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Efficacy of Pulsed Dye Laser Plus Topical Calcipotriol and Corticosteroid Combination versus Topical Calcipotriol and Corticosteroid Combination Alone in Treatment of Nail Psoriasis

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ABSTRACT

Background: psoriasis is a chronic, inflammatory skin disease that causes significant distress and morbidity.

Objective: the aim of this study was to compare the efficacy of PDL plus topical calcipotriol and corticosteroid combination versus topical calcipotriol and corticosteroid combination in the treatment of nail psoriasis.

Patients and methods: thirty patients with bilateral fingernail psoriasis were recruited from the Dermatology Outpatient Clinic at Al Hussein Hospital, Al Azhar University and Al-Haud Al-Marsoud Hospital between September 2014 and February 2017.

Results: regarding treatment sessions, total treatment sessions, follow up sessions or total follow up sessions, there was no statistically significant difference (p-value > 0.05) between right hand and left hand. There was no statistically significant difference (p-value > 0.05) between the 2 subgroups (< 30 years and > 30 years), (male and female) or (skin type 3 and type 4) as regard 1st, 2nd, and 3rd treatment session. There was highly statistically significant (p-value < 0.001) positive correlation between (1st Rt. Vs 2nd Rt.) and (2nd Rt. Vs 3rd Rt.) treatment sessions. Also, statistically significant (p-value < 0.05) positive correlation between (first Rt. Vs 3rd Rt.) treatment sessions.

Conclusion: laser therapy had been shown to be effective and safe for nail psoriasis. It could be used alone or combined with different therapeutic modalities, being especially beneficial with topical treatments.

Keywords: Pulsed Dye Laser Plus, Topical calcipotriol, Corticosteroid combination, Psoriasis.

INTRODUCTION

Psoriasis is an immunologic disease with a genetic predisposing predominantly triggered by abnormal CD4 and CD8 T-cell expansion. This activation eventually leads to the infiltration of inflammatory cells into the epidermis, resulting in the characteristic cutaneous lesions found in psoriasis. The maintenance of these lesions requires an expanded superficial vascular network, which begins prior to the onset of lesion formation [(1)]. Psoriasis varies in presentation and can involve the skin, joints, and nails, either alone or in combination. Nail psoriasis is common in those suffering from psoriasis, with reported incidences varying from 10% to 78% [(2)]. Nail involvement is more commonly found in patients with psoriatic arthropathy than in those with uncomplicated psoriasis [(3)].

The nail lesions were identified as nail matrix disease (pitting, leukonychia, red spots in lunula, nail plate crumbling) and nail bed disease (oil drop discoloration, onycholysis, nail bed hyperkeratosis, splinter hemorrhage). The Nail Psoriasis Severity Index (NAPSI) is an objective numeric grading tool used to evaluate disease severity. To obtain a patient's NAPSI score, the nail is divided into 4 quadrants; each quadrant then is evaluated based on the presence or absence of signs of the nail bed and/or nail matrix disease and is given a score.

The sum of the individual scores for each quadrant is the patient's NAPSI score [(4)]. Nail psoriasis has a significant adverse influence on the quality of life of patients. **De Jong and colleagues** [(5)] reported that 93% of patients with psoriasis with nail disease considered their condition to be a significant cosmetic handicap, 58% found that it interfered with their job, and 52% described the pain as a symptom [(6)].

The treatment of nail psoriasis largely depends on the severity of symptoms. Local or topical therapies along with ultraviolet (UV) therapy should be attempted initially. However, the efficacy of these methods is limited, as penetration through the nail plate and nail matrix is difficult. Systemic therapy may be needed in patients with severe disease or if topical treatment fails. Systemic treatment is not recommended for patients with psoriasis limited to the nails [(7)].

