CLINICAL REPORT

Adverse Events Leading to Discontinuation of Phototherapy: An Observational Study

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The aim of this prospective study in a phototherapy unit was to describe adverse events (AEs) associated with discontinuation of phototherapy in a clinical setting. A total of 872 included patients received 1,256 courses of phototherapy treatment: 76.9% narrow-band UVB (NBUVB); 9.6% systemic psoralen plus UVA (PUVA); 11.4% topical PUVA; and 2.1% UVA. Approximately a fifth of the treatments ($n = 240$, 19.1%) were associated with AEs, the most frequent of which was erythema (8.8%). Systemic PUVA had the highest rate of AEs (32.5%). Mycosis fungoides was the dermatosis with the highest rate of AE (36.9%). A total of 216 (17.2%) patients stopped treatment: 23.6% because of AEs (4.1% of all treatments). Treatment suspension due to AEs was associated with PUVA, both topical and systemic ($p < 0.001$), and diagnoses of mycosis fungoides ($p < 0.001$), palmoplantar psoriasis ($p = 0.002$), hand eczema ($p = 0.002$) and pityriasis lichenoides ($p = 0.01$). In conclusion, one in every 5 patients receiving phototherapy had an AE, but few stopped treatment for this reason.

Key words: phototherapy; adverse events; discontinuation; narrow-band UVB; psoralen plus UVA.

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SIGNIFICANCE

Phototherapy has proven to be an effective treatment for several dermatoses. However, little is known about the adverse events (AE) that lead to discontinuation in clinical practice. This prospective study included 872 patients who received 1,256 phototherapy treatments. Approximately a fifth of patients receiving phototherapy had an AE, but few stopped treatment for this reason. Erythema was the most frequent AE, and mycosis fungoides was the dermatosis with the highest rate of AE. Patients treated with psolaren plus UVA, and those with mycosis fungoides, hand eczema or palmoplantar psoriasis, were more likely to stop their treatment due to AE.

Narrow-band ultraviolet B (NBUVB) phototherapy and photochemotherapy with psoralen and ultraviolet A (PUVA) have proven to be both effective and efficient treatments for several dermatological diseases (1, 2), including psoriasis (3, 4), atopic dermatitis (5–7), vitiligo (8) and cutaneous lymphomas (9, 10).

Despite being a common treatment modality, there have been few studies of the adverse events (AEs) of phototherapy in clinical practice, particularly in regions with extended hours of sun exposure, such as the Mediterranean coast. An improved understanding of the reasons that patients stop their treatment, including AEs, may help physicians to better advise patients, potentially allowing prevention of the AEs.

To better assess the safety of phototherapy, the aim of this study was to describe the AEs related to phototherapy and their association with discontinuation of treatment in patients treated in a phototherapy unit on the Mediterranean coast.

MATERIALS AND METHODS

A single-centre, prospective, observational study was performed, collecting data from all patients who attended the Phototherapy Unit of the General University Hospital of Alicante from January 2005 to March 2018. This unit, located on the south-eastern Mediterranean coast of Spain, serves a population of approximately 267,000 people. Treatments included in the study were: NBUVB, systemic PUVA, palmoplantar topical PUVA and ultraviolet A (UVA). In all cases of systemic and topical PUVA, 8-methoxypsoralen (8-MOP) was used. The phototherapy systems were Waldmann UV 7001K (PUVA/TL01) and UV 181/200 AL, (Waldmann GmbH & Co. KG, Villingen-Schwenningen, Germany) and standard operating procedures were based on published guidelines from the Spanish Photobiology Group (11–13). The pre-phototherapy investigations in cases of systemic PUVA included an eye examination by an ophthalmologist, and a blood test with liver function panel and antinuclear antibodies (ANA), which were also tested in other treatment modalities if there was a clinical concern of lupus. The initial doses of UV were chosen following the proposed fixed doses depending on patient's Fitzpatrick skin type in the Spanish guidelines (11–13).

The following information were collected prospectively: age, sex, Fitzpatrick skin type, dermatological disease to treat, location of the lesions, previous and current treatments, number of sessions, cumulative doses received, efficacy, AEs, timing of the AE, and its impact on treatment discontinuation (yes/no). The AE considered were: erythema (defined as redness of skin with no blisters), hyperpigmentation, pruritus and erythema, UV-burn, phototoxicity (defined as a second-degree UV-burn, involving epidermis and superficial dermis), pruritus, pain, cutaneous lupus

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and gastrointestinal symptoms (pyrosis, abdominal pain, etc.). The reasons for stopping treatment were categorized as: patient's decision, lack of efficacy (no response or worsening of cutaneous lesions), or AEs.

