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Efficacy of long pulsed ND-yag laser in the treatment of nail psoriasis:

A clinical and dermoscopic evaluation

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Running head: Ndyag laser for nail psoriasis

Abstract

Background: Nail psoriasis is frequently seen in psoriatic patients. It is difficult to treat and shows unsatisfactory response to topical preparations. Recently, different types of Lasers have been shown to be effective in some nail disorders. **Aim:** The aim was to evaluate the efficacy and safety of long pulsed Nd: YAG laser 1,064 nm as a method for nail psoriasis treatment. **Methods:** A prospective intra-patient left-to-right, randomized, placebo-controlled study conducted on twenty-two patients with bilateral fingernail psoriasis, randomly assigned into right or left-side therapy with either 4 sessions of long pulsed Nd:YAG laser once monthly or daily topical placebo for 4 months , followed by 3 months follow up. Evaluation was done using nail psoriasis severity index at baseline, 2nd month, 4th month and after follow up period. Clinical and dermoscopic photographs were taken both at baseline and at 4th month. **Results:** There was a statistical significant improvement in both nail psoriasis severity index and dermoscopic features in laser side, along with significant difference between laser and placebo side. Nail bed showed obvious improvement than nail matrix. **Conclusion:** Nd:YAG laser represents an effective and safe modality for nail psoriasis treatment and dermoscopy is a useful tool for treatment efficacy assessment.

Keywords: nail psoriasis, Ndyag laser, NAPSI score

1 Introduction

Nail psoriasis (NP) is a common finding, affecting up to 80% of psoriatic patients with 5-10% of them having isolated nail affection 1, 2. NP is strongly associated with psoriatic arthritis 3, with a direct correlation between the duration of psoriasis and the severity of nail involvement 4. Nail involvement in psoriatic patients causes restrictions in patients' daily activities with a significant impact on their quality of life 5.

Nail psoriasis presents with different clinical signs according to the structure involved within the nail unit. In the nail plate, it may present by onycholysis, oil stains, subungual hyperkeratosis, and splinter hemorrhage; and, in the nail matrix, pitting, leukonychia, crumbling, red spots on the lunula and transverse grooves are often seen 2, 6.

Current treatment modalities for NP can be classified into topical therapy, intralesional injections, photochemotherapy, radiotherapy, and systemic therapy, including the use of biologics 7. Although many effective therapies are available for psoriasis, unfortunately the same level of response is usually not seen for the nail involvement 8.NP is refractory to treatment, with conventional therapies owing to the difficulty in penetrating the nail or its matrix 9. Patient satisfaction and compliance with current treatment modalities are often low 10.

Laser therapy has gained much attention in NP treatment due to the possibility of improved penetration of the nail and/or nail matrix 11. It is shown to be a safe and effective therapy for NP, alone or in combination with other therapeutic modalities, especially topical treatments 12.

The long-pulsed 1,064-nm Nd:YAG laser has been recently suggested as a promising treatment option for NP 13. The action of Nd: YAG laser 1,064 nm depends on selective photothermolysis of hemoglobin with the ability to penetrate deeper targeting dermal vasculature, which is believed to be the site of the earliest changes occurring in new psoriatic lesions, making it a suitable option for NP treatment 13. The aim of the study was to evaluate the efficacy and safety of long pulsed Nd: YAG laser 1,064 nm as a method for the treatment of NP.

2 Materials and methods

2.1 Patients:

This is a prospective intra-patient left-to-right, randomized, placebo-controlled study conducted on twenty-two patients with bilateral fingernail psoriasis, who was diagnosed based on clinical signs of nail psoriasis, associated cutaneous psoriatic lesions together with a dermoscopic examination of fingernails. Patients were selected from the outpatient clinic of Dermatology, Venereology and Andrology Department,Zagazig University Hospitals.

The study was approved by the Institutional Review Board (IRB) (ZU-IRB #3796-12-6-2017). Signed written informed consents were obtained from all participants before inclusion in the study.

Patients, who are in need for systemic therapy for psoriasis were excluded from the study, along with patients with onychomycosis, proved by KOH smear and/or fungal culture, subungual hematoma or subungual nevus, history of nail trauma, or using concomitant drug therapy affecting the nail.

Patients were randomly assigned into a right or left-side therapy of fingernails with either 4 sessions of long pulsed Nd:YAG laser once monthly or daily topical placebo for 4 months , followed by 3 months follow up.

2.2Methods

All patients were subjected to complete history taking and full clinical examination including general and dermatological examination of skin and nails regarding fingernail psoriasis clinical findings in nail bed and matrix.

Nail psoriasis severity was scored in each patient using the total Nail Psoriasis Severity Index**(**NAPSI)score, which evaluates presence or absence of signs in the nail bed (onycholysis, splinter hemorrhages, oil drop discoloration and subungual hyperkeratosis) and on the nail matrix (pitting, leukonychia, red spots in the lunula and nail plate crumbling) in all 10 fingernails. The nail is divided by imaginary horizontal and longitudinal lines into quadrants. Each nail is given

a score for nail bed (0-4) and nail matrix (0-4) depending on the presence of any of the features of NP in that quadrant 14. All 5 fingernails in each side were scored providing a maximum total NAPSI score of 40 and a minimum of zero. The score was assessed at baseline, at the 2nd and 4th month and at the end of three months follow-up period.

Dermoscopic examination of fingernails on both sides was done using DermLite DL3N, 3Gen (Juan Capistrano, CA, USA) connected to a cell phone camera. According to **Hashimoto et al** 15 dermoscopic features were detected; nail plate criteria includes diffuse scaling of the nail plate (DSP), transverse step-like notches (TSN), thickened white-yellow nail plates (TWY), whitish scaly streaks (WSS) and multiple white dots (MWD) and nail bed criteria includes erythematous borders of onycholytic area (EBO), distal onycholysis (DO), splinter hemorrhages of the nail bed (SHB), multiple black hemorrhagic dots (MBH) and agminated capillary dots (ACD). Digital dermoscopic photographs were taken both at baseline and 4th month.

Patients were randomly subjected to the right or left side therapy of their fingernails, after receiving comprehensive information regarding the nature of the treatment. Lesions were photo-documented on both sides before therapy.

