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Long Pulsed Nd-YAG Lasers versus Q Switched Nd-YAG Lasers in the treatment of recalcitrant Plantar Warts - Comparative Randomized Study

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Long Pulsed Nd-YAG Lasers versus Q Switched Nd-YAG Lasers in the treatment of recalcitrant Plantar Warts - Comparative Randomized Study

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Abstract

Background: The human papillomavirus (HPV) causes verrucae, or warts, which are epidermal growths on the skin. Seven to ten percent of the general population is afflicted with warts, the most prevalent viral infection of the skin.

Objective: In order to determine if Q-Switched Nd-YAG lasers or Long Pulsed Nd-YAG lasers are safe and effective in treating plantar warts that have become resistant to previous treatments.

Patients and Methods: Between June 2022 and June 2023, fifty (50) patients with clinically identified intractable plantar warts participated in an interventional randomized comparison trial held in the Dermatology and Venereology Departments of Al-Hussein University Hospital and Kobry El-Kobra Military Hospital.

Results: A comparable lack of statistical significance was observed in response, recurrence, and evaluation data as well as in demographic data when comparing the two groups.

Conclusion: Long-pulsed (1064 nm) and Q-Switched (1064 nm) Nd-YAG (1064 nm) laser systems are both safe and effective ways to treat plantar warts, particularly in individuals who cannot or will not undergo oral therapy.

Keywords: Pulsed Nd-YAG Laser; Plantar Warts; Q-Switched Nd-YAG Laser

1. Introduction

On the plantar side of the foot or toes, plantar warts appear, mainly ascribed to strains 1, 2, and 4 of the human papillomavirus (HPV), although HPV 57, 60, 63, 65, and 66 can also be involved. The hue of their color is generally akin to that of the epidermis. Frequently, the surface exhibits the presence of tiny black specks. Multiple occurrences may be present within a given geographical region. Applying pressure to these structures can elicit pain, leading to difficulties in ambulation. Mosaic warts refer to a collection of closely grouped plantar-type warts typically discovered on the hands or foot soles. Myrmecia refers to subcutaneous lesions characterized by extensive burrowing beneath the epidermis, often resulting in significant discomfort.

The postulation posits that lesion formation occurs due to external pressure exerted on the skin surface. Recalcitrance needs a precise delineation. Nevertheless, it generally refers to warts that endure despite undergoing conventional therapy for many months. Approximately 33% of non-genital warts, particularly plantar and periungual warts, have a persistent or resistant nature. Various therapeutic approaches are available for the treatment of plantar warts, encompassing surgical removal, pulsed dye laser treatment, salicylic acid topical application, administration of 5-fluorouracil, utilization of cantharidin, immunotherapy, cryotherapy, and electrodesiccation. Patients generally well-tolerated the treatment, and using local anesthetics is typically unnecessary.
Plantar warts can now be effectively and dependably treated with long-pulsed Nd-YAG laser, exhibiting response rates surpassing conventional therapies. Furthermore, the associated side effects are generally mild and temporary, including hemorrhagic bullae, temporary discomfort during therapy, numbness following treatment, and hyper and hypopigmentation.7

The frequency-doubled Q-switched Nd-YAG laser was set up to treat pigmented flat warts that were resistant to treatment with a fluence of 2.5 J/cm2 at a wavelength of 532 nm.8

In order to manage chronic plantar warts, this study aims to compare and contrast the safety and efficacy of Long Pulsed Nd-YAG laser with Q Switched Nd-YAG laser.

2. Patients and methods

This study is a randomized comparative intervention conducted on 50 patients clinically diagnosed with recalcitrant plantar warts. It was carried out in the Department of Dermatology and Venereology at Al-Hussein University Hospital and Kobya El-Kobba Military Hospital from June 2022 to June 2023.

Inclusion criteria: Patients with recalcitrant plantar warts who failed to respond to conventional treatments or showed recurrences after several months and ages ranging from 10 up to 60 years.

Exclusion criteria:

Those who have a history of keloid formation, those who are pregnant or nursing, and those who have used alternative methods to cure plantar warts within the last three months are not eligible.

