



**ORIGINAL ARTICLE**

# Therapeutic Efficacy of Long-Pulsed 1064-nm Nd: YAG Laser for Seborrheic keratoses.

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**ABSTRACT**

**Background:** Evaluation of the clinical efficacy and adverse effects of long-pulsed Nd: YAG laser for the treatment of SKs.

**Methods:** A randomized prospective placebo-controlled study was conducted on 14 patients clinically diagnosed with bilateral seborrheic keratoses. We selected the participants from the outpatient clinic of the Dermatology, Venereology, and Andrology Department of Zagazig University Hospitals through the period June 2018 to July 2019.

**Results:** Complete response of the SKs lesions occurred in 78.6% of patients on the laser side after one to two sessions of long-pulsed Nd:YAG laser therapy with no recurrence after 3 months after the end of our study. Regarding the placebo side, 100% showed no response to topical saline after 2 months. Comparison of the clinical response of the two sides after therapy showed high statistical significance ( $P < 0.0001$ ).

**Conclusions:** Long-pulsed Nd: YAG laser may represent an effective, well-tolerated therapeutic modality for seborrheic keratoses. Large randomized controlled studies are wanted to evaluate its efficacy and possible recurrences compared with other common treatment modalities such as curettage and cryotherapy

**Keywords:** Carbon dioxide laser; Erbium Yttrium Aluminum Garnet Laser; Pedunculated seborrheic keratosis; Amyloid protein precursor; Neodymium Yttrium Aluminum Garnet Laser



**INTRODUCTION**

Seborrheic keratosis is one of the most frequent Epithelial tumors which develop in adults. It appears as warty lesions having sharp borders and a stuck-on appearance. It has many clinical types such as dermatosis papulosa nigra and stucco keratosis [1]. They are very common in old age, especially in sun-exposed areas, and develop anywhere on the skin but never in the palm-planter areas [2].

The etiology and pathogenesis of Seborrheic keratosis are unclear until now. They may be due to the process of aging and ultraviolet light exposure; also the human papillomaviruses may play a role in the pathogenesis of the disease [3, 4].

Despite the benign nature of SKs, the patients need treatment due to the associated pain and cosmetic reasons. Several modalities can be used such as cryosurgery, curettage, and electrocautery. Some of these procedures can leave scars if it's not done properly [5]. In addition, several types of ablative lasers are currently available for example erbium:

Yttrium Aluminum Garnet laser also carbon dioxide resurfacing lasers, were used for the removal of these lesions as they damage water-containing tissue. But they are highly accompanied by many complications especially in dark skin populations, as post-treatment hyper or hypopigmentation [6].

There are types of lasers that act by the principle of selective photo-thermolysis, for example, Q-switched alexandrite laser (755 nm) and Q-Switched Nd: YAG lasers (532nm/1064 nm) also were described to successfully destruct SKs through aiming tissue containing melanin pigments [7].

Therefore the Q-Switched Nd: YAG laser (1064 nm) is a selective photothermolysis device that is broadly available with minimal side effects such as post-laser bleeding or crust development, and transient erythema [8].

Using the concept of selective photothermolysis, a 1064 nm wavelength of long-pulsed Nd:YAG laser would effectively target cell nests in SKs. Additionally, it has the benefit of deeper

penetration and high fluence. This laser destructs these warty lesions effectively without affection of surrounding tissue which will decrease the laser complications[9].

This study aimed to evaluate the clinical efficacy and adverse effects of long-pulsed Nd: YAG laser for the treatment of SKs.

## METHODS

*Site of study:* This was a randomized controlled prospective intra-patient left-to-right study on 14 participants with seborrheic keratosis on both sides. Patients were of both sexes. They were aged between 39 and 61 years old. All participants were with skin photo-type III and IV.

Written informed consent was obtained from all participants, the study was approved by the research ethics committee of the Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

*Inclusion criteria:* We selected patients with bilateral SKs (face & body), who had been diagnosed as clinically stable typical SK.