In 2009, **Fernandez-Guarino *et al.*** [(8)] were the first to study the efficacy of 595 nm pulsed dye laser (PDL) in nail psoriasis treatment, using a 6-millisecond pulse duration which is longer than the pulse duration used in previous psoriasis vulgaris studies. The study revealed excellent results, with a 33% improvement after 12 weeks of monthly sessions and 58% improvement after 24 weeks of treatment from the PDL treatment group.

A more recent study, **Oram *et al.*** [(9)] used a 1.5-millisecond pulse duration, which also demonstrated good results of PDL treatment of nail psoriasis [(7, 9)].

AIM OF THE STUDY

The aim of this study was to compare the efficacy of PDL plus topical calcipotriol and corticosteroid

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combination versus topical calcipotriol and corticosteroid combination in the treatment of nail psoriasis.

PATIENTS AND METHODS

Patient Selection

Thirty patients with bilateral fingernail psoriasis were recruited from the Dermatology Outpatient Clinic at Al Hussein Hospital, Al Azhar University and Al-Haud Al-Marsoud Hospital. The study was conducted between September 2014 and February 2017.

Ethical approval:

The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study.

The diagnosis was based upon the clinical characteristics of nail psoriasis. Patients with nail psoriasis that was refractory to the treatment they were receiving could be included in our study.

Exclusion criteria: - Pregnancy or lactation and history of photosensitivity.

- Patients who discontinued or just started to receive new systemic therapy or phototherapy during the study period were dropped from the study.

Study Protocol

The patients' characteristics and medical history were recorded. Each patient received topical calcipotriol and corticosteroid combination daily for six months on both hands. One session of 595 nm PDL was applied on the right hand every month for six months. Spots were directed to lunula, proximal and lateral nail fold.

Modified NAPSI scores were calculated and digital photographs of the nails were taken at baseline, 3 months and 6 months. Patients who used topical agents to treat plaque psoriasis elsewhere on the body were instructed to avoid transfer to the fingernails [(10)].

Efficacy and Safety Assessment

Modified NAPSI were assessed at baseline, 3 months and 6 months from digital photographs. Modified NAPSI scores were evaluated for the nail matrix, nail bed, and total nail of each finger. The highest possible score was 8 for the nail matrix, 6 for the nail bed, and 14 for the whole nail (the sum of the nail matrix and nail bed scores) [(10)].

As recommended in the guidelines for clinical trials on psoriasis, another blinded dermatologist evaluated the physician's global assessment scores as an outcome parameter using digital photographs at 3 and 6 months. Improvement of the fingernail was scored on a scale from 0 to 6 (0: total clearance [100% improvement]; 1: almost total clearance [90% improvement]; 2: distinct clearance [75% improvement]; 3: moderate clearance [50% improvement]; 4: mild clearance [25% improvement], and 5: no change, 6: worse).

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

Independent-samples t-test of significance was used when comparing two means. A one-way analysis of variance (ANOVA) was used when comparing more than two means. Pearson's correlation coefficient (r) was used for correlating data.

Probability (P-value)

- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

RESULTS

Table (1): Description of demographic data

Demographic data		Studied patients (N = 30)
Age (Years)	Mean	24.5
	± SD	14.9
	Min	6
	Max	65
Gender	Male	7 (23%)
	Female	23 (77%)
Skin type	Type 3	9 (30%)
	Type 4	21 (70%)

Table (1) showed that the mean age of studied patients was 24.5 ± 14.9 years. 77% of the studied patients were females and the other 23% were males. Regarding skin type, 70% of studied patients were type 3 and the other 30% were type 4.

Table (2): Comparison between total mNAPSI score of Rt and Lt hand in treatment sessions as regard age

Variables \ Groups		< 30 Years (N = 20)	> 30 years (N = 10)	T-test p-value
pretreatment Total score	Mean	31.8	39.7	0.3
	± SD	10.1	22.6	
3rd session Total score	Mean	26.2	34	0.1
	± SD	11.1	18.2	
6th session Total score	Mean	28.7	32.6	0.5
	± SD	18.7	11.5	

This table showed no statistical significant difference (p-value > 0.05) between the 2 subgroups (< 30 years

and > 30 years) as regard pretreatment, 3rd and 6th treatment session.