2.1. Study procedure:

All participants underwent a standardized protocol that included obtaining informed consent, conducting a comprehensive medical history interview and thorough physical examination, performing dermatological assessments to identify lesions, and capturing digital photographs. Specifically, standardized photographs of each lesion were taken at the beginning of the study and every four weeks after that, utilizing a digital camera for a total treatment duration of 20 weeks.

2.2. Treatment:

Each patient was randomly assigned to either a Q-Switched Nd-YAG laser or a Long Pulsed Nd-YAG laser therapy based on the information they found in their treatment envelope. The participants were allocated into two cohorts, each group comprising 25 individuals. The experimental group designated as Group A received treatment using the Long Pulsed Nd-YAG laser Synchro excellium HP (DEKA, Florence, Italy), employing the following parameters: a 5 mm spot size and a 20 millisecond pulse duration. The fluence value ranges from 60 to 80 J/cm2, with a 3-fluence condition.

The process involves the application of 2-3 pulses of pressure until a greyish discoloration is observed at the endpoints. The experimental group, Group B, received treatment with Q-plus QUANTA, an intervention developed in Italy. Q-Switched Nd-YAG laser by 5-10 successive pulses with the following parameters: The spot size is 6 mm. The fluence was set at 2 J/cm2 and gradually increased to 3-4 J/cm2 until a grayish discoloration, which served as the endpoint, was achieved.

Before the laser sessions, EMLA® cream or a lidocaine 2% injection the physical removal of hyperkeratotic lesions using a razor blade followed by the physical removal of hyperkeratotic lesions….etc. The entire wart and the surrounding skin’s margin measuring 2-3 mm were exposed to radiation, ensuring the laser pulses overlapped by 10% to 20%. Each participant underwent a maximum of four treatment sessions, with a four-week break between each session.

2.3. Evaluation:

One month following the fourth session. A comparison of the baseline and 20-week measurements in the photos was used to calculate changes in the surface areas of the warts. The results were categorized into one of five improvement levels using a five-grade rating system. Full clearance, a 100% improvement, signifies a complete enhancement, while a noticeable improvement refers to an increase ranging from 81% to 99%. A moderate improvement indicates progress ranging from 51% to 80%, and a mild improvement denotes a slight enhancement. The potential for improvement ranges from 10% to 50%, while there is a possibility for no change or even a decline in performance with less than a 10% improvement.

A clinically evident wart must be absent in order for the term “clearance” to be operationally defined. When a lesion still exists after four rounds of therapy, it was determined that the treatment had failed.

Follow-up: 6 months after the last session to evaluate the recurrence rate in both groups.

Ethical Consideration:

All participants in the study provided written consent. The study’s objective and any potential risks were thoroughly deliberated with the participants. All patients received appropriate medical treatment, and all data collected from patients were exclusively utilized for research objectives. The participants were provided with the researcher’s contact information, including their phone number and other communication means, to facilitate their ability to seek clarification or further information at any given time.
Statistical Analysis:
The researchers used IBM SPSS version 20 to enter the updated and coded data that they had obtained. Using numerical numbers and proportions was an integral part of presenting qualitative data. On the other hand, quantitative data is typically presented using statistical measurements like ranges, standard deviations, and means, presuming that the data follows a parametric distribution. To compare two groups using qualitative data, the Chi-square test was utilized. When the predicted count in any cell was less than 5, the Fisher exact test was utilized instead of the Chi-square test.

The Independent t-test was employed to compare two independent groups with quantitative data and a parametric distribution. The confidence level was established at 95%, with a corresponding margin of error of 5%, which was acceptable. The p-value was deemed statistically significant based on the following analysis. In statistical analysis, a p-value more than 0.05 is considered non-significant (NS), indicating insufficient evidence to reject the null hypothesis. Conversely, a p-value less than 0.05 is deemed significant (S), suggesting enough evidence to reject the null hypothesis and support the alternative hypothesis. Furthermore, a p-value of less than 0.01 was classified as highly significant (HS), indicating more substantial evidence against the null hypothesis.

