

The Comparison of Diphenylcyclopropenone and Nd:YAG in the Treatment of Palmar Verrucae

Palmar Siğillerin Tedavisinde Difenilsiklopropenon ve Nd:YAG Tedavilerinin Karşılaştırılması

Özge AŞKIN^a, Defne ÖZKOCA^a, Tuğba Kevser ÜSTÜNBAŞ UZUNÇAKMAK^a,
Zekayi KUTLUBAY^a, Burhan ENGİN^a, Server SERDAROĞLU^a

^aDepartment of Dermatology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, TURKEY

ABSTRACT Objective: Palmar verrucae are often recalcitrant to treatment. Diphenylcyclopropenone (DPCP) and Nd:YAG laser are treatment modalities that may be used in cases which are resistant to conventional treatment modalities. The aim of this study is to compare the treatment efficacies and safety of DPCP and Nd:YAG laser in the treatment of palmar verrucae. **Material and Methods:** A total of 30 patients with single or multiple palmar verrucae were divided into two equal groups: DPCP group and the Nd:YAG group with 15 patients in each. Informed consent of each patient was taken before treatment. Pre-treatment photos of each patient were taken. The age, gender, location and number of lesions of each patient were noted. One group received monthly Nd:YAG treatments and the other group received weekly DPCP treatments until complete remission. **Results:** The mean number of sessions required for remission was 1.6 in the Nd:YAG group and 4 in the DPCP group. Nd:YAG treatment requires a statistically significantly lower number of treatment sessions compared to DPCP treatment ($p<0.05$). The mean treatment duration was 6.4 weeks for the Nd:YAG group and 4 weeks for the DPCP group. A statistically significant difference was found between the two groups in terms of treatment duration the patients achieved complete remission in the DPCP group faster than the Nd:YAG group ($p=0.005$). **Conclusion:** Our study has shown that DPCP is a faster modality than Nd:YAG in the treatment of palmar verrucae. On the other hand, Nd:YAG is more effective per treatment session and therefore requires less hospital visits than Nd:YAG. The treatment efficacy was independent of the patient's age and number of lesions. DPCP was better tolerated than Nd:YAG.

ÖZET Amaç: Palmar siğiller sıklıkla tedaviye dirençlidirler. Difenilsiklopropenon (DPCP) ve Nd:YAG lazer, tedaviye dirençli siğil hastalarında kullanılabilen yöntemlerdir. Bu çalışmadaki amacımız, palmar siğillerin tedavisinde DPCP ve Nd:YAG tedavilerini karşılaştırmaktır. **Gereç ve Yöntemler:** Çalışmamıza palmar bölgede siğilleri olan toplam 30 hasta dâhil edilip, 2 eşit gruba randomize edildi: 1. gruba DPCP tedavisi verilirken, 2. gruba Nd:YAG tedavisi verildi. Hastalardan tedavi öncesi onam alındı ve fotoğrafları çekildi. Her hastanın yaşı, cinsiyeti, lezyon sayısı ve lokalizasyonu not edildi. Hastalara, tam yanıt elde edene kadar, Nd:YAG tedavisi aylık, DPCP tedavisi de haftalık olarak verildi. **Bulgular:** Remisyon için gereken seans sayısının ortalaması Nd:YAG grubu için 1,6, DPCP grubu için 4 idi. Nd:YAG grubu istatistiksel olarak daha az seans gerektirmektedir ($p<0,05$). Nd:YAG grubu için gereken ortalama tedavi süresi 6,4 hafta iken, bu süre DPCP için 4 haftadır. DPCP ile daha hızlı remisyon elde edilmektedir ($p=0,005$). İki grup arasında tedavi süresi açısından istatistiksel olarak anlamlı fark bulunmuştur: DPCP grubundaki hastalarda Nd: YAG grubuna göre daha hızlı tam remisyon elde edilmiştir. **Sonuç:** Çalışmamızda, palmar siğillerin tedavisinde DPCP'nin Nd:YAG'ye göre daha hızlı bir metod olduğunu, buna karşılık Nd:YAG'nin etkinliği seans başına daha fazla olup, daha az hastane ziyareti gerektirdiğini gösterdik. Tedavi etkinliği, hastanın yaşından ve lezyon sayısından bağımsızdır. DPCP, Nd:YAG'ye göre daha iyi tolere edilebilmektedir.

