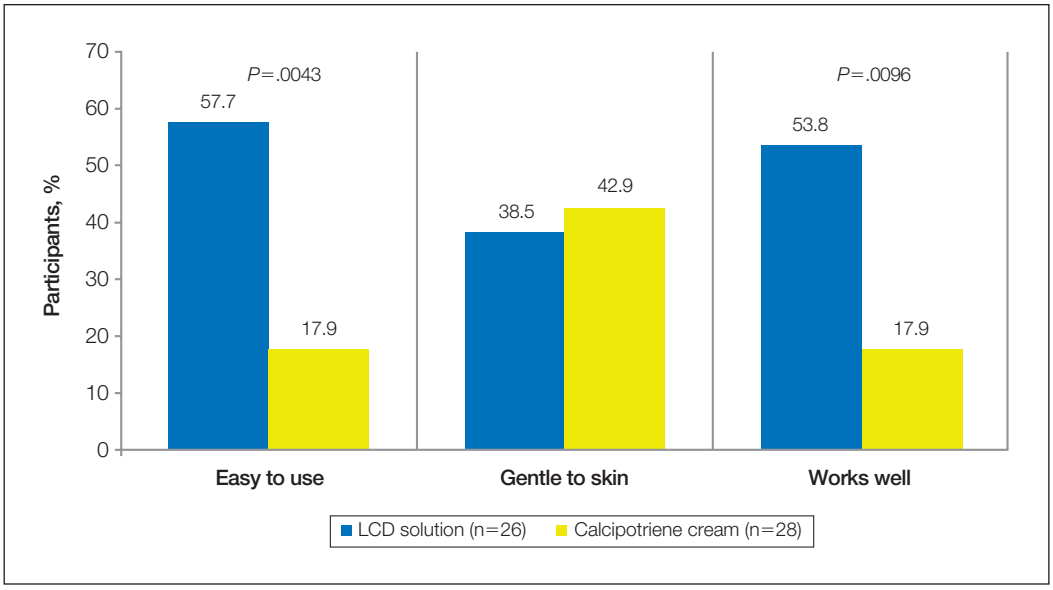

Figure 3. Percentage of participants who rated their study medication (liquor carbonis distillate [LCD] solution 15% or calcipotriene cream 0.005%) as much better than prior topical psoriasis therapies at the end of treatment (week 12). Participants rated each parameter on a 5-grade scale (6=much better; 4=somewhat better; 2=slightly better; 0=about the same; −2=worse) with 1-point increments.

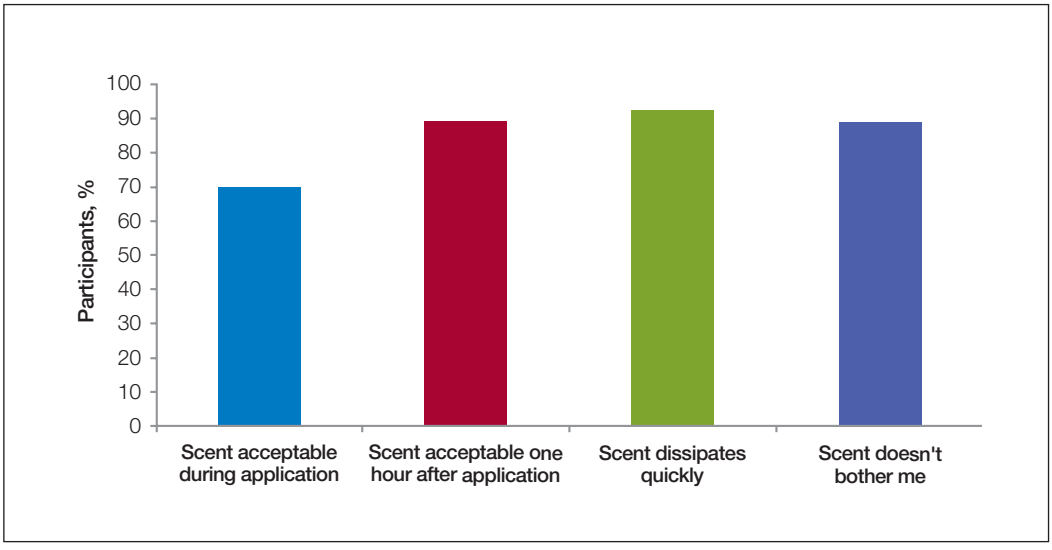

Figure 4. Percentage of participants who rated the scent properties of liquor carbonis distillate (LCD) solution 15% as neutral or positive at the end of treatment (week 12). Responses were collected from 26 participants who used LCD solution.

study men and women with moderate plaque psoriasis used a commercially formulated coal tar solution for 12 weeks. They found that LCD solution was easy to apply to up to 15% of their body surface area, had acceptable aesthetic properties that did not interfere with adherence to therapy, was a desirable product to treat psoriasis, and worked better than previously used topical products. This study demonstrated that coal tar can be formulated as a cosmetically acceptable preparation (LCD solution) that can compete with a white, unscented, cream formulation such as calcipotriene cream and is suitable for twice daily use at home.