3. Results

Table 1. Based on demographic information, the distribution of the cases being studied is categorized.

<table>
<thead>
<tr>
<th></th>
<th>All Cases</th>
<th>Sex</th>
<th>Age</th>
<th>Disease Duration</th>
<th>Size of wart before</th>
<th>No. session</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.= 50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td>Female</td>
<td>10 (20.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>40 (80.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Mean ± SD</td>
<td></td>
<td></td>
<td>37.42 ± 8.50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td>18 – 50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease. Duration Mean ± SD</td>
<td></td>
<td></td>
<td>32.26 ± 11.56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td>3 – 50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size of wart .before Mean ± SD</td>
<td></td>
<td></td>
<td>5.66 ± 1.61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td>3 – 8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. session Mean ± SD</td>
<td></td>
<td></td>
<td>4.24 ± 0.82</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td>3 – 5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As illustrated in Table 1, there were 40 cases were male and 10 were female and their ages ranged from 18 to 50 years (mean 37.42 years) the mean disease duration were 32.26±11.56, the size wart .before ranged from 3 to 8 (mean 5.66) and the mean No. session were 4.24 ± 0.82.

Figure 1. Sex-wise distribution of the cases under study.

Table 2. Compare between two groups, Group A (n=25) and Group B (n=25), in terms of age and gender demographics.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Test value</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.= 25</td>
<td>25</td>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Mean ± SD</td>
<td>37.84 ± 9.25</td>
<td>37.00 ± 7.86</td>
<td>-0.346*</td>
<td>0.731</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>18-50</td>
<td>18-50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4 (16.0%)</td>
<td>6 (24.0%)</td>
<td>0.500*</td>
<td>0.480</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>21 (84.0%)</td>
<td>19 (76.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P-value > 0.05: Non-significant (NS); P-value< 0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test, •: Independent t-test

The mean age of the participants in Group A was 37.84±9.25 years, as shown in Table 2, whereas the average age of participants in Group B was 37.00±7.86. In Group A, 84.0% of the participants identified as men while 16.0% identified as females. In contrast, in Group B 76.0% identified as males and 24.0% identified as females. Neither group A nor group B differed significantly from one another in terms of age or gender.

Figure 2. To compare the age distribution between group A and group B.
Figure 3: Compare the demographics of gender between groups A and B. Table 3 presents a comparative analysis of group A, consisting of 25 individuals, and group B, also comprising 25 individuals in relation to the duration and size of a wart, as well as the number of treatment sessions required.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Test</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. = 24</td>
<td>29.64 ± 12.39</td>
<td>34.88 ± 10.26</td>
<td>1.629*</td>
<td>0.110</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>3 – 50</td>
<td>15 – 50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size of wart before</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. = 24</td>
<td>5.38 ± 1.64</td>
<td>5.94 ± 1.56</td>
<td>1.218*</td>
<td>0.229</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>3 – 8</td>
<td>3 – 8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. session</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. = 24</td>
<td>4.08 ± 0.86</td>
<td>4.40 ± 0.76</td>
<td>1.389*</td>
<td>0.171</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>3 – 5</td>
<td>3 – 5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

An independent t-test is performed if the p-value is less than 0.05, a chi-square test is performed if the p-value is greater than 0.05, and a highly significant (HS) result is obtained if the p-value is less than 0.01.

As illustrated in Table 3, when we compared between group A & group B regarding disease duration, size of warts and number of sessions, we found that the average disease duration in group A was 29.64±12.39, while average disease duration in group B was 34.88±10.26, the average size of wart before in group A was 5.38±1.64, while average size of wart before in group B was 5.94±1.56 and the average No. session in group A was 4.08±0.86, while average No. session in group B was 4.40±0.76.

When comparing group A and group B, there were no statistically significant differences in the length of the disease, the size of the wart prior to treatment, or the number of treatment sessions.

Figure 4. illustrates a comparative analysis of disease duration when comparing groups A and B.

