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Clinical Evaluation of Sequential Application of Pulsed Dye Laser with 1064 Neodymium: Yttrium-Aluminum-Garnet Laser in the Treatment of Psoriasis

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Abstract
Background: *Angiogenesis has a crucial role in the pathogenesis and the maintenance of psoriasis. Dilated tortuous blood vessels can be acted upon by vascular lasers according to the principle of Anderson and Parrish.*
Objective: *The goal of this study was to evaluate the efficacy of the sequential application of pulsed dye laser (PDL) with Nd: YAG laser in the treatment of plaque psoriasis.*
Design: *This was a prospective clinical trial with a three-month follow-up.*
Patients and Methods: *Thirty three patients with chronic and stable plaque type psoriasis were included in this study. Patients received 7 sequential PDL + Nd: YAG laser treatments at two weeks intervals.*
Intervention: *Intervention included the application of seven sequential PDL and Nd: YAG laser treatments at two weeks intervals.*
Outcome Assessment: *Evaluation of clinical improvement by examination and photography.*
Results: *All patients showed a significant decrease in modified Psoriasis Area and Severity Index (m PASI) score.*
Conclusion: *Combined PDL + Nd: YAG presents a new therapeutic option for the treatment of plaque psoriasis.*
Keywords: *Angiogenesis, Cynosure, Nd: YAG, psoriasis vulgaris, Pulsed Dye Laser.*
Abbreviations: *L40: international classification of disease (ICD-10), Nd: YAG: Neodymium: Yttrium - Aluminum- Garnet, PDL: Pulsed Dye Laser, VEGFR; Vascular endothelial growth factor receptor.*

Psoriasis is the most prevalent chronic autoimmune skin disease affecting about 2% - 5% of the world. [1] Psoriasis vulgaris or plaque psoriasis (L40.0) represents about 90% of psoriatics. It starts as red macules or papules that extend peripherally forming red scaly plaques. Any part of the body can be affected but plaques are usually distributed symmetrically over elbows and knees. [2] .Because psoriasis is a chronic relapsing disease, many therapeutic options are available. These include topical treatments, systemic treatments, phototherapy, biologics and lasers. [3, 4].

Patients and Methods

Patients and lesions

After approval of the research ethical committee of laser institute, Cairo University, this study was performed between October 2012 and April 2013. Fourteen females and nineteen males with chronic stable psoriasis vulgaris were enrolled in this study. They were all diagnosed clinically. They had a mean age of 36±9.7 years. Patients included in this research are those with no history of keloids or hypertrophic scar, photosensitivity and seizure disorders. Pregnant and lactating females as well as patients treated during the two months prior to the study were excluded. Every patient served as his own control. Nothing was applied during the treatment period to the control psoriatic lesions. A written informed consent was signed by each patient before initiation of the sessions. Pre and post treatment clinical assessment was performed by using the modified PASI score (Table 2). Percentage of change in the m PASI score from the starting point to the end of the sessions was calculated. Follow up for three months after the last session was carried on and the m PASI score at the end of the follow up period was assessed. Pre and post treatment photographs were taken to assess clinical response to treatment. Number and percentage of completely cleared plaques at the end of the treatment period as well as at the end of the follow up period were assessed. Number of laser sessions achieving clearance, time elapsed before relapse, frequency of side effects were considered as secondary outcome measures.

Treatment Strategy

After estimation of m PASI and xylocaine cream application, each patient received seven sessions with two weeks intervals of combined PDL and Nd: YAG using the cynergy laser. It is manufactured by Cynosure in MA, USA. Multiplex laser parameters used were about 7 J/cm^2, 2 msec pulse duration for PDL followed after a long delay by Nd: YAG with about 35 j/cm^2 and 15 msec pulse duration and the spot size was 10 mm in diameter (Table 1).Using a hand piece held perpendicular to the skin, contiguous non overlapping pulses were delivered with concurrent air cooling which was supplied by Cynosure's Smart Cool device. An antibiotic ointment was applied to the lased plaques twice a day for five days after each session (Fusidic acid, Leo).

