Photodiagnosis and Photodynamic Therapy 27 (2019) 340–344

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

Efficacy of the combination of superficial shaving with photodynamic therapy for recalcitrant periungual warts

Lisha Wu[a,b,c], Wangqing Chen[a,b,c], Juan Su[a,b,c], Fangfang Li[a,b,c], Mingliang Chen[a], Wu Zhu[a], Xiang Chen[a,b,c], Shuang Zhao[a,b,c,d,*]

[a] Department of Dermatology, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha, Hunan, 41008, China
[b] Hunan Key Laboratory of Skin Cancer and Psoriasis, Changsha, Hunan, 410008, China
[c] Hunan Engineering Research Center of Skin Health and Disease, Changsha, Hunan, 410008, China
[d] National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, Hunan, 410008, China

ARTICLE INFO

Keywords:
Periungual warts
Superficial shaving
Photodynamic therapy
Recalcitrant

ABSTRACT

Background: Periungual warts **are** a viral infectious disease that occurs in a particular location. **It is** difficult to eliminate **completely,** and recurrence is common. Photodynamic therapy (PDT) as an option **that** has been widely recommended to treat viral warts. However, there are always a few patients with poor efficacy after PDT treatment. We have considered that the reason is the limitation of PDT penetrating **deep into** tissue. Thus, we combined superficial shaving with PDT to treat recalcitrant periungual warts.

Methods: Twenty-three patients **had** a total of 61 periungual **wart** lesions. All patients had recalcitrant periungual warts that had failed to respond to various treatments **that had** poor curative effects. After local injection of anesthesia, the lesions were shaved in situ, and PDT was performed immediately. A total of three sessions **of** PDT **were** applied for each patient after only one superficial shaving. **The overall** clinical response rate, recurrence rates, cosmetic outcomes, adverse events, **patient** satisfaction and quality of life were assessed. The potential risk factors **have** also been recorded.

Results: We achieved a 96% success rate (defined as more than 50% on clearance) in our 23 patients using combination superficial shaving with PDT after treatment **for** 3 months. At **the 12-month** follow-up, 21 patients (91%) had excellent cosmetic **outcomes. All** patients **had satisfactory** therapeutic effects and significant improvement in the quality of life. Pain during the illumination process was the main adverse event, but all patients were able to tolerate it. **We** also found that **frequent** or continuous hand activity, such as playing **Mah-jong, may be** a potential risk factor for periungual warts.

Conclusion: Our results offer promise for **combining** superficial shaving with PDT as an effective and safe therapy for patients with periungual **warts, especially** for those periungual warts **that** are **recurrent, have** multiple lesions, and thickness corneum stratum **of lesions**. **For** nails that are not suitable for routine surgery, combined superficial shaving with PDT is recommended.

1. Introduction

Warts are caused by human papillomaviruses (HPVs), of **which there are** more than 100 genotypes [1]. The prevalence rate of warts probably varies widely based on different age groups, **populations** and periods of time [2]. Although warts can be found throughout the whole body, **they** are most commonly seen **on the hands** and feet. Periungual warts are located around the nail **fold;** they usually extend under the nail plate and may lie adjacent to the nail matrix [3]. Due to the special location of periungual warts, **they are difficult to** access. **In addition to causing** major cosmetic disfigurement of the nail, **as well as** functional and social problems, periungual warts **(especially recalcitrant warts) are** a therapeutic challenge **that are** characterized by **resistance** to various treatments and frequent recurrence.

Multiple therapeutic options for periungual warts are currently available, including salicylic acid, cryotherapy, laser **therapy**, topical **Imiquimod**, intralesional bleomycin and immunotherapy [4]. For instance, cryotherapy or laser therapy may directly **destroy** warts by **the** physical principle. Intralesional bleomycin, as an antimitotic cytotoxic polypeptide, could bind to the viral DNA in warts and **prevent** replication, resulting in cell death [5]. Immunotherapy may **stimulate** local immunity, leading to **viral** clearance. However, no single therapy

* Correspondence to: the Department of Dermatology, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha, 41008, Hunan, China.
E-mail address: shuangxy@csu.edu.cn (S. Zhao).

