Phototherapy and photochemotherapy for polymorphic light eruption desensitisation

Aslam, A.; Fullerton, L.; Ibbotson, S. H.

Published in:
Photodermatology, Photoimmunology & Photomedicine

DOI:
10.1111/phpp.12310

Publication date:
2017

Document Version
Peer reviewed version

Phototherapy and photochemotherapy for polymorphic light eruption desensitisation

Aslam, A.; Fullerton, L.; Ibbotson, Sally

Published in:
Photodermatology, Photoimmunology & Photomedicine

DOI:
10.1111/phpp.12310

Publication date:
2017

Document Version
Peer reviewed version

Letter to the Editor

Phototherapy and photochemotherapy for polymorphic light eruption desensitisation: a five year case series review from a university teaching hospital

Aslam A[1,2], Fullerton L[1] and Ibbotson SH[1]

[1]Photobiology Unit, University Department of Dermatology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK

[2]Dermatology Department, St Helens and Knowsley Teaching Hospitals NHS Trust, Marshalls Cross Road, St Helens, UK, WA9 3DA

Corresponding author email: s.h.ibbotson@dundee.ac.uk

Key words

Phototherapy

Polymorphic light eruption

Desensitisation

UVB

Dear Editor

Polymorphic light eruption (PLE) is the most common immunological photodermatosis, with a prevalence of 18% in Europe[1]. The pathogenesis of PLE appears to involve delayed cell mediated hypersensitivity and aberrant Langerhans cell function[2,3]. Phototherapy, using narrowband UVB (UVB) or psoralen-ultraviolet A (PUVA) photochemotherapy, is widely used for prophylactic desensitisation in PLE, with benefit experienced in 90% of patients[4,5]. The mechanism of desensitisation is poorly understood but that stratum corneum thickening, induction of immunomodulatory cytokines and changes in Langerhans cells and dermal mast cells may be implicated.[6,7]

We describe five years' experience (2008-2013) of phototherapeutic desensitisation for PLE. Patients with suspected photosensitivity (n=1475) referred to the Scottish Photobiology Service, based at the Photobiology Unit, Ninewells Hospital and Medical School, Dundee, underwent investigations (including monochromator phototesting across the solar spectrum, UVA provocation testing, narrowband UVB minimal erythema dose (MED) testing and lupus serology). Of these 1475 patients, 370 (25%) were diagnosed with PLE. Of these 370 patients, phototherapeutic desensitisation was offered to 109 and local Tayside case notes were available for review in 79 of these patients (76 UVB and 3 UVA1). Treatment numbers, occurrence of provoked PLE, and response, as defined by use of repeat treatment courses in subsequent years, were recorded.

The standard regimens used were:

Narrowband UVB phototherapy (or UVA1) three times a week (50% MED starting dose and 20% dose increments each treatment, unless erythema or PLE induced, in which case increments were reduced to 10% after erythema or PLE settled) for 15 treatments; PUVA (oral 8-methoxypsoralen 25mg/m^2) twice-weekly for 15 treatments (70% minimal phototoxic dose (MPD) starting dose and 40%, reducing to 20% if erythema or PLE, dose increments at each treatment). If PLE was provoked,

topical betamethasone valerate 0.1% ointment/cream was prescribed and treatment adjusted as described above.

For the first course of desensitisation 46 patients (59%) received photo-exposed site treatment and 32 (41%) received whole body exposure (data missing for one patient). Following each treatment course patients were encouraged to cautiously seek top-up sunlight exposure to maintain desensitisation. Patients were followed up in autumn and, if deemed successful, the treatment was repeated yearly in spring. For patients who failed to obtain adequate desensitisation after two consecutive years of UVB, PUVA was offered.

Of the 79 patients with PLE who underwent desensitisation, 67 were female; 12 male (median age 41 (range 12-69) years). Fitzpatrick skin phototypes were: I (n=18), II (n=42), III (n=16) and IV (n=3). Twenty eight patients had been investigated using monochromator phototesting, with normal responses in 27 (96%). The patient with abnormal responses showed borderline UVA and visible light photosensitivity. Eight of the 15 patients (53%) who underwent provocation testing had abnormal erythemal and/or papular broadband UVA reactions.

Seventy six patients (96%) received narrowband UVB. The median UVB MED was 0.147 (range 0.048-0.4) J/cm^2. The median starting dose was 0.07 (range 0.02-0.2) J/cm^2.

