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**Is The Addition Of A Topical Agent To Narrowband UVB  
Treatment More Effective In Treating Male And Female  
Adults With Psoriasis Than Narrowband Treatment Alone?**

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies  
Philadelphia College of Osteopathic Medicine  
Philadelphia, Pennsylvania

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## ABSTRACT

**Objective:** The objective of this selective EBM review is to determine whether or not the addition of a topical agent to narrowband UVB treatment is more effective in treating adults with psoriasis than narrowband UVB treatment alone.

**Study Design:** Review of three English language primary randomized trials that were published between 2003 and 2012.

**Data Sources:** A randomized left-right comparison, placebo controlled clinical trial, a randomized trial, and a randomized placebo controlled, blinded clinical trial each comparing the addition of a topical agent to narrowband UVB treatment to narrowband UVB treatment alone were found using PubMed and Cochrane databases.

**Outcomes Measured:** The outcomes were measured by a single investigator in each trial by analyzing the improvement of the lesions based on the induration size, redness, and scaliness using Psoriasis Area and Severity Index (PASI) and Psoriasis Severity Index (PSI) scores.

**Results:** The results of these trials indicate that the addition of a topical agent to narrowband UVB can be effective in treating psoriasis. The Ehsani et al study concluded that while the use of 8MOP resulted in a greater score decrease, the decrease between groups was not significant. The Woo et al study concluded that while the difference in PASI scores between the groups was not significant, the active group using calcipotriol for psoriasis received less UVB. The Ozkan et al study concluded that the group treated with calcipotriol had statistically significant improvement compared to UVB monotherapy.

**Conclusions:** The results indicate that the addition of a topical agent to UVB therapy for adults with psoriasis is just as effective as NBUVB alone. While the use of 8MOP didn't produce statistically significant results, the trials that used calcipotriol had favorable outcomes. The Woo et al study concluded that calcipotriol may produce UVB enhancing effects resulting in less cumulative UVB exposure. The Ozkan study concluded that the addition of calcipotriol to UVB phototherapy is more effective and efficient in treating the lesions. Further study is warranted to evaluate the use of calcipotriol and NBUVB phototherapy for the treatment of psoriasis.

**Key Words:** psoriasis; narrowband UVB; phototherapy; topical psoriasis; ultraviolet B; plaque psoriasis

## INTRODUCTION

Psoriasis is a relatively common, chronic inflammatory dermatologic condition characterized by well demarcated, erythematous plaques with silver scales that can be caused by injury of the skin, infections, heightened stress levels or even medications.<sup>1</sup> The exact etiology of psoriasis is unknown but it is theorized to have a genetic component and thought to be due to over-activation of T-cells and inflammatory cytokines because of the positive response to treatment regimens. Although there are multiple types of psoriasis, plaque psoriasis makes up about 80% of all cases and is commonly characterized by red plaques with scales that typically occur on the patient's scalp, knees, elbows, and back. Although the disease is often asymptomatic, mild to severe itching may occur, as well as burning, skin pain, or Auspitz sign, which is tiny pin point bleeding when a scale is removed.<sup>2</sup> Despite the lack of symptoms, psoriasis can lead to disfiguring disability and decreased quality of life. Therefore, the decision to start treatment is often based on the social and psychological impact it has on the patient.

Psoriasis is a common dermatologic and the most common autoimmune problem in the United States. It affects over 125 million people worldwide and 7.5 million of those cases are in the United States.<sup>3</sup> With that many people affected by the disease, it is no surprise that around 11.25 billion dollars are spent annually on health care costs related to psoriasis. This estimate also includes the cost of days of work patients had to miss due to their disease. It is also estimated that there are 3 million visits to dermatologists each year for psoriasis.<sup>2</sup> This topic is important for all practitioners to be educated about because it is such a common problem and it can have such a negative impact on patients' lives, not only physically but also financially and emotionally.