Keywords: Diphenylcyclopropenone; Nd:YAG; palmar verrucae

Anahtar Kelimeler: Difenilsiklopropenon; Nd:YAG; palmar siğil

Palmar verrucae are slightly elevated tan-colored papules with surface scale. They are caused by various types of human papilloma viruses; mainly 1.3 and

10. Depending on the localisation of the lesion and the number of lesions, there are many treatment modalities. However, palmar verrucae are frequently

Correspondence: Defne ÖZKOCA

Department of Dermatology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, TURKEY/TÜRKİYE

E-mail: defneozkoca@yahoo.com



Peer review under responsibility of Türkiye Klinikleri Journal of Dermatology.

Received: 02 Feb 2021

Received in revised form: 23 Mar 2021

Accepted: 23 Mar 2021

Available online: 31 Mar 2021

2146-9016 / Copyright © 2021 by Türkiye Klinikleri. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

resistant to treatment. Cryotherapy, photodynamic therapy, topical salicylic acid, intralesional bleomycin, topical or systemic retinoids, topical podophyllin, topical trichloroacetic acid, topical imiquimod, intralesional interferon, electrocautery, immunotherapy, carbon dioxide laser, pulsed dye laser and Nd:YAG laser are examples of these modalities.¹

Diphenylcyclopropenone (DPCP) is a contact sensitizer that can be used in the treatment of treatment-resistant verrucae via immunotherapy. It has a treatment success of up to 85%. It has been found to be more successful than cryotherapy and pulse-dye laser in previous studies. The location that responds to DPCP immunotherapy the most is the proximal nail fold.²⁻⁴

Long-pulse 1,064 nm Nd:YAG laser has been used in the treatment of verrucae since 1999. Its mechanism of action is via the coagulation of vessels. Several studies have shown that Nd:YAG laser is as effective as pulse-dye laser in the treatment of verruca plantaris although it has a higher complication rate and is more painful. The recommended treatment parameters are a spot size of 7 mm, fluence of 100 J/cm² and a pulse duration of 20 ms.⁵⁻⁸

With this study, we aim to compare the treatment efficacies and safety of DPCP and Nd:YAG laser in the treatment of palmar verrucae. The secondary aim is to compare the efficacies of DPCP and Nd:YAG depending on the patient's gender, age and number of lesions.

MATERIAL AND METHODS

PATIENT SELECTION

The patients who have applied to the outpatient clinic of İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Dermatology and Venerology Department with the diagnosis of palmar verrucae and who have not received any treatment in the previous 3 months were included in this study. The patients with a history of photosensitive diseases, pregnant or nursing patients, immunosuppressed patients, patients with acute/critical illnesses, disabled patients, patients with verrucae elsewhere and patients younger than 18 years of age were excluded from this study. The included patients were randomized into two different

groups of equal sample sizes: DPCP group and the Nd:YAG group with 15 patients in each. Informed consent of each patient was taken before treatment. Pre-treatment photos of each patient were taken. The age, gender, location and number of lesions of each patient were noted. The post-treatment photos of the patients were taken when all lesions were cleared and the total number of sessions required for complete remission were noted.

DIPHENYLCYCLOPROPENONE TREATMENT

The patients in the DPCP group were first sensitized with 2% DPCP solution. Two weeks after sensitization, each patient received weekly 2% DPCP treatments. A total of 16 sessions (4 months) weekly was planned for the DPCP group. The patients were told not to wash their hands for 6 hours after each treatment session. Treatment was continued weekly until all lesions cleared.

ND:YAG TREATMENT

The patients in the Nd:YAG group received monthly treatment sessions with the following parameters: a fluence of 200 J/cm², a pulse duration of 15 ms, a frequency of 1.3 Hz and a spot size of 4 mm. The R33 head-piece of the 1,064 nm Nd:YAG laser (Fotona; Dualis SP, Ljubljana, Slovenia). The patients received topical EMLA cream before treatment in order to decrease pain. A total of 4 sessions monthly (4 months) were planned for the Nd:YAG group. Treatment was continued monthly until all lesions cleared.

ETHICAL STATEMENT

The approval of İstanbul University-Cerrahpaşa Medical Faculty Ethics Committee was taken before the study was initiated (23.01.2020, 39122051-604.01.01-13006). We conducted our research according to the World Medical Association Declaration of Helsinki.

