Comparative Study of Safety and Efficacy of Narrow Band Ultraviolet B (NBUVB) and Psoralen Ultraviolet A (PUVA) Therapy in Psoriasis Vulgaris

Utkarsh Shukla[1]

ABSTRACT

Introduction: Psoriasis is a group of chronic, inflammatory and proliferative condition of skin, associated with systemic manifestations in many organ systems. The most characteristic lesions consist of erythematous, scaly, sharply demarcated indurated plaques, present particularly over the extensor surfaces and scalp). Phototherapy is one of the most efficacious treatment options for psoriasis. New, emerging studies are beginning to define the biological mechanisms by which phototherapy improves psoriasis- with NBUVB and psoralen ultraviolet A (PUVA) as the most widely used applications.

Material and methods: This prospective study was carried out on 76 patients attending OPD of Rohilkhand medical college and hospital in one year from November 2017 to October 2018. The patients were randomly divided into two groups;Systemic PUVA (Trimethylpsoralen+UVA) and NBUVB groups and therapy will be administered thrice per week on non-consecutive days.

Results: The initial mean PASI score was 17.43 and 17.01 in group A and group B patients respectively, while post treatment PASI score was 3.08 and 2.01 in respective groups. The average cumulative dose for 80% clearance with PUVA was found to be 60.51 J/cm^2 while with NBUVB it was found to be 6.76 J/cm^2. Side effects were observed in 28.94% patients in group A while 5.2% patientsin group B. Amongst group A 18.42%, 7.8% and 2.6% patients presented with erythema, burning and vesiculations respectively while under group B 2.6% patients in each group presented with erythema and burning.

Conclusion: Both PUVA and NBUVB are effective for the treatment of psoriasis vulgaris. However, NBUVB has a distinct edge over PUVA in terms of efficacy and lesser side effects. The advantages of NBUVB therapy over PUVA therapy includes lack of psoralen-related side effects and less mean cumulative dose for clearance and so, good adherence.

Keywords: Psoriasis Vulgaris, PUVA: Systemic Psoralen and Ultraviolet- A,NBUVB: Narrow band ultraviolet-B, TMP: Trimethylpsoralen, PASI: Psoriasis Area and Severity Index

INTRODUCTION

Psoriasis was primarily believed to be a disorder of keratinization, however after successful use of traditional immunosupressants, and newer immunomodulatory drugs it is now believed to be a disease of Th1 dysregulation.[1] Th-17 is also considered to be involved in the pathogenesis.[1]Four categories of action were proposed in the literature to describe the effects of phototherapy in psoriasis: 1) alteration of cytokine profile, 2) induction of apoptosis, 3) promotion of immunosuppression, and 4) all other mechanisms.[2]

The ultraviolet light therapy Psoriasis was primarily believed to be a disorder of keratinization, however after successful use of traditional immunosupressants, and newer immunomodulatory drugs it is now believed to be a of psoriasis consists of, broadband UVB, narrow band UVB and psoralen along with UVA (PUVA). Ultraviolet B phototherapy irradiation encompasses the sun burning wavelengths of 300-320 nm. UVB is considered to be safer but is less effective than PUVA.[3] Clinical improvement of psoriasis by NBUVB is linked to suppression of Th17 and type I and type II IFN signaling pathways, which are critical in the pathogenesis of the disease.[4]

UVB phototherapy is recommended for patients of psoriasis that is refractory to various topical therapies and for patients with generalized plaque or guttate psoriasis in whom topical applications would be difficult or time consuming.[5] Psoralen and UVA(PUVA) is widely accepted as one of the standard treatment modalities for severe form of psoriasis.

Application of psoralen photochemotherapy

The first treatment exposure depends on the skin typing or on the determination of the MED and the patient is exposed to 1.5 J/cm^2 of UVA radiation, after 2 hours of ingestion of 0.6mg/kg body weight or oral 8 methoxasalen or trimethylpsoralen.[6] The patients are treated for thrice a week with dose increments of 0.5 J/cm^2, after every three sittings depending on erythema production and therapeutic response.