Of those patients who received UVB phototherapy: 52 (68%) completed 15 treatments; 11 (14%) received 10 to 14 treatments; 7 (9%) had less than 10 treatments and 6 (8%) received more than 15 exposures (median 15 range (1-33) (Figure 1). Of those who did not complete 15 treatments: 1 patient stopped after the first treatment as it provoked severe PLE, 1 patient stopped as she was diagnosed with chronic fatigue, 3 patients failed to attend (data missing for 2). Those who underwent 10 – 14 treatments deemed this to be satisfactory and did not complete 15 sessions. The maximum number of treatments was 33, in a patient with co-existing chronic idiopathic urticaria. Of the 58 patients (76%) who completed 15 or more treatments, 37 (64%) had a second course the

following year. Sixteen patients (28%) had three or more UVB courses in this five-year period (Figure 2). Thus, 53 of the 58 patients (91%) who completed at least 15 treatments had a successful treatment outcome, as defined by going on to have further courses in subsequent years, indicative of efficacy and suitability of treatment.

Four of the patients who received UVB went on to have either PUVA (n=2) or UVA1 (n=2) after failing to respond to two consecutive annual courses of UVB. Of these, two patients successfully received PUVA for two consecutive years and one of the patients who received UVA1 went on to have a second course the following year (Figure 2).

Three patients underwent a primary course of UVA1 desensitisation, having failed UVB phototherapy in previous years: all 3 completed 15 or more treatments and subsequent treatment courses were planned for the following year for all three patients (Figure 1).

Of the 79 patients who underwent desensitisation 44, (56%) had provoked PLE during treatment and one patient receiving UVB developed herpes simplex labialis. PLE induction was most likely to occur at treatment eight (median 8 (range 1-14)). The increments were reduced to 10% for all patients who developed PLE and 22 (50%) required a topical corticosteroid. Systemic steroids were not required. Of the eight patients who had a positive abnormal erythemal and/or papular reaction on UVA provocation testing, 7 (88%) had PLE induced during treatment, whereas of the 7 who had a negative provocation test, only 3 developed PLE during treatment; (50%; data missing from one).

Discussion

We have confirmed that phototherapeutic desensitisation can be effective for PLE. In a randomized, controlled comparative study of narrowband UVB with PUVA in 25 patients with PLE, equivalent efficacy was shown[4]. However, UVB is almost invariably the treatment of choice, given the need for psoralen and proven photocarcinogenic risk with PUVA and the lack of reported cancer risk with UVB to date[8]. Certainly, in our study 96% of patients received narrowband UVB.

Although PLE is commonly provoked during treatment (56% in this case series), our review suggests this occurs most commonly at the eighth treatment session which can thus help to plan ahead and advise patients accordingly. It is not known whether prophylactic use of topical corticosteroid during week three of treatment may limit the frequency of this adverse effect. Indeed, further studies are warranted to investigate this or the role of other potential suppressive therapies, such as Polypodium Leucotomas. Treatment is usually well tolerated and patients are able to complete a treatment course, with dose increment reductions and topical corticosteroid use. In our experience, those patients who, on investigation, had PLE induced on UVA provocation testing, are most at risk of developing PLE during treatment. Of the patients with abnormal erythemal and/or papular broadband UVA provocation test site reactions, 88% had provocation of PLE during treatment, indicating that if this investigation is positive then patients can be advised that it is very likely that they will develop PLE during desensitisation therapy. The patients that we included in this review were those who had been referred to the SPS and, as such, represent the more severe/most troublesome end of the spectrum of PLE, as only the minority of patients with PLE will be formally phototested. However, with this caveat, the group of patients with positive photoprovocation tests would be the most suitable to target with adjuvant prophylactic or concurrent topical glucocorticoid or other suppressive therapy and, as highlighted above, this merits further study.

Most patients received treatment to photo-exposed sites only (59%), and although PLE was provoked in 56% of patients during desensitisation, this figure may have been higher if whole body irradiation had been used in all patients[5].

The photoprotective effects of UVA and PUVA are temporary and need to be repeated. Fifty-eight patients completed fifteen or more UVB treatments (76%) and, as defined by going on to repeat treatment courses in subsequent years, 91% of these subjects found treatment to be effective, with no apparent loss of efficacy with subsequent courses. We commonly advise patients who have had three or four years of successful desensitisation to try a year without treatment.

Our review demonstrates that phototherapeutic desensitisation for PLE, predominantly with UVB, is safe, generally well tolerated and effective. These data provide us with practical information and guidance with respect to risk of PLE induction during a treatment course and the most likely time for this to develop, which is informative for patients embarking on desensitisation phototherapy.

References

1 Rhodes LE, Bock M, Janssens AS *et al.* Polymorphic Light Eruption Occurs in 18% of Europeans and Does Not Show Higher Prevalence with Increasing Latitude: Multicenter Survey of 6,895 Individuals Residing from the Mediterranean to Scandinavia. *J Invest Dermatol.* 2010; **130**: 626-8.

