



SAFETY AND EFFICACY OF LONG PULSED 1064NM ND:YAG LASER VERSUS LIQUID NITROGEN CRYOTHERAPY FOR THE TREATMENT OF WARTS – A COMPARATIVE STUDY.

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ABSTRACT

Background

Warts are benign epidermal growths on the skin and mucous membrane caused by infection with human papillomavirus. Complete clearance is not always achieved with the conventional therapies. Previous studies have shown the effectiveness of long pulsed 1064 nm Nd: YAG laser in the treatment of warts.

Objective

To compare the safety and efficacy of LP 1064 nm Nd: YAG laser with liquid nitrogen cryotherapy for the treatment of warts.

Methods

A total of sixty patients with warts were equally divided into two groups. First group received LP Nd: YAG laser treatment once in every four weeks for 16 weeks. Second group received liquid nitrogen cryotherapy once weekly for 4 weeks or until clearance of warts, whichever was earlier. Follow up was done at 4 and 8 weeks in laser group and at 2 and 4 weeks in cryotherapy group.

Results

The laser group demonstrated a significantly higher clearance rate (90.0% vs. 56.6%, $p < 0.01$), requiring fewer treatment sessions (1.3 ± 0.5 vs. 2.8 ± 1.1 , $p < 0.01$) compared to cryotherapy group. Laser group also had lesser complications and a lower relapse rate (0.0% vs. 13.3%, $p = 0.05$) compared to cryotherapy group.

Conclusion

LP 1064nm Nd: YAG laser is a safer and therapeutically more effective treatment modality requiring lesser number of treatment sessions, lesser complications and lower relapse rates compared to liquid nitrogen cryotherapy.

KEYWORDS

Warts, long-pulsed 1064 nm Nd: YAG laser, liquid nitrogen cryotherapy.

INTRODUCTION

Warts are benign epidermal growths on the skin and mucous membrane caused by infection with human papillomavirus (HPV). Prevalence ranges from 5 to 20 % in children and young adults [1]. Warts are caused by over 150 serotypes of HPV. They are subdivided into genital and non-genital types [2]. Transmission occurs through direct skin contact or indirectly via contaminated objects. Complications include pain, discomfort, bleeding, unsightly appearance, interference of function and social embarrassment [3].

Several treatment options are available for warts including chemical cautery, keratolytics, cryotherapy, electrocautery, immunotherapy and laser therapy [4]. Liquid nitrogen cryotherapy is widely employed in the treatment of warts [5]. Tissue hypoxia and acute cell damage result from rapid freezing, which also forms intracellular and extracellular ice crystals. Additionally, the freezing process damages the microcirculation, leading to ischemic necrosis and the destruction of affected tissues [6].

Neodymium-doped yttrium aluminum garnet (Nd:YAG), carbon dioxide, and pulsed dye lasers are among the many types of lasers that have been used to treat warts [7]. Among these, long-pulsed 1064nm Nd:YAG laser is particularly notable for its deep penetration into the skin and its selective absorption properties for hemoglobin and melanin. Its effectiveness in targeting wart lesions has made it a widely recognized choice in dermatological applications. The visible light emitted by long pulsed 1064nm Nd:YAG (LP Nd:YAG) laser transfers energy to thickened and hyperkeratotic epidermis, while also specifically targeting enlarged blood vessels. This causes the vessels to heat up and rupture quickly, leading to purpura and blister formation and eventual clearance of warts [8]. While LP Nd: YAG laser has proven to be effective in treating warts, there is a need for comparative studies to evaluate its safety and efficacy against other well-established treatments such as liquid nitrogen cryotherapy.

Only few studies have directly compared the effectiveness of LP Nd:YAG laser with liquid nitrogen cryotherapy in the treatment of warts to date. Therefore, the purpose of our study was to evaluate the safety and efficacy of long pulsed 1064nm Nd:YAG laser with liquid nitrogen cryotherapy for the treatment of warts.

METHODOLOGY

Study Design

This study was carried out over a period of six months, from May 2023 to October 2023, at Hassan Institute of Medical Sciences, Hassan, Department of Dermatology, Venereology, and Leprosy. Study was approved by the Institutional Ethics Committee, and prior to enrolment, written informed consent was obtained from each participant.

Patients

A total of 60 cases having non-genital warts, aged 12 years and above were enrolled in the study. Pregnant and lactating women, patients with a past history of keloids and bleeding tendencies, and immunocompromised patients were excluded from the study. Participants were randomly allocated to either laser group (LP Nd:YAG laser treatment) or cryotherapy group (liquid nitrogen cryotherapy treatment) in a 1:1 ratio using a computer-generated randomization sequence.