Laser-treated side: topical anesthetic cream (EMLA cream) was applied to nails under occlusion one hour before laser therapy. All patients and personnel in the

operating room wore wavelength specific laser safety goggles. Using the 1064nm long pulsed Nd:YAG laser (Synchro-FT laser system, DEKA, Italy), all nail plates including the lunula and proximal nail fold were treated using a 5 mm spot size, 35ms pulse duration and 40 J/cm² fluence, in partially overlapping mode 13. Pre-cooling of nails for 3-5 seconds was done by integrated contact cooling using the smart cooler handpiece. Further cooling by ice packs was used. Sessions were performed monthly for 4 sessions.

Placebo-treated side: patients were instructed to apply topical Vaseline as a placebo once daily at night to fingernails of the other side for a total of 4 months.

Patients were evaluated using consecutive photographic documentation, clinical assessment of nails and NAPSI score recording on each side at the 2nd, the 4thmonth and at the end of 3 months follow up period and dermoscopic examination at 4th month.

Any side effect of laser therapy was recorded. The severity of pain was scored using the visual analogue scale of 0-10, where (0) for no pain and (10) for worst pain 16. All patients were asked to grade the overall percentage of satisfaction with therapy on each side as highly satisfied (7-9), moderately satisfied (4-6), mildly satisfied (1-3) or unsatisfied (0) 17.

2.3 Statistical Analysis

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA2011). Quantitative data were expressed as the mean ± SD and range, and qualitative data were expressed as number and percentage. T-test was used to compare between two groups of normally distributed variables. Mann Whitney U test was used to compare between two groups of non-normally distributed variables. Repeated measure ANOVA test was used to compare more than two dependent variables normally distributed. Friedman-test was used to compare between more than two dependent variables non –normally distributed and post Hoc test was used to detect significant between each pair. Percent of categorical variables were compared using the Chi-square test or Fisher exact test when appropriate. MC Nemar test was used to compare between two dependent categorical variables. All tests were two-sided. P-value < 0.05 was considered statistically significant (S), and p-value ≥ 0.05 was considered statistically insignificant (NS).

3 Results

The study included 22 patients with bilateral nail psoriasis, sixteen male patients (72.7%) and 6 females (27.3%), their ages ranged from 12-54 years with a mean of 32 ± 15 years. The duration of the disease ranged from 1 to 10 years with a mean of 4.6 ± 3 years. Three patients (13.6%) showed a positive family history of psoriasis.

3.1. NAPSI score evaluation

Regarding laser-treated side, at 4^{th} month evaluation, all patients experienced statistical significant improvement in the nail matrix, bed and total NAPSI scores ($p < 0.001$) **figure (1, 2, 3)**

On comparing mean total NAPSI score of laser-treated and placebo side, there was a reduction with statistical significance in scores after 4 months ($p = 0.005$), and after 3 months follow up ($p= 0.009$). The statistically significant difference was obvious in nail bed than nail matrix scores as ($p=0.0001$), **table (1)**

3.2. Clinical evaluation

In laser-treated side, before treatment, the most frequent clinical features were oncholysis followed by pitting, subungual hyperkeratosis, salmon patch, splinter hemorrhage, crumbling and leukonychia. After treatment, there was an

improvement in all clinical findings, most significantly in onycholysis, subungual hyperkeratosis and salmon patch ($p < 0.05$), **figure (4)**

In the placebo treated side, the most frequent clinical findings before placebo were onycholysis followed by pitting, salmon patch, subungual hyperkeratosis, splinter hemorrhage, crumbling and leukonychia. After treatment, there was no statistically significant decrease in any findings, but there was an increase in subungual hyperkeratosis, splinter hemorrhage and crumbling.

On comparing individual clinical signs between laser and placebo after treatment, there was a reduction in all signs with a statistically significant difference in onycholysis, subungual hyperkeratosis, salmon patch and crumbling ($p<0.05$), **figure (5)**

3.3. Dermoscopic evaluation

Dermoscopy is a non-invasive useful tool in the evaluation of psoriatic nail. Ten dermoscopic findings had been used to evaluate NP. In laser side, before treatment, the most frequent dermoscopic features were MHB followed by TWY, DO, TSN, MWD, DSP, SHB, EBO, WSS, ACD. After treatment there was an improvement in all findings with statistically significant improvement in TWY, DSP, SHB, MWD, DO and MHB ($p < 0.05$), **figure (6, 7, 8)**

The most frequent dermoscopic features before placebo were TWY and MHB followed by TSN, DSP, DO, MWD, WWS, SHB, EBO. After treatment, not

only there was no significant improvement in any findings, but also there was an increase in TWY, TSN and SHB, **figure (9)**

On comparing dermoscopic findings between laser and placebo after treatment, there was a decrease in most findings in laser than placebo side with a high statistically significant difference in DSP and TWY as ($p \leq 0.0001$) and significant difference in MHB ($p < 0.05$), **figure (10)**

3.4. Patient satisfaction and pain assessment

Patient satisfaction was evaluated from 0 to 9. On the laser side, there were four patients (18.2%) with mild satisfaction, thirteen patients (59.1%) with moderate satisfaction and five patients (22.7%) with high satisfaction with mean 5±1.6. On the placebo side, all patients weren't satisfied. The only adverse effect observed in all patients on a laser treated side was a tolerable mild pain, evaluated by visual analogue scale for pain showing a mean score of 2.4 ± 0.6 and controlled by using topical anesthesia.

4. Discussion

Nail psoriasis is a common finding observed in psoriatic patients with a negative impact on the quality of life. The nail and joint disease may be linked to tissue-specific factors, including tissue biochemical stressing and the microtrauma that leads to activation of aberrant innate immune responses. NP has a wide spectrum of clinical presentations depending on the structure affected whether the nail matrix or nail bed 18, 19.

Management of NP is usually challenging due to difficult penetration of topical therapy through nail plate and prolonged therapy to obtain clinical response because of the slow growth of nail plate 20.