2 Palmer RA, Friedmann PS. Ultraviolet radiation causes less immunosuppression in patients with polymorphic light eruption than in controls. *J Invest Dermatol.* 2004; **122**: 291-4.

3 Wolf P, Byrne SN, Gruber-Wackernagel A. New insights into the mechanisms of polymorphic light eruption: resistance to ultraviolet radiation-induced immune suppression as an aetiological factor. *Exp. Dermatol.* 2009; **18**: 350-6.

4 Bilsland D, George SA, Gibbs NK *et al.* A comparison of narrow-band phototherapy (TL-01) and photchemotherapy (PUVA) in the management of polymorphic light eruption. *Br J Dermatol* 1993; **129**: 708-12.

5 Man I, Dawe RS, Ferguson J. Artificial hardening for polymorphic light eruption: Practical points from ten years' experience. *Photoderm Photoimmun Photomed* 1999; **15**: 96-9.

6 Wolf P, Gruber-Wackernagel A, Rinner B *et al.* Phototherapeutic hardening modulates systemic cytokine levels in patients with polymorphic light eruption. *Photochem. Photobiol. Sci.* 2013; **12**: 166-73.

7 Wolf P, Gruber-Wackernagel A, Bambach I *et al.* Photohardening of polymorphic light eruption patients decreases baseline epidermal Langerhans cell density while increasing mast cell numbers in the papillary dermis. *Exp. Dermatol.* 2014; **23**: 428-30.

8 Hearn RMR, Kerr AC, Rahim KF *et al.* Incidence of skin cancers in 3867 patients treated with narrow-band ultraviolet B phototherapy. *Br J Dermatol* 2008; **159**: 931-5.