Interventions

LP 1064 nm Nd:YAG laser therapy with a spot size of 2 mm, pulse duration of 10 msec, and fluence of 333 J/cm² was administered to the patients in the laser group. An injection of 1% lidocaine anaesthetic was administered around the lesions, particularly around their borders before the laser treatment, to improve patient comfort throughout the procedure. During the treatment sessions, both patient and clinician wore protective goggles and masks, and a smoke evacuator was used to eliminate any airborne viral particles. Laser was administered to an entire area of wart with 2 to 3 passes, ensuring 10-20% overlap. Additionally, a single set of slightly overlapping pulse was administered to the surrounding 1mm normal skin. Patients received treatment for a maximum of four sessions or until complete clearance, with an interval of four weeks between each session. Follow-up assessments were conducted at 4 weeks and 8 weeks. Patients in cryotherapy group underwent liquid nitrogen cryotherapy treatment using the open spray technique. In this technique, lesion was sprayed with liquid nitrogen by holding the tip of instrument 1cm away from the lesion. Freezing time used was 15-30 seconds or until freezing occurred up to 2mm around the lesion. Then it was allowed to thaw until freezing disappeared. Two freeze-thaw cycles were given in one session. Weekly liquid nitrogen cryotherapy was given for 4 weeks or until clearance of warts, whichever was earlier. Follow up was done at 2 weeks and 4 weeks. Follow up for all the patients was conducted after 6 months to look for relapse of warts.

Data Collection and Outcome Assessment

Baseline characteristics including age, sex, wart number, size, location, history of previous treatment received and clinical photographs were recorded for all patients. Treatment outcomes, side effects and patient satisfaction were assessed during follow-up visits.

Effectiveness of the treatment was evaluated by analysing photographs taken before and after the procedure and during each follow up, alongside results from clinical examination. The physician Global Improvement Scale (GIS) was used to grade the improvement in wart size and number. The GIS included five distinct grades. Grade 0 indicated no improvement, while Grade 1 represented mild improvement, characterized by a reduction in size and number of warts by 25% or less. Grade 2 signified moderate improvement with a reduction of 26% to 50%. Grade 3 denoted marked improvement, reflecting a reduction of 51% to 75%. Finally, Grade 4 indicated near-total or total improvement, achieving a decrease of at least 76% in both size and number. Safety was assessed by any negative occurrences or side effects that were reported by patients or noticed by the investigators.

Statistical Analysis

Categorical variables were expressed as count and percentage of patients, and comparisons between groups were made using Pearson's Chi-Square test for independence. Continuous variables were expressed as mean and standard deviation. Comparison between the two groups was performed using the Z test for two means. Data was analysed using SPSS software, version 24.0. An alpha level of 5% was set, indicating that a p-value below 0.05 was taken as statistically significant.

RESULTS

Sixty patients with non-genital warts participated in this study. Thirty patients were assigned to LP Nd: YAG laser group, while other thirty were assigned to liquid nitrogen cryotherapy group. Patients in the both groups had similar demographic characteristics, with no significant differences noted in age or gender distribution (Table 1). Patients in laser group had an average age of 27.5 years, whereas in cryotherapy group average age of patients was 29.4 years ($p = 0.45$). The laser treatment group included 15 males and 15 females, each representing 50% of the group. In contrast, the cryotherapy group comprised of 14 (46.7%) males and 16 females (53.3%) ($p = 0.80$).

Table 1: Baseline characteristics

Characteristics	Laser Group (n=30)	Cryotherapy Group (n=30)	p-value
Demographics			
Average Age (Years)	27.5 ± 5.6	29.4 ± 6.2	0.45
Gender, n (%)			
- Male	15 (50%)	14 (46.7%)	0.8
- Female	15 (50%)	16 (53.3%)	
Types of warts			
Palmar	7 (23.3%)	4 (13.3%)	
Plantar	8 (26.7%)	16 (53.3%)	
Verruca Vulgaris	10 (33.3%)	8 (26.7%)	
Periungual	5 (16.7%)	2 (6.7%)	
Characteristics of wart			
Number of Warts	1.5 ± 0.8	1.7 ± 1.0	0.37
Size of Warts (mm)	7.0 ± 2.5	8.0 ± 2.8	0.29
Duration of Warts (Weeks)	10.0 ± 5.2	11.0 ± 6.1	0.29

