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THERAPEUTIC HOTLINE

A large scale analytical study on efficacy of different photo(chemo)therapeutic modalities in the treatment of psoriasis, vitiligo and mycosis fungoides

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ABSTRACT: Psoriasis, vitiligo, and mycosis fungoides (MF) are among the most frequently treated dermatological diseases by photo(chemo)therapy. The objectives are to determine which photo (chemo) therapeutic modality could achieve the best response in the treatment of psoriasis, vitiligo, and MF. The design used in this study is retrospective analytical study. The study included 745 patients' records; 293 with psoriasis, 309 with vitiligo, and 143 with early MF, treated in the Phototherapy Unit, Dermatology Department, Kasr El-Aini Hospital, Cairo University by either psoralen and ultraviolet A (PUVA), narrow band ultraviolet B (NB-UVB), psoralen and narrow band UVB (P-NBUVB), broad band UVB (BB-UVB), or broad band UVA (BB-UVA). Data were retrieved from the computer database of the unit and statistically analyzed. In psoriasis, oral and topical PUVA and NB-UVB were found to be equally effective, whereas oral PUVA had significantly better results than both UVA and BB-UVB at the end of therapy. In generalized vitiligo, PUVA and P-NBUVB had significantly better results than NB-UVB alone. In early MF, there was no statistically significant difference between the response to oral PUVA and NB-UVB. PUVA and NB-UVB are good choices in patients with psoriasis and early stage MF, whereas PUVA appears the best choice in the treatment of vitiligo.

KEYWORDS: mycosis fungoides, photo(chemo)therapy, phototherapy, P-NBUVB, psoriasis, vitiligo

Introduction

Psoriasis, vitiligo, and mycosis fungoides (MF) are among the most common dermatological diseases treated with photo (chemo) therapy. Phototherapy is the exposure to nonionizing radiation for therapeutic benefits. It involves exposure to ultraviolet A

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(UVA) or ultraviolet B (UVB). UVA lamps emit either broad band UVA or UVA-1. Photo(chemo) therapy comprises the use of photosensitizers, psoralen, or khellin in combination with UVA (psoralen and ultraviolet A (PUVA) or khellin and UVA (KUVA), respectively) (1). UVB lamps emit either broad band UVB (BB-UVB) or narrow band UVB (NB-UVB). The efficacy of NB-UVB may be enhanced by addition of psoralen (P-NBUVB) (2).

Aim of the study

The aim of the study was to determine which form of photo (chemo) therapy could achieve the best response in the treatment of psoriasis, vitiligo, and MF. The effects of age, sex, disease duration, course, extent, and clinical variant or stage of the disease were evaluated as possible parameters for future optimization of individual patient treatment.

Patients and methods

Patients

This study included 745 patients; 293 with psoriasis, 309 with vitiligo and 143 with early MF. Patients were of both sexes, different age groups and skin types III-V. All patients were treated in the Phototherapy Unit, Dermatology Department, Kasr Al-Aini Hospital, Cairo University by different phototherapeutic modalities.

Equipment and dosing schedules

UVA light was delivered by UVA cabins (PUVA 7001& PUVA 1000, Waldmann GmbH, Germany) with F85/100 W fluorescent lamps (40 and 26 lamps, respectively), that emitted UV light in the wavelength range of 315–400 nm with a peak emission at 365 nm and an integrated UV photometer. In PUVA-treated patients, the initial UVA dose and subsequent increments were dependent on the skin type (3). When UVA (320–400 nm) without psoralen was used, the dose was fixed, at 10 J/cm^2 for psoriasis and 15 J/cm^2 for vitiligo patients.

NB-UVB was delivered by a UV cabin (Waldmann GmbH, Germany) equipped with an integrated UV photometer, having 16 TL-01/ 100W fluorescent lamps producing NB-UVB with a peak emission at 311 nm, whereas BB-UVB was delivered by a UV cabin (BB-UVB 1000 Waldman lighting) equipped with UVB lamps with a radiation spectrum of 285–350 nm and a peak at 310–315 nm). The initial UVB dose and subsequent increments were adjusted according to readily calibrated tables supplied by the manufacturer. In case of P-NBUVB, patients ingested psoralen tablets followed by exposure to NB-UVB 311 nm 90 minutes later.

