

Combination Effect of Super Pulsed Carbon Dioxide Laser and Photodynamic Therapy for Recalcitrant Facial Flat Warts: A Preliminary Study

Changbing Shen¹, Jing Gao², Randy Ko³, Zhongying Wang¹, Shengxiu Liu¹, Yongjiang Li¹, Mingjun Tang¹, Weiwei Yin¹, Chunjun Yang^{1*} and Xuejun Zhang^{1,2*}

¹Institute and Department of Dermatology, the First Affiliated Hospital, Anhui Medical University, Hefei 230032, Anhui, China

²Department of Dermatology, the Second Affiliated Hospital, Anhui Medical University, Hefei 230601, Anhui, China

³Department of Biochemistry, University of New Mexico, Albuquerque, NM 87131, New Mexico, USA

*Corresponding author: Dr. Chunjun Yang, Institute and Department of Dermatology, the First Affiliated Hospital, Anhui Medical University, Hefei 230032, China, Tel: +86-551-65138576; Fax: +86-551-65138576; E-mail: yangchunjun9@163.com

*Corresponding author: Professor Xuejun Zhang, Institute and Department of Dermatology, the First Affiliated Hospital, Anhui Medical University, Hefei 230032, China, Tel: +86-551-65138576; Fax: +86-551-65138576; E-mail: ayzxj@vip.sina.com

Received date: Mar 14, 2015, Accepted date: Mar 24, 2015, Published date: Mar 24, 2015

Copyright: © 2015 Shen C, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Dear Editor:

Flat wart is caused by human papilloma virus, frequently affects adolescents and adults. The warts are small sized (1-5 mm), flat or slightly elevated lesions, usually present as skin-colored or greyish-yellow papules on the forehead, cheeks, perioral area, chins, and dorsum of hands [1-3]. Many therapies for the treatment of flat wart with varying curative ratio. Pulsed dye laser and photodynamic therapy have been adopted in treating flat wart respectively, but neither of them achieved absolute restoration. There are no records of the combination therapy of super pulse carbon dioxide (CO₂) laser and photodynamic therapy in recalcitrant facial flat wart. We conducted a preliminary, non-blinded, non-randomized study at the

department of dermatology, the first affiliated hospital, Anhui Medical University, Anhui, China, from August, 2012 to November, 2013, to assess the safety and efficacy of combination of super pulse CO₂ laser and photodynamic therapy and provide a new approach for recalcitrant facial flat wart.

In this study, six recalcitrant facial flat wart patients with Fitzpatrick skin type IV were enrolled, including one male and five females aged from 17 to 48 years old. All of the patients suffered from the facial flat wart more than 2 years, with multiple facial flat warts (average 30) (Table 1). The detailed process of this combination treatment and the adverse events were explained to patients, and the written informed consent was obtained.

Patients	Sex	Age	Duration of warts (year)	Previous treatment	Treatment courses	Effect	Side-effects
1	F	17	2.5	Topical agents keratolytic	4	Cure	Erythema, post-inflammatory pigmentation
2	M	48	4.0	Topical agents, cryotherapy keratolytic	2	Cure	Erythema
3	F	34	3.5	Topical agents, CO ₂ laser keratolytic	3	Cure	Erythema
4	F	32	3.3	Topical agents keratolytic	2	Cure	Erythema
5	F	32	3.0	Topical agents, cryotherapy keratolytic	3	Cure	Erythema, post-inflammatory pigmentation
6	F	25	2.8	Cryotherapy, topical keratolytic agents	2	Cure	Erythema

Table 1: The basic conditions and treatment responses of patients.

The treatment course consisted of two steps: super pulse CO₂ laser irradiated firstly, followed with local photodynamic therapy with topical application of 5-aminolevulinic acid (ALA-PDT). First of all, the lesion was occluded with EMLA cream (2.5% lignocaine+2.5% prilocaine) for 30-45 minutes prior to the procedure. Then, treatment with the super pulsed CO₂ laser, using the following parameters: pulse mode, fluence of 0.5 J/cm², pulse interval 0.1 s, power output 0.5-0.8 W. The threshold of single pulse was the treatment area presenting white with desquamation. Next, the lesions were occluded with 5% ALA ointment (Fudan Zhang Jiang Biomedical Corp., Shanghai,

China) for 3.5 hours immediately, and then irradiated by a 633 nm laser (Yage[®], Wuhan, China) for 20 minutes with the energy from 100 to 120 J/cm².

The treatment procedure was repeated with an interval of 7-10 days. The patients were advised with strict sun protection by high-SPF sunscreen during the day and epidermal growth factor gel (Yifu[®], Guilin, China) was used postoperatively. Lesion changes were assessed by clinical observations through comparing pre-treatment with post-treatment photographs by operators and patients themselves. The efficacy and side-effects of the treatment were recorded at each visit.

The final effect and relapse were assessed by following up at least 3 months after the last treatment.