A study limitation is the relatively small number of participants with moderate psoriasis studied over 18 weeks. Experience with LCD solution in patients with more severe disease or over a longer period of use was not determined. Additionally, it is not known if participant responses to the cosmetic acceptability survey were influenced by the fact that both products were

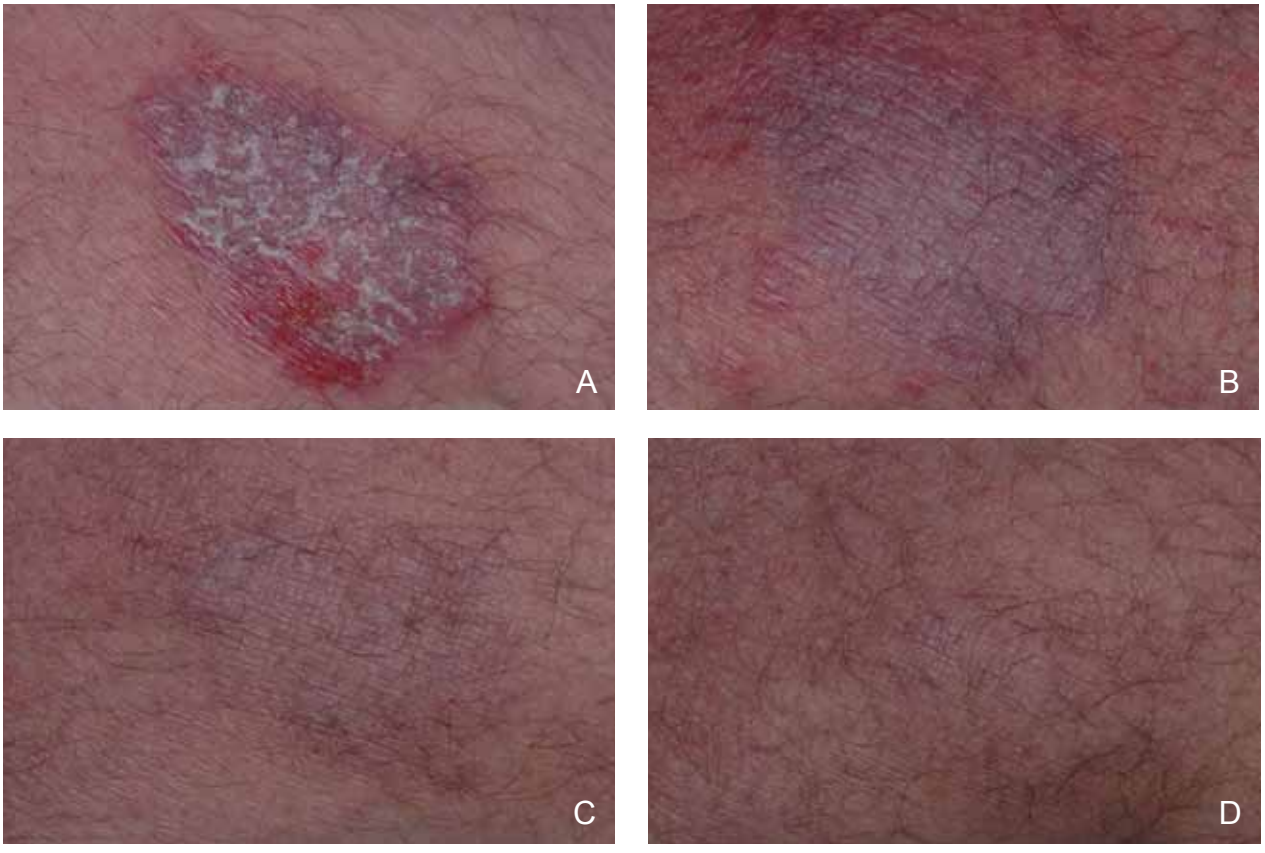

Figure 5. Abdominal lesion at baseline (A), week 4 (B), week 8 (C), and week 12 (D). The participant applied liquor carbonis distillate solution 15% twice daily for 12 weeks. No staining was apparent during clinical evaluations.

available to them at no cost during the study, or how cost considerations may translate into actual preference for and/or willingness to use a particular topical product in clinical practice. Finally, no attempt was made to limit enrollment or otherwise account for participants' prior experiences with psoriasis therapies, particularly tar- or calcipotriene-based formulations, which is a potential source of bias in the participants' opinions of both study products. Excluding patients with prior use of topical therapies would have placed severe restrictions on recruitment, as patients with mild to moderate psoriasis typically are exposed to multiple topical psoriasis therapies[16,17] because of the chronic nature of the disease. The study participants were representative of patients in clinical practice. The study demonstrated that patients who typically use topical agents to treat psoriasis were able to use LCD solution twice daily at home for 12 weeks and accepted the product as a convenient and desirable therapy for psoriasis.

Conclusion

The results from this study indicate that the newly formulated LCD solution 15% is a well-tolerated, convenient, and cosmetically acceptable over-the-counter topical formulation for successfully treating plaque psoriasis in adults and can be a viable treatment alternative to prescribed topical therapies for patients with mild to moderate psoriasis.

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