There is currently no cure for psoriasis, so treatment is aimed at the reduction in the size and appearance of the lesions based on the extent of the disease. Even patients with mild disease are very self-conscious of these red, scaly lesions. Patients with mild disease are advised to keep their skin moisturized with creams and for flares they can use topical corticosteroid creams, such as triamcinolone 0.1%, over the affected area. These steroid creams have side effects and can eventually be less effective, therefore a vitamin D analog, such as calcipotriene ointment 0.005% or calcitriol ointment 0.003% is often added to the treatment. For patients that have lesions on their scalp, it is possible to get the corticosteroids in solution form or they can also use an over the counter tar shampoo.<sup>4</sup> In patients with more generalized disease, the use of phototherapy, both UVB and UVA, has been proven to be effective in controlling the lesions, but comes with risks of its own, including melanoma. There are also various systemic agents that can be used to treat severe cases of psoriasis including methotrexate, cyclosporine, and retinoids such as acitretin. Another option for treatment includes TNF inhibitors such as etanercept, infliximab, and adalimumab.<sup>2,4</sup>

All of the agents mentioned above can be used to control the symptoms of the psoriasis, however it is important to consider the possible adverse reactions and side effects the medications will have and whether or not the benefits of treatment outweigh the risks. While phototherapy has been proven to be effective in the treatment of psoriasis, it is costly, prolonged and is likely to have issues with compliance in addition to its physical side effects. Therefore, this paper investigates the use of an adjunctive topical therapy to enhance the efficacy of narrowband UVB treatments.

**OBJECTIVE**

The objective of this selective EBM review is to determine whether or not the addition of a topical agent to narrowband UVB treatment is more effective in treating adults with psoriasis than narrowband UVB treatment alone.

**METHODS**

In order to be considered satisfactory, the population studied had to be patients over the age of 18 who had been clinically diagnosed with chronic psoriasis. The study had to be a randomized trial that used narrowband UVB phototherapy monotherapy compared to narrowband UVB therapy with the addition of a topical agent. The control group in each study was a group who only received narrowband UVB monotherapy, with or without the addition of a placebo. The topical interventions studied included 0.1% 8-methoxypsoralen (8MOP) cream<sup>5</sup>, 0.1% psoralen gel<sup>6</sup>, .005% calcipotriol ointment<sup>6</sup>, and 50 µg g<sup>-1</sup> calcipotriol cream<sup>7</sup>. The outcomes were based on the overall improvement of the psoriasis lesions based on redness, induration size, and scaliness of the lesions all of which affect the patients' quality of life. The studies used included one randomized left-right comparison, placebo controlled clinical trial, one randomized trial, and one randomized placebo controlled, blinded clinical trial.

In order to find appropriate articles, the keywords that were used included: psoriasis; narrowband UVB; phototherapy; topical psoriasis; ultraviolet B; plaque psoriasis. Only articles written in English were considered and they had to be published in peer-reviewed journals. The author used the previously mentioned keywords to search the PubMed and Cochrane databases that addressed the

questions and had patient centered outcomes based on the appearance of the lesions. In order to be considered, the articles had to be randomized trials that used narrowband UVB treatment and were published after the year 1996 in order to ensure up to date information. Reasons an article would be rejected included consenting patients under the age of 18, broadband UVB phototherapy, or UVA phototherapy.

**Table 1: Demographics and Characteristics of Included Studies**

Study	Type	# pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Ehsani, 2011 (5)	RCT	10	25-65	Pts >18 y/o with stable plaque type psoriasis (<20% BSA); no systemic tx for 8 wks & no topical tx for 4 wks	Pts who were pregnant, lactating, have a hypersensitivity to 8MOP, and photosensitive disorders	0	0.1% 8MOP cream 15 min before NBUVB treatment VS. placebo cream 15 min before NBUVB treatment
Ozkan, 2012 (6)	Rando- mized trial	30	>18	Pts >18 y/o with stable, localized, chronic, plaque-type psoriasis, pts had no systemic tx for 12 wks and no topical tx for 2 weeks prior	Pts who were pregnant, lactating, have photosensitive disorders or hypersensitivity to 8MOP or calcipotriol	0	NBUVB therapy alone VS. NBUVB plus psoralen gel VS. NBUVB plus calcipotriol ointment
Woo, 2003 (7)	RCT	50	>18	Pts >18 y/o with a clinical diagnosis of psoriasis and informed consent, pts had no phototherapy or systemic antipsoriatic treatment for 2 months prior	Pts who had contraindications to phototherapy, hypercalcemia, hypersensitivity to calcipotriol, cetomacrogol, cetostearyl alcohol, or paraffin,	14	Twice daily Calcipotriol cream 50 µg g <sup>-1</sup> plus NBUVB cream VS. twice daily topical emollient as a placebo plus NBUVB