Pulsed dye laser has emerged as an effective therapeutic option for NP, targeting increased vasculature and dermal angiogenesis. Recently, the long pulsed Nd:YAG laser has been suggested as a treatment modality for NP due to its efficacy in the therapy of vascular lesions with deep penetration 11, 21.

The objective of this randomized intrapatient, left-to-right controlled study was to evaluate the efficacy and safety of long pulsed Nd:YAG laser as a suitable option for NP treatment.

The study showed a highly statistically significant reduction in the nail matrix, nail bed and total NAPSI scores after four sessions of Nd:YAG laser therapy ($P<0.00001$), with a statistically significant difference when compared with

placebo therapy (P<0.005). However, the statistical difference was obvious in the nail bed than nail matrix score both after therapy and at follow-up.

Similarly, **Kartal et al.**21 reported a significant response of both nail bed and matrix lesions of NP after three sessions of Nd:YAG laser therapy. Although different parameters were used (6-mm beam diameter, 15-milliseconds pulse duration, and 10J/cm² energy),a statistically significant reduction of total NAPSI score was reported. Also **Arango-Duque et al.** 13**,** in their comparative study of PDL versus Nd:YAG laser therapy in 11 patients with NP reported that both lasers were significantly effective for nail matrix and nail bed lesions with a significant decrease in total NAPSI score. No statistically significant difference was found between the two treatments.

In our study, among the clinical findings detected in NP, the signs that responded significantly to Nd:YAG laser were onycholysis, subungual hyperkeratosis and salmon patch respectively, showing that the response of nail bed lesions was more prominent than nail matrix. This may be due to the more vascular structures in nail bed than matrix rendering it a more suitable target to Nd:YAG laser with selective photothermolysis of hemoglobin in dermal vasculature.

Pitting was the least responsive to Nd:YAG laser (6.7% improvement) and still can be seen in most of the cases, as it occurs from a defect in the upper-most

layers of the nail plate which arise from the proximal matrix. It is most probable that clearance of pitting after laser therapy will be seen later with the complete growth of nail plate from the matrix to hyponychium 22.

On the contrary, **Arango-Duque et al.** 13**,** using same parameters as our study, reported no statistically significant difference between improvement of the nail bed and nail matrix lesions after PDL or Nd:YAG laser therapy. **Kartal et al.**21, reported that at the end of three Nd:YAG laser sessions, both nail bed and matrix lesions almost cleared.

In this study, patients showed sustainable improvement with no recurrence of NP after the 3-month follow-up period. No significant difference was detected in total NAPSI, matrix NAPSI and bed NAPSI scores compared to end of laser therapy ($P>0.05$). This suggests that the Nd:YAG laser is a reliable treatment for nail psoriasis with long-lasting response.

In recent years, dermoscopy has become increasingly appreciated as an effective tool to facilitate the clinical assessment of nail diseases. It is a non-invasive rapidly applied and inexpensive tool that facilitates the visualization of subclinical signs and the vascular involvement of nail psoriasis. Dermoscopic findings vary depending on the affected area of the nail 23.

Few studies have evaluated the dermoscopic features of psoriatic nails. The present study identified 10 dermoscopic nail findings in psoriatic patients before

therapy. The most frequently observed dermoscopic features of nail bed were MBH (77.3%), DO (68.2%) and SHB (40.9%). TWY (72.7%), TSN (68.2%), MWD (50%) and DSP (45.4%) were the most frequent matrix findings. These results coincided with that of **Hashimoto et al.**15 who reported that TWY, TSN, DSP; SHB and EBO may serve as markers of psoriatic nail activity.

Comparison of dermoscopic signs before and after placebo showed no improvement with a statistically non-significant difference. While after laser therapy, improvement of all dermoscopic findings was detected; the nail bed signs that showed a statistically significant improvement after laser therapy were SHB, DO and MBH respectively and nail matrix signs that showed significant improvement were TWY, DSP and MWD, respectively. Thus both the nail matrix and nail bed dermoscopic findings improved equally to Nd:YAG laser therapy, which might be due to the early detection of any improvement by dermoscopy than clinically.

In the present study, dermoscopic improvement corresponded with clinical improvement in some findings as distal onycholysis and subungual hyperkeratosis but does not correspond to pitting and splinter hemorrhages. This may be explained by the more detailed and easy evaluation by dermoscopy of superficial abnormalities associated with nail matrix involvement as pitting. Also, dermoscopy improves the visualization of splinter hemorrhages, which are more vivid when newer and are darker when older 23, 24, 25**.**

No adverse side effects to Nd:YAG laser therapy were recorded in this work, except mild tolerable pain not enough to interrupt the treatment sessions. Patients were very satisfied with this modality; moderate satisfaction in 59.1% of patients and high satisfaction in 22.7%. However, **Arango-Duque et al.** 13**,** reported that Nd:YAG laser was more painful when compared with PDL therapy in NP, although patient's satisfaction was high in both modalities.

In conclusion, this study suggests that Nd: YAG laser can represent an effective, minimally invasive and safe modality for the treatment of nail psoriasis and dermoscopy is a useful objective tool for evaluation of psoriatic nails and should be used for assessment of treatment efficacy.