Results

Of the thirty three patients, a total of thirty patients completed the study. Most patients were of skin phototype *IV* (twenty one) while the rest (nine) were of type Ⅲ. All patients were evaluated before the start of sessions, every four weeks and three months after the last sessions. Clinical assessment was performed by using the modified PASI score (Table 2, 3). Photographs were taken before and after treatment (Figures1&2). Comparison of the baseline score with that of the fourteenth week revealed a significant decrease with a p-value less than 0.001. Percentage of improvement was 76.77%. Mean improvement of m PASI score was greater in multiplex than in control plaques ($p< 0.001$). Collectively in all patients, eight plaques (26.6%) showed complete clinical response especially at the elbows after a mean of five sessions.

Side effects

They were slight in the form of mild burning sensation or mild pain during the sessions (two). Some patients (four) exhibited moderate post-inflammatory hyperpigmentation which were treated by a bleacher for two months following the sessions.

Follow –up

All patients were followed up for three months. Modified PASI scores were estimated by the end of the follow-up period and compared with the baseline scores (Table 3). Expansion of the lesions occurred after a mean of 1.35 months and the mean m PASI was less than the initial one but without significant difference. Follow up of the completely cured plaques showed no relapse of the lesions.

TABLE 1. Multiplex parameters.

	PDL	Nd: YAG
wavelength	585nm	1064nm
spot size	10mm	10 mm
Fluence	6-10 J/cm^2	30-40 J/cm^2
Pulse duration	2 msec	15 msec

TABLE 2. Mean modified psoriasis Area and Severity index score.

skin sign	Erythema	Induration	scales	Total score
lesions score	0-4	0-4	0-4	0-12

TABLE 3. Changes in mean modified PASI scores during treatment period and at the end of the follow-up period.

zero week	4th week	8th week	12th week	14th week	follow-up period
7.903	3.760	2.620	2.030	1.835	7.463

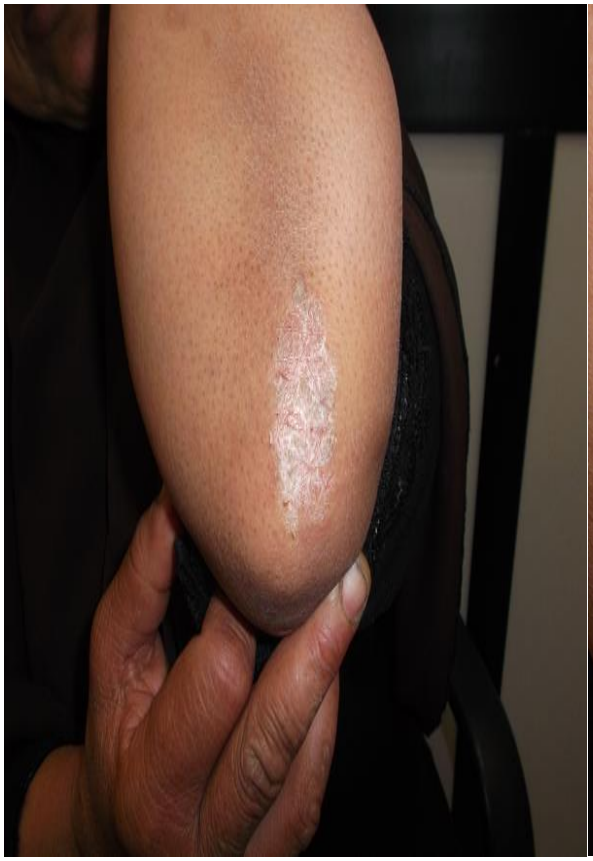


Fig.1A. Pretreatment of psoriatic plaques.

