IJMAMR 5 (2017) 1-6 ISSN 2053-1834

International Journal of Modern and Alternative Medicine Research
www.bluepenjournals.org/ijmamr

Comparison of the efficacy of PUVA versus BBUVB in the treatment of psoriasis vulgaris

Tran Hau Khang* and Le Huu Doanh

National Hospital of Dermatology and Venereology, Hanoi, Vietnam.

Article History
Received 05 August, 2017
Received in revised form 04 September, 2017
Accepted 08 September, 2017

Keywords:
Psoriasis vulgaris, Phototherapy, Photochemotherapy, Skin clearance, Relapse.

Article Type:
Full Length Research Article

ABSTRACT

Psoriasis vulgaris is estimated to be about 85% of all types of psoriasis presented at Vietnam National Hospital of Dermatology and Venereology (NHDV). Psoriasis is still not completely curable, although a wide variety of treatment modalities are available. This study was aimed at comparing the therapeutic effects of psoralen plus ultraviolet A (PUVA) and broadband ultraviolet B (BBUVB) in the treatment of psoriasis vulgaris. Sixty psoriasis vulgaris patients who presented at NHDV were randomly divided into PUVA-treated group (34 patients) and BBUVB-treated group (26 patients). The dose of UV was based on the skin type. Psoriasis area and severity index (PASI) score was measured at the beginning and after every two weeks in both groups. The patients were followed up for 1 year after skin clearance to monitor the relapse. Median time reaching PASI75 (75% reduction of PASI) were 28 days and 35 days for BBUVB and PUVA, respectively (p=0.0216). There was no significantly different skin clearance (PASI100) rate in BBUVB- and PUVA-treated groups (p=0.317). However, BBUVB treatment involved higher adverse effects with erythema, burning, moderated hyperpigmentation and itchiness. PUVA-treated patients had significantly longer remission (p=0.0053), with the median weeks to relapse being 31.5 weeks versus 12 weeks among patients treated with BBUVB. BBUVB is more effective than PUVA in a short duration reaching PASI75 and PASI100 with higher photo side effects. However, PUVA treatment prolongs the regression of psoriasis. Therefore, the combination of BBUVB and PUVA will be an effective phototherapy for skin clearance and prevent the recurrence.

INTRODUCTION

Psoriasis is a skin disease that involved 2.91% of total out-patients in Vietnam Hospital of Dermatology and Venereology (NHDV). The disease may present in several different forms, but the most common (85% of psoriasis cases in NHDV) is chronic plaque psoriasis. In histology, plaques of psoriasis show abnormal proliferation and differentiation of epidermal keratinocytes.

Current opinion considers that psoriasis is T cell-mediated skin chronic disease (Chamian and Krueger, 2004). Psoriasis is still not completely curable, although a wide variety of treatment modalities, both topical in the form of salicylic acid, corticosteroids, tar, dithranol and ultraviolet B (UVB), and systemic agents like photo-therapy, photochemotherapy, retinoids, methotrexate and cyclosporine are available for its control (Farber and Nall, 1984; Fredriksson and Pettersson, 1978). The goal of treatment is to clear each episode of psoriasis and prevent a recurrence for as long as possible (Luba and Stullberg, 2006). Phototherapy, photochemotherapy and systemic immunosuppressive agents are good therapeu-tic options for chronic plaque psoriasis resistant to topical emollients and keratolytics (Greaves and Weinstein, 1995).

The present study was designed to compare the

*Corresponding author. E-mail: khangquocduc@fpt.vn.

Table 1. Pre-treatment evaluation of Psoralen plus ultraviolet A- and broadband ultraviolet B-treated groups.

	Psoralen plus ultraviolet A			Broadband ultraviolet B			*p*
	N	Mean	SEM	N	Mean	SEM	
Psoriasis area and severity index (PASI) score	17	10.98	0.81	13	9.15	0.52	0.09
Age	17	39.71	2.98	13	45.85	4.53	0.25
Duration of psoriasis (months)	17	82.12	14.12	13	103.77	20.46	0.38

effectiveness and safety of broadband ultraviolet B (BBUVB) and oral psoralen plus ultraviolet A (PUVA) in the treatment of chronic plaque psoriasis.