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Figure legend

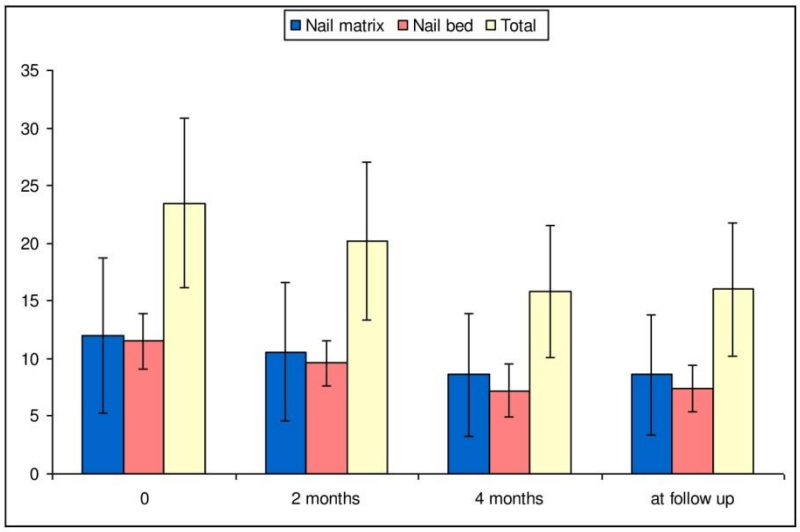
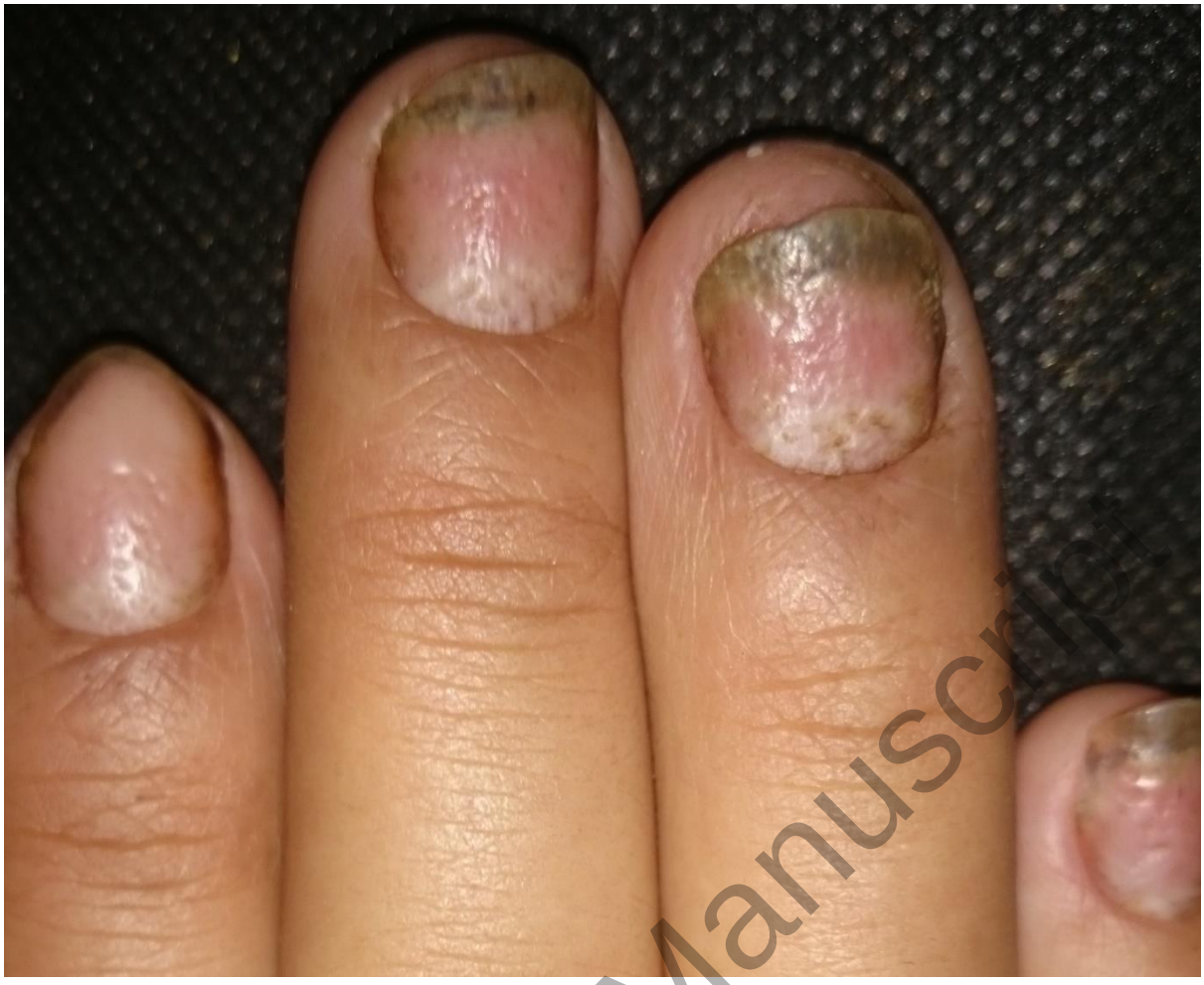


Figure (1): Evaluation of nail matrix, bed and total NAPSI scores of laser side at zero, two months, four months and after three months follow up.