Methods

Evaluation schedule

All patients were evaluated early, at mid-therapy and at the anticipated session of clearance for each disease. Evaluation was done at 10, 30, and 50 sessions in psoriatics, and at 10, 50, and 70 sessions in vitiligo patients. In MF patients, evaluation was done at sessions 10, 40, and 60. Although the final evaluation of MF patients was done at Session 60, patients were routinely discharged from the Phototherapy Unit when complete clinical clearance occurred and maintenance sessions were given according to Phototherapy Unit Guidelines.

Data sources

This retrospective patient record analysis used data from a computerized medical record database of the Phototherapy Unit. The program used was: Kasr El Aini PUVA System (KEPUVA System): Microsoft Access XP-based Database engine: JET Scripting: VBA Description: specially designed program at the Phototherapy Unit, Dermatology Department, Kasr Al-Aini Hospital, Cairo University.

Data used

Each record contains personal data, disease history, examination, investigations, and treatment data. Type of photo (chemo) therapy, dose of psoralen (if used), achieved final response, and follow-up were recorded.

Data analysis

Data included in the statistical analysis were only those of records showing “excellent” response (80–100% clearance of the lesions) or “good” response (60–80% clearance of the lesions) on clinical evaluation.

Data were retrieved and tabulated. Data in the present study were all categorical, thus comparison between the different study groups was done using Chi-square (χ^2) test. Yates correction

equation was used instead when the expected frequency was less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs statistical Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA).

Results

Psoriasis

Oral and topical PUVA, UVA, NB-UVB, and BB-UVB were used in the treatment of 293 psoriatics. The number and percentage of patients achieving excellent or good response are summarized in Table 1, and the effects of treatment modalities in relation to the session number were compared. Oral and topical PUVA and NB-UVB were found to be equally effective, whereas oral PUVA had significantly better results than both UVA ($p = 0.039$) and BB-UVB ($p = 0.015$) at the end of therapy.

None of the parameters chosen to act as predictors to the outcome of various therapies had any influence on the treatment outcome of psoriasis, irrespective of the treatment modality.

Vitiligo

Oral and topical PUVA, UVA, NB-UVB, BB-UVB, and P-NBUVB were used in the treatment of 309 vitiligo patients. At the 70th session, patients treated with oral PUVA or P-NBUVB showed statistically better results than those treated with NB-UVB. Approximately 55% of vitiligo cases who received topical PUVA, UVA phototherapy, NB-UVB, or BB-UVB achieved an excellent or good response at the end of therapy (Table 2).

Among treated vitiligo patients, those with progressive course achieved good results. They constituted 90% of PUVA treated patients and 87% of NB-UVB treated patients, where excellent or good

Table 1. Comparison of the beneficial effect of various treatment modalities in psoriatic patients in relation to session number

	Treatment modality					
Number of sessions	Oral PUVA ($n = 173$)	Topical PUVA ($n = 21$)	UVA ($n = 6$)	NB-UVB ($n = 69$)	BB-UVB ($n = 24$)	P Value
10	13/173 (7.51%)	1/21 (4.76%)	0/6 (0%)	5/69 (7.24%)	2/24 (8.33%)	0.948
30	71/173 (41.04%)	7/21 (33.33%)	1/6 (16.67%)	23/69 (33.33%)	6/24 (25%)	0.369
50	152/173 (87.86%)	15/21 (71.42%)	2/6 (33.33%)	56/69 (81.16%)	16/24 (66.67%)	0.008*

n, number of patients.
*Significant P value.
BB-UVB, broad band ultraviolet B; NB-UVB, narrow band ultraviolet B; PUVA, psoralen and ultraviolet A.

Table 2. Comparison of the beneficial effect of various treatment modalities in vitiligo patients in relation to session number

	Treatment modality						
Number of sessions	Oral PUVA ($n = 150$)	Topical PUVA ($n = 18$)	UVA ($n = 16$)	NB-UVB ($n = 96$)	P-NB UVB ($n = 17$)	BB-UVB ($n = 12$)	P Value
10	0/150	0/18	0/16	0/96	0/17	0/12	–
50	39/150	4/18	2/16	14/96	5/17	1/12	0.320
	26%	22.2%	12.5%	14.6%	29.4%	8.3%	
70	114/150	10/18	8/16	52/96	15/17	7/12	0.001*
	76%	55.6%	50%	54.2%	88.2%	58.3%	

n, number of patients.
*Significant P value.
BB-UVB, broad band ultraviolet B; NB-UVB, narrow band ultraviolet B; PUVA, psoralen and ultraviolet A; UVA, ultraviolet A.

response was achieved in 79% and in 55% of cases, respectively. Patients with generalized vitiligo without acral lesions showed significantly higher excellent or good response to both PUVA and NB-UVB than those with generalized vitiligo with acral lesions ($p = 0.000$ and $p = 0.015$, respectively). The only effect of gender on vitiligo treated patients in the study was the significantly higher incidence of excellent or good results in NB-UVB-treated females as compared to males ($p = 0.02$).