EXPERIMENTAL SUBJECTS AND METHODS

Patients

Seventy-two eligible patients (men and women) aged 18 years and above with moderate to severe chronic plaque psoriasis affecting ≥10% body surface area were randomly selected from all the patients who presented with psoriasis cases in NHDV. The study exclusion criteria included a history of phototoxic reactions, liver or kidney failure, HIV positive, history of skin cancer or other cancers, and erythrodermic, pustular, or guttate psoriasis. The washout period for prior to psoriasis therapies was 2 weeks for topical medications and 4 weeks for photo-therapy and systemic therapies. Concomitant psoriasis therapies were not allowed. The study was approved by the NHDV and written informed consent was obtained from all patients.

The patients diagnosed with stable plaque type psoriasis were enrolled and randomly divided into PUVA-treated group and BBUVB- treated group. After excluding the patients lost to follow-up, 60 patients were analyzed (PUVA: 34 patients and BBUVB: 26 patients).

Ultraviolet therapy

Psoralen plus ultraviolet A-treatment group

Oral dose of 8-methoxypsoralen was 0.5 to 0.6 mg/kg body weight two hours before ultraviolet A (UVA) exposure (HOUVA, Beachwood, OH). The UVA treatment was initiated at 2 J/cm^2 with subsequent increase of 1.0 J/cm^2. PUVA treatment was carried out 3 times per week. The patients were advised to wear UVA protective glasses when exposed to ultraviolet light (natural or artificial) for the next 24 h.

Broadband ultraviolet B-treatment group

Parafine oil was applied on the skin lesion before exposure to BBUVB (HOUVA, Beachwood, OH). The BBUVB treatment was initiated at 40 mJ/cm^2 with subsequent increase of 20 mJ/cm^2. BBUVB treatment was done 5 times per week. The patients were advised to wear UVB protective glasses when exposed to ultraviolet light.

The patients were assessed weekly for any adverse effects of phototherapy. Liver and renal function tests were performed before treatment and repeated monthly. Ophthalmological examination was carried out before commencement and at the end of treatment. Psoriasis area and severity index (PASI) score was measured at the beginning and after every 2 weeks in both treatment groups. When PASI had reduced by 75% (PASI75), the last UV dose was delayed until the patients reached skin clearance (PASI100), then the phototherapy was stopped. The patients were followed up for 1 year after skin clearance to monitor the relapse of skin lesion.

Statistical analyses

Patients who enrolled in the study but withdrew before starting treatment were excluded from statistical analysis, whereas all those who commenced therapy were included regardless of withdrawal for any reason thereafter. Comparisons between the 2 treatment groups were made by means of the χ^2 test for nominal data and the Mann-Whitney test for ordinal data. For those who achieved PASI75, PASI100, relapse, Kaplan-Meier survival analysis using the log-rank test was used to compare remission in the 2 treatment groups. Analysis was performed using statistical software (SPSS version 13; SPSS Inc, Chicago, Ill). All tests of significance were 2-sided, and statistical significance was assumed at $p<0.05$.

RESULTS

Seventy-two patients were enrolled in the study and randomly divided into two groups of UV therapy (PUVA: 36 patients and BBUVB: 36 patients). Twelve patients withdrew before UV treatment and lost after follow-up. Sixty patients were included in pre-treatment evaluation of UV therapy (Table 1). All of the patient skin types were