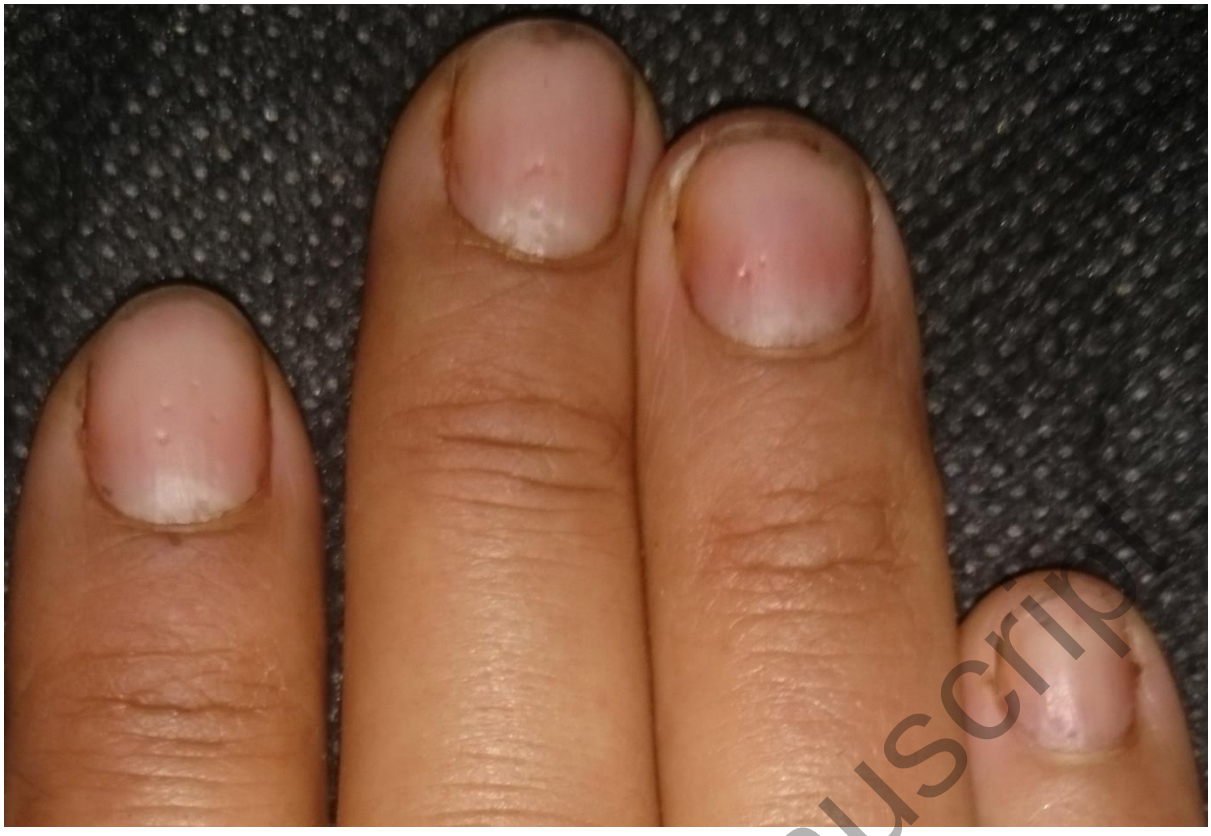
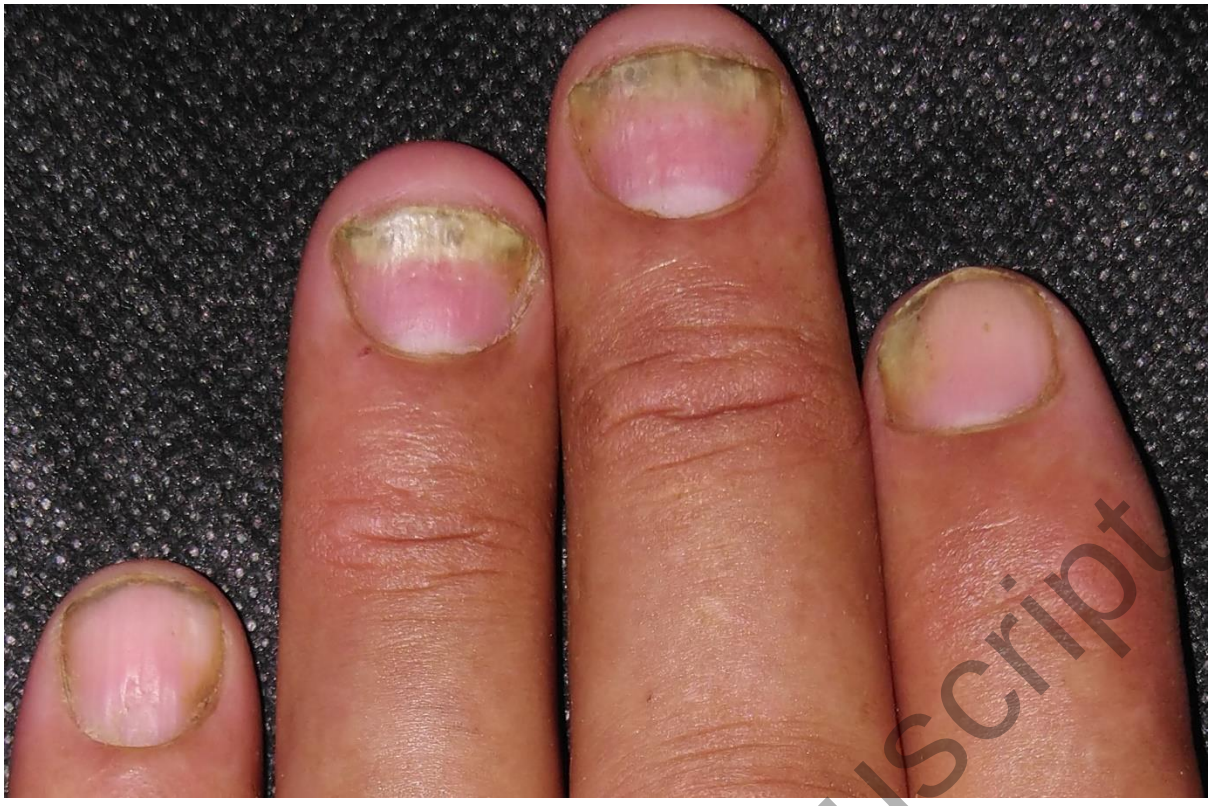


Figure (2): (a) Right fingernails before treatment showed pitting, onycholysis, splinter hemorrhage, (b) After Nd: YAG laser therapy showed marked clinical improvement and decrease in NAPSI.



