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Efficacy of the pulsed dye laser in the treatment of localized recalcitrant plaque psoriasis: a comparative study

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Conflicts of interest
None declared.

Summary

Background Localized chronic plaque psoriasis, resistant to local therapy, may be very hard to treat. The treatment of these lesions with a pulsed dye laser (PDL) has been described before, but a comparative study between the PDL and a potent topical treatment has never been performed.

Objectives To compare the efficacy of the PDL in the treatment of localized, recalcitrant plaque psoriasis with a potent topical therapy, using calcipotriol/betamethasone dipropionate (Dovobet®) as an active comparator.

Methods Eight patients with psoriasis were treated with both PDL (585 nm) and calcipotriol/betamethasone dipropionate in an open, intrapatient, left–right comparison. A plaque severity score (sum score) and photographs were used to document the course of therapy. Patients reported pain on a visual analogue scale.

Results Both treatments were well tolerated, although one patient left the study due to post-PDL treatment pain. A significant difference in the sum score 12 weeks after treatment was seen in favour of the PDL (62% vs. 19% reduction; $P < 0{\cdot}05$). Scores for erythema declined significantly at week 12 in both the PDL and the calcipotriol/betamethasone dipropionate group ($P < 0{\cdot}001$). Induration and desquamation scores were significantly reduced at week 12 in the PDL group, without a statistically significant reduction in calcipotriol/betamethasone-treated lesions. The pain scores declined with progressive PDL treatments, although not statistically significantly.

Conclusions PDL treatment might be considered for the treatment of localized, recalcitrant plaque psoriasis, when other topical therapies have failed.

So far, no consensus exists on the position of the pulsed dye laser (PDL) in the treatment of psoriasis. Multiple previous studies have shown different results, ranging from complete remission to no improvement at all.[1–7] It is difficult to compare the results of these studies, because they all used different treatment modalities. The number of treatments varied from only one treatment up to five. There was also a wide variation in laser parameters such as spot size (diameter 5–7 mm), energy fluence (2–9 J cm^{-2}) and pulse duration (0·2–1·5 ms). There are no studies comparing PDL treatment with other well-known treatments for psoriasis.

In plaque psoriasis, the first comparative study was done by Zelickson *et al.*[4] They compared two different pulse durations of PDL treatment with each other, using fluences varying between 7·5 and 8·5 J cm^{-2}, and with triamcinolone acetonide 0·1% ointment twice daily for 10 weeks. Using global scores, they found a statistically significant clinical improvement of the PDL-treated site, compared with the triamcinolone-treated site. Bjerring *et al.* compared the PDL (0·2 ms, 2–7 J cm^{-2}) with dermabrasion.[6] Dermabrasion gave complete remission in five of six patients, whereas such improvement was reached in only three of 11 patients treated with PDL.

Neither dermabrasion nor triamcinolone acetonide 0·1% ointment, however, are standard treatments for psoriasis. The latter is regarded as a relatively mild corticosteroid for the treatment of psoriasis. There are no comparative studies between PDL and first-line topical treatments of psoriasis. Because PDL treatment is time consuming, expensive and painful, it is not a first-choice treatment for psoriasis. In chronic, localized, therapy-resistant plaque psoriasis, however, PDL treatment might provide an adequate solution.[8,9]

In order to examine the position of the PDL in the treatment of localized recalcitrant plaque psoriasis, we compared its clinical efficacy and tolerability with an active comparator: calcipotriol 50 μg g^{-1} and betamethasone dipropionate 0·5 mg g^{-1} ointment (CB) (Daivobet®/Dovobet®; Leo Pharma, Ballerup,

Denmark). This two-compound product is a highly effective treatment for psoriasis. Clinical studies have demonstrated that up to 4 weeks of treatment with CB once daily gives superior efficacy and similar or better tolerability than once or twice daily application of its individual components.[10–13]

In a left–right comparison, patients with recalcitrant psoriasis were treated with both CB and the PDL. CB treatment was given for a period of 4 weeks. The number of PDL treatments varied between one and three, with a 2-week interval between treatments.