Table (3): Comparison between total mNAPSI score of Rt and Lt hand in treatment sessions as regard sex

Variables \ Groups		Male (N = 8)	Female (N = 22)	T-test p-value
pretreatment Total score	Mean	31.6	35.5	0.5
	± SD	16.5	15.3	
3rd session Total score	Mean	30.2	28.3	0.7
	± SD	18.2	12.7	
6th session Total score	Mean	37.5	27.3	0.1
	± SD	24.1	12.5	

This table showed no statistical significant difference (p-value > 0.05) between the 2 subgroups (male and female) as regards treatment session.

Table (4): Comparison between total mNAPSI score of Rt and Lt hand in treatment sessions as regard skin type

Variables \ Groups		Type 3 (N = 9)	Type 4 (N = 21)	T-test p-value
pretreatment Total score	Mean	29.7	36.5	0.3
	± SD	9.7	17.2	
3rd session Total score	Mean	23.7	31.1	0.2
	± SD	12.7	14.3	
6th session Total score	Mean	24.1	32.6	0.2
	± SD	15.7	16.6	

Table (4) showed no statistical significant difference (p-value > 0.05) between the 2 subgroups (skin type 3 and type 4) as regards treatment session.

Table (5): Correlation study between mNAPSI score of treatment sessions as regard Rt. Hand

Parameters \ Groups	Pearson correlation coefficient	
	(r)	p-value
pretreatment Rt. Vs 3rd Rt.	0.8	< 0.001**
pretreatmentt Rt. Vs 6th Rt.	0.4	0.02*
3rd Rt. Vs 6th Rt.	0.6	< 0.001**

(r): Pearson correlation coefficient

*: p-value < 0.05 is considered significant.

**: p-value < 0.001 is considered highly significant.

This table showed:

- Highly statistical significant (p-value < 0.001) positive correlation between 1st Rt. Vs 2nd Rt. and 2nd Rt. Vs 3rd Rt. treatment sessions.
- Statistically significant (p-value < 0.05) positive correlation between 1st Rt. Vs 3rd Rt. treatment sessions.

Table (6): Comparison between quality of life (QOL) before and after treatment

Variables \ Groups		Before (N = 30)	After (N = 30)	T-test p-value
QOL	Mean	6.3	3.8	0.001*
	± SD	2.9	2.5	

*: p-value < 0.05 is considered significant.

This table showed statistically significant difference (p-value < 0.05) between QOL before and after treatment.

Table (7): Comparison between QOL before and after treatment

Variables \ Groups		Before (N = 30)	After (N = 30)	T-test p-value
QOL	Good	19 (63.3%)	27 (90%)	0.01*
	Moderate	11 (36.7%)	3 (10%)	

*: p-value < 0.05 is considered significant.

This table shows statistically significant difference (p-value < 0.05) between QOL before and after treatment.

Table (8): Correlation study between QOL and age (before treatment)

Before treatment / Variables		QOL		p-value
		Good (N = 19)	Moderate (N = 11)	
Age (years)	Mean	22.2	28.4	0.28
	± SD	12.1	18.7	

Table (8) showed no statistical significant difference (p-value > 0.05) between patients with good QOL and patients with moderate QOL as regards age before treatment.

Table (9): Correlation study between QOL and age (after treatment)

After treatment / Variables		QOL		p-value
		Good (N = 27)	Moderate (N = 3)	
Age (years)	Mean	23.3	35.3	0.18
	± SD	12.9	29.02	

This table showed no statistical significant difference (p-value > 0.05) between patients with good QOL and patients with moderate QOL as regards age after treatment.

Table (10): Correlation study between QOL and sex (before treatment)

Before treatment / Variables		QOL		p-value
		Good (N = 19)	Moderate (N = 11)	
Sex	Male	5 (26.3%)	3 (27.3%)	0.95
	Female	14 (73.7%)	8 (72.7%)	

This table showed no statistical significant difference (p-value > 0.05) between patients with good QOL and patients with moderate QOL as regards sex before treatment.