Figure 5. illustrates a comparative analysis of the wart size before to treatment for both group A and group B.

Figure 6. illustrates a comparative analysis of the number of sessions conducted by group A and group B.

Table 4 presents a comparative analysis of Group A, consisting of 25 individuals, and Group B, also comprising 25 individuals, with respect to the occurrence of recurrence.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Test</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. %</td>
<td>1 4.0%</td>
<td>2 8.0%</td>
<td>0.355</td>
<td>0.552</td>
<td>NS</td>
</tr>
</tbody>
</table>

Chi-square test, independent t-test, and non-significant (NS) when p-value > 0.05, significant (S) when p < 0.05, and highly significant (HS) when p < 0.01.
Table 5. presents a comparative analysis of clinical improvement between two groups, namely Group A (n=25) and Group B (n=25).

<table>
<thead>
<tr>
<th>Clinical Improvement</th>
<th>Group A</th>
<th>Group B</th>
<th>Test value*</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Complete Clearance</td>
<td>10</td>
<td>40.0%</td>
<td>3</td>
<td>12.0%</td>
<td>10.206 0.016 S</td>
</tr>
<tr>
<td>Marked Improvement</td>
<td>2</td>
<td>8.0%</td>
<td>10</td>
<td>40.0%</td>
<td></td>
</tr>
<tr>
<td>Mild Improvement</td>
<td>6</td>
<td>24.0%</td>
<td>8</td>
<td>32.0%</td>
<td></td>
</tr>
<tr>
<td>Moderate Improvement</td>
<td>7</td>
<td>28.0%</td>
<td>4</td>
<td>16.0%</td>
<td></td>
</tr>
</tbody>
</table>

Table 6. analyzes the satisfaction levels of two groups, Group A (n=25) and Group B (n=25), and compares them.

<table>
<thead>
<tr>
<th>Satisfaction</th>
<th>Group A</th>
<th>Group B</th>
<th>Test value*</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td>6</td>
<td>24.0%</td>
<td>7</td>
<td>28.0%</td>
<td>0.773 0.679 NS</td>
</tr>
<tr>
<td>Satisfied</td>
<td>8</td>
<td>32.0%</td>
<td>10</td>
<td>40.0%</td>
<td></td>
</tr>
<tr>
<td>Unsatisfied</td>
<td>11</td>
<td>44.0%</td>
<td>8</td>
<td>32.0%</td>
<td></td>
</tr>
</tbody>
</table>

As illustrated in Table 4, 5 and 6, response results show significantly improvement in both groups. In group A there was one patient recurrence while, in group B 2(8.0%) patients were recurrence. For the evaluation in group A, 12.0% of them were complete clearance, 28.0% were marked improvement, 32.0% were mild improvement and 16.0% were moderate improvement. While, in group B 16.0% of them were complete clearance, 28.0% were marked improvement, 24.0% were mild improvement and 32.0% were moderate improvement.

There was a lack of statistical significance observed when comparing the response, recurrence, and evaluation outcomes between group A and group B.

Cases

Cases treated with (Long pulsed Nd YAG) lasers

(Post) (Female patient 33 years old) (Pre)
4. Discussion

Warts are classified as benign epithelial neoplasms that develop on the skin and mucosa due to infection by the human papillomavirus (HPV). Dermatologic complaints of this nature are frequently encountered, with an estimated prevalence of 10% among individuals in the pediatric and young adult age groups.9

There are various therapy modalities for the management of warts, yet the majority of these approaches are associated with distinct drawbacks and adverse consequences. Invasive procedures are associated with the disadvantages of experiencing discomfort and enduring extended recovery times. The effective care of a specific condition necessitates the prolonged administration of pharmaceutical agents, and the achievement of treatment goals is consequently heavily contingent upon patients’ adherence to prescribed regimens.7

Using photo-dermal or photomechanical deterioration to target tissue is the basic concept of the laser treatment technique. Structures that serve as targets can soak up monochromatic coherent light at specific frequencies and wavelengths. Light energy is transformed into thermal energy, which causes the target structure to deteriorate. The photomechanical effect or coagulation, which refers to the coagulation of these structures, could happen based on the energy density and pulse length.10

Numerous studies have assessed the efficacy of Long-Pulsed Nd-YAG lasers and Q-switched Nd-YAG lasers in treating various dermatological conditions. However, our work represents the first attempt to directly examine the effects of these two types of Nd-YAG lasers (Long-Pulsed Nd-YAG laser and Q-switched Nd-YAG laser) specifically...
on plantar warts.