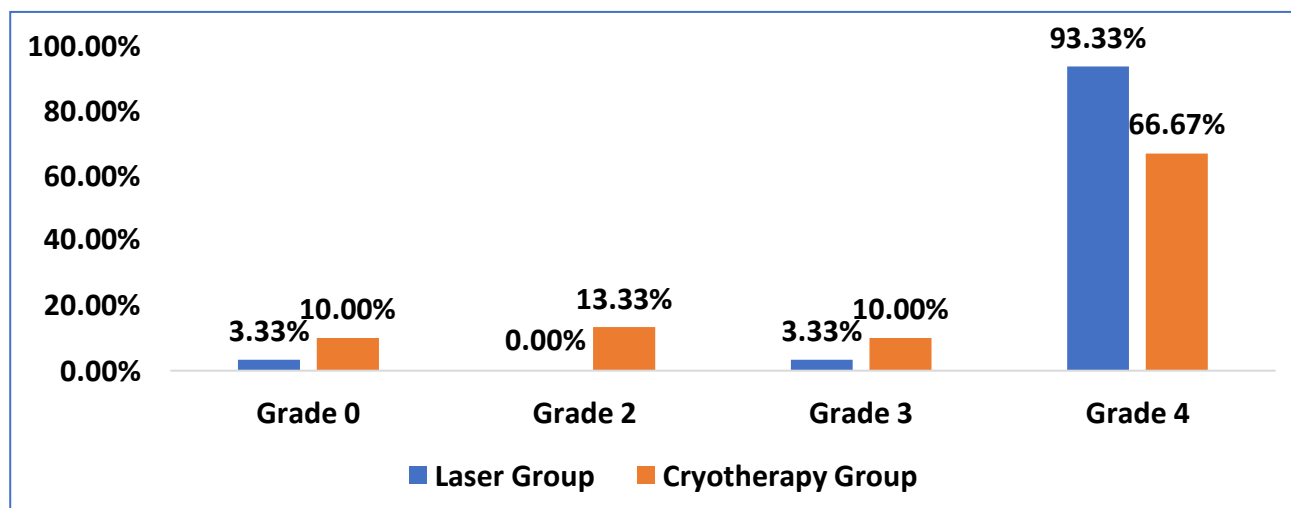
The distribution of wart types varied across the two groups (Table 1). In the laser treatment group, the most prevalent type was verruca vulgaris, accounting for 33.3%, followed by plantar warts (26.7%), palmar warts (23.3%), and periungual warts (16.7%). In the cryotherapy group, plantar warts were the most prevalent (53.3%) followed by verruca vulgaris (26.7%), palmar warts (13.3%), and periungual warts (6.7%).

The baseline features of the warts showed no significant differences between the two groups (Table 1). There were 1.5 ± 0.8 warts on average in the laser treatment group and 1.7 ± 1.0 warts on average (p = 0.37) in the cryotherapy group. The average size of the warts in the laser treatment group measured 7.0 ± 2.5 mm, whereas in the cryotherapy group, the mean size was 8.0 ± 2.8 mm (p = 0.29). Furthermore, the average duration of the warts was reported as 10.0 ± 5.2 weeks in the laser group, while in the cryotherapy group, average duration of warts was 11.0 ± 6.1 weeks (p = 0.29).

At the end of the study, results from Global Improvement Scale indicated a significant difference between the two treatment groups (p-value-0.001) (Table 2 and Graph 1). In the laser group, 28 (93.3%) patients achieved grade 4, while only 20 (66.7%) patients in the cryotherapy group reached this grade. One patient (3.3%) from the laser group exhibited a grade 3 improvement, whereas three patients (10%) from the cryotherapy group had the same improvement. In the cryotherapy group, four patients (13.3%) experienced grade 2 improvement, but no such improvement was seen in the laser group. One patient (3.3%) in the laser group showed grade 0 improvement, whereas three patients (10%) in the cryotherapy group showed the same grade.