The local research ethics committee approved the study protocol. All patients provided written informed consent on enrolment, and the study was performed according to the Declaration of Helsinki.

Statistical analysis

Demographic and descriptive data were expressed as absolute and relative frequencies for categorical variables, and as medians and interquartile range (IQR) for non-normally distributed quantitative variables. The χ^2 test was used to compare AE incidence between phototherapy modalities or dermatoses treated; the Mann-Whitney test, to compare non-normally distributed quantitative variables; and a logistic regression model, to test significant associations from the univariable analysis. *p*-values <0.05 were considered statistically significant. The magnitude of associations was measured using odds ratio (OR) with 95% confidence intervals (95% CI). All analyses were performed using IBM SPSS Statistics for Macintosh, Version 21.0 (IBM Corp., Armonk, NY, USA, 2012).

RESULTS

During the study period, 1,256 treatment courses in 872 patients (43.9% male; median age 44 years) were included. Fifty-two treatment courses (4.1%) were in patients aged under 18 years, and 86.6% of patients had Fitzpatrick skin type II or III. The main dermatosis treated was plaque psoriasis (65%), followed by palmoplantar psoriasis (10%), mycosis fungoides (5.2%), atopic dermatitis (4.4%) and guttate psoriasis (2.8%). NBUVB was the most frequently given treatment (76.9%), whereas systemic PUVA accounted for 9.6%, topical PUVA for 11.4%, and UVA for 2.1% of treatments. Just under a third (30.7%) of patients had previously received phototherapy, usually NBUVB (277 cases), with a minority receiving UVA ($n=20$), topical PUVA ($n=15$) and systemic PUVA ($n=54$). Treatment had a mean duration of 78 days, with treatment courses of 20–30 sessions given twice or 3 times a week, following the Spanish Photobiology Group guidelines. Participants' characteristics are shown in **Table I**.

There were 240 (19.1%) acute AEs recorded during the study period; the most frequent was erythema (8.8%). Erythema in patients treated with NBUVB appeared in the first 6 h and had a duration of 1.5–2 days, while in patients treated with PUVA appeared after 24–36 h and had a duration of 6–7 days. **Table II** presents AEs according to phototherapy modality. NBUVB had a rate of acute AE of 18.1%, similar to topical PUVA (16.1%) and lower than systemic PUVA (32.5%). Compared with NBUVB, systemic PUVA therapy showed a higher frequency of any AE (OR 2.2; 95% CI 1.4, 3.3), cutaneous lupus (OR 8.1; 95% CI 1.1, 58.2), and phototoxic reactions (OR 34.2; 95% CI 7.2, 163.1). Patients receiving topical PUVA reported pain (OR 20.7; 95% CI 2.1, 200.3) and phototoxic reactions (OR 24.8; 95% CI 5.1, 120.8) more frequently than those treated with NBUVB.

Table III shows AEs according to treated dermatoses and phototherapy modalities. Mycosis fungoides was the dermatoses with the highest rate of AEs (36.9%). In patients treated with systemic PUVA, compared with patients with plaque psoriasis, those with mycosis fungoides had higher odds of experiencing any AE (OR 3; 95% CI 1.1, 8.3). On the other hand, between patients treated with NBUVB, atopic dermatitis increased the odds of pruritus plus erythema (OR 4.2; CI 95% 1.1, 15.7). By type of psoriasis, guttate psoriasis showed the highest frequency of erythema (17.1%) and palmoplantar psoriasis was the dermatosis with the lowest rate of AEs (11.9%).

