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, Shengxue Liu1, Yongjiang Li1, Mingjun Tang1, Weiwei Yin1, Chunjun Yang1* and Xuejun Zhang1,2*

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

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 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) and photodynamic therapy and provide a new approach for recalcitrant facial flat wart.

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.

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

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex</th>
<th>Age (year)</th>
<th>Duration of warts (year)</th>
<th>Previous treatment</th>
<th>Treatment courses</th>
<th>Effect</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>17</td>
<td>2.5</td>
<td>Topical keratolytic agents</td>
<td>4</td>
<td>Cure</td>
<td>Erythema, post-inflammatory pigmentations</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>48</td>
<td>4.0</td>
<td>Topical keratolytic agents, cryotherapy</td>
<td>2</td>
<td>Cure</td>
<td>Erythema</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>34</td>
<td>3.5</td>
<td>Topical keratolytic agents, CO2 laser</td>
<td>3</td>
<td>Cure</td>
<td>Erythema</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>32</td>
<td>3.3</td>
<td>Topical keratolytic agents</td>
<td>2</td>
<td>Cure</td>
<td>Erythema</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>32</td>
<td>3.0</td>
<td>Topical keratolytic agents, cryotherapy</td>
<td>3</td>
<td>Cure</td>
<td>Erythema, post-inflammatory pigmentations</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>25</td>
<td>2.8</td>
<td>Cryotherapy, topical keratolytic agents</td>
<td>2</td>
<td>Cure</td>
<td>Erythema</td>
</tr>
</tbody>
</table>

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 pulse 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 irratated 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.
Photoporphyrin IX (PpIX) when applied topically to the skin. Cells follow-up (Figures 1a and 1b) in this primary study. No relapsed cases completely restoration after two to four treatment courses by 3 months 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.

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, owning 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