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS version 21. The number of treatment sessions needed in order to achieve remission and the other variables were analyzed using histograms, probability graphics and Kolmogorov-Smirnov/Shapiro-Wilk tests. The spearman correlation test was used in order to

TABLE 1: Treatment results.

	Mean number of sessions	Minimum number of sessions	Maximum number of sessions	Mean treatment duration	Minimum treatment duration	Maximum treatment duration
DPCP	4	2	10	4 (p=0.005)	2	10
Nd:YAG	1.6 (p<0.05)	1	4	6.4	3	16

DPCP: Diphenylcyclopropanone.

analyse the variables that are not distributed normally. Mann-Whitney U test was used in order to compare the treatment efficacies of DPCP and Nd:YAG.

RESULTS

A total of 30 patients were included in this study. Fifteen of these patients received DPCP treatment and 15 received Nd:YAG treatment. Of these patients, thirteen were male and 17 were female. Six male patients received DPCP treatment and 7 male patients received Nd:YAG treatment. Nine female patients received DPCP treatment and eight female patients received Nd:YAG treatment. Overall, the mean age of the patients was 29.3 years: minimum of 18 and maximum of 44 years. Overall, the mean number of lesions of each patient was 2.8: minimum 1 and maximum 8. All of the patients achieved complete remission and both methods were successful in the treatment of palmar verrucae. Overall, the mean number of sessions required for remission was 2.8: minimum 1 and maximum 10.

The mean number of sessions required for remission was 1.6 (minimum 1 and maximum 4) in the Nd:YAG group. This number was 4 (minimum 2 and maximum 10) in the DPCP group. Nd:YAG treatment requires a statistically significantly lower number of treatment sessions compared to DPCP treatment (p<0.05). Furthermore, this difference was found to be significant in both genders: Nd:YAG treatment requires less sessions than DPCP both in females and males (p-values 0.003 and 0.004 respectively).

The mean treatment duration for the Nd:YAG group was 6.4 (minimum 3 maximum 16) weeks and the mean treatment duration for the DPCP group was 4 (minimum 2 maximum 10) weeks. The Nd:YAG treatment was applied every 4 weeks and the DPCP treatment was applied every week. A statistically sig-

nificant difference in terms of treatment duration was found between the two groups: the patients achieved complete remission in the DPCP group faster than the Nd:YAG group (p=0.005). The treatment results are summarized in Table 1.

Figure 1a shows the pre-treatment lesion of a patient treated with Nd:YAG; and Figure 1b shows the same lesion after only 1 treatment session. Figure 2a shows the pre-treatment lesion of a patient treated with DPCP; and Figure 2b shows the same lesion after 10 treatment sessions.

There is no relationship between the patient’s age and the number of treatment sessions required in both DPCP and Nd:YAG groups (p= 0.671 and 0.389, respectively). Moreover, there is no relationship between the number of lesions and the number of treatment sessions required for both DPCP and Nd:YAG groups (p= 0.901 and 0.333, respectively). Thus, the number of treatment sessions is independant of the number of lesions.

As for the side effects, three patients complained of pain during and after treatment. All of these patients were in the Nd:YAG group. Ulceration and bullae formation were observed in one of the Nd:YAG



FIGURE 1: a) A single lesion on the index finger of a patient before Nd:YAG treatment was initiated; b) The same lesion 1 month after a single session of Nd:YAG treatment. Complete remission was observed.



FIGURE 2: a) A lesion on the thumb of a patient before diphenylcyclopropanone treatment was initiated; b) The same lesion 1 month after 10 treatment sessions of diphenylcyclopropanone.



FIGURE 3: a) Ulceration following Nd:YAG therapy; b) Bullae formation following Nd:YAG therapy.

patients; the scar resolved in a month. [Figures 3a](#) and [3b](#) show ulceration and bullae formation following Nd:YAG therapy. The same patients two months follow-up is seen in [Figure 4](#). No side effects were reported in the DPCP group.