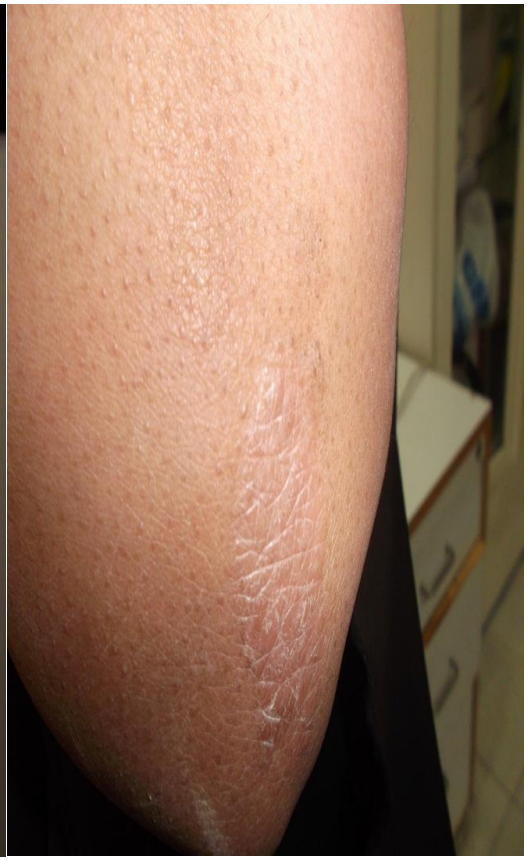


Fig.1B.Post-treatment psoriatic plaques.