Regarding treatment discontinuation, 1,040 of the 1,256 treatments (82.8%) were completed, while 216 treatments (17.2%) were not. The most frequent reason for discontinuation was the patient's non attendance (for work, personal or unknown reasons, 112 cases, 51.9%). The remainder of the patients stopping their treatment did so because of lack of treatment efficacy (53 cases, 24.5%) and AEs (51 cases, 23.6% of treatment discon-

Table I. Clinical and epidemiological characteristics of total courses of phototherapy treatment

Variables	Total courses of treatment ($n=1,256$)	NBUVB ($n=966$)	Systemic PUVA ($n=120$)	Topical PUVA ($n=143$)	UVA ($n=27$)
Sex, *n* (%)					
Male	552 (43.9)	432 (44.7)	61 (50.8)	43 (30.1)	16 (59.3)
Female	704 (56.1)	534 (55.3)	59 (49.2)	100 (69.9)	11 (40.7)
Age, years, median (IQR)	44 (31–57)	41 (30–55)	50 (40–60)	50 (37–70)	45 (38–54.25)
Skin type, *n* (%)					
I	4 (0.3)	2 (0.2)	0 (0)	2 (1.4)	0 (0)
II	387 (30.8)	307 (31.8)	30 (25)	43 (30.1)	7 (25.9)
III	696 (55.8)	534 (55.3)	62 (51.7)	83 (58.0)	17 (63.0)
IV	154 (12.3)	112 (11.6)	24 (20.0)	15 (10.5)	3 (11.1)
V and VI	11 (0.8)	7 (0.7)	4 (3.3)	0 (0)	0 (0)
Dermatosis, *n* (%)					
Plaque psoriasis	816 (65)	755 (78.2)	44 (36.7)	6 (4.2)	11 (40.7)
Palmoplantar psoriasis[a]	126 (10.0)	3 (0.3)	4 (3.3)	112 (78.3)	7 (25.9)
Mycosis fungoides	65 (5.2)	32 (3.3)	32 (26.7)	1 (0.7)	0 (0)
Atopic dermatitis	55 (4.4)	51 (5.3)	1 (0.8)	2 (1.4)	1 (3.7)
Guttate psoriasis	35 (2.8)	35 (3.6)	0 (0)	0 (0)	0 (0)
Vitiligo	25 (2.0)	23 (2.4)	2 (1.7)	0 (0)	0 (0)
Hand eczema	21 (1.7)	0 (0)	1 (0.8)	19 (13.3)	1 (3.7)
Pityriasis lichenoides	16 (1.3)	10 (1)	4 (3.3)	0 (0)	0 (0)
Lymphomatoid papulosis	11 (0.9)	3 (0.3)	8 (6.7)	0 (0)	0 (0)
Lichen planus	9 (0.7)	6 (0.6)	1 (0.8)	2 (1.4)	0 (0)
Mastocytosis	7 (0.6)	2 (0.2)	5 (4.2)	0 (0)	0 (0)
Other[b]	70 (5.5)	44 (4.6)	18 (15)	1 (0.7)	7 (25.7)

[a]Palmoplantar psoriasis includes pustulosis palmoplantaris (n=18 of the treatment courses) and psoriatic hyperkeratotic lesions localized predominantly in palms and soles ($n=108$). [b]Includes: granuloma annulare ($n=14$), nodular prurigo ($n=11$), solar urticaria ($n=8$), pruritus ($n=8$), chronic superficial dermatitis ($n=7$), morphea ($n=5$), lichen sclerosus et atrophicus ($n=3$), alopecia areata, ($n=3$), actinic prurigo ($n=2$), Sézary syndrome ($n=1$), pityriasis lichenoides et varioliformis acuta ($n=1$), perforating dermatoses ($n=2$), keratosis lichenoides chronica ($n=1$), hypomelanosis ($n=1$), chronic graft-versus-host disease ($n=1$), peripheral T-cell lymphoma ($n=1$), and lichen nitidus ($n=1$). PUVA: psolaren + ultraviolet A; NBUVB: narrow-band ultraviolet B; UVA: ultraviolet A; IQR: interquartile range.