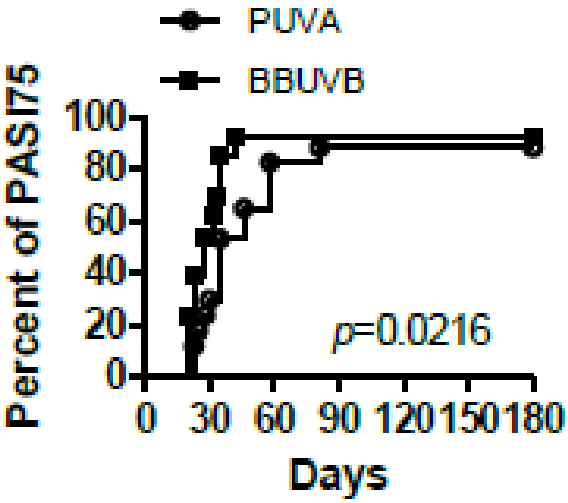

Figure 1. The percentage of patients reaching PASI75. With 5 UV-exposures per week for BBUVB and 3 UV-exposure per week for PUVA, BBUVB-treated patients had earlier reached PASI75 than PUVA groups (median reaching PASI75 were 28 days and 35 days for BBUVB and PUVA, respectively, and p=0.0216).

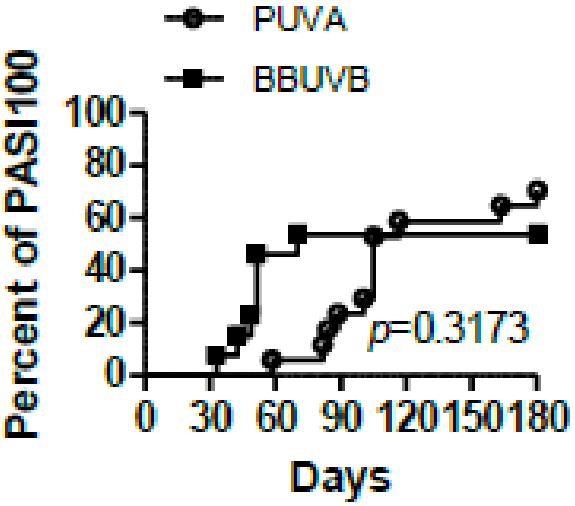

Figure 2. The percentage of patients reaching PASI100. 24/34 patients cleared (64.7% PASI100) on PUVA therapy and 14/26 patients cleared (53.8% PASI100) on BBUVB therapy after 6-month assessment (p=0.317).

type III and IV (Data are not shown). The two groups were well matched for baseline PASI score, age and duration of psoriasis. No patients in both groups had ever been previously treated with phototherapy or photo-chemotherapy.

These patients began UV therapy using skin type-based initial and subsequently increased doses. With five UV-exposures per week for BBUVB and three UV-exposures per week for PUVA, BBUVB-treated patients reached PASI75 earlier than PUVA-treated group (median time for reaching PASI75 were 28 and 35 days for BBUVB and PUVA, respectively; p=0.0216) (Figure 1). There were four patients in PUVA-treated group and 2 patients in BBUVB-treated group who could not reach PASI75.

When the patients had attained PASI75, the last UV dose was delayed until the patients reach skin clearance (PASI100), thereafter the phototherapy was stopped. When three-month assessment was analyzed, BBUVB treatment significantly increased its rate (PASI100) (7/26=26.9% for BBUVB and 4/34=8.8% for PUVA, p=0.0194). However, 22 out of 34 patients had their skin lesions cleared (PASI100 was 64.7%) on PUVA therapy and 14 out of 26 patients had their skin lesions cleared (PASI100 was 53.8%) on BBUVB therapy after 6-month assessment. There was no significant difference in PASI100 rate in BBUVB- and PUVA-treated groups, p=0.317 (Figure 2).

During the treatment period, the cumulative UV dose when the patient obtained PASI75 (cumulative UV dose at PASI75) was calculated, and when the patient attained PASI100 (cumulative UV dose at PASI100) in PUVA- and BBUVB-treated groups (Table 2). The cumulative UV doses were higher in the PUVA-treated group than that in the BBUVB-treated group (p<0.0001).

In patients treated with BBUVA, they had a higher incidence of the development of erythema (100%), burning (31%), moderated hyperpigmentation (100%), itchiness (100%) and eye vision effect (7%), but lower incidence of the development of seborrheic reaction (0%) when compared with the PUVA-treated patients (Figure 3). Percentages of the adverse effects in the BBUVB-treated group were higher when compared to the PUVA-treated group. The hyperpigmentation markedly appeared on the previous lesion skin in PUVA-treated patients. Whereas, it appeared more severe on the non-previous lesion skin in BBUVB-treated patients (Figures 4 and 5).