Application of nbuvb

Prior to phototherapy, the patient's minimal erythema dose (MED) must be determined in order to establish the dosage schedule. Pai G.S. et al in their study noticed that MED

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was higher in darkly pigmented skin individual. Initial doses should be reduced and gradually stepped up by 20% in subsequent sitting, depending on the patient's erythema response. For 311nm therapy, the intial dose should be equal to 0.7 MED. Patients are treated three to five times a week. If the initial dose is tolerated, a 20% incremental increase of the previous dose is used at each visit.[7]

This study was aimed at comparing the side effects and efficacy of NBUVB and PUVA in patients of psoriasis vulgaris.

MATERIAL AND METHODS

This was a prospective study carried out in Outpatient Department of Dermatology Venereology

and Leprosy, Rohilkhand Medical College and Hospital, Bareilly, a tertiary care hospital in western Uttar Pradesh during the period of November 2017 to October 2018. The patients were randomly divided into two groups; Systemic PUVA (Trimethylpsoralen+UVA) and NBUVB groups and therapy were administered thrice per week on non-consecutive days.

Methods

A written consent was obtained from patient/guardian. Relevant history was taken and clinical examination done, including general, systemic and local examinations. The patients were examined clinically and PASI calculated. The eligible patient for the study were allocated into two groups namely GROUP A and GROUP B. Patient in Group A will be treated with systemic PUVA and Patient in Group B were treated with NBUVB thrice weekly on non-consecutive days. Both the groups were explained about the nature and course of the disease and advised to come for follow up regularly. Initial dose was decided in respect to skin type. Patient were assessed for 1 year at 6 weeks interval. At each visit assessment was done.

Study Treatment Groups

Group A (PUVA therapy): Standard PUVA treatment protocol was followed in regards of dosing of Trimethylpsoralen, irradiation and photoprotection71-72. Patients in this group were given 0.6mg/kg Trimethylpsoralen (Tablet Neosoralen Mac laboratories Pharmaceuticals Pvt. Ltd.) orally two hours before the light session. Patient received three sessions per week on non-consecutive days. Initial dose of UVA varied from 0.5 to 2.5 J/cm^2 according to Fitzpatrick skin type; subsequent increment in dose by 0.5 J/cm^2 was given in each session until minimal erythemogenic dose (MED) was met.

Group B (NBUVB therapy): Standard NBUVB treatment protocol was followed in regards of dosing of irradiation and photoprotection21, 72-73. NBUVB phototherapy was administered thrice weekly on non-consecutive days. Photo-testing was not performed and standard initial dose of 280 mJ/cm^2 was started in all patients. The irradiation was increased by 20% of previous dose until optimal constant dose of minimal erythema was achieved. Patient was then maintained on MED dose and continued until complete remission was achieved or till completion of therapy, whichever was earlier.

Therapy with PUVA and NBUVB was administered in Dermaindia Spiegel series Whole body Phototherapy chamber, 6KVA 24 tubes, TL 100w/10R (or) TL 100/01 Phillips Holland.

Assesment was done by calculating PASI score which was calculated by dividing lesions into four sites of affection head (h), upper limb (u) trunk (t) and lowerlimb (l) were separately scored. Morphologic scoring of psoriasis was done by evaluation of three parameters: erythema, induration and desquamation.

Results were assesed in terms of reduction in PASI scores i.e. <30% reduction was considered as poor response, 31% -79% as average response and 80% or more reduction was considered as good response.

RESULTS

Out of a total of 76 patients taken up for the study, 35(46.05%) were females while 41(53.94%) were males while the The mean age group for PUVA therapy was 36.59 years whereas for NBUVB was 36.79 years including patients ranging between age group of 18 to 60 years.

Majority of cases were found to be between 18-33 years of age group. Out of 38 patients of PUVA therapy 2 patients had a history of diabetes mellitus while 2patients had hypertension and 1 patient presented with deranged thyroid profile. While 3, 2 and 2 patients in NBUVB therapy had history of diabetes mellitus, thyroid disorder and hypertension respectively.

