Journal of Clinical & Experimental Dermatology Research

Lacarrubba et al., J Clin Exp Dermatol Res 2014, 5:6
DOI: 10.4172/2155-9554.1000243

Research Article Open Access

Corticosteroid Cream Once Daily plus an Emollient Cream in comparison with Corticosteroid Cream Twice Daily in Plaque Psoriasis: An Intra-Patient, Randomized Assessor-Blinded, Ultrasound Evaluation Study

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Abstract

Background: Emollients and keratolytics creams with corticosteroids have been demonstrated to be useful in plaque psoriasis (PP), improving clinical response with a steroid-sparing effect. However, so far, no trials with objective measurement evaluations are available. Aim of this intra-patient randomized, assessor-blinded, 4-week study was to evaluate, by means of ultrasound imaging, the efficacy of the combination of hydrocortisone valerate 0.1% cream (HVC) once daily with an emollient, keratolytic, keratoplastic and anti-inflammatory cream (EKC) containing urea 20%, salicylic acid 2% and niacinamide (2%) once-daily vs. HVC alone applied twice-daily in PP.

Methods: Fifteen patients with mild-to-moderate PP were enrolled. For each patient two symmetrical, target lesions were selected and randomized to receive HVC+EKC or HVC alone for 4 weeks. Primary efficacy parameter was the reduction of skin thickness by ultrasound evaluation using a 22 MHz B-mode high-resolution system. Secondary endpoint was the assessment of Target Lesion Score (TLS) evaluating erythema, scaling, infiltration and itching with a 5-point scale (0=none, 1=mild, 2=moderate, 3=severe, 4=very severe).

Results: Twelve patients were randomised and concluded the trial. Combination therapy with HVC+EKC was as effective as corticosteroid twice-daily with a similar reduction of psoriatic skin thickness at week 4 in comparison with baseline (combination therapy: from 2.59 ± 0.4 mm at baseline to 2.19 ± 0.4 mm at week 4; mono-therapy from 2.56 ± 0.4 mm to 2.14 ± 0.37 mm). TLS reductions observed at the end of the study were similar in the two treatment regimens. Combination therapy (HVC+EKC) was as effective as mono-therapy (HVC) twice daily with a similar reduction, objectively evaluated, of skin thickness at week 4 in comparisons with baseline. The efficacy results were paralleled by the reduction of TLS.

Conclusion: Our results confirm that the concomitant use of emollients with topical corticosteroids is efficacious in plaque psoriasis, with a steroid-sparing effect.

Keywords: Plaque psoriasis; Emollients; Skin B-mode ultrasound evaluation

Introduction

Chronic plaque psoriasis is the most common type of psoriasis [1]. The aim of plaque psoriasis treatments should be the decrease or inducing remission of inflammation, scaling, itching, burning, and sky dryness [2]. Topical therapies are usually tried as first line treatments [3]. Evidence based data show that initial management of chronic plaque psoriasis is made mainly with topical corticosteroids, applied most commonly twice daily [4,5]. However there are several adverse effects of corticosteroids including cutaneous atrophy, rebound after discontinuation of treatment and decreasing response to the drug (tachyphylaxis) [6-8]. For these reasons steroid-sparing therapeutic strategies could be important in the treatment approach of chronic plaque psoriasis [9]. In this regards emollient, keratolytic and moisturizer agents can act as an important adjunctive therapy of topical treatments in psoriatic patients [10]. Salicylic acid and high concentration of urea could be used in the initial keratolytic phase, whereas moisturizing products and emollients are especially suitable in the intermediate phase and the chronic/remission phase of psoriasis [11,12]. Concomitant use of keratolytics and emollients with topical corticosteroids has been demonstrated to be efficacious in plaque psoriasis, improving clinical response with a steroid-sparing effect [13]. However, so far, no trials with objective measurement evaluations, i.e. ultrasound assessment of plaque thickness reduction, of the use of keratolytic/emollient treatment with a topical corticosteroid are available.

Methods

Study aim

We evaluated using a pilot intra-patient (left vs. right site) randomized, assessor-blinded, 4-week study design, the efficacy of the combination of hydrocortisone valerate 0.1% cream (HVC) once daily with an emollient, keratolytic, keratoplastic and anti-inflammatory cream (EKC) containing urea 20%, salicylic acid 2% and niacinamide 2% (Iralfaris cream, ISDIN, Spain) once daily vs. HVC alone, applied twice daily, for the treatment of plaque psoriasis by means of ultrasound imaging.