*Exclusion criteria:*

We excluded patients who had clinically atypical and rapidly growing SK lesions or had a tendency of multiple eruptive SK lesions (a sign of laser-treat). Patients with a history of keloid formation and lesions on eyelids or within 5 mm of the orbital rim were also excluded

*Methods:* We took a complete medical history and made a complete clinical examination for all patients. In this study (intra-patient side-to-side comparison). Patients were classified indiscriminately to right or to left side treatment of SKs by either long pulsed Nd: YAG laser or by topical placebo for up to 2 months.

*A-Laser session:*

All participants received laser therapy on one side of the body at Al-Solaymanyah Laser Unit.

*Preparation of Patients:*

All patients received full suitable information about the treatment. We took photos of both sides of the body before therapy. We used topical anesthetic cream for lesions one hour prior to laser treatment, Also wavelength-specific laser glasses were used by all personnel in the operating room.

*Procedure:* Fourteen SKs patients received right or left-side treatment of facial and body lesions in a random manner by the long pulsed Nd:YAG laser 1064nm (Candela Max Pro-USA). By means of 12-millimeter spot size, 1.5-millisecond pulse duration, and 60 Joul/cm<sup>2</sup> fluencies. Precooling of the lesions was made by a cooler handpiece.

Sessions were performed every month for up to 3 sessions.

*Post-operative:* Another cooling with ice dressings can be used after the session for 5- 10 minutes to decrease erythema & pain. Fusidic acid +Betamethasone cream was applied twice daily for 3 days following each laser session. Sunscreen was prescribed according to the patient's daily work.

*B-Placebo therapy:* We advised all participants to put topical saline solution one time daily at night on the lesions of the opposite side of the body for at least 2 months.

*Evaluation of patients and Follow-up:* It consisted of consecutive photographic documentation on both sides of the body one month after the last session and also at the end of the follow-up period (3 months after the end of laser sessions). We evaluated the response to treatment by the approximate decrease in size and color of lesions and photographic comparison. Patients showing complete disappearance of lesions were defined as responders(CR). Patients showing more than 50% clearance of lesions were defined as partial responders(PR), while patients showing less than 50% clearance of lesions were defined as nonresponders (NR). Also, we recorded any adverse effects such as erythema, crusts, burns, pain, scarring, or hyperpigmentation.

*Patient self-assessment:*

Patient satisfaction percentages about the used treatment on each body side were rated as regards cosmetic appearance from 0 to 9 (0: unsatisfied, 1-3: mildly satisfied, 4-6: moderately satisfied, 7-9: highly satisfied).

*Statistical analysis*

The collected data were tabulated and statistically analyzed by SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA 2011). Quantitative data were articulated as (the mean  $\pm$  SD) and qualitative data were articulated as numbers and percentages. The percentage of categorical variables was matched by Fisher exact test or Chi-square test once suitable. The McNemar test was also applied to compare dependent categorical variables. P value < 0.05 was considered statistically significant.

## RESULTS

The patient's ages ranged between 39 and 61 with a mean age of (53 $\pm$  8 years) & a mean disease period was (2.4 $\pm$  1 year). Most of the patients were females (57.1%) with only 42.9% males. Ten patients were of skin photo type IV (71.4%) and four patients were of type III (28.6%). The commonest site of lesions was on the face (85.7%) of patients followed by the back (14.3%). Eleven patients have multiple lesions on both sides (78.6%) but only three patients have only a single lesion on both sides (21.4%). Twelve patients have

popular lesions (85.7%) while one patient has macular lesions (7.14%) and one patient has verrucous lesions (7.14%). Common seborrheic keratoses were seen in 71.4% of patients, while dermatosis papulosa nigra was seen in 28.6%. Five patients (42.8. %) have their lesions black in color (table 1).

(78.6%) of patients in the laser, the side showed a complete response of their lesions after one to two sessions of long-pulsed Nd:YAG laser therapy (figure 1) with no recurrence after three months after the end of our study, while 21.4% showed partial response to therapy. Regarding the placebo

side, 100% showed no response to topical saline (figure 2) after 2 months. Comparison of the clinical response of the two sides after therapy showed high statistical significance ( $P < 0.0001$ ) (table 2), (figure 3).