Our study’s conclusions show no statistically significant difference in the demographic features of the two groups. Additionally, our investigation revealed no statistically significant distinction between the two groups regarding response, recurrence, and evaluation.

In the laser group, a study conducted by El-Mohamady et al. \(^\text{11}\) carried out a comparative analysis to evaluate the efficacy of two laser types, namely PDL and Nd-YAG, in the treatment of resistant plantar warts. The results indicated that complete clearance of the warts was accomplished in 73.9% of cases treated with PDL, while the cure rate for Nd-YAG laser treatment was found to be 78.3%.

Han et al. \(^\text{7}\) found a 44% response rate in deep palmoplantar warts after the initial treatment. They also noted that most patients required multiple treatments. Based on these findings, including long-pulsed Nd-YAG laser in the available therapeutic choices should be considered a reasonable approach.

In contrast, Huilgol et al. \(^\text{12}\) found that their patients experienced partial remission and symptom reduction with PDL treatment. However, as stated in previous investigations, a complete resolution still needs to be achieved; several factors may contribute to the observed outcome, including the individual's immunological health, warts’ quantity and location, persistence, and the number of laser sessions conducted.

Our study’s findings show that groups A and B significantly differed in patient satisfaction and pain levels. This difference is statistically significant.

Hence, the findings of El-Mohamady et al. \(^\text{11}\) establish that photodynamic therapy (PDL) is deemed safe and linked to reduced adverse effects. However, a higher frequency of treatments is necessary to achieve complete resolution of the lesions. Conversely, Nd-YAG laser treatment is more efficacious and necessitates fewer treatments, albeit accompanied by heightened discomfort and a higher prevalence of side effects.

Zorman et al. \(^\text{13}\) conducted a study wherein the Nd-YAG laser was employed without administering an anesthetic to treat warts in 85 individuals. Utilizing alternate procedures, such as using chilly air or applying ice cubes every three to four laser pulses, is safe and successful in mitigating discomfort and minimizing thermal damage to the surrounding tissues throughout the treatment process. No notable adverse effects were observed among the patients after the treatment. Specifically, four individuals exhibited the presence of blisters; 14 patients, however, claimed to have experienced minor pain in the days that followed.

Furthermore, there were no patient reports of scars or hypo- or hyperpigmentation. The participants in the study said that they experienced pain levels comparable to those associated with cryotherapy procedures and reported mild discomfort in the subsequent days. Based on their respective experiences, the implementation of topical anesthetic did not yield a substantial reduction in pain compared to the administration of a placebo. Moreover, the response rates achieved by topical anesthesia were comparable to or even higher than those achieved using traditional therapeutic approaches.

Our study’s findings indicate that there is no statistically significant disparity in complications between groups A and B.

Yeh, Y.T. \(^\text{14}\) concurs with this statement. In the days following the therapy, it is feasible to discern alterations via microscopic assessment. These changes include a splitting of the dermal-epidermal junction, necrosis of the epidermis, extravasation of red blood cells, and the presence of obliterated blood vessels accompanied by a concentrated infiltration of inflammatory cells within the dermal layer.

5. Conclusion

Nd-YAG with a long pulse (1,064 nm) It is safe and successful to treat plantar warts with Q-Switched Nd-YAG (1064 nm) laser technologies. For those who prefer not to or are unable to undergo oral treatment, these laser techniques provide an excellent alternative.

5.1. Recommendations

It is recommended to do this study on a large number of patients to support our results, and it is necessary to increase the usage of both techniques for a better outcome with a low recurrence rate.

Disclosure

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Conflicts of interest

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References