Table II. Sessions, cumulative doses and adverse events (AE) by phototherapy modality

Treatment- and AE-related variables	NBUVB ($n=966$)	Systemic PUVA ($n=120$)	Topical PUVA ($n=143$)	UVA ($n=27$)	Total
Sessions, mean±SD	25.3±11.1	24.3±12.4	25.3±11.1	24±9.3	–
Cumulative doses, J/cm^2, mean±SD	41.1±68.2	133.9±104.1	154.9±100.1	177.5±94.3	–
Any adverse event, *n* (%)	175 (18.1)	39 (32.5)[a]	23 (16.1)	3 (11.1)	240 (19.1)
Erythema	91 (9.4)	10 (8.3)	8 (5.6)	2 (7.4)	111 (8.8)
Hyperpigmentation	44 (4.6)	10 (8.3)	1 (0.7)	1 (3.7)	56 (4.5)
Pruritus and erythema	18 (1.9)	4 (3.3)	2 (1.4)	0 (0)	24 (1.9)
UV-burn	2 (0.2)	8 (6.7)[a]	7 (4.9)[a]	0 (0)	17 (1.4)
Pruritus	13 (1.4)	3 (2.5)	0 (0)	0 (0)	16 (1.3)
Pain	1 (0.1)	1 (0.8)	3 (2.1)[b]	0 (0)	5 (0.4)
Cutaneous lupus	2 (0.2)	2 (1.7)[c]	0 (0)	0 (0)	4 (0.3)
Gastrointestinal symptoms	1 (0.1)	1 (0.8)	2 (1.4)	0 (0)	4 (0.3)
Post-inflammatory hypopigmentation	3 (0.3)	0 (0)	0 (0)	0 (0)	3 (0.2)

[a]$p<0.001$; [b]$p<0.01$; [c]$p=0.04$.
NBUVB: narrow-band ultraviolet B; PUVA: psolaren + ultraviolet A; UVA: ultraviolet A; SD: standard deviation.
Note: odds of experiencing adverse event compared with reference category of NBUVB.

Table III. Adverse events by dermatoses under treatment

	Dermatosis					
Adverse event	Plaque psoriasis ($n=816$) *n* (%)	Palmoplantar psoriasis ($n=126$) *n* (%)	Mycosis fungoides ($n=65$) *n* (%)	Guttate psoriasis ($n=35$) *n* (%)	Atopic dermatitis ($n=55$) *n* (%)	Hand eczema ($n=21$) *n* (%)
Any treatment						
Any adverse event	149 (18.3)	15 (11.9)	24 (36.9)	8 (22.9)	11 (20.0)	4 (19.0)
Erythema	75 (9.2)	3 (2.4)	8 (12.3)	6 (17.1)	5 (9.1)	2 (9.5)
Hyperpigmentation	40 (4.9)	1 (0.8)	5 (7.7)	2 (5.7)	1 (1.8)	0 (0)
Pruritus and erythema	13 (1.6)	2 (1.6)	2 (3.1)	0 (0)	4 (7.3)	0 (0)
UV-burn	3 (0.4)	5 (4)	4 (6.2)	0 (0)	0 (0)	2 (9.5)
Pruritus	11 (1.3)	0 (0)	2 (3.1)	0 (0)	1 (1.8)	0 (0)
Pain	1 (0.1)	2 (1.6)	1 (1.5)	0 (0)	0 (0)	0 (0)
Cutaneous lupus	2 (0.2)	0 (0)	2 (3.1)	0 (0)	0 (0)	0 (0)
Gastrointestinal symptoms	1 (0.1)	2 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)
Post-inflammatory hypopigmentation	3 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
NBUVB treatment	755	3	32	35	51	0
Any adverse event	136 (18)	0 (0)	9 (28.1)	8 (22.9)	8 (15.7)	0 (0)
Erythema	69 (9.1)	0 (0)	5 (15.6)	6 (17.1)	3 (5.9)	0 (0)
Hyperpigmentation	38 (5.0)	0 (0)	2 (6.3)	2 (5.7)	1 (2.0)	0 (0)
Pruritus and erythema	11 (1.5)	0 (0)	1 (3.1)	0 (0)	3 (5.9)[a]	0 (0)
UV-burn	2 (0.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pruritus	9 (1.2)	0 (0)	1 (3.1)	0 (0)	1 (2.0)	0 (0)
Pain	1 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cutaneous lupus	2 (0.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Gastrointestinal symptoms	1 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Post-inflammatory hypopigmentation	3 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Systemic PUVA treatment	44	4	32	0	1	1
Any adverse event	9 (20.5)	0 (0)	14 (43.8)[b]	0 (0)	1 (100)	0 (0)
Erythema	3 (6.8)	0 (0)	3 (9.4)	0 (0)	0 (0)	0 (0)
Hyperpigmentation	1 (2.3)	0 (0)	3 (9.4)	0 (0)	0 (0)	0 (0)
Pruritus and erythema	2 (4.5)	0 (0)	1 (3.1)	0 (0)	1 (100)	0 (0)
UV-burn	1 (2.3)	0 (0)	4 (12.5)	0 (0)	0 (0)	0 (0)
Pruritus	2 (4.5)	0 (0)	1 (3.1)	0 (0)	0 (0)	0 (0)
Pain	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cutaneous lupus	0 (0)	0 (0)	2 (6.3)	0 (0)	0 (0)	0 (0)
Gastrointestinal symptoms	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Post-inflammatory hypopigmentation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Topical PUVA treatment	6	112	1	0	2	19
Any adverse event	1 (16.7)	15 (13.4)	1 (100)	0 (0)	2 (100)	4 (21.1)
Erythema	1 (16.7)	3 (20)	0 (0)	0 (0)	2 (100)	2 (10.5)
Hyperpigmentation	0 (0)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)
Pruritus and erythema	0 (0)	2 (1.8)	0 (0)	0 (0)	0 (0)	0 (0)
UV-burn	0 (0)	5 (4.5)	0 (0)	0 (0)	0 (0)	2 (10.5)
Pruritus	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pain	0 (0)	2 (1.8)	1 (100)	0 (0)	0 (0)	0 (0)
Cutaneous lupus	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Gastrointestinal symptoms	0 (0)	2 (1.8)	0 (0)	0 (0)	0 (0)	0 (0)
Post-inflammatory hypopigmentation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