Materials and methods

Patients

Eight patients aged at least 18 years with stable, symmetrical, recalcitrant plaque psoriasis were included in the study. Recalcitrant psoriasis was defined as: 'not responding to any topical therapy (ointments and creams), including ultrapotent corticosteroids and vitamin D_3 derivatives and combination products or combination therapy with more than one topical treatment'. Patients were excluded if they had received systemic antipsoriatic agents within 8 weeks prior to the study, or phototherapy [psoralen plus ultraviolet (UV) A or UVB] within 4 weeks prior to the start of the study. Patients had used no topical treatment for at least 2 weeks. Other exclusion criteria were pregnancy, lactation and a history of photosensitivity. This study was approved by the medical ethics committee. Written informed consent was obtained from all patients.

Study design

Two weeks before the start of treatment, 10% salicylic acid in white vaseline was prescribed for 2 weeks in order to standardize and optimize the pretreatment situation for both topical treatment and laser treatment. It is particularly necessary to minimize scaling before PDL treatment. At the initial visit, two similar, contralateral psoriatic lesions of at least 12 cm^2 were selected. These plaques were similar in terms of body localization and clinical severity score. One of the plaques was treated with CB once daily, for a period of 4 weeks. The contralateral lesion was treated with the PDL (Photogenica V laser; Cynosure, Chelmsfort, CA, U.S.A.) at the initial visit and after 2 and 4 weeks. A pulse duration of 0·45 ms with a wavelength of 585 nm was constantly used. Comparing all previous studies with different fluences, spot sizes and time intervals between two treatments, the best results were achieved with a fluence of 8·5 J cm^{-2}, a spot size with a diameter of 5 mm and a treatment interval of 2 weeks. In order to compare these findings with our own experience, a psoriatic plaque of a patient not included in our study was treated with four different fluences: 5·5, 6·5, 7·5 and 8·5 J cm^{-2}. One month after PDL treatment, pictures were taken of the treated area and complete clearance was noticed at the site treated with 8·5 J cm^{-2} (Fig. 1). We therefore used an energy fluence of 8·5 J cm^{-2} and a spot size of 5 mm in all patients and during all three treatments. The area treated with laser had an overlap of 10–20% per shot. Prior to the PDL treatment, arachis oil was applied on the psoriatic plaques, in order to reduce the amount of scattering. Local anaesthesia was given during and shortly after the laser treatment, using a cooling device (Cryo 5 cooling device; Zimmer Elektromedizin, Neu-Ulm, Germany).

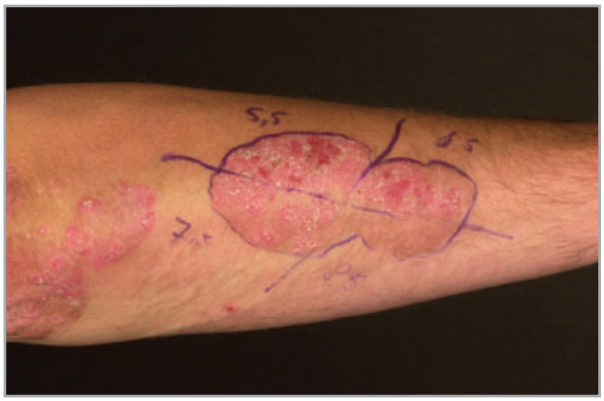

Fig 1. Clinical photograph of a psoriatic plaque treated with 5·5, 6·5, 7·5 and 8·5 J cm^{-2} in four quadrants, when determining the fluence used in the present study (8·5 J cm^{-2}).

After the 4 weeks of treatment with both PDL and CB, patients entered the follow-up period of 8 weeks. If the PDL-treated plaque showed residual crusting at the planned second and third visits, PDL treatment was postponed for 1 week, until the crusting had resolved, for safety and to optimize efficacy. Clinical efficacy was scored at baseline, and after 4 and 12 weeks. Adverse events were recorded and patients reported pain on a visual analogue scale (VAS).