Twelve of thirty-four patients for PUVA-treated group and seven of twenty-six patients for BBUVB-treated group whose psoriasis cleared were followed up until relapse or for a maximum of 12 months. Kaplan-Meier survival analysis also showed that PUVA-treated patients had significantly longer remissions (p=0.0053), with the median time to relapse being 31.5 weeks versus 12 weeks among patients treated with BBUVB (Figure 6).

DISCUSSION

In the present study, improvement in the clinical scores of patients treated with PUVA therapy was achieved, but the results were better in the BBUVA-treated sides where the

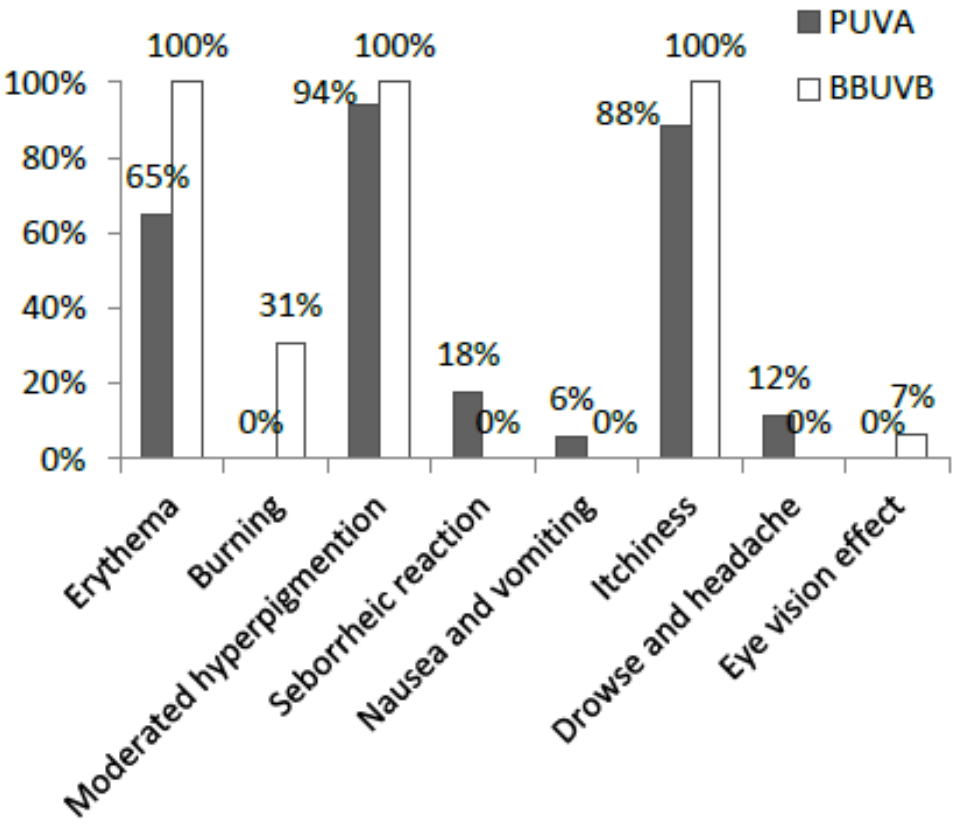

Figure 3. Adverse effects of UV therapy. BBUVB induced higher incidences of the development of erythema (100%), burning (31%), moderated hyperpigmented (100%), itching (100%), and eye vision effect (7%), but lower incidence of the development of seborrheic reation (0%) when compared with the PUVA-treated patients.

Table 2. Cumulative UV dose at time point of PASI75 and PASI100.