[a]$p=0.031$; [b]$p=0.032$.
PUVA: psolaren + ultraviolet A; NBUVB: narrow-band ultraviolet B: UVA: ultraviolet A.
Odds of experiencing adverse event compared with reference category of plaque psoriasis.

Table IV. Causes of treatment discontinuation according to phototherapy modality

Reason for treatment discontinuation	Treatment modality				
	NBUVB (*n* = 966) *n* (%)	Systemic PUVA (*n* = 120) *n* (%)	Topical PUVA (*n* = 143) *n* (%)	UVA (*n* = 27) *n* (%)	Total *n* (%)
Patient's decision	91 (9.4)	6 (5)	11 (7.7)	4 (14.8)	112 (8.9)
Adverse event	20 (2.1)	18 (15)	13 (9.1)	0 (0)	51 (4.1)
Lack of efficacy	36 (3.7)	9 (7.5)	8 (5.6)	0 (0)	53 (4.2)
Total	147 (15.2)	33 (27.5)	32 (22.4)	4 (14.8)	216

NBUVB: narrow-band ultraviolet B; PUVA: psolaren + ultraviolet A UVA: ultraviolet A.

tinuations and 4.1% of treatments given). Causes of treatment interruption according to treatment modality are shown in **Table IV**. Of the 240 patients with AEs, 51 (21.3%) discontinued treatment for that reason. **Table V** shows the factors related to treatment discontinuation and to treatment discontinuation due to AEs. Patients who stopped treatment due to AEs were older ($p = 0.01$) than those who continued. No sex-related differences were observed.

Compared with NBUVB, patients treated with systemic PUVA were at higher risk for interruption of phototherapy treatment for any reason (OR 2.1; 95% CI 1.4, 3.3) and due to AEs (OR 8.3, 95% CI 4.2, 16.2). Topical PUVA also conferred a higher risk of all-cause discontinuation (OR 1.6, 95% CI 1.1, 2.5) and discontinuation due to AEs (OR 4.7, 95% CI 2.3, 9.7).

According to the dermatosis requiring treatment, rates of all-cause treatment discontinuation were higher for atopic dermatitis (OR 2.4, 95% CI 1.3, 4.4), hand eczema (OR 2.7, 95% CI 1.1, 6.8) and pityriasis lichenoides (OR 4.1, 95% CI 1.4, 11.9) than for plaque psoriasis. Patients were more likely to discontinue treatment due to an AE if they had a diagnosis of palmoplantar psoriasis (OR 3.6, 95% CI 1.6, 8.3), hand eczema (OR 7.8, 95% CI 2.1, 29.1), pityriasis lichenoides (OR 7.8, 95% CI 1.6, 37.7) and mycosis fungoides (OR 9.6, 95% CI 4.3, 21.4).