Table 2: Global Improvement Scale (Grade)

Global Improvement Scale (Grade)	Laser Group	Cryotherapy Group	p-value
Grade 0	1 (3.3%)	3 (10.0%)	0.001
Grade 1	0 (0.0%)	0 (0.0%)	
Grade 2	0 (0.0%)	4 (13.3%)	
Grade 3	1 (3.3%)	3 (10.0%)	
Grade 4	28 (93.3%)	20 (66.7%)	



Graph 1: Physician global improvement scale

Both treatment modalities were associated with a range of complications, all of which were classified as mild in severity (Table 3). Pain was the most common complaint among them, as reported by 24 patients (80%) in the cryotherapy group and 21 patients (70%) in the laser group ($p = 0.25$). 18 patients (60.0%) in the laser group (Fig. 1) and 22 patients (73.3%) in cryotherapy group had blistering ($p = 0.15$). Furthermore, it was noted that 4 patients (13.3%) in the laser group and 3 patients (10.0%) in the cryotherapy group experienced post-inflammatory hypopigmentation ($p = 0.45$) (Fig 2). Hemorrhagic bulla was found in 6 patients (20%) in the cryotherapy group, whereas it was found in 1 patient (3.3%) in the laser group ($p = 0.045$). In the laser treatment group, none of the patients had secondary infection. Conversely, secondary infection was noted in one patient (3.3%) from the cryotherapy group ($p = 0.10$). Furthermore, 3 patients (10%) in the cryotherapy group and 1 patient (3.3%) in the laser group both experienced ulceration ($p = 0.20$). Post procedure adverse events like pain, blistering and ulceration were managed accordingly.

Table 3: Complications

Complications	Laser Group	Cryotherapy Group	p-value
Pain	21 (70.0%)	24 (80.0%)	0.25
Blister	18 (60.0%)	22 (73.3%)	0.15
Postinflammatory hypopigmentation	4 (13.3%)	3 (10.0%)	0.45
Hemorrhagic bulla	1 (3.3%)	6 (20.0%)	0.045
Secondary infection	0 (0.0%)	1 (3.3%)	0.10
Ulceration	1 (3.3%)	3 (10.0%)	0.20



Fig. 1 A 21-year-old woman with a plantar wart underwent treatment with 1064 nm LP Nd:YAG laser, (a) - before treatment, (b) - blister at the site of treatment at 1 week and (c) - complete clearance

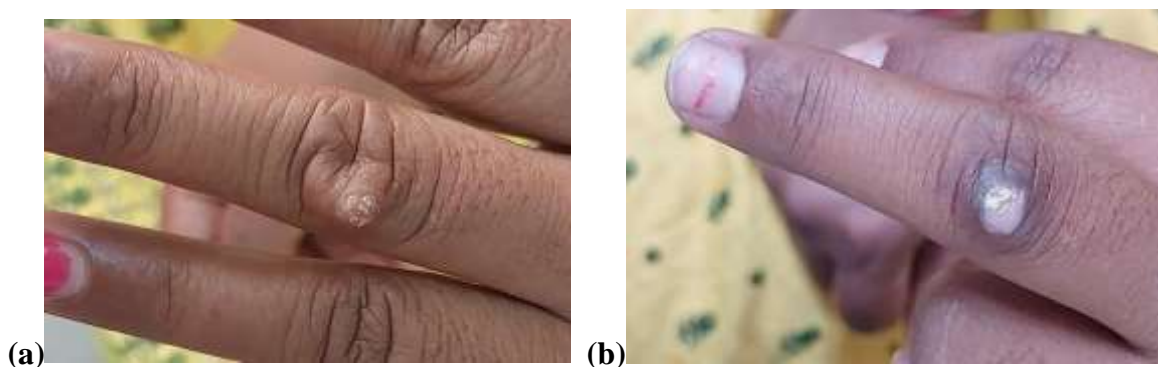


Fig. 2 (a) - common wart in a 32-year-old female treated with liquid nitrogen cryotherapy before treatment, (b) – complete clearance with PIH

Table 4: Treatment Outcomes

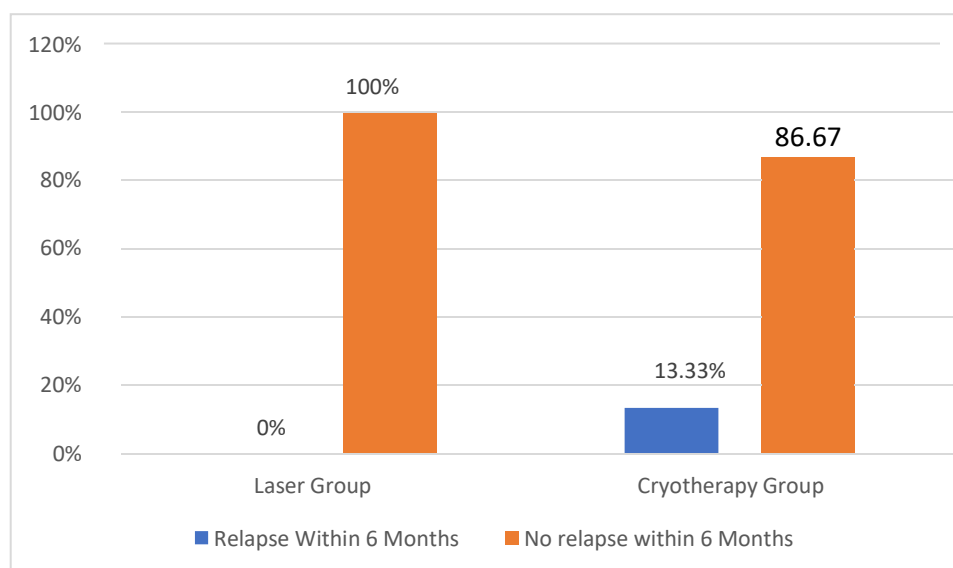
Outcome	Laser Group	Cryotherapy Group	p-value
Clearance Rate	27 (90.0%)	17 (56.6%)	<0.01
Average Number of Sessions Required	1.3 ± 0.5	2.8 ± 1.1	<0.01