Mycosis fungoides

PUVA and NB-UVB were used in the treatment of 143 early stage MF patients. No statistically significant difference was found between PUVA and NB-UVB at Sessions 10, 40, and 60 (Table 3). Of the 91 patients who achieved excellent or good response with PUVA therapy, 30% showed recurrence after an average remission period of 27 months and 27% continued maintenance therapy without evidence of recurrence during the maintenance period (average 19 months). The remaining 43% of patients did not return to follow up after clinical clearance. Of the 14 patients treated with NB-UVB showing excellent or good response, six patients continued to receive maintenance therapy for 3 years on average and eight patients did not return for maintenance therapy after clinical clearance.

Considering the effects of the chosen parameters on therapeutic response, PUVA treated MF patients with shorter disease duration and females aged 10–30 years tended to show higher excellent and good responses. On the other hand, in NB-UVB treated MF patients none of the different parameters influenced response to therapy.

Table 3. Comparison of the beneficial effect of various treatment modalities in mycosis fungoides patients in relation to session number

	Treatment modality		
Number of sessions	Oral PUVA ($n = 123$)	NB-UVB ($n = 20$)	P Value
10	5/123 4.1%	0/20	0.794
40	30/123 24.4%	6/20 30%	0.791
60	91/123 74%	14/20 70%	0.919

n, number of patients.

NB-UVB, narrow band ultraviolet B; PUVA, psoralen and ultraviolet A.

Side effects encountered during therapy

Phototoxic reactions (in the form of itching or mild to moderate erythema) were the most frequently encountered side effects. They were more commonly reported with BB-UVB followed by both NB-UVB and topical PUVA in psoriasis, whereas in vitiligo, they were equally reported with oral PUVA, topical PUVA, and P-NBUVB. In MF, phototoxic reactions occurred more commonly with NB-UVB followed by PUVA. On the other hand, itching was most frequently encountered with topical PUVA and P-NBUVB than in oral PUVA- and NB-UVB-treated patients in all three diseases. In patients who received oral psoralen, gastrointestinal (GIT) side effects were encountered.

Discussion

Photo (chemo) therapies are among the most efficiently used modalities in the treatment of psoriasis, vitiligo, and MF, with high success rates and low incidence of side effects (4). The comparative efficacy of the different photo(chemo)therapeutic modalities in the treatment of those diseases was our main concern, besides the parameters used as predictors of response.

Psoriasis group

Analysis of our data highlights that oral PUVA and NB-UVB are equally effective in achieving excellent or good response in psoriatics. A similar result was obtained in a right-left comparative study (5). On the other hand, the superiority of PUVA over NB-UVB was reported in two randomized controlled trials (6,7). It is noteworthy that the number of patients in our study was almost double the patients in the previous studies.

Oral PUVA was found to be superior to both UVA and BB-UVB at the end of therapy. It could be expected that oral psoralen adds to the therapeutic efficacy of UVA radiation, inducing a better response of oral PUVA over UVA phototherapy. It is likely that the higher penetration power of UVA induced a better response over BB-UVB in psoriatics. It was reported that BB-UVB achieved better results in patients with eruptive and seborrheic psoriasis than in those with chronic plaque psoriasis (8), the latter comprised most of the patients in this study. Only one study could be retrieved from published literature comparing oral PUVA to BB-UVB, which found them to be of equal efficacy (9). However, some of their patients were receiving

topical anthralin or calcipotriol in addition to BB-UVB, which could bias their study results. As for the parameters studied in patients with psoriasis, they did not influence response, irrespective of the treatment modality. On the other hand, a previous study showed that severe cases of psoriasis responded better to oral PUVA than to NB-UVB (10), and when plaques were thick or on the lower limbs they showed poor response to NB-UVB, irrespective of the clinical variant (11).