Study design

The present study was a mono-centre prospective, intra-patient,

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Received September 04, 2014; **Accepted** October 08, 2014; **Published** October 16, 2014

Citation: Lacarrubba F, Musumeci ML, Milani M, Micali G (2014) Corticosteroid Cream Once Daily plus an Emollient Cream in comparison with Corticosteroid Cream Twice Daily in Plaque Psoriasis: An Intra-Patient, Randomized Assessor-Blinded, Ultrasound Evaluation Study. J Clin Exp Dermatol Res 5: 243. doi:10.4172/2155-9554.1000243

randomised (left vs. right), assessor-blinded trial. Randomisation list with a 1:1 ratio and with a block of 4 was generated by the mean of statistical software (G-Power, Los Angeles, US). Study was performed between March 2013 and September 2013.

Subjects

Patients were enrolled in the trial after their written informed consent according to the Declaration of Helsinki [14]. Study protocol was approved by IRB University of Catania. Fifteen patients (12 M, 3 F, age range: 30-76 years) with mild-to-moderate plaque psoriasis were enrolled. For each patient two symmetrical, target lesions were selected and randomized to receive either HVC+EKC, both applied once daily, (HVC applied in the morning and EKC applied in the afternoon, both applied without occlusion) or HVC alone twice daily (one application in the morning and one application in the afternoon, applied without occlusion) for 4 consecutive weeks. Mean daily amount of HVC for application was 3 grams for the twice daily schedule and 1.5 gram of HVC and 1.5 grams for EKC. Exclusion criteria were: age <18 years, no symmetrical psoriatic lesions, localized palmo-plantar psoriasis, pregnancy, lactation, renal or liver diseases. Patients receiving in the previous six months systemic therapy for psoriasis, such as acitretin or methotrexate or biological compounds, were excluded, as were those who had received any form of topical therapy within the preceding 4 weeks. Additionally, enrolment excluded patients with guttate, erythrodermic or pustular psoriasis.

Study outcomes

The primary efficacy parameter was the reduction of skin thickness by ultrasound evaluation, which was made using a 22 MHz B-mode high-resolution system (EasyScan Echo®, Business Enterprise, Trapani, Italy). A secondary endpoint was the clinical evaluation of a Target Lesion Score (TLS) including degree of erythema, scaling, infiltration and itching with a 5-point scale (0=none, 1=mild, 2=moderate, 3=severe, 4=very severe). Both assessments were performed by an investigator unaware of treatment allocation of the patients (operator-blinded fashion).

Statistical analysis

Statistical analyses were done using SPSS (Statistical Package for Social Science) statistical software (version 13.0). Data were expressed as mean (SD). All P values were two-sided. According to the pilot nature of the present trial, a formal sample size calculation was not performed. However we fixed, in an arbitrary manner, in at least 12 evaluable subjects a reasonable sample size for an intra-patient evaluation. Two-tailed Mann–Whitney (unpaired) and Wilcoxon (paired) tests were applied to compare treatments and to compare baseline levels with values at the end of study period. Analysis was based on the intention-to-treat principle and involved all randomised patients. A P-value ≤ 0.05 was considered statistically significant. Data are presented as mean ± SD.

Results and Discussion

A total of fifteen patients were enrolled in the study. Twelve subjects were randomised and concluded the trial. Three subjects (2 men and 1 woman) not satisfying inclusion criteria were not randomised in the trial. Trial initiated March 2013 with First Patient First visit and was concluded, last patient last visit, September 2013. Patients' baseline characteristics are summarized in Table 1. Combination therapy with HVC+EKC was as effective as corticosteroid twice daily treatment with a similar reduction of psoriatic skin thickness at week 4 in comparison with baseline (Figure 1) (combination therapy: from 2.59 ± 0.4 mm at baseline to 2.19 ± 0.4 mm at week 4 (a 16% reduction), p=0.005; mono-therapy: from 2.56 ± 0.4 mm to 2.14 ± 0.37 mm, (a 16% reduction), p=0.005). No statistically significant differences were observed between the two treatment regimens at the end of the study period (Figure 2). The efficacy results were paralleled by the TLS decrease observed at the end of the study (from 8.8 ± 2.1 to 5.4 ± 2.3 (representing a 39% reduction) in the combination therapy treated sites and from 8.8 ± 2.1 to 5.5 ± 2.2 (representing a 38% reduction) in the mono-therapy treated sites) with no differences between the two treatment regimens (Figure 3). Trial medications were well tolerated. No serious adverse events were observed during the trial. Glucocorticosteroids remain a cornerstone treatment of chronic plaque psoriasis due to their potent anti-inflammatory and antiproliferative effects [15]. However, the same mechanisms of action responsible for the improvement of dermatologic inflammatory conditions can cause adverse effects [16]. Therefore steroid-sparing therapeutic strategies could be important in the treatment of chronic plaque psoriasis. Emollients or moisturizers might act as an effective adjunctive therapy of topical treatments in psoriatic patients. Use of emollient or keratolytic agents in combination with corticosteroid has been shown to be efficacious in the treatment of plaque psoriasis. In particular, emollients are generally used in a supportive role as an addition to topical treatments, to normalise hyperproliferation, differentiation, and to exert antiinflammatory effects [17]. In addition, keratolytic and some moisturizing agents (e.g. urea) could enhance penetration of topically applied antipsoriatic drugs, representing an additional therapeutic rationale for this combination [18]. Watsky et al. [19] in an open study in 96 psoriatic patients have