Clinical assessments

At every visit photographs of the two target plaques were taken and sum scores were assessed. The sum score is a cumulative measure which includes scores for erythema, induration (plaque thickness) and scaling on the following scale: 0, absent; 1, minimal (very light pink, hardly any elevation, rare scale); 2, mild (light red/pink, slight elevation, poorly defined scale); 3, moderate (red, moderate elevation, defined scales); 4, severe (very red, marked ridge, heavy scaling). Finally, a global sum score (range 0–12) was defined as the sum of all three scores together, reflecting plaque severity.

VAS scores (range 0–10) were used to measure the level of pain during treatment. A score of 0 represented a total absence of pain and 10 represented maximum pain. Patients reported these scores after PDL treatment.

Statistical analysis

All analyses were carried out using Statistica® statistical software, version 6·0 (StatSoft, Tulsa, OK, U.S.A.). To compare sum scores between different moments in time during

Patient	Number of PDL sessions	Residual crusting	Postponed 1 week?	Remarks
1	3	No	No	Excellent response; hyperpigmentation
2	3	No	No	Excellent response; hyperpigmentation
3	3	No	No	–
4	1	No	No	Dropped out due to pain, data not analysed
5	3	Yes	Yes	PDL treatment at weeks 0, 3 and 6; excellent response; hyperpigmentation
6	1	Yes	No	Excellent response; hyperpigmentation
7	3	No	No	–
8	3	Yes	Yes	PDL treatment at weeks 0, 3 and 6

Table 1 Number of pulsed dye laser (PDL) sessions, time span between these sessions, efficacy and drop-out

treatments, we performed two-way analyses of variance. If significant, Duncan's *post hoc* comparison was performed. $P < 0{\cdot}05$ denoted the presence of a statistically significant difference.

Results

Patient population

Eight Caucasian patients, four men and four women, with localized recalcitrant moderate-to-severe symmetrical plaque psoriasis, participated in this investigation. Their mean ± SEM age was 52 ± 10 years, and the mean ± SEM duration of psoriasis was 21 ± 8 years. One patient terminated the trial early due to an adverse event after the first PDL treatment. This patient considered the treatment too painful. Data of this patient were not analysed. A further patient required only one PDL session to achieve an excellent response. Two patients had PDL sessions at weeks 0, 3 and 6 instead of 0, 2 and 4, because of residual crusting (Table 1).

Sum scores during therapy

At baseline, sum scores (mean ± SEM) were 7·6 ± 0·3 in the PDL group and 7·4 ± 0·3 in the CB group. Four weeks after the start of treatment no statistically significant change had been observed, although a tendency to lower sum scores was seen in both groups. Twelve weeks after treatment, however, the sum score declined to 2·9 ± 1·4 in the PDL group ($P = 0{\cdot}001$), whereas in the CB group the sum score dropped only to 6·0 ± 0·7 ($P = 0{\cdot}10$). Figure 2 illustrates these results.

Differences in sum score (mean ± SEM) between the PDL and CB groups were 0·2 ± 0·1, 0·7 ± 0·8 and 3·1 ± 1·6, at weeks 0, 4 and 12, respectively, and in favour of PDL at week 12. The sum score difference at week 12 was statistically significant compared with week 0 ($P = 0{\cdot}04$) and week 4 ($P = 0{\cdot}02$). These results are depicted in Figure 2.

Erythema, induration and desquamation

Four weeks after the start of treatment no statistically significant result was observed for separate erythema, induration and desquamation scores, although a tendency towards lower scores was observed.

