

Real-Life Effectiveness of Topical Vitamin D and Corticosteroid Combination Therapy in Psoriasis

Moving Beyond Clinical Trials

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ABSTRACT

To provide successful care for psoriasis patients, treatments must be efficacious and safe as well as improve the patients' overall well-being. Efficacy and safety are generally established by randomized, controlled clinical trials. However, because of the rigid conditions under which randomized, controlled clinical trials are conducted, they do not reflect patient experience in real-life clinical practice; that is, they do not measure treatment effectiveness in the real world. Factors such as adherence to therapy, treatment satisfaction, and quality of life may be rated unrealistically high in randomized, controlled clinical trials. Observational studies using real-life patient populations, and capturing patient-reported outcomes, are useful at better assessing a treatment's effectiveness. Healthcare professionals and payers may gain valuable insights from patient-reported outcomes data that can be used in making treatment decisions. For localized plaque psoriasis, topical vitamin D analog and corticosteroid combination therapy is recommended as a first-line treatment. This commentary addresses the concept of clinical trial efficacy versus real-life effectiveness in psoriasis treatment using vitamin D and corticosteroid topical combination therapy as a model. (*J Clin Aesthet Dermatol.* 2015;8(2):48–50.)

The chronic and irritative nature of psoriasis is associated with physical and psychological stresses.

In some cases, the stress related to having psoriasis itself serves as a trigger or exacerbating factor for the disease.¹ Patient feedback on psoriasis-related symptom assessments and health-related quality of life (QoL) provides the dermatologist with information needed to ensure treatment success.

Topical therapy is considered first-line therapy for the majority of patients with mild-to-moderate plaque psoriasis.² Combination therapy using a vitamin D analog and a corticosteroid is among the preferred treatment options.² Topical calcipotriene and betamethasone dipropionate (CBD) in a fixed-combination formulation has been shown in randomized, controlled clinical trials (RCTs) to be both efficacious and safe in the treatment of patients with plaque psoriasis.^{3,4} The limitation of these efficacy studies and all RCTs, however, is that the

treatment intervention is not evaluated under real-life conditions.⁵ RCT efficacy studies do not consider patient, provider, or system-level factors that may confound the treatment effect.⁵ While patient-reported outcomes (PROs), such as treatment satisfaction and QoL, are often considered secondary efficacy end points in clinical trials, these real-life outcomes are often of primary concern to patients. Study data that include PROs may help to establish the effectiveness of the therapy in actual use. This approach is well suited to a condition such as psoriasis.

This commentary explores the role of PROs in psoriasis using a vitamin D and corticosteroid fixed-combination topical treatment as a model. Dermatologists may find information from PROs useful, as they provide insights to consider in formulating plans that can lead to a more satisfactory and successful treatment experience for their patients.¹

DISCLOSURE: Dr. Zeichner has served as an advisor for LEO Pharma Inc.

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EFFICACY VERSUS EFFECTIVENESS IN PSORIASIS

The methodology used in RCTs is designed to reduce factors that can bias results while generating credible conclusions about the efficacy of a treatment studied under ideal and controlled circumstances. In clinical trials for psoriasis, the Psoriasis Area and Severity Index (PASI) and the Investigator's Global Assessment (IGA) scores are two commonly used primary efficacy end points. Results from one RCT showed that CBD topical combination therapy provided a significantly larger reduction in PASI (73.2%) following four weeks of twice-daily treatment than calcipotriene (48.8%), betamethasone dipropionate (63.1%), or vehicle alone (28.8%) (all $P < 0.001$).⁴ In another RCT, controlled disease (the achievement of "clear" or "almost clear" skin according to the IGA scale and a minimum 2-point change from baseline) was reached in a statistically significant greater proportion of subjects in the CBD group than in the other treatment groups at Week 8 (combination [29.0%], betamethasone dipropionate [21.5%; $P = 0.008$], calcipotriene [14.6%; $P = 0.002$], vehicle [6.3%; $P < 0.001$]).³