Table (11): Correlation study between QOL and sex (after treatment)

After treatment / Variables		QOL		p-value
		Good (N = 27)	Moderate (N = 3)	
Sex	Male	8 (29.6%)	0 (0%)	0.27
	Female	19 (70.4%)	3 (100%)	

Table (11) showed no statistical significant difference (p-value > 0.05) between patients with good QOL and patients with moderate QOL as regards sex after treatment.

DISCUSSION

The purpose of the present study was to compare the efficacy of PDL plus topical calcipotriol and corticosteroid combination versus topical calcipotriol and corticosteroid combination in the treatment of nail psoriasis.

The mean age of studied patients was 24.5 ± 14.9 years and 77% of studied patients were females while 23% were males. 70% of studied patients were skin type 3 and the other 30% were type 4.

To our knowledge, there are scanty studies that have either evaluated the efficacy of pulsed dye laser plus topical corticosteroids and calcipotriol in the treatment of nail psoriasis or compared topical corticosteroids and calcipotriol efficacy to PDL alone. The combination of laser and topical treatment can enhance the positive results of the therapy. Therefore, we used a coadjuvant treatment with betamethasone calcipotriol to improve the outcome.

Our study compared between right hands (received PDL plus topical combination) and left hands (received topical calcipotriol and corticosteroid combination daily). With respect to the number of treatment sessions; Modified NAPSI scores were slightly decreased in right hands between the 1st, 2nd and 3rd sessions than in left hands of the patients. The mean of the score was 18.1, 14.6 and 15.1 in 1st,2nd and 3rd sessions of right hands treatment respectively, while the mean of the score was 16.3, 13.8 and 14.9 1 in 1st, 2nd and 3rd sessions of left hands treatment respectively. But, there was no noted statistical significant difference (p-value > 0.05) between right hand and left hand as regards treatment sessions. Also, there was no statistically significant difference (p-value > 0.05) between treatment sessions as regards total sessions.

A Comparison between Rt. hand and Lt. hand regarding follow up sessions showed that the mean was 14.5 and 14.6 in 1st and 2nd follow up of the Rt. hand respectively, while the mean was 14.8 and 15.2 in 1st and 2nd follow up of the Lt. hand. There were no differences between 1st and 2nd follow up in both hands and no statistically significant difference (p-value > 0.05) between right hand and left hand as regards follow up sessions. Also no statistically significant difference (p-value > 0.05) between follow up sessions as regards total. We found an improvement in the right hands with a slight difference that privileges PDL but the results were not statistically significant. These results suggest the benefits of this combination therapy, especially for those patients who have exclusive nail involvement. **Erceg and colleagues** [11] compared the effectiveness 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. A significant difference in the sum score 12 weeks after treatment was seen in favor of the PDL (62 % versus 19 % reduction; p < 0.05). The authors concluded that PDL treatment might be considered for the treatment of localized, recalcitrant plaque psoriasis when other topical therapies have failed. Our data showed that 20 patients were < 30 years old and 10 patients were >30 years old. Mean of Modified NAPSI scores decreased from 31.8 to 28.7 between 1st and 3rd in subgroup < 30 years while mean of Modified NAPSI scores decreased from 39.7 to 32.6 between 1st and 3rd in subgroup > 30 years with no statistically significant difference (p-value > 0.05) between the 2 subgroups (< 30 years and > 30 years) as regard 1st, 2nd and 3rd treatment session. As regards the sex our results showed better improvement in females (n=22) than males (n=8) no statistically significant difference (p-value > 0.05) between the 2 subgroups (male and female) as regards treatment session.