	PUVA			BBUVB			*p*
	N	Mean	SEM	N	Mean	SEM	
Cumulative UV dose at PASI75 (J/cm^2)	15	183.87	32.82	12	2.36	0.35	<0.0001
Cumulative UV dose at PASI100 (J/cm^2)	12	284.83	36.36	7	3.64	0.28	<0.0001

PASI was reduced by 75% (PASI75). With five exposures per week, BBUVB reached PASI75 earlier when compared with PUVA. The difference is significant statistically (p=0.0216). Other observations of this study were that BBUVB could clear slightly better when compared with PUVA within three months period. This difference is, however, not significant statistically (p=0.317) within six months period. Kabat-Zinn et al. (1998) achieved median day of treatment to clearance with UVB treatment within 84 to 98 days and with PUVA, it was within 45 to 95 days. Our results obtained showed that the median day with BBUVB was 70 days, and was longer for median day with PUVA treatment.

The results of this study could be compared to previous studies with Narrowband UVB (NBUVB) that were randomized in comparison studies on the treatment of chronic plaque psoriasis (Gorden et al., 1999; Markham et al., 2003; Tahir and Mujtaba, 2004). Gordon et al. (1999) repoeted median day of treatments to clearance with PUVA in 35 to 45 days, and with NB-UVB in 30 to 35 days. According to Tahir 's report, the PASI100 rates were 84 to 85% with PUVA and 60 to 65% with NBUVB. PUVA seems to be more efficacious than NBUVB in the treatment of chronic plaque psoriasis in previous studies.

However, this study demonstrated that BBUVB significantly reduced and cleared the skin lesions.

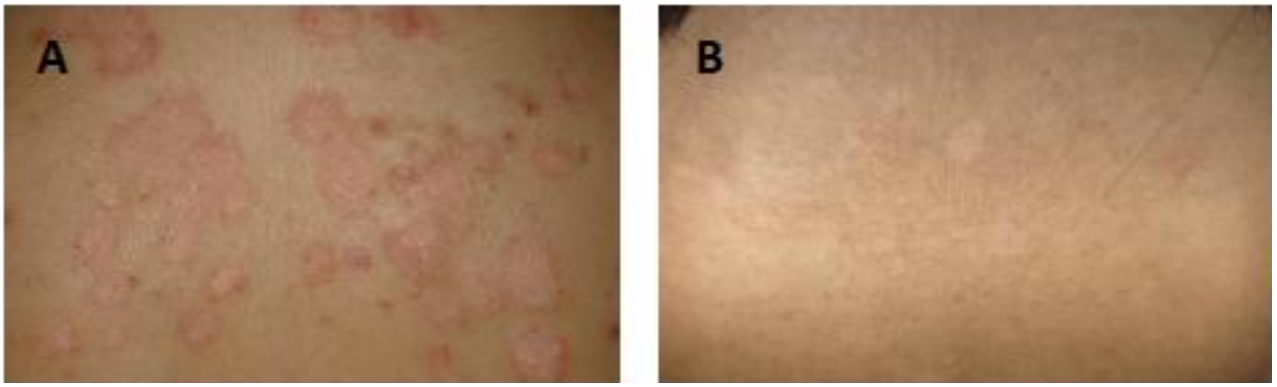

Figure 4. A, Psoriasis before treatment; **B**, clearance of the lesions was achieved with BBUVB at the end of 10 weeks of treatment. Moderated hyperpigmentation appeared on non-previous lesion skin.