Despite the merits of RCTs in determining efficacy, they do not give the full picture of treatment effectiveness. Effectiveness can also be defined as the performance of a treatment intervention under pragmatic or real-life conditions.⁵ Under the conditions of a RCT, adherence rates, for example, may be unrealistically high. As evidence-based medicine and pay-for-performance continue to be emphasized in modern clinical practice, effectiveness data have assumed more importance. Both healthcare professionals and payers are increasingly interested in study data that include PRO findings, which will aid in making treatment decisions. PROs represent the patient's evaluation of the issue being studied, free from intermediary interpretation by a clinician or other healthcare professional.⁶ PRO data are important in psoriasis, since the patient's acceptance of and adherence to topical therapy is a significant component of treatment effectiveness.

Interventional studies can be designed to include PRO measures and thereby provide data on clinical effectiveness. The United States Food and Drug Administration (FDA) recognizes the value of incorporating PROs in clinical trials to help establish the real-life effectiveness of a treatment and in support of labeling claims.⁶ PROs can be used as primary or secondary end points. Although the FDA guidance does not address dermatology-specific issues, it recommends using a validated PRO instrument to assess concepts that are best measured from the patient's perspective.

Studies using PROs are conducted under conditions more closely resembling real-life clinical practice with less-standardized treatment protocols, a more heterogeneous patient population, and individualized patient therapy.⁵ Clinical trials with CBD fixed-combination topical therapy have reported data related to treatment effectiveness. Results from two clinical trials showed better treatment effectiveness⁷ and a higher level

of treatment satisfaction⁸ with the CBD fixed-combination topical suspension compared with individual agents alone.^{7,8} A trial that evaluated Dermatology Life Quality Index scores in an exploratory, *post hoc* analysis, reported improvements of 5.8 and 6.4 points at Week 4 and Week 8, respectively, for the CBD topical suspension.³

REAL-LIFE EFFECTIVENESS DATA MODEL

Lambert et al⁹ recently conducted an observational study, the PRO-long study (Patient Reported Outcomes in a long-term study), to evaluate the clinical effectiveness of CBD combination topical treatment for psoriasis.⁹ The study compared patients' perspectives on two formulations, a suspension and an ointment, in a prospective, 52-week study of real-life effectiveness. Data from the 12-week interim analysis have been published.

The primary end point was the difference in clinical effectiveness between the two formulations. Effectiveness was assessed by measuring the proportion of patients with controlled disease, defined as "mild" or "very mild" by the Patient's Global Assessment of disease severity. Effectiveness was also evaluated using patient responses to questionnaires on adherence behavior, treatment satisfaction, and QoL.

At Week 12, a similar proportion of patients in each group (71.9% suspension vs. 65.7% ointment, numbers were not significantly different) reported controlled disease. Thus, as one might expect, overall differences were not seen in the effectiveness domain of the nine-item Treatment Satisfaction Questionnaire for Medication (TSQM-9) among the two treatment groups; the only item in this domain where there was a significant difference was application time, where the suspension scored significantly higher than the ointment ($P = 0.013$). However, a significant difference was seen in the overall score of the convenience domain, with the suspension group scoring significantly higher than the ointment group ($P = 0.014$). More patients using the suspension responded positively to questions about ease of treatment use ($P = 0.050$) and ease of treatment planning ($P = 0.014$) than did patients using the ointment. Collectively, these data show that patients considered the suspension formulation faster, easier to use, and more convenient than the ointment formulation. These findings are consistent with previously reported PRO data from CBD fixed-combination topical suspension clinical trials and suggest that treatment with CBD topical suspension is efficacious and well tolerated and improves QoL in patients with psoriasis vulgaris.^{3,4}

CONCLUSION

PRO data are an important component in assessing the patient's perspective on topical psoriasis therapy. While RCTs can determine the effectiveness and safety profile of a drug, PRO data provide important information about patient acceptance and adherence. PRO data from a 12-week observational study showed that a CBD topical suspension improved QoL in patients with psoriasis vulgaris. These data highlight the importance to

dermatologists of using data on patient preferences, such as reported in effectiveness studies, in conjunction with efficacy and safety data in making treatment decisions for their patients with psoriasis.

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