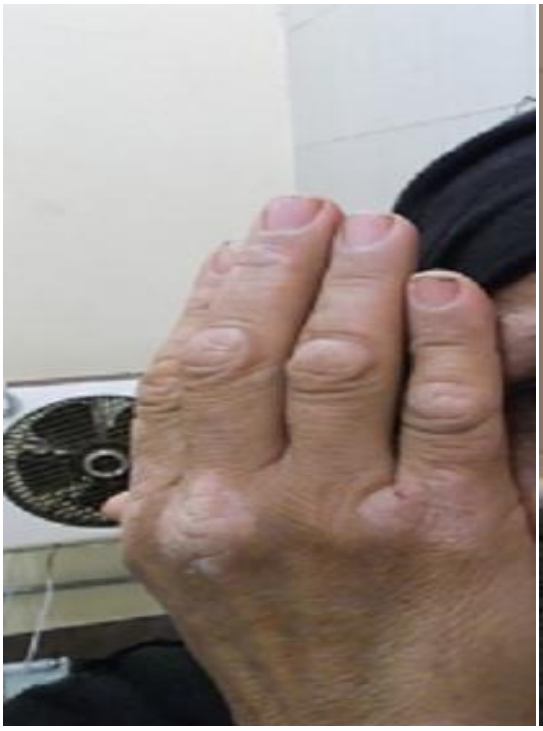


Fig. 2A. Pre-treatment psoriatic plaques

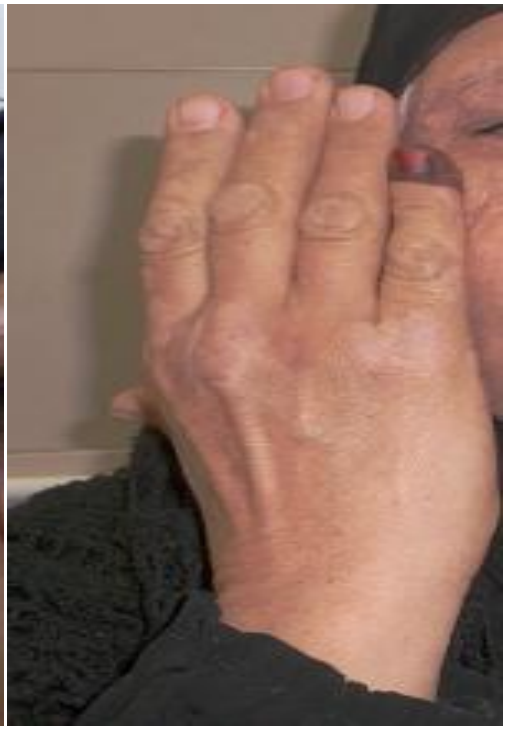
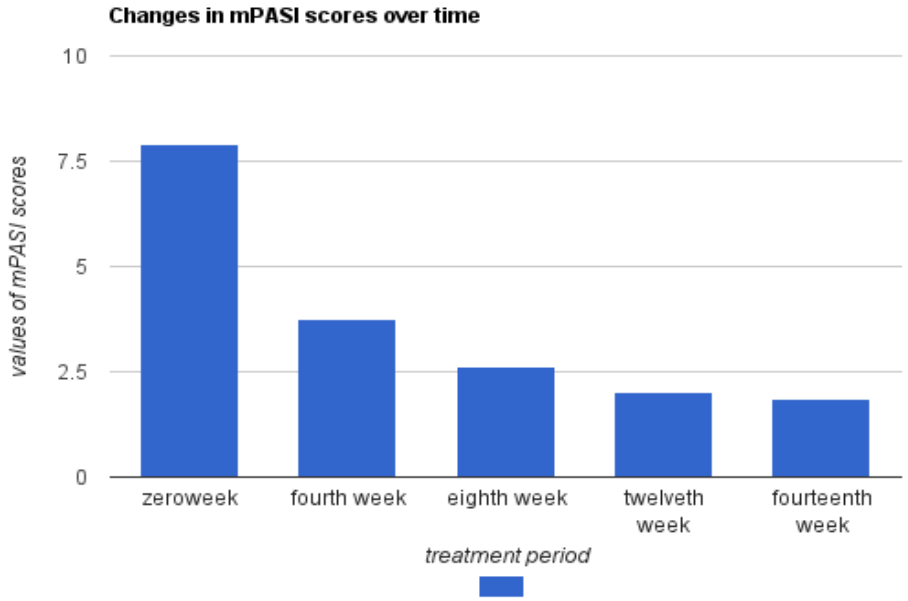


Fig. 2B. Post-treatment psoriatic plaques



Discussion

Psoriasis is described as a chronic inflammatory disease of the skin. Extracutaneous manifestations as uveitis, psoriatic arthritis and inflammatory bowel disease may present.[4] Because of the strong interplay between genetics, triggering factors and immunology, psoriasis is believed to be a multifactorial disease.[5] Some authors considered it as a metabolic syndrome.[6] Main features of psoriasis pathogenesis include: (a) abnormal differentiation and hyperproliferation of keratinocytes (b) T lymphocyte infiltration (c) dermal vascular alterations as angiogenesis, high endothelial venule formation and dilatation.[6] Many therapeutic modalities for psoriasis are available. However, laser is restricted to chronic, stable, localized plaque psoriasis resistant to topical treatment. Patients seeking for longer remissions or bored with the frequent applications of creams and ointments can also try lasers. Laser can also be used as an additive tool with systemic therapy for recalcitrant plaques. Co_2 laser, excimer laser, Erbium: YAG laser and PDL have been used with various results. [4, 8]

PDL has been used for the treatment of many inflammatory skin diseases including psoriasis.

Hacker and Rasmussen in 1992 reported for the first time the therapy of an inflammatory skin disease, psoriasis vulgaris with the PDL. [9] Studies of PDL in psoriasis revealed various results. It acts through several mechanisms and its effects is confined to the superficial microvasculature. [9] Migration of lymphocytes from blood vessels decreases as PDL reduces intracellular adhesion molecule 1 (ICAM-1). [4] Transforming growth factor beta which increases after PDL therapy suppresses the activities of T-lymphocytes. Also, reduction in recruitment of lymphocytes occurs probably secondary to decreased vascular endothelial area. Hern et al. reported partial inhibition of endothelial cell proliferation by PDL. [10] Downregulation of angiopoietin 2, a destabilizer of mature blood vessels can also occur. In addition, oxyhemoglobin strongly absorbs PDL leading to the formation of microthrombi. [11] PDL treatment normalizes epidermal cell turnover. [8] Racz et al. in 2010 mentioned that PDL decreases the expression of epidermal activation markers. These include immune cell derived Tumor necrosis factor- alpha, endothelial E- Selectin, epidermal beta-defensin 2, VEGFR 2 and VEGFR 3.This is followed by TNF-alpha mRNA and IL23P19 downregulation. [13] Moreover, PDL transforms oxyhemoglobin into methemoglobin (MetHb). Heating of hemoglobin causes oxidative reactions to form MetHb where ferrous ions are oxidized into ferric ones. [14, 15]