Average cumulative dose- The average cumulative dose of PUVA for 80% clearance was found to be around 60.51J/cm^2 and cumulative dose for 80% clearance by NBUVB was found to be around 6.76J/cm^2. Data was statistically significant p<0.05.(Fig1)

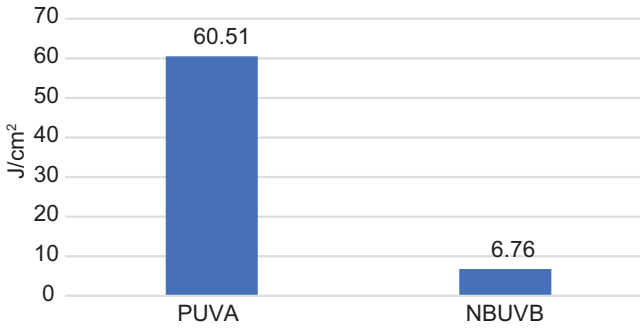


Figure-1: Average cumulative dose

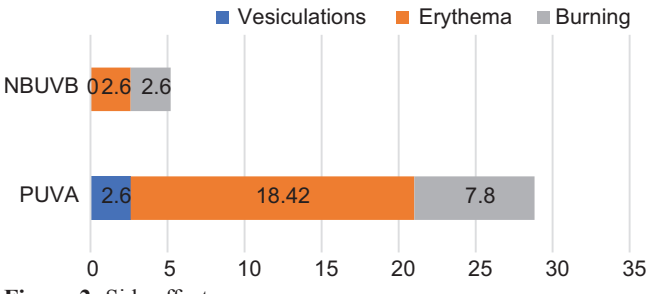
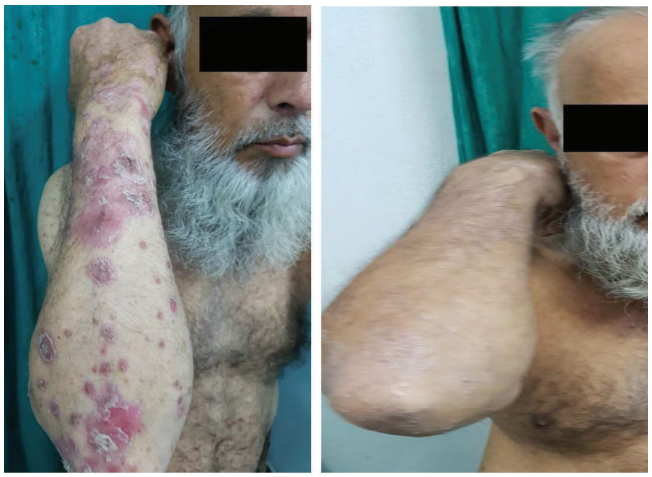
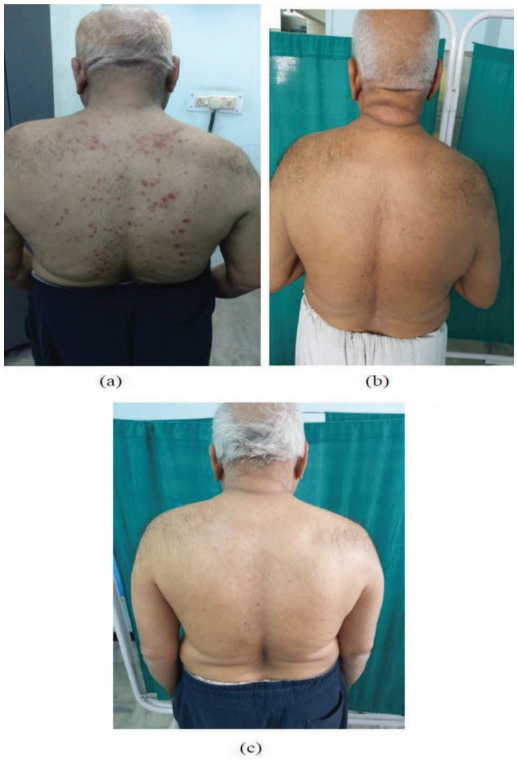


Figure-2: Side effects.