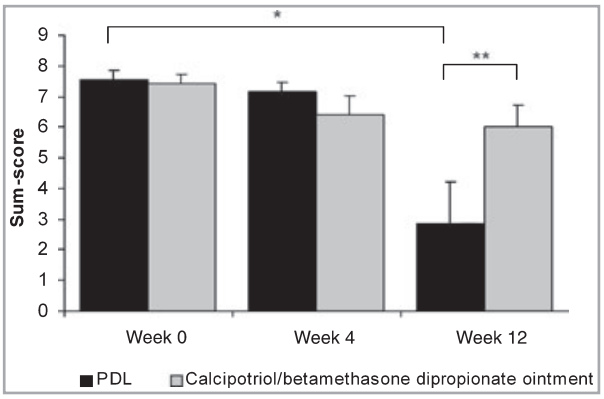

Fig 2. Sum scores (0–12) during pulsed dye laser (PDL) treatment, compared with topical calcipotriol/betamethasone dipropionate ointment therapy (mean ± SEM). Statistical significance: *$P = 0{\cdot}001$; **$P = 0{\cdot}04$.

Scores for erythema declined statistically significantly at week 12 in both the PDL (3·3 ± 0·2 at week 0 to 1·1 ± 0·6 at week 12; $P < 0{\cdot}001$) and the CB groups (3·1 ± 0·1 at week 0 to 2·4 ± 0·2 at week 12; $P < 0{\cdot}01$). Induration and desquamation scores were significantly reduced at week 12 in the PDL group, but not in the CB group (Fig. 3).

Side-effects

Patients reported pain at the treated site as the major side-effect of PDL therapy. The overall pain score (mean ± SEM) on a 0–10 VAS was 6·5 ± 0·4. No correlation was found between pain score and treatment success. Interestingly, pain scores declined from 7·0 ± 0·6 after the first, to 6·7 ± 0·9 and 5·7 ± 0·8 after the second and third PDL sessions, respectively ($P > 0{\cdot}05$). Four patients developed residual hyperpigmentation after the PDL treatment.

Long-term follow-up

After more than 6 months of follow-up, the four patients with a complete response to PDL still had clearance of the