https://doi.org/10.1016/j.pdpdt.2019.06.021
Received 3 May 2019; Received in revised form 7 June 2019; Accepted 24 June 2019
Available online 25 June 2019
1572-1000/ © 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

has been proven effective at achieving complete remission and stable long-term efficacy, particularly for recalcitrant periungual warts [6]. **In contrast**, these modalities may have undesirable side effects, such as cryotherapy or intralesional bleomycin **causing** obvious pain **and** infection **causing** nail plate **damage, etc.**

Clinically, photodynamic therapy (PDT) is a safe, less invasive, effective and good cosmetic therapy option for various dermatologic conditions, such as actinic keratosis **and** superficial nonmelanoma skin cancer. An increasing number of **studies** have shown that PDT generates endogenous molecular oxygen to kill microbes or viruses [7,8]. **To date**, PDT has been demonstrated to successfully treat several viral warts, including condyloma acuminate [9], common warts and flat warts [10]. Originally, Stender et al. performed a pilot study of PDT treatment for recalcitrant hand and foot warts. Their results **showed** that only 42% of the warts through 5-aminolaevulinic acid (ALA)-PDT with red light treatment were completely healed [11]. Subsequently, several studies have reported that the clearance rate of hand and foot warts via single PDT treatment **ranged from** 56 to 100% [12,13]. We have considered that inadequate penetration of topically applied **photosensitizers** through **the** tissue in PDT treatment might be caused by **an** unstable clearance response. Otherwise, current clinical PDT guidelines [14] also recommend pretreatment of thick lesions prior to PDT to enhance the distribution and uptake of topically applied **photosensitizers** to improve curative effects **and** reduce recurrence.

Based on our successful experience **with treatment in** Bowen disease [15], we combined a simple and practical pretreatment with PDT to treat recalcitrant periungual warts that had failed to respond to various treatments and **had** poor therapeutic **effects** (Table 1), **e.g., patients with multiple thickened** and unclear border lesions **and** patients were not suitable for surgical excision due to large lesions **involving** the nail. A total 23 cases with recalcitrant periungual warts were treated with the combination of superficial shaving with PDT. We evaluated the clearance rate, recurrence rate, adverse events, **patient** satisfaction, quality of life and potential risk factors after 12 months **of** follow-up.

2. Materials and methods

2.1. Patients

According to the Declaration of Helsinki, the study was subjected to approval by the Ethics Committee of Xiangya Hospital of Central South University, and each patient signed an informed consent before being enrolled in the study. This retrospective observational study included 41 patients with periungual warts who were treated in the Department of Dermatology, Xiangya Hospital, Central South University from January 2016 to March 2017. The enrollment criteria were **as follows:** 1) patients showed multiple recurrences after other treatments; 2) patients **had** multiple hyperkeratotic or unclear border lesions; **and** 3) patients were not suitable for surgical excision due to large lesions involved in the nail. A diagnosis of periungual warts was determined by **three** independent senior dermatologists. The exclusion criteria were as follows: photosensitizer or lidocaine allergy, pregnancy, lactation, any active systemic infectious diseases, and immunosuppressive therapy. Among 41 patients, 18 were excluded due to withdrawal. Finally, we collected the data for the remaining 23 patients (Fig. 1).

Table 1
Previous treatments for periungual warts.

Modality	Number of treatments
Cryotherapy	35 (43.2%)
Laser	20 (24.7)
Imiquimod	4 (4.9%)
Intralesional 5-fluorouracil	16 (19.8%)
The others (Armour, Traditional Chinese Medicine et al.)	6 (7.4%)
Total	81

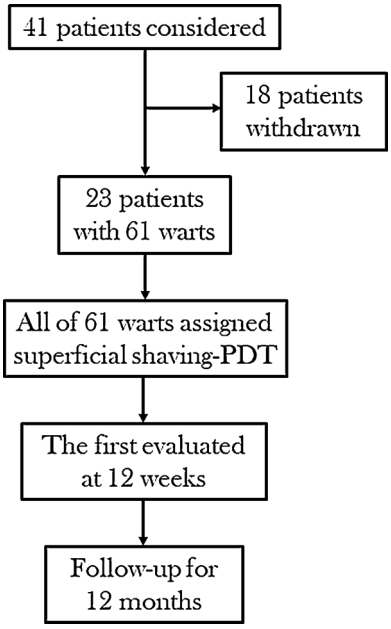

Fig. 1. Profile of clinical recruitment and evaluation.