(a) (b)

Picture-1: (a) lesion at base (b) At 48 weeks after PUVA therapy



(a) (b) (c)

Picture-2: (a) At baseline (b)At 48 weeks of therapy with NBUVB (c)After 3 weeks of follow up.

Mean pasi scores

	Initial	At 6 months	At completion	P > 0.05
PUVA	17.43	8.2	3.08	
NBUVB	17.01	7.24	2.01	

Side effects: Side effects like erythema, itching and vesiculations were noted and it was
found that 11(28.94%) out 38 patients treated by PUVA showed side effects wherein 7 patients (18.42%) presented with erythema, 3 patients (7.8%) with mild burning and 1(2.6%) patient presented with vesiculations. Whereas in patients who underwent NBUVB only 2 (5.2%) patients presented with mild erythema and burning. (Fig 2)

Follow up (Picture 1 and 2)

	PUVA	NBUVB
Patients with more than 80% reduction in PASI scores	28(73.68%)	36(94.73%)
Patients with 31%-79% clinical improvement	6(15.78%)	2(5.2%)
Patients with no signifi-cant clinical improvement while on treatment (<30%)	4(10.52%)	0
Patients with relapse while on treatment	9(23.68%)	2(5.2%)
Patients with relapse 3 months after treatment	0	5(13.15%)

DISCUSSION

In our study total 76 psoriasis patients were enrolled out of which 35(46.05%) were females and 41(53.94%) were males, with mean age of 36.59 years and 36.8 years respectively in PUVA and NBUVB group. Gordon PM et al.[8] in their study found mean age group to be 43.3 and 41 years for NBUVB and PUVA respectively in 100 patients which was in accordance with our study.

In our study out of 38 patients assigned to NBUVB group 18(47.36%) were females and in PUVA group out of 38 patients, 17(44.73%) were females with a slight male preponderance. Similarly, in a study involving 34 psoriatic patients by Salem et al[9] 16(47.05: %) patients were females which corresponds to our study. Van Weldeen[10] et al in there study including palmoplantar psoriasis found a male preponderance in the ratio of 4:1.

Frequency of therapy: Patients in our study were called thrice weekly for follow up. Similarly Sezar et al[11] did similar study in patients with palmoplantar psoriasis with 25 patients and therapy was given thrice a week until complete or almost remission of lesions and found better results with topical PUVA therapy. Similarly Tenew et al.[12] in their study administered PUVA and NBUVB in thrice weekly follow up.

Dosage: Chauhan et al[13] in there study titled Narrowband Ultraviolet B versus Psoralen plus Ultraviolet A therapy for severe plaque psoriasis: an indian perspective, intial dosage was given according to Fitzpatrick skin type i.e. type 4 and 5 and intitial dosage was 2.0 J/cm^2 for type 4 and 1.5 J/cm^2 for type 5 for PUVA. Dosage was increased by 1-1.5 J/cm^2 every second visit. While for NBUVB initial starting dose of 280 mj/cm^2 was given and dosage were increased by 20% at each subsequent visit.

Gordon et al[8] in their study took initial dose of PUVA of 1-2.5 J/cm^2 according to skin type.

In our study PUVA and NBUVB were initially given at a dose of 2.0 J/cm^2 and 150 mj/cm^2 with fixed increments of 0.5 J/cm^2 in PUVA and by 20% in cases of NBUVB in each subsequent visit.

Cumulative Dosage: In our study mean cumulative dosage for 80% clearance in PUVA was found to be about 60.51

J/cm^2. and for NBUVB was found to be about 6.76 J/cm^2, similarly
Sezer et al[11] reported 34.9 J/cm2 in NBUVB and 111.5 J/cm^2 of PUVA in cases of
palmoplantar psoriasis. Chauhan et al[13] in their study found mean cumulative dose of 93.8 J/cm^2 in case of PUVA and 30.1 J/cm^2 while on PUVA.