Vitiligo group

In vitiligo patients, no difference in the response was observed between all modalities at early sessions. But given a longer time, oral PUVA and P-NBUVB showed statistically significant better results than NB-UVB, yet it is not recommended to use psoralen with NB-UVB as it may carry a higher risk probability (2). In NB-UVB-treated vitiligo patients, excellent or good response was observed in about 50% of cases at the 70th session, which was almost equivalent to the results obtained by topical PUVA, UVA, and BB-UVB. PUVA can create a favorable milieu for promoting the growth of melanocytes in patients with vitiligo and can also slow down the destruction of melanocytes in active stage of the disease; while in the stable stage, NB-UVB irradiation should be used to stimulate melanocyte proliferation and migration directly (12). In addition, PUVA has immunological effects on circulating lymphocytes and reduces antimelanocyte antibodies that are elevated in proportion to disease activity (13). The finding that almost 90% of our cases treated with PUVA or NB-UVB were in the active stages of the disease might explain the better achieved response with PUVA therapy. Other study groups stated that NB-UVB was more effective than oral PUVA in treating vitiligo (14–16). No study on the effect of P-NBUVB in vitiligo could be retrieved from the published literature except that of Mofty et al. in 2001 (2), whose data are included in the current study.

Some of the parameters had an influence on the response to therapy in vitiligo patients in the present study. In PUVA treated patients, those with progressive course achieved better results. This might be explained by the immunological effect of PUVA on circulating lymphocytes in active disease stages. A previous retrospective study, documented that disease stability did not influence the extent of re-pigmentation (17). Acral lesions showed a worse response to either oral PUVA or NB-UVB therapy than lesions in other sites, as previously documented (18–20). This would be due to the low number of hair follicles in acral parts that act as a reservoir for melanocytes (21). More female patients with vitiligo achieved excellent or good response to NB-UVB therapy than males. Age, disease duration, and disease extent had no effect on the response of the vitiligo patients to any of the used treatment modalities.

Mycosis fungoides group

Comparable results were found in our MF patients treated with oral PUVA and NB-UVB. Diederen et al. (2003) reported equal efficacy of both oral PUVA and NB-UVB after conducting a retrospective comparative study on 46 patients with early stage MF (22). None of the parameters seemed to affect the outcome of NB-UVB therapy in MF patients. However, a better response to oral PUVA therapy was observed in females, in the age group 19–30 years and those with shorter disease duration. Two studies concluded that early onset MF is less aggressive than that appearing in adult life (23,24).

Delay in achieving good response was observed in psoriatics and in MF patients in this study when compared with other reported trials, where the average sessions needed for clearance of psoriasis varied between 20–25 sessions with oral PUVA and NB-UVB (25–27). Similarly, clearance of MF lesions was reported to occur in about half the sessions (mean 29 sessions) (28) needed to treat patients of the present study. A possible explanation is the darker skin types in our patients (III, IV and V). Yones et al. (2006) reported that psoriatic patients with skin types V and VI showed a lower rate of clearance than those with skin types I through IV (7).

Side effects

The most commonly encountered side effects in our patients with psoriasis were phototoxic reactions (itching, mild-to-moderate erythema), which occurred more frequently with UVB radiation whether broad band or narrow band. This falls in the same range as other studies, where one fifth of psoriatic cases treated with oral PUVA (29) or NB-UVB (30) experienced phototoxic reactions. Itching was mainly encountered with NB-UVB in our study. In vitiligo patients phototoxic reactions, followed by thick skin and itching were found common with PUVA (whether oral or topical) followed by P-NBUVB, followed by NB-UVB. In MF, phototoxic reactions occurred more with NB-UVB than oral PUVA, whereas itching occurred with oral PUVA.

Conclusions

- Oral PUVA, topical PUVA and NB-UVB are equally effective as treatment modalities in psoriasis.
- Oral PUVA and P-NBUVB are the most effective modalities regarding photo(chemo)therapy in vitiligo, yet it is not recommended to use psoralen with NB-UVB as it may carry a higher risk probability. NB-UVB could be used if psoralens are contraindicated.
- Oral PUVA and NB-UVB are equally effective in treatment of MF. An additional value for PUVA is the longer remission period.

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Erratum

Dr. Piergiacomo Calzavara-Pinton was incorrectly listed as Piergiacomo Calzavara Pinton in "Cost-effectiveness analysis of TNF-α blockers for the treatment of chronic plaque psoriasis in the perspective of the Italian health-care system" (Dermatol Ther 2010;23supp1:S7–S13). We apologize for this error.