Of the participant patients, all facial flat warts lesions showed completely restoration after two to four treatment courses by 3 months follow-up (Figures 1a and 1b) in this primary study. No relapsed cases were recorded by following up 3-18 months. The side effects were mild erythema and temporary post-inflammatory pigmentation, all of six patients presented mild to moderate erythema with different irritation after operations per times. Erythema disappeared in the next few days, and pigmentation restored within 4-7 weeks. No other severe side effects were recorded.



Figure 1: Facial flat warts lesions restoration pre-treatment and post treatment photographs.

Super pulsed CO₂ laser is widely used in the treatment of nevi and small skin neoplasm because of its ultra-pulse mode which can avoid thermal injury of normal skin tissue to the greatest extent based on selective photothermolysis [4]. In recent years, owing to its noninvasive and good cosmetic results, ALA-PDT has been successfully used for acne [5], and warts [6]. ALA is absorbed into the epidermal cells and biosynthesized to the light-sensitive metabolite photoporphyrin IX (PpIX) when applied topically to the skin. Cells with accumulated PpIX are exposed to light of certain wavelengths, free radicals are released as singlet oxygen, leading to cell death. The stratum corneum is the main obstacle to the uptake of the photosensitizer into the skin and the hyperkeratotic areas inhibit photosensitizer penetration into the skin. Yoo KH et al. [7] reported that removing the upper parts of the hyperkeratotic wart lesions by CO₂ laser initially may enhance the absorption of the photosensitizer in the PDT treatment. In our study, all of lesions were cleared by super pulsed CO₂ laser followed with ALA-PDT after two to four treatment courses, and 3 of the 6 patients showed completely restoration with only two treatments. We infer the flat wart can absorb 5-ALA better after melted by pre-therapy with super pulsed CO₂ laser, and the lesions were better treated by photodynamic therapy subsequently.

In order to avoid side effect caused by super pulsed CO₂ laser, the parameters here we used were lower than routine treatment, the

treatment area presenting white with desquamation immediately after super pulsed CO₂ laser was considered proper procedure. The side effects were mild erythema and temporary post-inflammatory pigmentation; erythema with mild irritation emerged immediately after treatment every times, which disappeared in the next few days. Two patients (1 male and 1 female) complained of severe irritation with erythema, and with dispersive facial edema, these discomfort diminished gradually when using wet compress with 3% boric acid solution. Post-inflammatory pigmentation disappeared gradually within 1-3 months follow-up. The results were consistent with Wang et al. study [8], which also suggested that there was no apparent increased risk of hyperpigmentation for the treatment of recalcitrant viral warts by photodynamic therapy with 20% 5-ALA in Asian population (mainly skin types III, IV, and V). It may be a new available and effective approach for recalcitrant facial flat wart to combine super pulsed CO₂ laser and ALA-PDT, and it is well tolerated by our patients. Due to the limited cases, we could not affirm the accurate therapy effect of this treatment; further studies expanding patient number are needed.

Acknowledgement

We acknowledge the individuals who participated in this project and their families. We also appreciated the help from Randy Ko from University of New Mexico for collaborating with us in revising this manuscript.

References

1. Hultgren TL, Srinivasan SK, DiMaio DJ (2007) Epidermodysplasia verruciformis occurring in a patient with human immunodeficiency virus: a case report. *Cutis* 79: 307-311.
2. Iarikov D, Duke W, Skiest D (2008) Extensive development of flat warts as a cutaneous manifestation of immune reconstitution syndrome. *AIDS Read* 18: 524-527.
3. Pavithra S, Mallya H, Pai GS (2011) Extensive presentation of verruca plana in a healthy individual. *Indian J Dermatol* 56: 324-325.
4. Sardana K, Garg VK (2009) Successful treatment of nevus comedonicus with ultrapulse CO₂ laser. *Indian J Dermatol Venereol Leprol* 75: 534-535.
5. Wang HW, Lv T, Zhang LL, Guo MX, Stepp H, et al. (2012) Prospective study of topical 5-aminolevulinic acid photodynamic therapy for the treatment of moderate to severe acne vulgaris in Chinese patients. *J Cutan Med Surg* 16: 324-333.
6. Yu YE, Kuohung V, Gilchrest BA, Penrose C, Shim H (2012) Photodynamic therapy for treatment of hand warts. *Dermatol Surg* 38: 818-820.
7. Yoo KH, Kim BJ, Kim MN (2009) Enhanced efficacy of photodynamic therapy with methyl 5-aminolevulinic acid in recalcitrant periungual warts after ablative carbon dioxide fractional laser: a pilot study. *Dermatol Surg* 35: 1927-1932.
8. Wang YS, Tay YK, Kwok C, Tan E (2007) Photodynamic therapy with 20% aminolevulinic acid for the treatment of recalcitrant viral warts in an Asian population. *Int J Dermatol* 46: 1180-1184.