	Total number of randomised patients (n=15)
Gender	
Men	10
Women	2
Age (years): mean ± SD	53 ± 14
Duration of psoriasis (years): mean ± SD	18 ± 4
Target lesion clinical score	8.8 ± 2
Target lesion thickness (mm): mean ± SD	2.58 ± 0.4

Table 1: Patients characteristics at baseline.

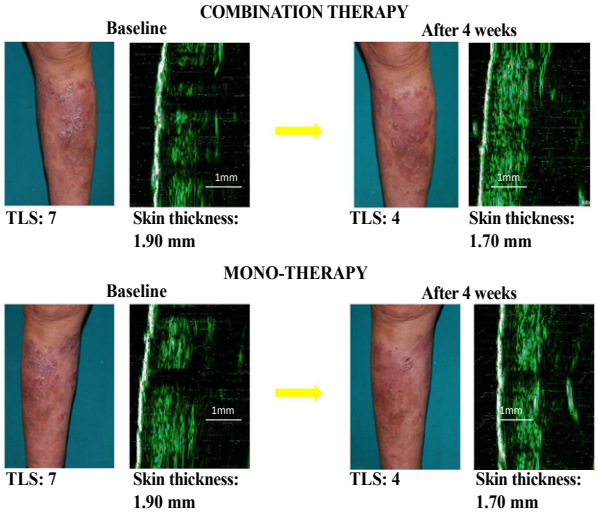
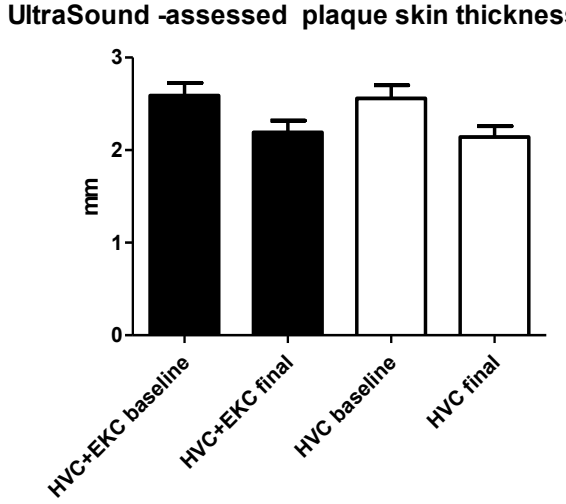


Figure 1: Clinical and ultrasound evolution of a target lesion: a study case.



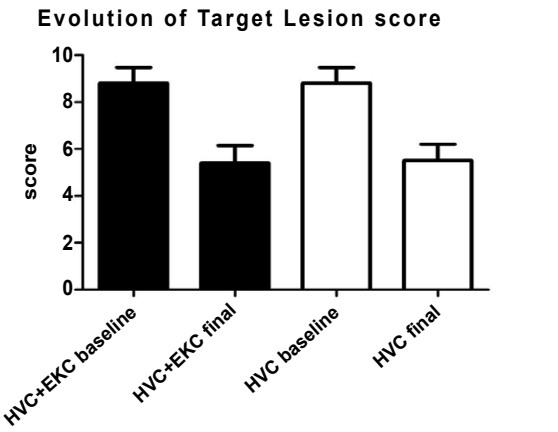
HVC= hydrocortisone valerate 0.1% cream

EKC= emollient, keratolytic, keratoplastic and anti-inflammatory cream

p=0.005 vs baseline for HVC and HVC+EKC

p=Not Significant within groups at baseline and at final visit

Figure 2: Evolution of target plaque thickness evaluated by ultrasound.