## **OUTCOMES MEASURED**

The outcomes were measured by a single investigator in each trial by analyzing the improvement of the lesions based on the induration size, redness, and scaliness using Psoriasis Area and Severity Index (PASI), Psoriasis and modified PASI scores, known as Psoriasis Severity Index (PSI) scores. Each study used a single trained investigator to measure the lesions. The measurements for all three studies were primarily made using the Psoriasis Area and Severity Index, which divides the body into four regions, and then assigns a score to each region based on the area and severity affected. The scores range from 0 = no disease, to 72 = maximal disease.<sup>8</sup>

## **RESULTS**

These three studies compared the addition of various topical agents to narrowband UVB phototherapy for adults with chronic psoriasis to evaluate if the combination therapy is more effective than UVB monotherapy. The first study was a randomized left-right comparison, placebo controlled clinical trial investigating the use of 8MOP with UVB.<sup>5</sup> The second was a randomized trial investigating the use of psoralen gel with UVB as well as the use of calcipotriol ointment with UVB.<sup>6</sup> The third was a randomized placebo controlled, blinded clinical trial investigating the use of calcipotriol cream with UVB.<sup>7</sup>

In the study by Ehsani et al, patients used were those who had symmetric lesions on their shins that would be useful in a left-right comparison study. The active arm of the study received 0.1% 8MOP cream while the control arm received a cold cream as a placebo. The researchers observed a significant improvement in

Psoriasis Severity Index score from baseline in both the control arm and the active arm (p-value <0.001), however the difference between the two treatment arms was not significant at p-value 0.069 (Table 2). It was noted, however that the side treated with 8MOP did have a greater decrease in mean percentage PSI score that occurred earlier than the control side. No patients in this study exhibited complete clearance of lesions. The investigator inspected for side effects of therapy each week, but the only side effect noted was pigmentation changes. Due to this visual side effect, the investigator could no longer be blind for the duration of the study. <sup>5</sup>

**Table 2: Statistical Significance of Interventions vs. UVB Monotherapy**

	UVB alone vs. 8MOP + UVB <sup>1</sup>	UVB alone vs. Psoralen + UVB <sup>2</sup>	Calcipotriol + UVB vs. UVB alone & Psoralen +UVB <sup>2</sup>	UVB alone vs. Calcipotriol + UVB <sup>3</sup>
P-value	0.069	> 0.05	< 0.05	0.3

*\*Statistical significance was considered to be a p-value <0.05*

The study by Ozkan et al had patients in the active groups apply their respective psoralen gel or calcipotriol ointment twice per day where the control group only received the UVB therapy. The study showed that all three groups had statistically significant improvement with p-value < 0.05, however only the comparison of Calcipotriol ointment + UVB treatment with the other two groups had a significant difference. Table 3 depicts the improvement in Mean PASI score from baseline compared to the end of the treatment at 10 weeks. In group 1, 40% of patients had more than 50% clearance of lesions. Group 2 had 10% of patients with more than 50% clearance of lesions. Group 3 had 100% of its patients with more than 50% clearance of lesions. With respect to the Calcipotriol ointment + UVB therapy, the Relative Benefit Increase (RBI) was calculated to be 1.5% and the

Absolute Benefit Increase (ABI) was calculated to be 0.6%. Numbers Needed to Treat (NNT) was calculated to be 2, indicating that for every two patients treated with the calcipotriol ointment + UVB phototherapy, one more patient would see more than 50% clearance of lesions.

**Table 3: Clinical Improvement of Mean PASI Scores from baseline to 10 weeks**

	Group 1 UVB monotherapy	Group 2 Psoralen + UVB	Group 3 Calcipotriol + UVB
Mean PASI score at Baseline	2.72 +/- 1.41	3.25 +/- 0.39	3.66 +/- 0.59
Mean PASI score at 10 weeks	1.80 +/- 0.88	2.28 +/- 0.42	1.20 +/- 0.42