2.2. Superficial shaving

Superficial shaving was only performed once before the first PDT, **and** no more shaving **was performed** for two additional **sessions of** PDT. After routine disinfection, 2% lidocaine was topically injected. Then, **a** razor blade (brand: Gillette) with routine sterilization was used to cut periungual warts in situ, resulting in a **slightly** bloody exudation. The epidermis was removed until **the** superficial dermal layer **was visible**. The operation of shaving should be softly and carefully **performed**. If necessary, electrocoagulation was utilized to stop bleeding.

2.3. Photodynamic therapy

PDT was immediately performed after shaving. Briefly, the shaving wound was covered with 10% 5-aminolaevulinic acid (5-ALA) cream (Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co. Ltd, Shanghai, China), and **a** compression bandage **was used to cover** the wound with gauze. After light-free incubation for **3 h**, the lesions were irradiated with **633 nm** red light at 80 mW/cm^2 for **20 min**. The distance between the lamp and the skin was adapted according to the degree of pain. Generally, the distance between the lamp and the skin is **20 cm**. The ALA-PDT procedure for each patient was repeated 3 times at one-week intervals, **with** no superficial shaving treatment for the next two **rounds of** PDT. Patients routinely wore protective glasses when irradiated.

2.4. Data collection

We recorded 23 patients' gender, age, number of lesions, number of previous treatments, healing time, curative effects (at 3 months), recurrence rate (after 12 months treatment) and potential risk factors (Table 2). **We** also evaluated **the** patients' satisfaction, dermatology life quality index (DLQI) and adverse events after 12 months **of** follow-up (Table 3). **Twenty-three** patients had a total of 61 periungual warts (15 males and 8 females included in under **7** age; age range: 5–60 years old; mean age: 25.96 ± 14.06). There were solitary lesions with 10 cases and thirteen patients with multiple lesions, **with** up to eight lesions in two patients.

Table 2
Characteristics of the patients with periungual warts treated with combination simple shaving with PDT.

ID	Gender [a]	Age (year)	Duration (month)	Number of Lesions	Number of Treatments	Healing Time (days)	Curative Effects (At 3 months)[b]	Recurrence (≥12 months)	Risk Factors[c]
1	F	58	40	2	5	7	Good	No	Frequently play Mah-jong
2	M	16	12	8	3	5	Excellent	No	Tear at the skin of fingers repeatedly
3	M	15	36	2	3	9	Excellent	No	None
4	M	33	40	4	5	14	Excellent	No	Frequently play Mah-jong
5	F	60	15	2	3	7	Good	Yes	Frequently play Mah-jong
6	F	26	8	3	3	9	Good	No	None
7	F	32	15	1	1	7	Good	No	None
8	M	10	18	5	3	10	Excellent	No	Tear at the skin of fingers repeatedly
9	F	39	22	4	3	10	Poor	Yes	Frequently play Mah-jong
10	M	46	15	1	2	7	Excellent	No	None
11	M	16	18	6	5	7	Excellent	No	None
12	F	30	24	2	1	10	Excellent	No	None
13	M	5	8	8	5	10	Excellent	No	None
14	M	13	6	1	1	7	Good	No	Finger-biting habits
15	M	18	6	1	1	3	Excellent	No	Finger-biting habits
16	M	26	3	1	2	3	Excellent	No	None
17	M	16	6	1	1	3	Excellent	No	None
18	M	26	10	1	3	7	Excellent	No	None
19	F	26	6	2	3	7	Good	No	None
20	M	18	6	3	3	7	Excellent	No	None
21	F	18	6	1	2	6	Excellent	No	None
22	M	22	8	1	2	3	Good	No	Occupational risk for computer worker
23	M	28	8	1	1	3	Good	No	Frequently play Mah-jong

[a] F indicated female, M is male.
[b] Evaluation of curative effects was graded as Excellent: complete clearance, Good: ≥50% clearance, Poor: < 50% clearance.
[c] Possible risk factors by our inquiry, Mah-jong is one of popular leisure activities in many Chinese communities.