Figure 1

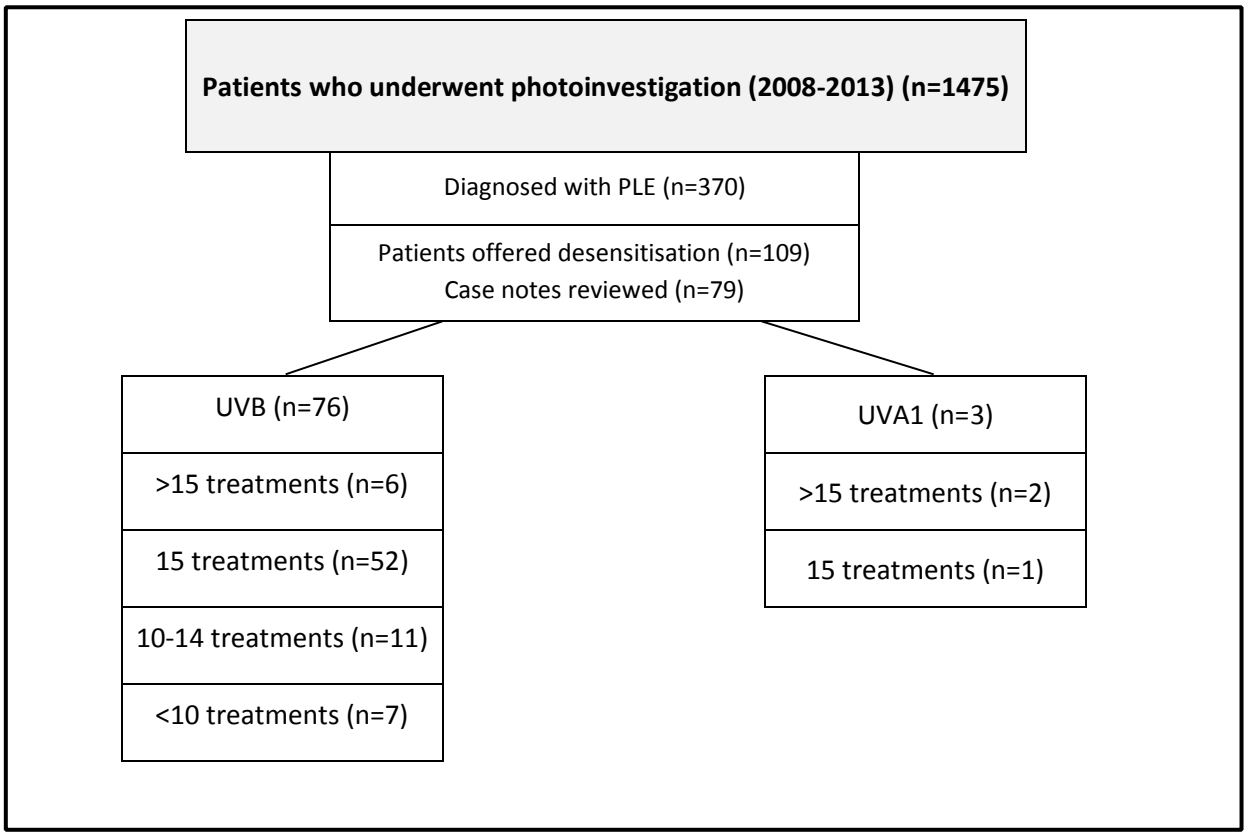
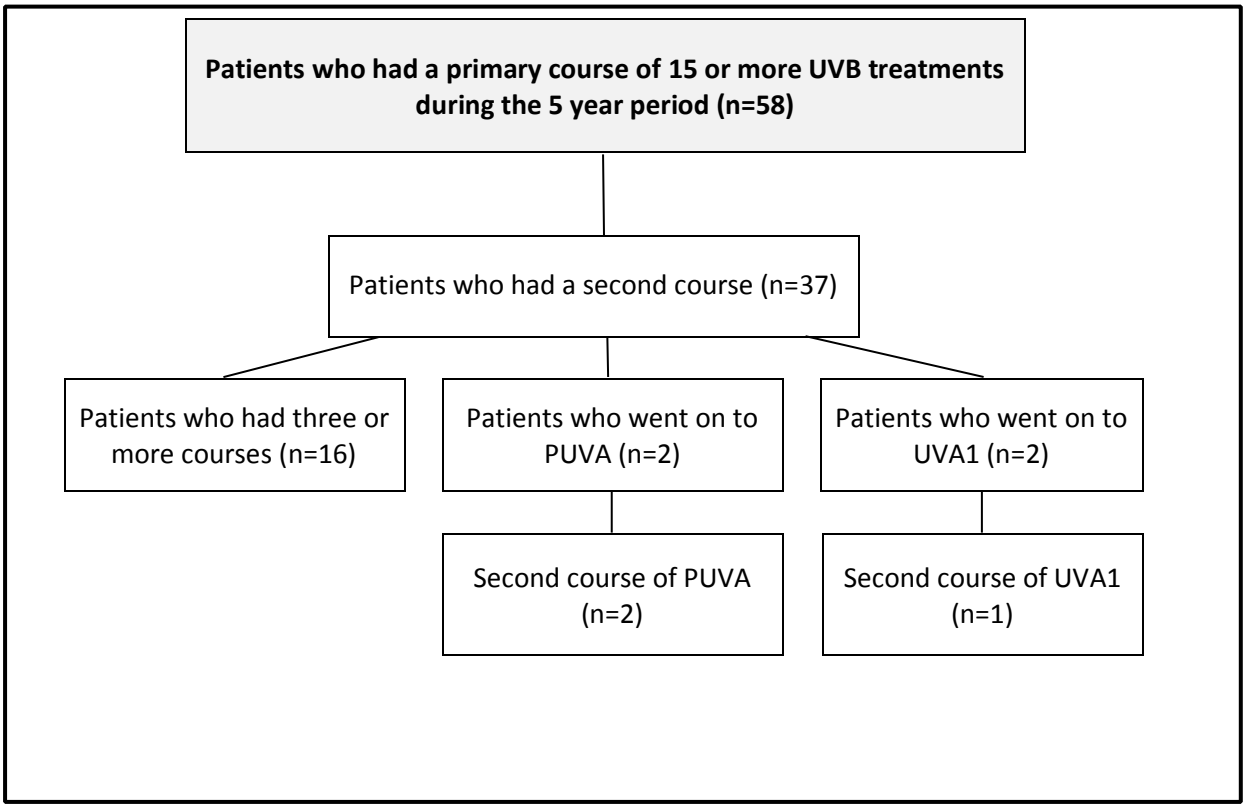

Patients who underwent photoinvestigation (2008-2013) (n=1475)
Diagnosed with PLE (n=370)
Patients offered desensitisation (n=109)
Case notes reviewed (n=79)
UVB (n=76)
>15 treatments (n=6)
15 treatments (n=52)
10-14 treatments (n=11)
<10 treatments (n=7)
UVA1 (n=3)
>15 treatments (n=2)
15 treatments (n=1)

Figure 2


Patients who had a primary course of 15 or more UVB treatments during the 5 year period (n=58)
Patients who had a second course (n=37)
Patients who had three or more courses (n=16)
Patients who went on to PUVA (n=2)
Patients who went on to UVA1 (n=2)
Second course of PUVA (n=2)
Second course of UVA1 (n=1)

Legends

Figure 1. Flowchart showing the number of patients undergoing the different desensitisation modalities

Figure 2. Flowchart showing the subsequent treatment course after a primary course of UVB (15 or more treatments)