HVC=hydrocortisone valerate 0.1% cream

EKC=emollient, keratolytic, keratoplastic and anti-inflammatory cream

Target Lesion Score includes degree of erythema, scaling, infiltration and itching with a 5-point scale (0=none, 1=mild, 2=moderate, 3=severe, 4=very severe).

p=0.005 vs baseline for HVC and HVC+EKC

p=Not Significant within groups at baseline and final visit

Figure 3: Evolution of clinical Target Lesions Score.

shown that once daily application of both a topical corticosteroid (betamethasone dipropionate) and either a water-in-oil based cream or lotion was significantly better than once daily application of betamethasone dipropionate cream alone. The conclusion of these authors was that water-in-oil emollients could be useful in the therapy of chronic, plaque-type psoriasis providing also a steroid-sparing effect. In 2009 Seite et al. [20] demonstrated that the use of an emollient can limit relapses after the end of corticosteroid therapy, and maintain the improvement obtained after 1 month corticosteroid therapy at clinical level evaluated through a physician global assessment. However, these trials did not use objective measurement evaluations, i.e. ultrasound assessment of plaque thickness reduction, in assessing the efficacy of this combination therapeutic strategy. High-frequency ultrasound (>20 MHz) is a non-invasive imaging technique that has been used both for diagnosis and therapeutic monitoring in psoriasis as well as in other dermatological conditions [21-24]. In our study we evaluated the clinical efficacy of combination therapy (topical corticosteroid once daily plus an emollient/keratolytic anti-inflammatory cream) in comparison with a twice daily corticosteroid application by means of ultrasound assessment of target psoriatic plaque lesions. The emollient/keratolytic and anti-inflammatory cream evaluated in this study contains urea (20%), salicylic acid (2%) and nicotinamide (2%). Salicylic acid is widely used as a keratolytic agent in the treatment of hyperkeratotic skin conditions, especially psoriasis and it is considered one of the most effective keratolytic compounds [25,26]. Urea is a well-known moisturizing agent. Urea is also known to exert a proteolytic, keratolytic, hydrating, hygroscopic, and antipruritic effect [27]. In addition urea could exert a penetration-enhancement effect when combined with other active compounds, like corticosteroids [28]. Topical niacinamide shows a potent antioxidant and anti-inflammatory effect on the skin [29]. Furthermore, niacinamide could improve skin barrier functions [30]. Therefore this combination has a strong rationale as adjunctive treatment in plaque psoriasis therapy [31]. The results of this pilot study show that combination of corticosteroid and emollient/keratolytic and anti-inflammatory cream, both applied once daily, has similar effects on the plaque thickness reduction as corticosteroid application twice daily, confirming, in an objective manner, the additional beneficial effect and the steroid-sparing action of this approach. Some limitation of the present study should be taken in account in evaluating the results we obtained. This is pilot trial and therefore the results should be confirmed by a larger sample size trial. However the primary outcome was the ultrasound evolution of target plaque psoriasis which should be considered a sensible and objective tool. We decided to perform an intra-patient trial design improving the power of study size. Finally, outcomes of the study have been evaluated in an assessor-blinded fashion, increasing the internal validity of the results. Another limiting aspect of our trial was treatment duration (4 weeks) not allowing us to evaluate and compare safety and tolerability data of the two regimens used. However the primary outcome of the trial was efficacy and 4 week period is in general the appropriate duration in order to evaluate therapeutic efficacy of a topical regimen in plaque psoriasis.

Conclusion

Combination therapy (HVC+EKC) was as effective as mono-therapy (HVC) twice daily with a similar reduction, objectively evaluated, of skin thickness at week 4 in comparisons with baseline. The efficacy results were paralleled by the clinical evaluation of Target Lesion Score. Our results confirm that the concomitant use of a keratolytic, emollients and anti-inflammatory cream with topical corticosteroid is efficacious in plaque psoriasis, with a steroid-sparing effect.

Funding Source

The present project was partially funded by a grant from ISDIN. The sponsor had no role in the study design and conduct, and was not involved in the collection, analysis, and interpretation of data. Massimo Milani is an employee of ISDIN.