The third study by Woo et al showed a significant decrease in PASI score for both the control and the active arm (p-value < 0.01). The mean PASI scores reduction was significantly lower in the group being treated with calcipotriol cream when measured at the eighth session (95% CI, 1.0-6.2, p-value = 0.008). The mean score reduction was not significant when measured at the fourteenth session (95% CI, -2.2-5.6, p-value = 0.4) or the final twentieth session (95% CI, -5.9-1.9, p-value = 0.3). This study also took into account the amount of UVB treatments. The active group received a mean of 18.7 treatments, compared to the control group's mean of 20.4, however this was not statistically significant. They reported that although the groups did not achieve significantly different results at the end, "we have identified a UVB-sparing effect and hence a possible reduction in the risk of skin carcinogenesis".<sup>7</sup>

## DISCUSSION

The goal of these studies was to determine if the addition of a topical agent to phototherapy for psoriasis enhanced the treatment's efficacy. The use of narrowband UVB is widely accepted as part of treatment of psoriasis, however it is not necessarily convenient or without side effects of its own. In order for the phototherapy to be effective, it is recommended that the patient gets three treatments per week, which usually has improvement of the lesions in around seven weeks, however they might need to continue in order to maintain the clearance.<sup>4</sup> This type of regimen might be difficult to adhere to for patients and therefore decreases the compliance and efficacy of the treatment. Some patients even run into issues convincing their insurance companies that it is a necessary part of therapy.

The study by Woo et al. demonstrated that although the addition of the calcipotriol agent did not necessarily produce statistically significant outcome differences, it did reduce the number of UVB treatments required for the active arm to achieve the same results as the control group.<sup>7</sup> The study by Ozkan et al came to a similar conclusion as they observed moderate improvement in the calcipotriol group compared to the psoralen and control groups who all had mild improvement. The study concluded that the combination of calcipotriol ointment with phototherapy and if used instead of monotherapy, that the total number of treatment sessions could be reduced. This is an important consideration because it would likely reduce the side effects of the phototherapy experienced by some patients, such as erythema, pruritis, and burning.<sup>6</sup> A noteworthy factor about this study is that the calcipotriol group showed the most significant improvements

despite starting out with the highest PASI scores as a result of the randomization process.<sup>6</sup>

Two of the three studies reported erythema and pruritis as an adverse effect of the phototherapy. This undesirable effect could potentially be due to the amount of UVB exposure the patients underwent during therapy, therefore it is important to determine if less exposure would produce less side effects. Another very important adverse effect that needs to be considered with UVB therapy is the possibility of long term exposure leading to skin cancer.<sup>1</sup> Contraindications for the use of phototherapy as treatment for psoriasis include a diagnosis of skin cancer, pregnancy, and photosensitizing medications that might put a patient at increased risk for adverse effects.

All of the studies dealt with relatively small sample sizes of 10, 30, and 50. Of the 50 patients in the third study, 14 withdrew leaving them with only 36 patients finishing the trial. The study was analyzed using an intention-to-treat, but the study would still be more reliable if it covered a larger population.<sup>7</sup> Another possible limitation within these studies was the side effect observed in the Ehsani et al study. The investigator was intended to be blind as to which group was the control and which was the active until the active group treated with the 8MOP exhibited pigmentation changes.<sup>5</sup> These studies were also limited by the lack of consistency with the treatments being compared. They each compare different topical agents, dosages, vehicles, and UVB exposures.

## CONCLUSION

The results of the three studies analyzed appear to be inconclusive and somewhat conflicting. The active arm in each study produced improvement of the lesions compared to the control arms, however only the study done by Ozkan et al was able to show statistically significant results by comparing the calcipotriol group with the control arm and the psoralen arm.<sup>6</sup> This study, as well as the Woo et al study, was able to show a potential UVB enhancing effect which is significant in that it could reduce the number of UVB treatments needed to achieve the desirable outcome.<sup>7</sup> Although this was not the primary goal of the study, it is worthy of further investigation because fewer treatment sessions would help with the compliance issues of the UVB phototherapy schedule.

One suggestion for future studies of the use of calcipotriol topical agents would be to aim to find the optimal vehicle and dosage to be used in combination therapy. For example, the Ozkan et al study using calcipotriol ointment achieved superior results to the control and the psoralen groups, whereas the Woo et al study using calcipotriol cream was only able to demonstrate that the active arm needed less UVB treatments to achieve the same results.<sup>7</sup> Further investigation of the calcipotriol ointment would benefit from a larger study than 30 patients. The research should also consist of a lengthy follow-up period during which the researchers can determine not only the effectiveness of the clearance of lesions, but also for how long the therapy induces remission.

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