Table 3
Evaluation of patients' satisfaction and adverse effects.

ID	Scores of satisfactions with treatment[a]	DLQI[b]		Adverse events	
		Before	After	Pain[c]	The others
1	9	16	4	5	Secondary Onychodystrophy
2	10	18	5	3	None
3	9	10	4	4	None
4	9	15	5	7	Mild itching, spontaneous remission after 2 days
5	8.5	14	12	6	None
6	7	15	6	6	None
7	9	25	4	10	Blister, vanish after 5 days by topical complex iodine
8	8	15	6	7	None
9	6	18	12	5	None
10	8	16	6	7	None
11	9	22	8	5	None
12	10	19	12	5	None
13	10	11	2	5	None
14	8	15	4	3	None
15	9	16	5	2	None
16	9	12	4	3	None
17	8	16	5	3	None
18	8	15	4	3	None
19	8	15	6	7	None
20	7	16	5	8	None
21	8	15	6	4	None
22	8	18	6	5	None
23	10	15	4	3	None

[a] Evaluation satisfaction with treatment by scoring at 12 months follow-up.
[b] Dermatology life quality index.
[c] Pain was assessed by visual analogue scale, ranging from no pain(0) to unbearable pain(10).

After 3 months, the outcome was assessed. **The curative** effect was graded as excellent (complete clearance), good (≥50% clearance), poor (< 50% clearance) and invalid. The evaluation of recurrence was based on clinical symptoms. Depending on the presence of signs and symptoms, including redness, change in pigmentation, scarring, atrophy, and dysfunction, **the cosmetic outcome was evaluated**. Clinical response and cosmetic outcome were evaluated at initial treatment, 3 months and 12 months after treatment. Satisfaction with treatment and **the** DLQI score were used to indicate improvement of **the** patients' quality of life.

2.5. Statistical analysis

SPSS 17.0 for Windows was used. **The statistical** analysis was performed using the **paired** sample t-test, and the significance level was $p < 0.05$.

3. Results

As **shown** in Table 2, the median duration of periungual warts at entry was 14 months (range 3–40 months). All of the patients had received at least one **of the** other treatments before **being** recruited into our trial. We considered that the healing time was significantly correlated with the location and size of periungual **wart** lesions. The average healing time through our **combined** treatment was 7 days (range 3–14 days), the longest wound healing time was 14 days and the shortest was 3 days. After treatment **for** 3 months, we achieved complete clearance of periungual warts in 14 of 23 patients (61%), 8 patients (35%) had a greater than 50% clearance, **and** one patient showed poor curative effects (clearance < 50%). **A total** 96% of patients **had** a satisfactory cosmetic outcome (Figs. 2 and 3). After more than 12 months **of** follow-up, 21 patients (91%) had excellent cosmetic outcomes better than at 3 months. However, two recurrences (9%) were recorded at **the 12-month** follow-up. Meanwhile, potential risk factors in our collection frequently **included playing** Mah-jong, **repeated tears in the** fingers,

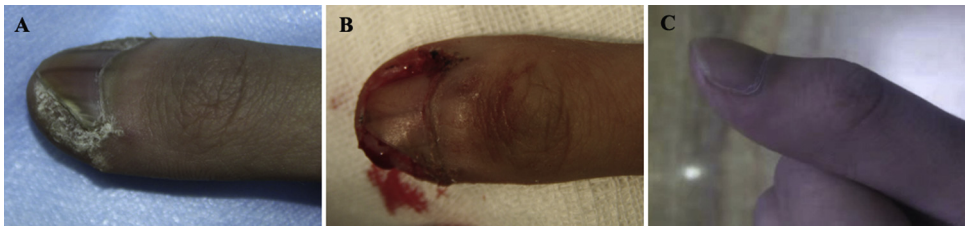

Fig. 2. Representative clinical pictures from one patient. **A**. Periungual warts before the combination treatment; **B**. After superficial shaving. **A razor** blade was used to cut the lesion in situ, resulting in a **small amount of** bloody exudation; **C**. After treatment **for** 3 months.

finger-biting habits and **an** occupational risk for computer **workers** (Table 2).