DISCUSSION

The conventional treatment modalities for verrucae are cryotherapy, electrocoagulation, topical therapies and surgical excision. Although these methods are effective, recurrences and incomplete remissions are common with these modalities. The 1,064 nm Nd:YAG laser is effective due to its ability to penetrate deeply into the tissue. However, this deeper penetration results in a greater sensation of pain

compared to other treatment modalities. As a result of pain, the patients tend to pull back their extremities, leading to a lower treatment success.^{9,10} The largest case series for the treatment of palmoplantar verrucae with Nd:YAG lasers was reported by Han et al. who reported a success rate of 96% and an average of 1.49 treatment sessions.⁸ Likewise, Zorman et al. reported a success rate of 91% with an average of 2.2 treatment sessions.⁹ All of the patients achieved complete remission in our patient series and the average number of treatment sessions was 1.6.

Previously, the use of Nd:YAG treatment was compared to the use of cantharidin–podophylline resin-salicylic acid in plantar warts and was found to be less effective than cantharidin-podophylline resin-salicylic acid.¹¹ Likewise, the efficacy of Nd:YAG was compared to the efficacy of cryotherapy in the treatment of acral verrucae. The modalities were equally effective, however, cryotherapy was less painful compared to Nd:YAG.¹² There are no previous studies comparing the treatment efficacy of Nd:YAG to DPCP. We report a 100% clearance rate in both treatment groups. The average number of treatment sessions required for clearance was 1.6 in the Nd:YAG group and 2.8 for the DPCP group. The

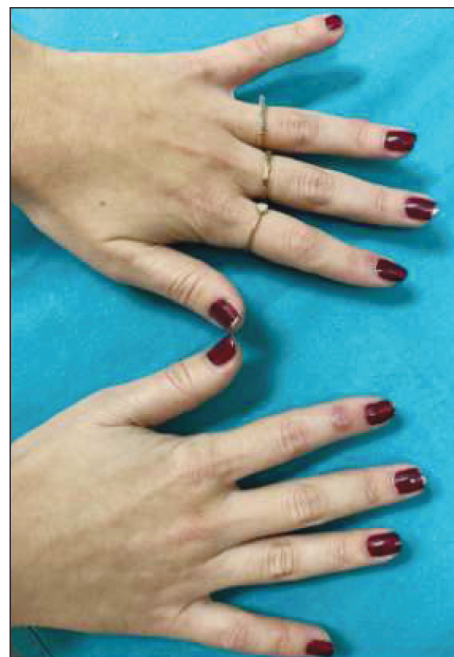


FIGURE 4: Two months after Nd:YAG therapy, all the side effects have subsided.

difference was statistically significant. Our results reveal that Nd:YAG is more effective than DPCP in a single session and requires less hospital visits. On the other hand, the mean treatment duration for Nd:YAG was 6.4 weeks and the mean treatment duration for DPCP was 4 weeks; this difference was statistically significant. DPCP is more effective than Nd:YAG in terms of treatment duration meaning that patients are treated faster with DPCP than Nd:YAG.

There are three previous studies regarding the treatment efficacy of DPCP in verrucae. Park et al. have reported a clearance rate of 75%, Choi et al. 85% and Suh et al. 85%. The treatment durations were 22 weeks, 7.8 to 54 weeks depending on the location of the lesion and 9 weeks, respectively.²⁻⁴ Among all palmar verrucae, DPCP was the most effective in periungual verrucae.³ On the other hand, DPCP, as a monotherapy, is less successful than cryotherapy and Pulse-dye Laser in the treatment of palmar verrucae.⁴ Again, our study is the first to compare the efficacies of DPCP and Nd:YAG in the treatment of palmar verrucae. Nd:YAG is more effective per session and requires less hospital visits; on the other hand DPCP treatment is faster.

Similar to the previous literature, no major adverse side effects were reported in our DPCP-treatment group.²⁻⁴ DPCP is a well-tolerated treatment modality for palmar verrucae. On the other hand, 3 (20%) of the Nd:YAG patients reported intolerable pain during the treatment sessions, this, again, is in line with the previous literature.^{9,10} Ulceration and scar formation were observed in a patient although she did not complain of pain during the procedure. This adverse effect resolved in a month following the use of topical antibiotic creams and epithelising agents.

CONCLUSION

Our study has shown that DPCP is a faster modality than Nd:YAG in the treatment of palmar verrucae. On the other hand, Nd:YAG is more effective per treatment session and therefore requires less hospital visits than DPCP. The treatment efficacy was independent of the patient's age and number of lesions. DPCP was better tolerated than Nd:YAG.