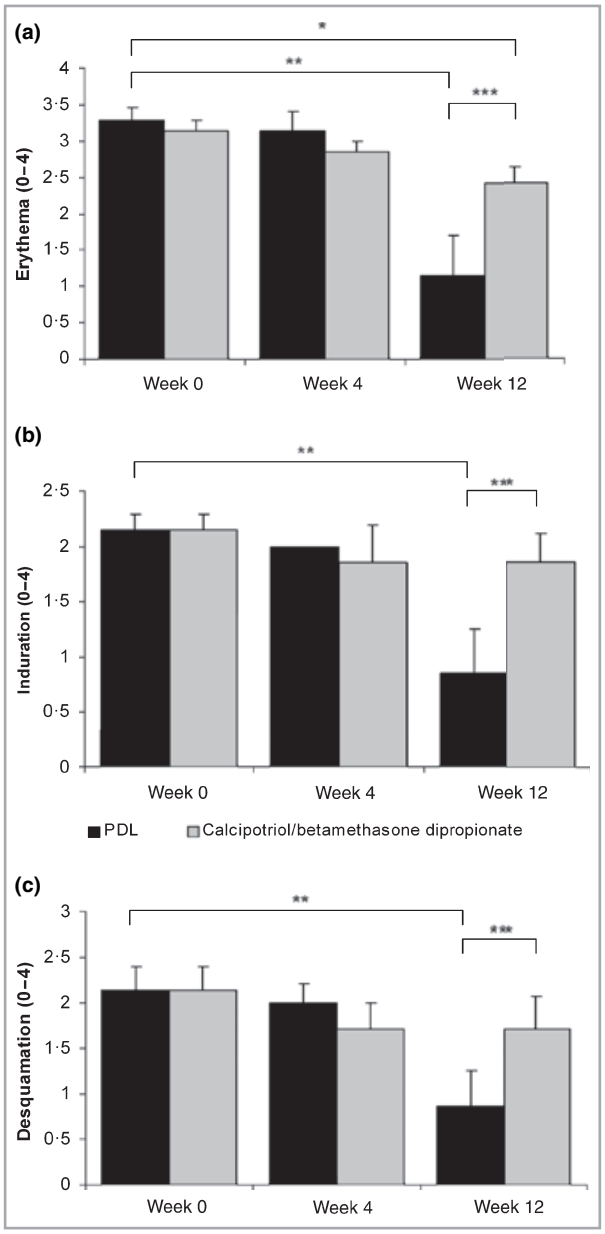

Fig 3. Separate clinical scores (0–4) for the individual components: erythema (a), induration (b) and desquamation (c) (mean ± SEM). Statistical significance: *$P < 0{\cdot}01$; **$P < 0{\cdot}001$; ***$P < 0{\cdot}05$.

treated plaque. Hyperpigmentation was still visible. However, three of these four patients had needed systemic treatment for an exacerbation of their psoriasis, and therefore the follow-up observation on the PDL-treated plaque was no longer reliable.

Discussion

In the present study patients were treated for 4 weeks with the PDL and CB in an open, intrapatient, left–right comparison. After 4 weeks of treatment, no statistically significant result was observed in either treatment. The majority of patients (five out of seven) received their third and last PDL treatment only at week 4; it is thus likely that at week 4 the clinical results of the PDL treatment were not yet apparent. The results after 4 weeks of CB treatment, however, were unexpected. Although a tendency to a decline in sum score was observed, there was no statistically significant improvement of the psoriatic lesions. This is in contrast with earlier studies, in which CB showed good results after 4 weeks of treatment.[10–13] The explanation for this may be that we selected patients with plaque psoriasis that had previously been resistant to potent topical treatments. Secondly, it is possible that patients' compliance may not have been optimal. Although all patients claimed to have applied the ointment once daily, we did not check the residual ointment after the 4 weeks of topical treatment.

In contrast, after 8 weeks of follow-up, at week 12, the sum score had significantly declined further in the PDL group. We also observed a reduction in the CB-treated group, but this decline was not significant. Remarkably, in both groups the score for erythema declined significantly after 12 weeks, whereas induration and desquamation scores declined significantly only in the PDL group.

Four of seven patients reached complete clearance of the psoriatic lesions 8 weeks after the final laser treatment. In these patients, all of whom had skin type I, II or III, there was some degree of hyperpigmentation visible at the treated area. Mild hyperpigmentation was also present in the patients treated with PDL in previous studies.[2–4] Although some studies mentioned other side-effects such as hypopigmentation and atrophic scarring, we did not see these effects in our patients.[3,4] Patients who had complete remission of the PDL-treated plaque had a prolonged remission: after approximately 6 months of extra follow-up there were still no signs of relapse.

There was a tendency towards a decline in the reported pain scores after successive laser treatments, although this was not significant. Pain has also been mentioned in previous studies as a disadvantage of the PDL treatment. By providing local anaesthesia with a cooling device during and shortly after the laser procedure, our patients considered the laser treatment to be reasonably tolerable.

Studies on the efficacy of treating chronic psoriatic plaques with the PDL, compared with a first-line topical therapy for psoriasis, have not previously been performed. Although we noticed a significant improvement in the laser-treated areas at week 12, compared with those treated with the active comparator, the utility of the PDL as a standard therapy for psoriasis is limited. Due to the small spot size and the post-treatment pain, laser treatment has to be restricted to only circumscribed and therapy-resistant psoriatic plaques.

Limitations of the present study include the lack of blinding, the small patient group and the possible poor compliance to topical treatment. Moreover, sum scores might have been influenced by the pretreatment with 10% salicylic acid, which is necessary for PDL treatment on severely scaling plaques. However, pretreatment might also have enhanced the penetration of CB.

In conclusion, PDL treatment might be considered for the treatment of localized, recalcitrant plaque psoriasis, when topical therapies have failed or are contraindicated. The treatment is well tolerated although pain and hyperpigmentation can be experienced. These side-effects were acceptable in most patients.

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