We evaluated patient satisfaction with treatment by scoring (0–10 points, the higher the score, the more satisfied with the treatment effect) at **the 12-month** follow-up. As **shown** in Table 3, the score ranged from 6 to 10 points (average score was 8.5), **indicating** that patients **were** quite satisfied with the treatment effects. **The mean** values of **the** DLQI before and 12 months after operation were 15.96 ± 3.21 and 5.87 ± 2.70, respectively. There was a significant difference between the two **DLQIs** ($p = 0.000 < 0.001$), **indicating** that the quality of life was remarkably improved. In addition, the adverse event during and after treatment was mostly pain. The pain was assessed by **the** visual analogue scale (VAS), ranging from 0 (no pain) to 10 (unbearable pain). **At** present, the highest score was 10 points, with an average score of 5.04 points. Additional adverse events included secondary onychodystrophy, **as well as** mild itching and **blisters**, and **the** patients did not need to stop treatment.

4. Discussion

Periungual **wart** therapy has always been a challenge, especially for recalcitrant periungual warts. There is no single therapy **that is proven** effective at achieving complete remission in patients [16]. Thus, **many** therapeutic options have been established with different success rates [17]. Consistent with this situation, there was **a** history of previous therapy for all 23 patients, including cryotherapy, laser **therapy**, Imiquimod, **and** intralesional 5-fluorouracil (Table 1). In **the present study**, we achieved a 96% success rate (defined as more than 50% on clearance) in our 23 patients using combination superficial shaving with PDT after treatment **for** 3 months. At **the 12-month** follow-up, 21 patients (91%) had excellent cosmetic outcomes, and **two recurrences were** observed (Table 2). Taken together, we have confirmed that the combination **of** superficial shaving with PDT may be an effective and safe alternative option for **the** treatment of recalcitrant periungual warts.

PDT has been extensively used in a variety of cutaneous warts, including condyloma acuminate [18], common warts and flat warts [19]. However, limitations for the topical PDT might be inadequate penetration of photosensitizer through tissue [20]. Thus, current clinical PDT guidelines recommend pretreatment, such as gentle curettage of thin lesions, prior to PDT treatment [21]. Caccavale et al. achieved 84.6% complete remission of 13 acral resistant wart patients by combining curettage + microneedling + ALA-PDT treatment [22]. Similarly, the main purpose of pretreatment with superficial shaving in our study was to increase the topical penetration of PDT photosensitizer in the periungual warts. **The results showed** that the combination treatment **had** an excellent effect (Figs. 2 and 3**). We** presumed that superficial shaving could remove **the** superficial stratum corneum, **expose** the deeper layer and augment the topical penetration of **the** PDT photosensitizer, leading to **improved** PDT efficiency. In addition, PDT could regulate the immune response and eliminate the invisible lesion, resulting in a low recurrence rate.

Carbon dioxide (CO2) laser therapy, which has been performed to treat various viral warts [23]**, may be a pretreatment option. However, treatment of warts with CO2 laser therapy can be complicated by substantial adverse effects, including scarring, hypopigmentation, and prolonged wound healing** [24,25]**. Additionally, given the special location of periungual warts, it is necessary to reduce the risk of side effects as much as possible, the purpose is to avoid causing major cosmetic disfigurement of the nail, or functional problems. Otherwise, it is** easy to operate for **superficial** shaving pretreatment in situ by using a razor blade, and the process of shaving pretreatment only takes **approximately** 2–3 min for each lesion. Routine wound dressing was performed after the initial PDT. Three days later, routine iodine complexation disinfection or erythromycin ointment was applied by **the** patients themselves. None of the patients had an infection. Thus, we believe that the combination **of** superficial shaving with PDT treatment periungual warts should be worth spreading in clinics, especially for recalcitrant or **repeatedly recurrent situations**.