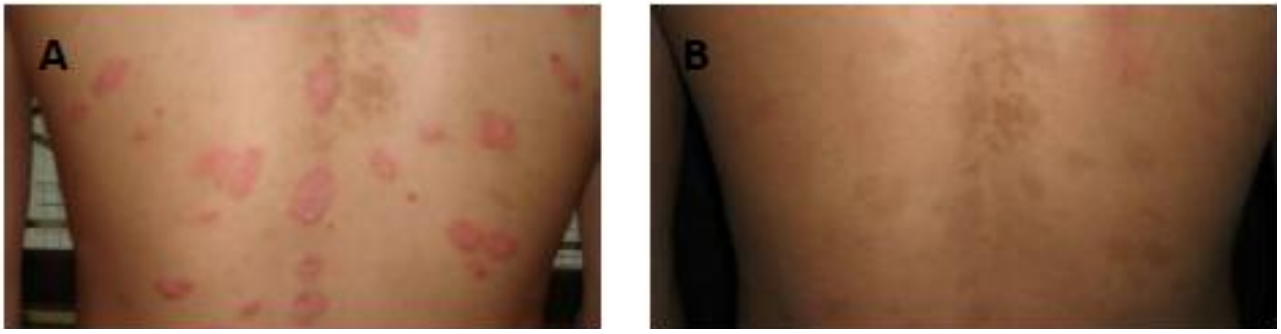

Figure 5. A, Psoriasis before treatment; **B**, clearance of the lesions was achieved with PUVA at the end of 10 weeks of treatment. Moderated hyperpigmentation appeared on previous lesion skin.

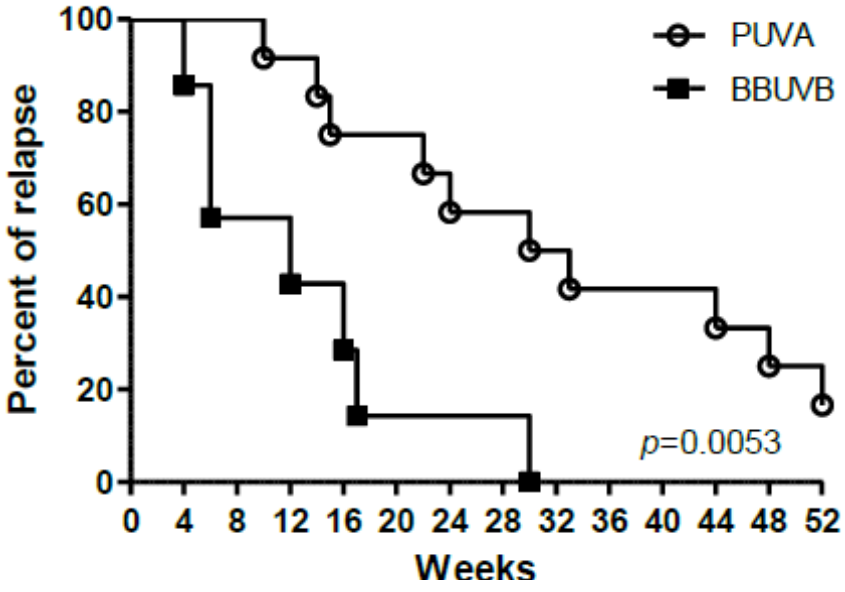

Figure 6. Relapsing rate after one year of follow-up. The median time to relapse was 31.5 week in PUVA group and was 12 week in BBUVB group (p=0.0053).

BBUVB phototherapy has also been in use since the 1920s (Perry et al., 1968). It has not been associated with the development of skin cancers despite the concomitant application of tars, which are considered carcinogenic (Pittelkow et al., 1981). This therapy remains one of the safest treatments for cutaneous psoriasis, but requires treatments at least three times per week for several months to be effective.

Though BBUVB could reduce the skin lesion shorter than PUVA, it also induces higher adverse effects than PUVA such as erythema, burning, moderated hyperpigmention, and itchiness. This was also because of the more erythemogenic wide-band (290-320 nm) source of radiation and the additive effect of this band with psoralen which we used compared to the less erythemogenic UVA (320-400 nm)[6]. Nausea, seborrheic reaction, and headache is no doubt a PUVA-related side effect, and therefore confined to the patients of PUVA. Itchiness and hyperpigmentation, which were the commonest complaints in our patients on either treatment, may not be solely related to ultraviolet therapy. Their frequencies were not significantly higher in BBUVB patients (100%) than those of PUVA patients (88 and 94%, respectively). Both NBUVB and BBUVB offer definite advantages over PUVA that make these modalities preferable for many patients. In particular, PUVA may cause nausea, requires the use of eye protection after treatment sessions, and cannot be used during pregnancy.