All patients who developed phototoxic reactions ($n = 17$) or lupus erythematous ($n = 4$) discontinued due to the AE, while there were no discontinuations due to pigmentation alterations. According to the type of AE and compared with erythema, pruritus plus erythema resulted in a higher frequency of treatment discontinuation due to an AE (OR 4.1; CI 95% 1.5, 11.2), as did pain (OR 10.3; 95% CI 1.6, 67.1).

Table V. Factors related to adverse events prompting treatment discontinuation

Variables	Treatment discontinuation for any reason *n*/N (%)	Treatment discontinuation due to adverse event *n*/N (%)	OR (95% CI) for discontinuation due to AE	*p*-value
Sex				
Male	102/552 (18.5)	22/552 (4.0)	NS	NS
Female	114/704 (16.2)	29/704 (4.1)	NS	NS
Age, years, median (IQR)	44 (29–56)	54 (34–60)	–	0.01[a]
Skin type				
I	1/4 (25.0)	0 /4 (0)	NS	NS
II	61/387 (15.8)	21/387 (5.4)	NS	NS
III	122/695 (17.6)	24 /695 (3.5)	NS	NS
IV	30/154 (19.5)	5/154 (3.2)	NS	NS
V and VI	2/11 (18.2)	1/11 (9.1)	NS	NS
Phototherapy modality				
NBUVB	147/965 (15.2)	20/965 (2.1)	1	
Topical PUVA	22/143 (15.4)[b]	13/143 (9.1)	4.7 (2.3, 9.7)	< 0.001
Systemic PUVA	33/120 (27.5)[c]	18/120 (15.0)	8.3 (4.2, 16.2)	< 0.001
UVA	4/27 (14.8)	0 (0)	NS	NS
Adverse event				
Erythema	–	14/111 (12.6)	–	–
Hyperpigmentation	–	0/56 (0)	–	–
Pruritus and erythema	–	9/24 (41.6)	4.1, (1.5, 11.2)	0.006
UV-burn	–	17/17 (100)	–	–
Pruritus	–	2/16 (12.5)	–	–
Pain	–	3/5 (60.0)	10.3 (1.6, 67.1)	0.015
Cutaneous lupus	–	4/4 (100)	–	–
Gastrointestinal symptoms	–	2/4 (50.0)	–	–
Post-inflammatory hypopigmentation	–	0/3 (0)	–	–
Dermatosis				
Plaque psoriasis	127/815 (15.6)	17/815 (2.1)	1	
Palmoplantar psoriasis	25/126 (19.8)	9/126 (7.1)	3.6 (1.6, 8.3)	0.002
Mycosis fungoides	15/65 (23.1)	11/65 (16.9)	9.6 (4.3, 21.4)	< 0.001
Guttate soriasis	1/35 (2.9)	0 (0)	NS	NS
Atopic dermatitis	17/55 (30.9)[d]	3/55 (5.5)	NS	NS
Hand eczema	7/21 (33.3)[e]	3/21 (14.3)	7.8 (2.1, 29.1)	0.002
Pityriasis lichenoides	6/16 (37.5)[f]	2/16 (12.5)	7.8 (1.6, 37.7)	0.01
Lymphomatoid papulosis	1/11 (9.1)	1/11 (9.1)	NS	NS

[a]Mann–Whitney test was performed to compare the non-normally variable. Odds of discontinuing treatment for any reason compared with reference categories of NBUVB treatment ([b,c]) or plaque psoriasis ([d–f]): [b]$p = 0.02$; [c]$p = 0.001$; [d]$p = 0.04$; [e]$p = 0.04$; [f]$p = 0.01$.
AE: adverse event; NBUVB: narrow-band ultraviolet B; PUVA: psolaren + ultraviolet A; UVA: ultraviolet A; OR: odds ratio; CI: confidence interval; NS: not significant; IQR: interquartile range.

DISCUSSION

There are few reports about AEs and interruption of phototherapy in clinical practice. In our setting, NBUVB was the main phototherapy modality, accounting for 76.9% of treatments, which is consistent with the most recent clinical guidelines and several national and international publications (14–17). The main dermatosis treated in our phototherapy unit is psoriasis, which is also in line with the existing literature. Phototherapy is a mainstay in psoriasis treatment, with the largest evidence-base and most experience of use for this dermatosis (14, 15).