However, PDT was associated with pain, which was the main adverse event in the procedure of our combination therapy (mean score was 5.04 by visual analogue scale evaluation) (Table 3). The pain usually occurs during and after PDT treatment, especially **when** the first light **is** irradiated. It may be that nerve endings were stimulated to generate an action potential, and the transmission of this impulse can be caused by the release of inflammatory factors such as histamine, bradykinin, and prostaglandins [26,27]. **Presently**, pain mainly occurred **with** light irradiation, which may be **alleviated** to the routine local injection of **epinephrine and lidocaine (1:5000)** [28] before the superficial **shaving. One** patient had secondary onchodystrophy after our **combined** treatment (Fig. 4). This adverse event is rarely **observed**. Photo-onycholysis, which is considered to be a phototoxic reaction, has occasionally occurred after PDT when **it** has been

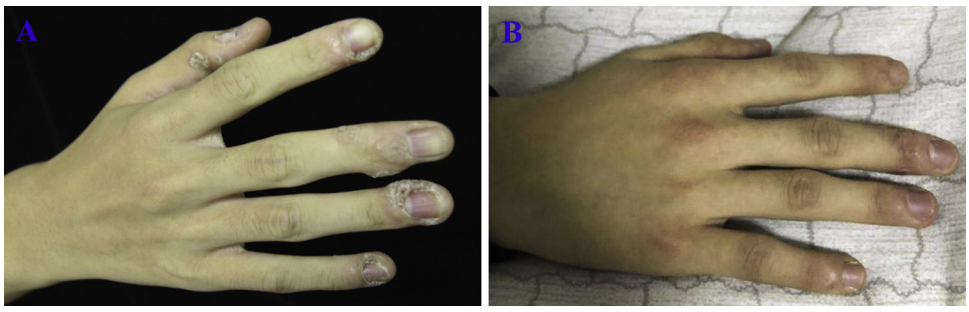

Fig. 3. Clinical photos from one patient with multiple lesions before (**A**) and after (**B**) the combination treatment.

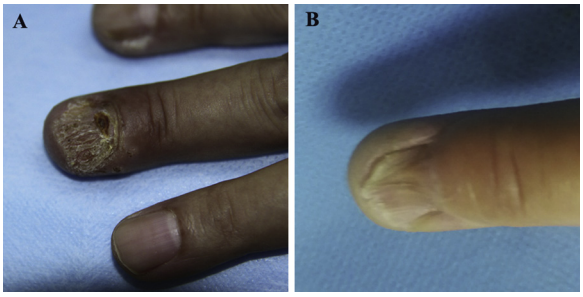

Fig. 4. One patient had secondary onchodystrophy after our combination treatment (**B**). Photo (**A**) **shows** the periungual warts before treatment.

undertaken at periungual sites, such as for viral warts [12] and actinic keratoses [29]; however, the underlying mechanisms have remained unclear. **We** speculated that secondary onchodystrophy could be either due to a direct traumatic effect of PDT on the nail plate or **perhaps** a coincidental event; **however**, there was no evidence in this case.

Meanwhile, we recorded potential risk factors of 23 patients with recalcitrant periungual warts by inquiry. As **shown** in Table 2, there were **subjects** frequently play Mah-jong, **repeated tears in the** fingers, finger-biting habits and occupational risk for computer **workers**. Warts are due to HPV. Lesions are most common at the site of trauma and probably result from inoculation of the virus into the minimally damaged area of the epithelium [30]. Severe hand warts showed an occupational risk among meat, fish and poultry **workers. It** has been suggested that the environment in which these workers are employed (such as cold and wet, with a high frequency of cuts and abrasions) is especially conductive to infection with and transmission of wart-causing HPV [31]. Interestingly, five (21.7%) of 23 patients have a **habit of playing** Mah-jong (Table 2), which is one of the popular leisure activities in various Chinese communities. **Playing the game of Mah-jong is similar to** playing poker; it involves continuous hand activity, and it takes a few hours to a whole day **to play**. Thus, we considered that the unique attributes of some environments during the process of playing Mah-jong may facilitate infection with HPV or enhance activation of latent infections, leading to **an** increased risk for periungual warts. Further research is needed to prove this assumption.

Our study is a retrospective **one** with only one arm from the treatment group. In the future, we need to strictly perform the standard protocol of a clinical trial to compare the therapeutic difference between PDT alone and **a** combination with PDT by **using multiple** clinical centers and further confirm the **value** of our combination therapy. **In addition**, long-term follow-up of patients is necessary to monitor for **recurrence**.