References

1. Levine D, Gottlieb A (2009) Evaluation and management of psoriasis: an internist's guide. Med Clin North Am 93: 1291-1303.
2. Menter A, Gottlieb A, Feldman SR, Van Voorhees AS, Leonardi CL, et al. (2008) Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol 58: 826-850.
3. Nast A, Boehncke WH, Mrowietz U, Ockenfels HM, Philipp S, et al. (2011) S3-guidelines for the treatment of psoriasis vulgaris Update 2011. J Dtsch Dermatol Ges 9 Suppl 2: S1-104.
4. Mason AR, Mason J, Cork M, Dooley G, Edwards G (2009) Topical treatments for chronic plaque psoriasis. Cochrane Database Syst Rev 15: CD005028.
5. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, et al. (2009) Guidelines of care for the management of psoriasis and psoriatic arthritis Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol 60: 643-659.
6. Lee JY, Maibach HI (1998) Corticosteroid skin atrophogenicity: assessment methods. Skin Res Technol 4: 161-166.
7. Kao JS, Fluhr JW, Man MQ, Fowler AJ, Hachem JP, et al. (2003) Short-term glucocorticoid treatment compromises both permeability barrier homeostasis and stratum corneum integrity: inhibition of epidermal lipid synthesis accounts for functional abnormalities. J Invest Dermatol 120: 456-464.
8. du Vivier A, Stoughton RB (1975) Tachyphylaxis to the action of topically applied corticosteroids. Arch Dermatol 111: 581-583.
9. Ghali FE (2005) Improved clinical outcomes with moisturization in dermatologic disease. Cutis 76: 13-18.
10. Fluhr JW, Cavallotti C, Berardesca E (2008) Emollients, moisturizers, and keratolytic agents in psoriasis. Clin Dermatol 26: 380-386.
11. Witman PM (2001) Topical therapies for localized psoriasis. Mayo Clin Proc 76: 943-949.
12. Bikowski J (2001) The use of therapeutic moisturizers in various dermatologic disorders. Cutis 68: 3-11.
13. Finlay AY (1997) Emollients as adjuvant therapy for psoriasis. J Dermatolog Treat 8: 25-27.
14. World Medical Association Inc (2009) Declaration of Helsinki. Ethical principles for medical research involving human subjects. J Indian Med Assoc 107: 403-405.
15. Robertson DB, Maibach HI (1982) Topical corticosteroids. Int J Dermatol 21: 59-67.
16. Hill CJ, Rostenberg A Jr (1978) Adverse effects from topical steroids. Cutis 21: 624-628.
17. Schöpf E, Mueller JM, Ostermann T (1995) Value of adjuvant basic therapy in chronic recurrent skin diseases. Neurodermatitis atopica/psoriasis vulgaris. Hautarzt 46: 451-454.
18. Wohlrab W (1984) The influence of urea on the penetration kinetics of topically applied corticosteroids. Acta Derm Venereol 64: 233-238.
19. Watsky KL, Freije L, Leneveu MC, Wenck HA, Leffell DJ (1992) Water-in-oil emollients as steroid-sparing adjunctive therapy in the treatment of psoriasis. Cutis 50: 383-386.
20. Seité S, Khemis A, Rougier A, Ortonne JP (2009) Emollient for maintenance therapy after topical corticotherapy in mild psoriasis. Exp Dermatol 18: 1076-1078.
21. Lacarrubba F, Nardone B, Musumeci ML, Micali G (2009) Ultrasound evaluation of clobetasol propionate 0.05% foam application in psoriatic and healthy skin: a pilot study. Dermatol Ther 22 Suppl 1: S19-21.
22. Musumeci ML, Lacarrubba F, Fusto CM, Micali G (2013) Combined clinical, capillaroscopic and ultrasound evaluation during treatment of plaque psoriasis with oral cyclosporine. Int J Immunopathol Pharmacol 26: 1027-1033.
23. Lacarrubba F, Tedeschi A, Nardone B, Micali G (2008) Mesotherapy for skin rejuvenation: assessment of the subepidermal low-echogenic band by ultrasound evaluation with cross-sectional B-mode scanning. Dermatol Ther 21 Suppl 3: S1-5.
24. Lacarrubba F, Verzì AE, Tedeschi A, Catalfo P, Nasca MR, et al. (2013) Clinical and ultrasonographic correlation of acne scars. Dermatol Surg 39: 1683-1688.
25. Lebwohl M (1999) The role of salicylic acid in the treatment of psoriasis. Int J Dermatol 38: 16-24.
26. Loden M (1996) Urea-containing moisturizers influence barrier properties of normal skin. Arch Dermatol Res 288: 103-107.
27. Muller KH, Pflugshaupt C (1989) Urea in dermatology I. Hautarzt 40: 1-12.
28. Feldmann RJ, Maibach HI (1974) Percutaneous penetration of hydrocortisone with urea. Arch Dermatol 109: 58-59.
29. Gehring W (2004) Nicotinic acid/niacinamide and the skin. J Cosmet Dermatol 3: 88-93.
30. Mohammed D, Crowther JM, Matts PJ, Hadgraft J, Lane ME (2013) Influence of niacinamide containing formulations on the molecular and biophysical properties of the stratum corneum. Int J Pharm 441: 192-201.
31. Luger T, Seite S, Humbert P, Krutmann J, Triller R, et al. (2014) Recommendations for adjunctive basic skin care in patients with psoriasis. Eur J Dermatol 24: 194-200.