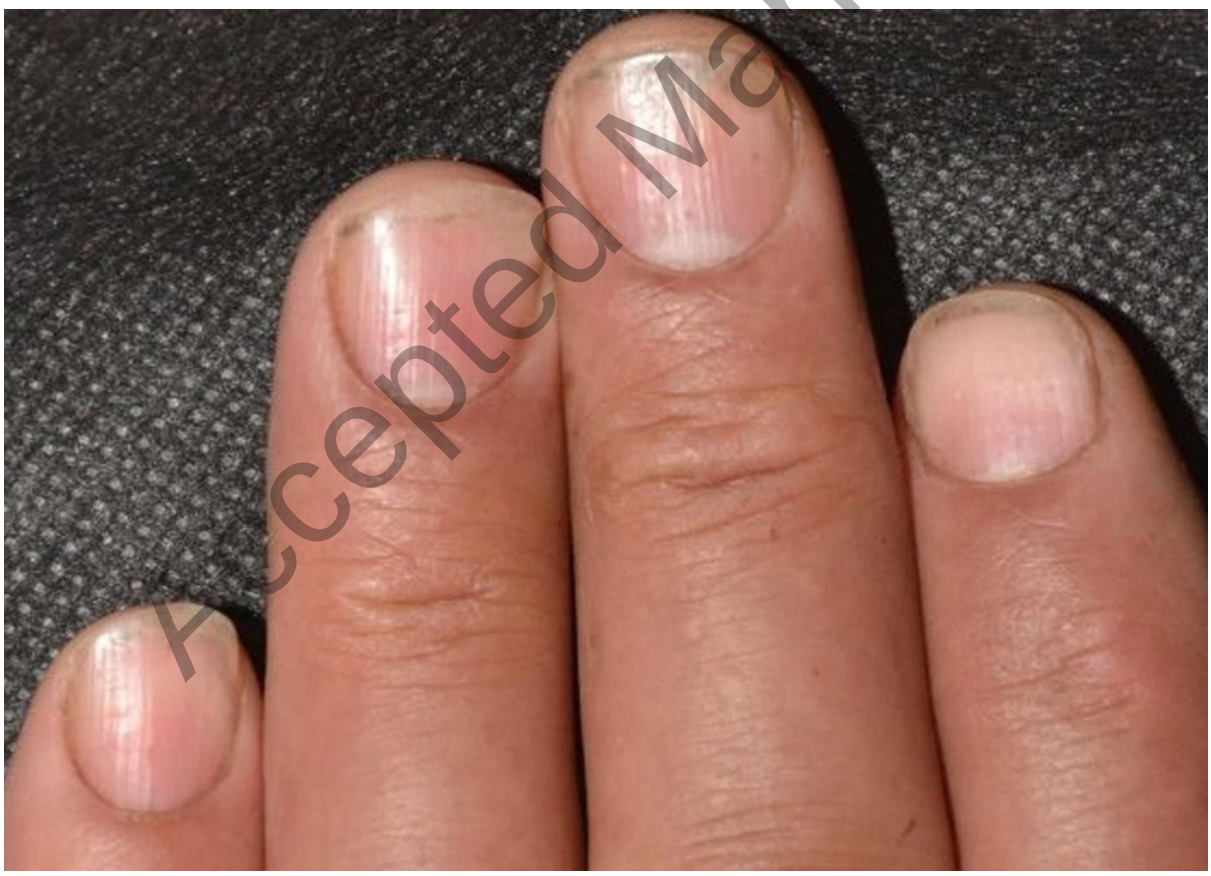


Figure (3): (a) Left fingernails before treatment showed onycholysis ,pitting, splinter hemorrhage, subungual hyperkeratosis and salmon patch, (b) After Nd:YAG laser therapy showed marked clinical improvement and decrease in NAPSI.

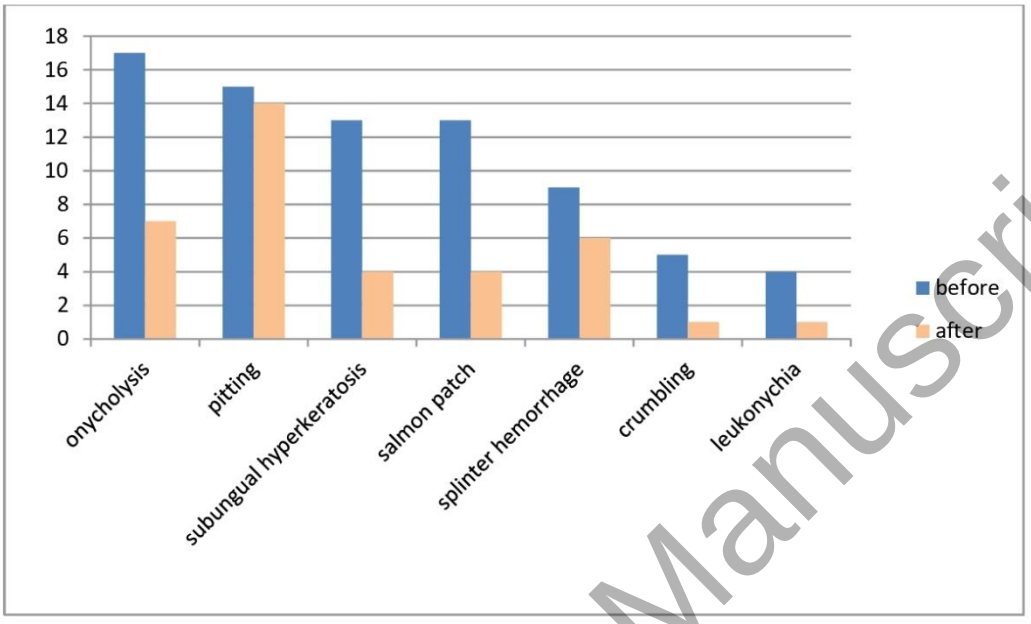


Figure (4): Comparison of nail psoriasis clinical signs before and after laser treatment

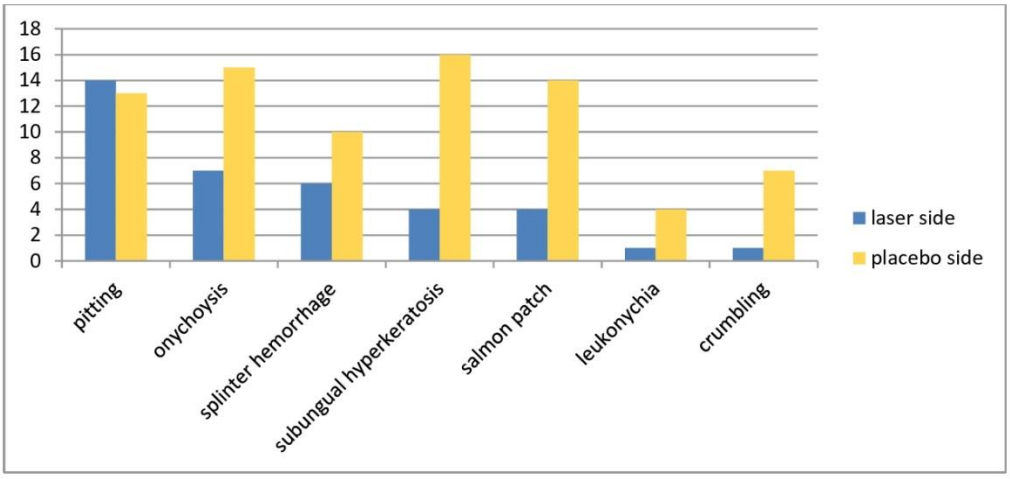


Figure (5): Comparison of nail psoriasis clinical signs between laser and placebo sides after treatment