During the 52-weeks follow-up period of this study, relapse of psoriasis (defined as the degree of skin involvement of 50% or more of that recorded at the time of entry into the study) was higher in BBUVB-treated group. The results of PUVA therapy in our study are comparable with that of the same therapy used by Yones et al. (2006). In psoriasis, the epidermis and dermis showed high numbers of dendritic cells (DCs) such as Langerhans cells (LCs) and dermal DCs (Sabat et al., 2007). Impairment of epidermal LC mobilization psoriasis associated with trigger of enhancement of psoriasis (Cumberbatch et al., 2006). Treatment of PUVA, UVB, and cyclosporine modalities equally reduce lymphocytes, macrophages, and DCs. However, PUVA is the only treatment that decreases epidermal LCs (Erkin et al., 2007).

Conclusion

It can be said that BBUVB is more effective than PUVA in shorter duration with lower cumulative dose of ultraviolet energy needed for 75% reduction of PASI and skin clearance with high photo-side effects. However, PUVA treatment prolongs the regression of psoriasis. Therefore, the combination of BBUVB and PUVA will be more effective in treatment of psoriasis.

REFERENCES

Chamian F. & Krueger J. G. (2004). Psoriasis vulgaris: An interplay of T lymphocytes, dendritic cells, and inflammatory cytokines in pathogenesis. Curr. Opin. Rheumatol. 16:331-337.

Farber E. M. & Nall L. (1984). Psoriasis. A review of recent advances in treatment. Drugs. 28:324-346.

Luba K. M. & Stulberg D. L. (2006). Chronic plaque psoriasis. Am. Family Phys. 73:636-644.

Greaves M. W. & Weinstein G. D. (1995). Treatment of psoriasis. The New England Journal of Medicine. 332:581-588.

Fredriksson T. & Pettersson U. (1978). Severe psoriasis-oral therapy with a new retinoid. Dermatologica. 157:238-244.

Kabat-Zinn J., Wheeler E., Light T., Skillings A., Scharf M. J., Cropley T. G.., Hosmer D. & Bernhard J. D. (1998). Influence of a mindfulness meditation-based stress reduction intervention on rates of skin clearing in patients with moderate to severe psoriasis undergoing phototherapy (UVB) and photochemotherapy (PUVA). Psychosomatic Medicine. 60:625-632.

Gordon P. M., Diffey B. L., Matthews J. N. & Farr P. M. (1999). A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. J. Am. Acad. Dermatol. 41:728-732.

Markham T., Rogers S. & Collins P. (2003). Narrowband UV-B (TL-01) phototherapy vs oral 8-methoxypsoralen psoralen-UV-A for the treatment of chronic plaque psoriasis. Arch. Dermatol. 139:325-328.

Tahir R. & Mujtaba G. (2004). Comparative efficacy of psoralen - UVA photochemotherapy versus narrow band UVB phototherapy in the treatment of psoriasis. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP. 14:593-595.

Perry H. O., Soderstrom C. W. & Schulze R. W. (1968). The Goeckerman treatment of psoriasis. Arch. Dermatol. 98:178-182.

Pittelkow M. R., Perry H. O., Muller S. A., Maughan W. Z. & O'Brien P. C. (1981). Skin cancer in patients with psoriasis treated with coal tar. A 25-year follow-up study. Arch. Dermatol. 117:465-468.

Yones S. S., Palmer R. A., Garibaldinos T. T. & Hawk J. L. (2006). Randomized double-blind trial of the treatment of chronic plaque psoriasis: Efficacy of psoralen-UV-A therapy vs narrowband UV-B therapy. Arch. Dermatol. 142:836-842.

Sabat R., Philipp S., Hoflich C., Kreutzer S., Wallace E., Asadullah K., Volk H. D., Sterry W. & Wolk K. (2007). Immunopathogenesis of psoriasis. Exp. Dermatol. 16:779-798.

Cumberbatch M., Singh M., Dearman R. J., Young H. S., Kimber I. & Griffiths C. E. (2006). Impaired Langerhans cell migration in psoriasis. J. Exp. Med. 203:953-960.

Erkin G., Ugur Y., Gurer C. K., Asan E., Korkusuz P., Sahin S. & Kolemen F. (2007). Effect of PUVA, narrow-band UVB and cyclosporin on inflammatory cells of the psoriatic plaque. J. Cutan. Pathol. 34:213-219.