PASI score: In our study the baseline PASI in PUVA and NBUVB was 17.43 and 17.01 respectively which reduced to 3.08(by 82.36%) in PUVA and 2.01(by 88.14%) in NBUVB. Overall decrement in PASI scores of the two regimen was not found to differ significantly although the later group showed slight higher decrement in the mean PASI value.
However in a similar study done by Salem et al[9] comparing results between Bath PUVA and NBUVB, 18 patients with initial mean baseline PASI score of 26.43 were given bath PUVA and 16 patients with initial mean PASI score of 20.74 were treated with NBUVB. Clinical response in PASI score post treatment in bath PUVA group was 3.92 (i.e. reduction by 85.44%) whereas in NBUVB was found to be 9.08 (i.e. reduction by 58.72%).

Side effects and safety profile: Side effects such as erythema, burning and vesiculation were noted in 7, 3 and 1 patients out of 38 patients treated with PUVA whereas 1 patient presented with increased erythema over psoriatic lesion after 2 days of increased dose of NBUVB and 1 patient with mild burning after next day of therapy. Tanew A et al[12] in their study reported similar comparable side effects along with complaint of nausea in a case after ingestion of psoralen which was not seen in any of our patients.
In our study erythema was seen in 18.42% of patients receiving PUVA whereas in a study done by Gordon PM et al[8] it was reported 35.7% patients developed erythema of varying grade. They reported that in 6 patients erythema was severe enough to miss few follow ups of PUVA. Relatable to our study where in 3 patients dose had to be lowered down in subsequent visit in PUVA because of erythema. Two patients who developed burning with erythema were lost to follow up.
Archier E et al[14] in their systemic literature search concluded that out of 49 published studies, 41 assessing the risk of non melanoma skin cancer by PUVA. An increased risk of Basal cell carcinoma was found in patients receiving more than 100
PUVA sessions, and no increased risk of skin cancer was evidenced in the four studies assessing potential carcinogenic risk of NBUVB in European and British population.
Although evidence of carcinogenic changes of PUVA and NBUVB were not reported in Indian studies, so it can be concluded that Fitzpatrick skin type IV and V are less prone to carcinogenic effect of UVR. Although it requires further research in Indian scenario.

Result and follow up: In our study relapse was seen in 23.68% patients under PUVA and 5.2% under NBUVB while on therapy probably due to non compliance of patient under this regimen due to increased adverse effects. However 3 months after completion of therapy no patient under PUVA presented with recurrence while 5 patients (13.15%) under NBUVB category came with recurrence. This corresponded to a study done by Yones et al[15] in which out of 88 psoriasis patients, patients who were treated with PUVA showed less recurrence (i.e. 32%) after 12 months as compared to NBUVB patients who showed about 75% recurrence.
Dayal et al[16] did their study in 60 patients of Chronic plaque psoriasis and found more than 75% reduction in PASI in both the groups, which was comparable to our study which showed more than 70% patients in both the groups presented with >80% reduction in PASI scores.

CONCLUSION

Like all the other previous studies in the past, this study also establishes that both PUVA and NBUVB are effective for the treatment of psoriasis vulgaris. However, NBUVB has a distinct edge over PUVA in terms of efficacy and lesser side effects. The advantages of NBUVB therapy over PUVA therapy includes lack of psoralen-related side effects and less mean cumulative dose for clearance and so, good adherence. In conclusion, we found no significant difference in efficacy between NBUVB and PUVA when treating chronic plaque psoriasis in patients with Fitzpatrick skin types IV and V.
However, NBUVB would be our preferred choice as the available data suggest no or minimal risk of carcinogenesis compared with PUVA, it is safer to use in children and pregnant patients, is devoid of drug-related (psoralen) side-effects and there is no requirement for post-treatment eye protection.

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