Limitations

The limited sample number is the main restriction of this research.

Data Availability Statement

Data openly available in a public repository that issues datasets with DOIs.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Server Serdaroğlu, Zekayi Kutlubay; **Design:** Zekayi Kutlubay, Özge Aşkın; **Control/Supervision:** Server Serdaroğlu, Zekayi Kutlubay; **Data Collection and/or Processing:** Defne Özkoca, Özge Aşkın; **Analysis and/or Interpretation:** Defne Özkoca, Tuğba Kevser Üstünbaş Uzunçakmak; **Literature Review:** Tuğba Kevser Üstünbaş Uzunçakmak, Defne Özkoca; **Writing the Article:** Defne Özkoca, Özge Aşkın; **Critical Review:** Burhan Engin, Server Serdaroğlu; **References and Fundings:** Server Serdaroğlu; **Materials:** Zekayi Kutlubay.

REFERENCES

1. Sterling JC, Handfield-Jones S, Hudson PM; British Association of Dermatologists. Guidelines for the management of cutaneous warts. *Br J Dermatol.* 2001;144(1):4-11. [[Crossref](#)] [[PubMed](#)]
2. Park JY, Park BW, Cho EB, Park EJ, Kim KH, Kim KJ. Clinical efficacy of diphenylcyclopropenone immunotherapy as monotherapy for multiple viral warts. *J Cutan Med Surg.* 2018;22(3):285-9. [[Crossref](#)] [[PubMed](#)]
3. Suh DW, Lew BL, Sim WY. Investigations of the efficacy of diphenylcyclopropenone immunotherapy for the treatment of warts. *Int J Dermatol.* 2014;53(12):e567-71. [[Crossref](#)] [[PubMed](#)]
4. Choi Y, Kim DH, Jin SY, Lee AY, Lee SH. Topical immunotherapy with diphenylcyclopropenone is effective and preferred in the treatment of periungual warts. *Ann Dermatol.* 2013;25:434-9. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
5. Goldberg DJ, Beckford AN, Mourin A. Verruca vulgaris: novel treatment with a 1064 nm Nd:YAG laser. *J Cosmet Laser Ther.* 2015;17(2):116-9. [[Crossref](#)] [[PubMed](#)]
6. Kimura U, Takeuchi K, Kinoshita A, Takamori K, Suga Y. Long-pulsed 1064-nm neodymium:yttrium-aluminum-garnet laser treatment for refractory warts on hands and feet. *J Dermatol.* 2014;41(3):252-7. [[Crossref](#)] [[PubMed](#)]
7. El-Mohamady Ael-S, Mearag I, El-Khalawany M, Elshahed A, Shokeir H, Mahmoud A. Pulsed dye laser versus Nd:YAG laser in the treatment of plantar warts: a comparative study. *Lasers Med Sci.* 2014;29(3):1111-6. [[Crossref](#)] [[PubMed](#)]
8. Han TY, Lee JH, Lee CK, Ahn JY, Seo SJ, Hong CK. Long-pulsed Nd:YAG laser treatment of warts: report on a series of 369 cases. *J Korean Med Sci.* 2009;24:889-93. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
9. Zorman A, Koron N. Wart removal without anesthesia using long-pulse 1064-nm Nd:YAG laser. *J Cosmet Dermatol.* 2021;20(2):506-12. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
10. Hsu VM, Aldahan AS, Tsatalis JP, Perper M, Nouri K. Efficacy of Nd:YAG laser therapy for the treatment of verrucae: a literature review. *Lasers Med Sci.* 2017;32(5):1207-11. [[Crossref](#)] [[PubMed](#)]
11. Ghonemy S. Treatment of recalcitrant plantar warts with long-pulsed Nd:YAG laser versus cantharidin-podophylline resin-salicylic acid. *J Cosmet Laser Ther.* 2017;19(6):347-52. [[Crossref](#)] [[PubMed](#)]
12. Gheisari M, Iranmanesh B, Nobari NN, Amani M. Comparison of long-pulsed Nd:YAG laser with cryotherapy in treatment of acral warts. *Lasers Med Sci.* 2019;34(2):397-403. [[Crossref](#)] [[PubMed](#)]