The laser group had better treatment outcomes (Table 4). There was a significant difference in the clearance rates between the treatment groups. Clearance rate in the laser group was 90%, whereas in cryotherapy group clearance rate was 56.6% ($p < 0.01$). Additionally, the mean number of sessions required for total clearance was 1.3 ± 0.5 in the laser group, while the cryotherapy group needed an average of 2.8 ± 1.1 sessions ($p < 0.01$).

Table 5: Relapse Rates

Relapse	Laser Group	Cryotherapy Group	p-value
Relapse Within 6 Months	0 (0.0%)	4 (13.3%)	0.05
No Relapse Within 6 Months	30 (100.0%)	26 (86.7%)	

Relapse rate within 6 months of treatment completion was significantly lower in the laser group (Table 5, graph 2). In the laser treatment group, there was no relapse (0%), while 4 patients (13.3%) in the cryotherapy group reported recurrence of warts ($p = 0.05$).



Graph 2 : Relapse rate

DISCUSSION

In this study, laser treatment attained a complete clearance rate of 93.3%, which is significantly greater than the 66.6% clearance rate observed with cryotherapy ($p < 0.01$). Additionally, 70% of the patients in the laser group experienced fewer side effects compared to 80% in the cryotherapy group. In comparison to cryotherapy group, laser group needed fewer treatment sessions on average for complete clearance (1.3 ± 0.5 vs. 2.8 ± 1.1 , $p < 0.01$). In the laser group, there was no case of relapse (0%). In contrast, 13.3% of the patients receiving cryotherapy reported relapse ($p = 0.05$).

Patients in LP Nd:YAG laser group had a far greater clearance rate of 96.7% than 79.3% clearance rate in the cryotherapy group, according to a study by Liu et al. [9]. This finding aligns with the results of our study. However, the laser group had higher incidence of mild adverse effects such as pain, erythema and edema compared to the cryotherapy group which is in contrast to our study findings. For the treatment of acral warts, Gheisari et al. [10] found that both treatment methods showed similar efficacy and that there was no significant difference in the clearance rates between the two groups (72.5% for laser and 67.5% for cryotherapy).

The differences between our findings and those of Liu et al. [9] and Gheisari et al. [10] may be due to variations in the study design, patient demographics, characteristics of the warts, treatment protocols, higher fluence (160–360 J/cm²) and shorter pulse duration (10ms) compared to our study (fluence: 150–200 J/cm², pulse duration: 20–30 ms) [9]. Differences in the laser parameters might have contributed to the higher incidence of adverse effects observed in their study.

The LP Nd:YAG laser is a potentially effective substitute for conventional cryotherapy in the treatment of warts. The advantages of LP Nd:YAG laser include higher clearance rates, fewer treatment sessions and a lower relapse rate. These benefits are attributed to the laser ability to selectively target and destroy the blood vessels supplying the wart, leading to its clearance. In contrast, cryotherapy has the potential to cause nonspecific damage to the nearby healthy tissue,

which leads to higher side effects [11].

Limitations of our study include, relatively small sample size, exclusion of pediatric patients and this was carried out at a single centre that can affect the generalizability of findings. Therefore, we recommend conducting more multicentre randomized controlled trials with a larger sample size.

CONCLUSION

Our study demonstrated that LP 1064 nm Nd: YAG laser is a safer and therapeutically more effective treatment modality requiring fewer treatment sessions, lesser complications, and lower relapse rates. These findings suggest that LP Nd: YAG laser could be considered as a preferable treatment modality for warts, particularly for recalcitrant cases.

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