About 70% of CSK patients had multiple lesions compared to 100% of DPN and the difference was statistically insignificant ( $P > 0.05$ ). Also, 80% of CSK patients showed a complete response to laser therapy compared to 75% of DPN patients without a statistically important difference ( $P > 0.05$ ), (table 3).

**Table 1:** Demographic data of patients.

Variables	No.	%
Age ( years):		
• Mean± SD	53.±8	
• Range	(39-61)	
Sex:	No.	%
• Male	6	42.9
• Female	8	57.1
Disease duration (years):	2.4±1	
• Mean± SD	(1-4)	
• Range		
	No.	%
Skin type:		
• III	4	28.6
• IV	10	71.4
Site of lesions:		
• Face	12	85.7
• Back	2	14.3
Number of lesions:		
• Single	3	21.4
• Multiple	11	78.6
Type of lesions:		
• Papular	12	85.7
• Macular	1	7.14
• Verrucous	1	7.14
Clinical type:		
• CSK	10	71.4
• DPN	4	28.6
Color of lesions:		
• light brown	2	14.3
• Dark brown	5	35.7
• Black	6	42.8
• Grey	1	7.1

**Table 2:** Comparison of clinical response to therapy on the laser side versus the placebo side.

Clinical response	Laser side		Placebo side		Test	P-value
	No.	%	No.	%		
Complete response (CR)	11	78.6	0	0	$\chi^2=18.1$	0.00002 (Hs)
Partial response (PR)	3	21.4	0	0	f	0.22
No response (NR)	0	0	14	100	$\chi^2=28$	0.00001 (Hs)

f= Fisher exact test

$\chi^2$  Chi-square test of significance

**Table 3:** Comparison between CSK and DPN as regards clinical picture, number of sessions, and clinical response.

	Clinical type				Test	P-value
	CSK(n=10)		DPN(n=4)			
	No.	%	No.	%		
Number of lesions:						
Single	3	30	0	0	f	0.51
Multiple	7	70	4	100		
Lesions color:						
Light Brown	2	20	0	0	$\chi^2 = 7.1$	0.07
Dark Brown	3	30	2	50		
Black	4	40	2	50		
Grey	1	10	0	0		
Number of sessions:						
One session	1	10	3	75	f	0.04(S)
Two sessions	9	90	1	25		
Clinical response:						
Complete response	8	80	3	75	f	0.99
Partial response	2	20	1	25		
No response	0	0	0	0		

f= Fisher exact test

$\chi^2$  Chi-square test of significance



**Figure 1:** Complete remission of the lesion in the Laser group.



Figure 2: Partial remission of the lesion in the Laser group.

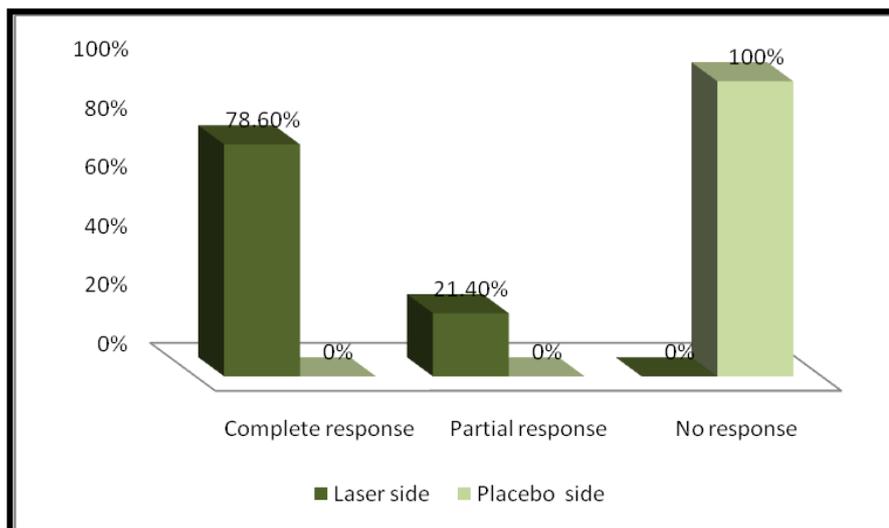


Figure 3: Comparison of the clinical response of the two sides after therapy showed high statistical significance

### DISCUSSION

Seborrheic keratoses (SKs) are pigmented papules, plaques, or nodules that appear on the trunk of old patients. These patches are of different colors, extents, and depths and are often related to sun-exposed areas [10].