Our rate of AEs was 19.1%, which is consistent with the previous study by Martin et al. (18). Our results are not fully comparable with other reports, since the studies published include different treatment modalities, regimens, settings, and definitions of AEs, and erythema is not always included in the accounting for AE. Previously reported rates of AEs with phototherapy in clinical practice vary widely, from 0.8% to 94% (14, 15). No differences were observed between the proportion of men and women who had AEs, and there were no significant differences between skin types. Patients who discontinued treatment due to AEs were slightly older.

According to existing literature (18), erythema is the most frequent AE in patients undergoing phototherapy in our region of Spain. In the present study, the rate of AEs was lower for NBUVB than for other therapeutic modalities. This coincides with a study by Chen et al. (19), who reported that NBUVB was associated with a 30% lower risk for AEs than PUVA. In our study, the rate of AEs in patients receiving PUVA therapy is within the range reported in the literature (1.3–72%), but lower than in other series that probably collected data for higher cumulative doses or longer treatments (18, 20–23).

A low rate of AEs was found in patients with palmoplantar psoriasis. In a previous series by Carrascosa et al., this rate was slightly higher, reaching 25% (24). The differences found in our study by type of psoriasis, guttate psoriasis being the one with the highest frequency of erythema (17.1%) and palmoplantar psoriasis the one with the lowest rate of AEs (11.9%), are likely to be due to the whole body being treated with NBUVB compared with hands and feet with topical PUVA. That said, patients with mycosis fungoides had the highest rate of AEs across all treatment modalities. In cases receiving systemic PUVA phototherapy, the rate of AEs in patients with mycosis fungoides was significantly higher than in another dermatosis. Physicians might thus consider increasing the dose only with caution and intensifying monitoring in patients with mycosis fungoides, especially if treated with systemic PUVA, in order to detect AEs early and address them appropriately.

Phototherapy withdrawal rates have been reported as various values, from 0% to 32% (20, 25). Schiener et al. (26) reported a discontinuation rate of NBUVB treatment of 24%; Dawe et al. (27), 32%; and Sapam et al. (21), 3.6%. These figures are in agreement with our study, with a withdrawal rate of 17.2%. Topical and systemic PUVA had higher rates of all-cause and AE-related discontinuation. The profile of AEs we observed in these treatment modalities (pain, gastrointestinal symptoms, and phototoxic reactions) could be more poorly tolerated than the AEs observed for other treatment modalities, leading to more discontinuations than in NBUVB.

Our results showed that the main reason for treatment discontinuation (8.9% of all treatments administered) was patients' non-appearance due to work, personal or unknown reasons. These findings are in accordance with those found in the literature, with work-related absences reported in 9.6% of patients in the study by Dawe et al. (27). We observed the highest rates of treatment disruption for atopic dermatitis, hand eczema and pityriasis lichenoides. In the case of atopic dermatitis, treatment interruption was due mainly to personal or unknown reasons. Implementing strategies to encourage therapeutic adherence in patients with this dermatosis could decrease treatment interruptions and help achieve therapeutic goals.

Patients with palmoplantar psoriasis, mycosis fungoides, hand eczema and pityriasis lichenoides had higher rates of treatment interruption due to AEs. Thus, providing more information to patients with these risk factors for AEs, as well as intensifying monitoring and control in these groups, could help prevent and quickly manage the AEs, favouring completion of the treatment regimen.

Study limitations

This study has some limitations. First, it is an observational study performed in a single centre, in a setting with a high number of hours of solar exposure, which could limit the generalization of the results. Secondly, the low frequency of some dermatoses may preclude conclusions related to dermatoses-related AEs. Thirdly, some patients discontinued treatment for unknown reasons, which could reflect an underestimation of the rate of AEs.

Conclusion

This study reports the rates of treatment interruption and prevalence of AEs in patients receiving phototherapy in a clinical practice setting. Erythema was the most frequent AE observed. There are numerous variables that can influence treatment discontinuation, many of them unrelated to the safety of phototherapy. The results showed that 4.1% of phototherapy treatment regimens were interrupted due to AEs. Patients treated with systemic and topical PUVA, and patients with mycosis fungoides if treated with systemic PUVA, were more likely to have AEs and to interrupt treatment because of them. Physicians should thus consider increasing the

dose only with caution and intensifying monitoring in patients with these risk factors, in order to detect AEs early and address them appropriately.

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