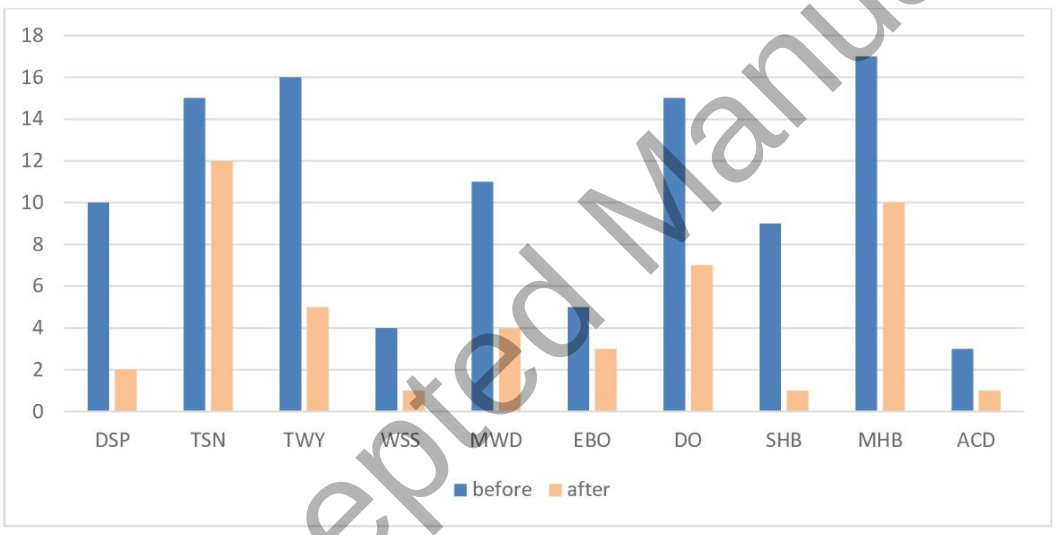
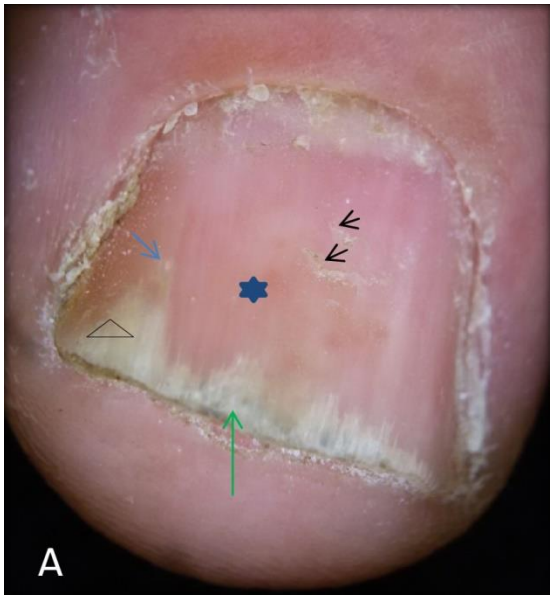


Figure (6): Comparison of dermoscopic findings of nail psoriasis before and after laser treatment



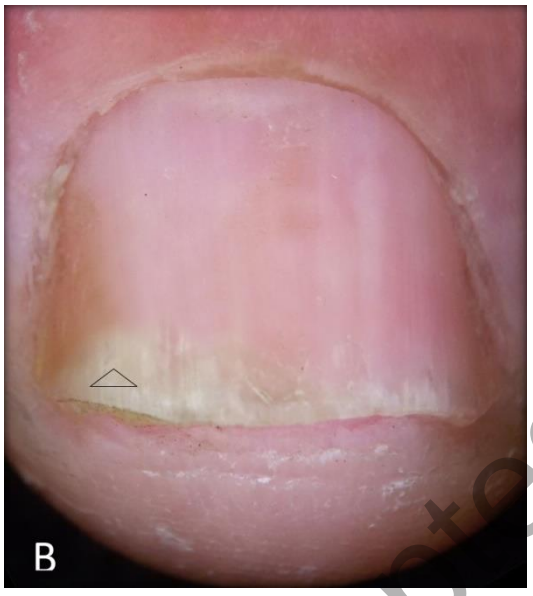
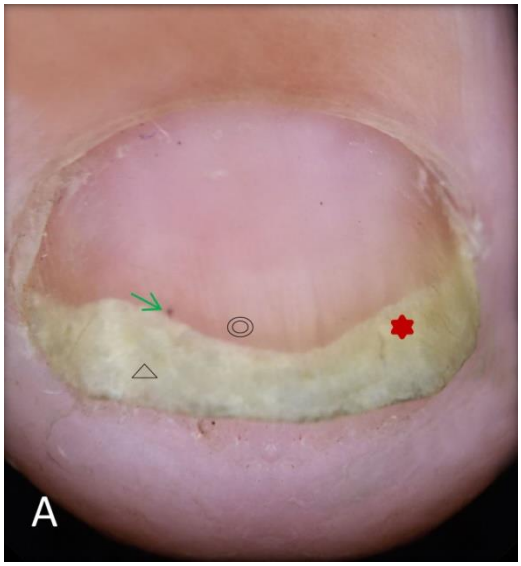


Figure (7): Dermoscopic examination of fingernails (a) before treatment showed transverse step like notches (→), distal onycholysis (△), multiple white dots (→), multiple black hemorrhagic dots (→) and agminated capillary dots (✿), (b) after Nd:YAG laser therapy showed marked improvement .