It was stated that laser devices were successfully used in the treatment of seborrheic keratoses, such as Alexandrite (755 nanometers) and Diode laser. No further studies about the ability of long-pulsed lasers in the treatment of seborrheic keratosis have been published. Its variability of action makes it promising to choose the exact wavelength which directed against the melanin-containing lesions[11].

Using the concept of selective photothermolysis, a 1064 nm wavelength of long-pulsed Nd: YAG laser would effectively target cell nests in SKs.

Additionally; it has the benefit of brilliant extent of penetration also emerging high fluencies.

This laser has the propriety to damage all lesions selectively without affecting the surrounding skin which will minimize all adverse effects related to laser treatment [9].

Similarly, Kim et al., [7] reported a significant response when working by an alexandrite laser (755-nanometer) using a pulse interval of 3 milliseconds and fluency of 35 Joul/cm<sup>2</sup> on seborrheic keratosis, especially on the face with many colors and various types and demonstrated that improvement of cases was stable and unaffected by the color or the type of SKs.

Also, Cho et al., [8] applied the long-pulsed alexandrite laser on many facial SKs, their colors ranged from light brown to deeply pigmented black. Despite their irregular surfaces, they were removed successfully through 2 sessions of long-pulsed alexandrite laser (755nanometer) without

notable complication. 80% of CSK patients showed a complete response to laser therapy compared to 75% in DPN patients without a statistically important difference ( $P>0.05$ )

Similarly, Schweiger et al., [12] reported the safety of long-pulsed Nd:YAG laser therapy for the destruction of dermatosis papulosa nigra. Two female cases received a single session with fluency of 145-155J/cm<sup>2</sup> and a pulse duration of 20 msec. Both patients had 70% to 90% resolution of the cured lesions.

Trafeli et al., [13] documented that long pulsed lasers directed against melanin were applied for destructing many pigmented epidermal lesions as lentigines, congenital melanocytic nevus, and seborrheic keratoses.

Chan et al., [14] reported that long pulsed Nd:YAG (532nanometer) laser showed the same efficacy in Chinese persons with lentigines on the face at settings (2 milliseconds pulse duration also a fluency from 9 to 12 Joul/cm<sup>2</sup>) paralleled to Q-Switched laser (532nanometer) treatment, conversely the long-pulsed laser had less adverse effects.

Likewise, Rosenbach et al., [15] demonstrated that alexandrite laser (755nanometer) therapy between 35 and 50 Joul/cm<sup>2</sup> for lentigines in cases had skin types II to IV using a pulse duration of 5 ms succeeded with good results with negligible complications.

Ho et al., [16] found that a long-pulsed alexandrite laser of 100  $\mu$ s-pulse width was preferred more than Q-Switched (alexandrite) laser with 50 nanosecond-pulse width due to fewer adverse events and high clinical results in the cure of lentigines.

Regarding the complication of Nd:YAG laser treatment noted in this study, All patients(100%) suffered from pain and erythema at the time of the session and persisted for three to four days after laser therapy, while,71.4% showed crust formation shortly after the laser session and 42.9% showed blistering. Also, atrophy occurs in two cases (14.3%) after two treatments of Nd:YAG long pulsed laser therapy.

Patients were pleased with this modality 57.1%, with moderate satisfaction in 28.6% of patients and mild satisfaction in 14.3%, while on the control side, all patients were unsatisfied.

### CONCLUSION

We may conclude that Nd: YAG laser may represent a valuable, well-tolerated therapeutic modality for seborrheic keratoses. Large studies are recommended to evaluate its efficacy, safety,

and possible recurrences compared to other common treatment modalities such as curettage and cryotherapy.

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