5. Conclusion

Our results offer promise for **combining** superficial shaving with photodynamic therapy as an effective and safe therapy for patients with periungual warts. **For** those periungual warts **that are, in particular,** recalcitrant, **recurrent, have** multiple lesions, and **have the thickness of the** corneum stratum, as well as involving nails that are not suitable for routine surgery, combined superficial shaving with PDT is recommended.

Funding

The study was supported by the National Natural Science Foundation of China (Grant number: 81673046).

References

[1] B. Pollock, R. Sheehan-Dare, Pulsed dye laser and intralesional bleomycin for treatment of resistant viol hand warts, Lasers Surg. Med. 30 (2) (2002) 135–140.
[2] S.K. Loo, W.Y. Tang, Warts (non-genital), BMJ Clin. Evid. 2014 (2014).
[3] D. Veitch, G. Kravvas, F. Al-Niaimi, et al., Pulsed dye laser therapy in the treatment of warts: a review of the literature, Dermatol. Surg. 43 (4) (2017) 485–493.
[4] R. Bacelieri, S.M. Johnson, Cutaneous warts: an evidence-based approach to therapy, Am. Fam. Physician. 72 (4) (2005) 647–652.
[5] M.J. Landsman, J.E. Mancuso, S.P. Abramow, Diagnosis, pathophysiology, and treatment of plantar verruca, Clin. Podiatr. Med. Surg. 13 (1) (1996) 55–71.
[6] J.C. Sterling, S. Handfield-Jones, P.M. Hudson, D. British Association of, Guidelines for the management of cutaneous warts, Br. J. Dermatol. 144 (1) (2001) 4–11.
[7] L. Milla Sanabria, M.E. Rodriguez, I.S. Cogno, N.B. Rumie Vittar, M.F. Pansa, M.J. Lamberti, V.A. Rivarola, Direct and indirect photodynamic therapy effects on the cellular and molecular components of the tumor microenvironment, Biochim. Biophys. Acta 1835 (1) (2013) 36–45.
[8] H.S. Hwang, H. Shin, J. Han, K. Na, Combination of photodynamic therapy (PDT) and anti-tumor immunity in cancer therapy, J. Pharm. Investig. 48 (2) (2018) 143–151.
[9] V. Nucci, D. Torchia, P. Cappugi, Treatment of anogenital condylomata acuminata with topical photodynamic therapy: report of 14 cases and review, Int. J. Infect. Dis. 14 (Suppl. 3) (2010) e280–e282.
[10] C.S. Kwok, S. Gibbs, C. Bennett, R. Holland, R. Abbott, Topical treatments for cutaneous warts, Cochrane Database Syst. Rev. 9 (2012) CD001781.
[11] I.M. Stender, J. Lock-Andersen, H.C. Wulf, Recalcitrant hand and foot warts successfully treated with photodynamic therapy with topical 5-aminolaevulinic acid: a pilot study, Clin. Exp. Dermatol. 24 (3) (1999) 154–159.
[12] C.A. Schroeter, L. Kaas, J.J. Waterval, P.M. Bos, H.A. Neumann, Successful treatment of periungual warts using photodynamic therapy: a pilot study, J Eur. Acad. Dermatol. Venereol.: JEADV 21 (9) (2007) 1170–1174.
[13] I.M. Stender, R. Na, H. Fogh, C. Gluud, H.C. Wulf, Photodynamic therapy with 5-aminolaevulinic acid or placebo for recalcitrant foot and hand warts: randomised double-blind trial, Lancet 355 (9208) (2000) 963–966.
[14] C.A. Morton, R.M. Szeimies, A. Sidoroff, L.R. Braathen, European guidelines for topical photodynamic therapy part 2: emerging indications–field cancerization, photorejuvenation and inflammatory/infective dermatoses, J. Eur. Acad. Dermatol. Venereol. 27 (6) (2013) 672–679.