Regards Skin type and outcomes of treatment in patients; The mean of Modified NAPSI scores decreased from 29.7 to 24.1 between 1st and 3rd in skin type 3 and scores decreased from 36.5 to 32.6 in skin type 4. However, no statistical significant difference (p-value > 0.05) between the 2 subgroups (skin type 3 and type 4) as regards treatment session. **Ventura *et al.*** [12] stated that approximately 90% of psoriatic patients develop nail psoriasis during their lifetimes, and it is not related to gender or age**.**

In the present study, the correlation between treatment sessions at right hand showed highly statistically significant (p-value < 0.001) positive correlation between 1st Rt. Vs 2nd Rt. and 2nd Rt. Vs 3rd Rt. treatment sessions. Also, statistically significant (p-value < 0.05) positive correlation between 1st Rt. Vs 3rd Rt. treatment sessions.

These results indicate that Increasing the number of PDL sessions accompanied by an increase in response in nail psoriasis treatment.

Before the start of treatment, the clinician should inform the patient that any noticeable nail improvement will take a long time and many treatments will show maximal results only after 1 year. The low growth rate of the nail plate is responsible for a delay of 3–9 months before clinical improvement can be noticed

in cases of effective treatment. Four to 6 months is a reasonable period of treatment before evaluating clinically relevant results. In the beginning, the improvement may be so limited that it is advisable to take photographs of the nails during each visit to convince both the patient and the physician that the treatment has positive results.

In agreement with our results, **Huang *et al.*** [10] evaluated the efficacy and safety of PDL with a topical retinoid in treating nail psoriasis in 25 patients with recalcitrant psoriasis of the bilateral fingernails. Marked reduction in mean NAPSI score from baseline to 6 months in the experimental group compared to the control group. A notably higher percentage of patients in the experimental group showed ≥75% improvement at 6 months versus the control group. Patient global assessment scores were higher in the experimental group versus the control group**.**

The quality of life data analysis showed highly statistically significant difference between QOL before and after treatment. The mean of QOL was 6.3 ± 2.9 and 3.8 ± 2.5 before and after treatment respectively. There was no statistical significant difference between patients with good QOL and patients with moderate QOL as regards mNAPSI score before and after treatment. There was no statistical significant difference between patients with good QOL and patients with moderate QOL before and after treatment as regards age and sex. Patients with only nail bed alterations scored significant lower QOL scores when compared to patients with only nail matrix features. The additional negative consequences of nail involvement in psoriasis on QOL may be explained by the fact that nail psoriasis is more than a highly visible variant. Complaints of patients with nail psoriasis include pain, inability to grasp small objects, tie shoe laces or button clothes and cause an altered sense of fine touch [13]**.**

Vitiello *et al.* [14] showed that the average baseline NAPSI score for the 13 patients was 22.3 and mNAPSI at week 0 was 6.3. The mean NAPSI score at the end of week 12 was 14.8 and the mean mNAPSI score for the target nail was 5.2. The mean percentages of reduction of the NAPSI score and mNAPSI score were 31.8% and 13.3%, respectively. At the end of week 12, for two of the 13 patients (15%), NAPSI scores remained the same. No improvement of the target nail's appearance was noted in 46% of the patients; however, the same amount of patients responded positively to treatment. **De Jong *et al.*** [5] reported that 93% of patients with psoriatic nail disease considered their condition to be a significant cosmetic handicap and to adversely impact their quality of life. The patient-reported outcomes were also an important index of the efficacy of treatment. Though the patient's global assessment of psoriatic nail disease indicated significant improvement by experimental treatment over the control treatment. Only, 47.3% of patients receiving experimental treatment thought it improved fingernail cosmoses. This might mean that the improvement was not obvious enough or was incompatible with their expectations [5, 10]**.**

Finally, the period of follow-up is of utmost importance in the judgment of the results because further improvement may occur up to 1 year. These reasons underline the need for studies in which several treatments are compared without other factors interfering with the outcome.

CONCLUSION

In conclusion, laser therapy has shown to be effective and safe for nail psoriasis. It could be used alone or combined with different therapeutic modalities, being especially beneficial with topical treatments.

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