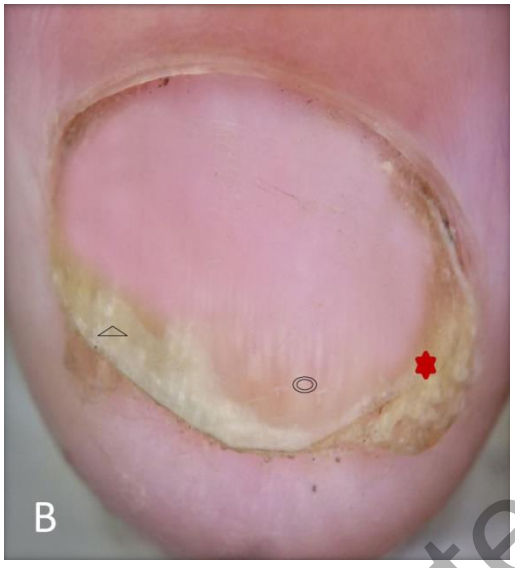


Figure (8): Dermoscopic examination of fingernails (a) before treatment showed thickened white yellow nail plate ( ), distal onycholysis ( ), black hemorrhagic dots ( ) and erythematous border of onycholytic area ( ), (b) after Nd:YAG laser therapy showed moderate improvement.

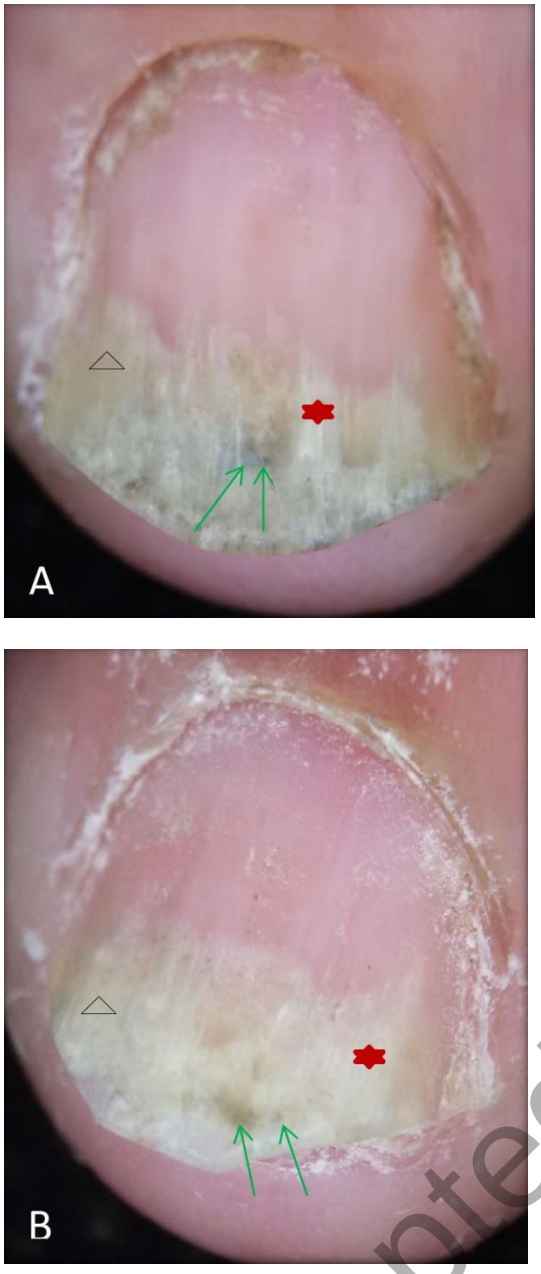


Figure (9): Dermoscopic examination of fingernails (a) before placebo showed thickened white yellow nail plate ( ), distal onycholysis ( ) and multiple black hemorrhagic dots (→) (b) after placebo showed no response.

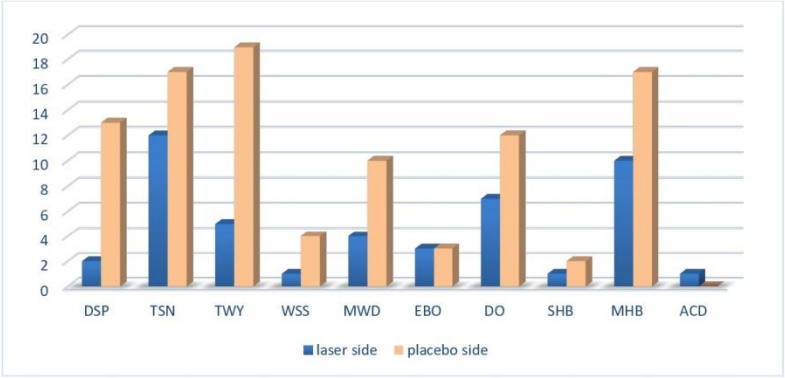


Figure (10): Comparison of dermoscopic findings of nail psoriasis between laser and placebo after treatment

Table legend

Table (1): Comparison of nail psoriasis NAPSI scores of laser treated side versus placebo at zero, two months, four months and after three months follow up.

	Nail matrix				**Nail bed**				**Total**			
	0	**2 m**	**4 m**	**at follow up**	**0**	**2 m**	**4 m**	**at follow up**	**0**	**2 m**	**4 m**	**at follow up**
Laser side Mean± SD Range	12±6.7 (0-20)	10.6±6 (0-20)	8.6±5.3 (0-20)	8.6±5.2 (0-20)	11.5±2.4 (7-17)	9.6±2 (6-15)	7.2±2.3 (4-14)	7.4±2 (4-14)	23.5±7.4 (12-34)	20.2±6.8 (6-31)	15.8±5.7 (4-27)	16±5.8 (4-24)
Placebo side Mean± SD Range	12±7.4 (0-20)	12±7.4 (0-20)	12±7.4 (0-20)	11.9±7.4 (0-20)	11±3.3 (5-18)	11±3.3 (5-18)	10.9±3.2 (5-17)	10.9±3.2 (5-17)	23±9 (6-36)	23±8.9 (6-36)	22.9±8.9 (6-36)	22.85±9 (6-36)
MW	0.071	0.86	1.68	1.68	0.74	1.53	4	3.8	0.11	1.15	2.8	2.61
P	0.94	0.39	0.09	0.09	0.46	0.13	0.0001**	0.0001**	0.92	0.25	0.005*	0.009*

MW =Mann-Whitnney test