[15] D. Liu, L. Wu, J. Li, W. Shi, F. Li, J. Su, K. Huang, Q. Zhou, S. Zhao, M. Chen, Combined the simple shaving with photodynamic therapy for refractory Bowen disease, Photodiagnosis Photodyn. Ther. (2019).
[16] J.C. Sterling, S. Gibbs, S.S. Haque Hussain, M.F. Mohd Mustapa, S.E. Handfield-Jones, British Association of Dermatologists' guidelines for the management of cutaneous warts 2014, Br. J. Dermatol. 171 (4) (2014) 696–712.
[17] F. Dall'oglio, V. D'Amico, M.R. Nasca, G. Micali, Treatment of cutaneous warts: an evidence-based review, Am. J. Clin. Dermatol. 13 (2) (2012) 73–96.
[18] K. Chen, B.Z. Chang, M. Ju, X.H. Zhang, H. Gu, Comparative study of photodynamic therapy vs CO2 laser vaporization in treatment of condylomata acuminata: a randomized clinical trial, Br. J. Dermatol. 156 (3) (2007) 516–520.
[19] X. Wen, Y. Li, M.R. Hamblin, Photodynamic therapy in dermatology beyond non-melanoma cancer: an update, Photodiagnosis Photodyn. Ther. 19 (2017) 140–152.
[20] U. Keyal, A.K. Bhatta, G. Zhang, X.L. Wang, Present and future perspectives of photodynamic therapy for cutaneous squamous cell carcinoma, J. Am. Acad. Dermatol. 80 (3) (2019) 765–773.
[21] C.A. Morton, H.C. Wulf, R.M. Szeimies, Y. Gilaberte, N. Basset-Seguin, E. Sotiriou, S. Piaserico, R.E. Hunger, S. Baharlou, A. Sidoroff, L.R. Braathen, Practical approach to the use of daylight photodynamic therapy with topical methyl aminolevulinate for actinic keratosis: a European consensus, J Eur. Acad. Dermatol. Venereol.: JEADV 29 (9) (2015) 1718–1723.
[22] S. Caccavale, A. Iocco, G. Pieretti, R. Alfano, G. Argenziano, Curettage + microneedling + topical ALA-PDT for the treatment of acral resistant warts: our experience, Photodiagnosis Photodyn. Ther. (2019).
[23] J. Nguyen, D.Z. Korta, L.W. Chapman, K.M. Kelly, Laser treatment of nongenital verrucae: a systematic review, JAMA Dermatol. 152 (9) (2016) 1025–1034.
[24] R.A. Logan, C.B. Zachary, Outcome of carbon dioxide laser therapy for persistent cutaneous viral warts, Br. J. Dermatol. 121 (1) (1989) 99–105.
[25] S. Takac, The CO2 laser and verruca vulgaris, Med. Pregl. 53 (7–8) (2000) 389–393.
[26] A. Kasche, S. Luderschmidt, J. Ring, R. Hein, Photodynamic therapy induces less pain in patients treated with methyl aminolevulinate compared to aminolevulinic acid, J. Drugs Dermatol. 5 (4) (2006) 353–356.
[27] S.M. Langan, P. Collins, Randomized, double-blind, placebo-controlled prospective study of the efficacy of topical anaesthesia with a eutetic mixture of lignocaine 2.5% and prilocaine 2.5% for topical 5-aminolaevulinic acid-photodynamic therapy for extensive scalp actinic keratoses, Br. J. Dermatol. 154 (1) (2006) 146–149.
[28] Y.N. Chaves, L.A. Torezan, A.B. Niwa, J.A. Sanches Junior, C. Festa Neto, Pain in photodynamic therapy: mechanism of action and management strategies, An. Bras. Dermatol. 87 (4) (2012) 521–526 quiz 527-9.
[29] S. Hanneken, U. Wessendorf, N.J. Neumann, Photodynamic onycholysis: first report of photo-onycholysis after photodynamic therapy, Clin. Exp. Dermatol. 33 (5) (2008) 659–660.
[30] S. Gibbs, I. Harvey, J. Sterling, R. Stark, Local treatments for cutaneous warts: systematic review, BMJ 325 (7362) (2002) 461.
[31] P.A. Stehr-Green, P. Hewer, G.E. Meekin, L.E. Judd, The aetiology and risk factors for warts among poultry processing workers, Int. J. Epidemiol. 22 (2) (1993) 294–298.