One of the very important properties of MetHb is that it has an increased absorption with increasing wavelength from 700-1000 nm. Also, it is well targeted by neodymium- yttrium aluminum-garnet (Nd: YAG). As regards the absorbance of MetHb, it has three times the absorbance of oxyhemoglobin and thirteen times that of deoxyhemoglobin. [16] MetHb and thrombus are formed when PDL is used but they are not acted upon or utilized for the benefit of the lesions. That's why the idea to use another vascular laser capable to act upon both MetHb and thrombus (Nd: YAG, 1064 nm) in conjunction with PDL emerges. Because of the increased absorption of 1064 nm by both MetHb and the thrombus, lower fluences of the 1064 nm Nd: YAG laser can produce specific damage to the blood vessels with diminished collateral thermal tissue damage. [17] A second reason for this combination is that the 1064 nm Nd: YAG laser has the capability to reach the microvessels of the upper reticular dermis which are not affected by PDL due to its limited penetration depth reaching only the superficial capillary bed. [8, 10]

By reviewing literature, only Van Lingen and colleagues in 2008 tried to use the Nd: YAG solely but failed to improve plaque type psoriasis. They partially attributed this to the lack of targeting the superficial microvasculature. [18] That's why we considered that this trial as a third reason implying the use of both lasers together. Also, the use of this combined technique in port wine stains with improved results inspired us to apply it to psoriasis. [17]

Regarding Nd: YAG laser and besides the above mentioned effects, it decreases CD3+ lymphocytes in the dermis significantly. However, the epidermal thickness decreased non significantly (-24.9%, $p > 0.05$). [18] Nd: YAG laser is also absorbed by a small hemoglobin peak at 900-1000 nm. [18] In addition, as a high percentage of human papillomavirus-carriage is of primary character in relation to the initiation of psoriasis, so long-pulsed Nd: YAG lasers can destroy blood vessels of the skin cutting-off the nutrient supply to the virus and to the rapidly dividing epidermal cells containing the virus. [20, 21]

Combined laser therapy in psoriasis has long been used to improve results, lessen side effects and decrease treatment periods. It can also offer a chance to treat resistant cases. PDL was used with topical salicylic acid, topical corticosteroids as well as with topical calcipotriol giving highly effective results. [22] Combination therapy of ultraviolet A phototherapy plus psoralen or acitretin resulted in beneficial results greater than using either alone. [23,24] Kragballe and colleagues concluded after their trial that a once daily application of combined calcipotriol and betamethasone dipropionate was more effective

and more tolerable than twice every day application of calcipotriol alone in the treatment of scalp psoriasis. [25]

As regards PDL+ Nd: YAG treatment of psoriasis, we used Google Scholar, PubMed search engine and Medline database to find any similar treatment combination but no studies revealed discussing the use of sequential PDL and Nd: YAG in treatment of psoriasis. Using both lasers once every two weeks for three months gave promising results. This may be due to the additive or synergistic effects of PDL and Nd: YAG. A decrease of 50% from pretreatment initial scores is generally accepted as a positive clinical response whereas a reduction of ≥ 75% is accepted as a superior response approaching clearance. [26] Side effects were minimal. However, recurrence started five weeks after the treatment period although some plaques on the elbows did not undergo any expansion of the lesions by the end of the follow up period.

Conclusion

This study demonstrates that sequential lasers in psoriasis (PDL+ Nd: YAG) is a new effective treatment modality. Probably it is needed to extend the treatment period to achieve a higher percentage of improvement. We deduce from this trial that manipulation of laser parameters according to each site of the body is recommended. A longer follow-up period is needed for plaques showing complete cure. This treatment is considered safe with minimal complications. Also, this study may pave the pathway for more types of sequential lasers in treatment of psoriasis.

Acknowledgments

Conflicts of interest

None declared.

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