The dual toning technique of 1064nm Nd:YAG picosecond and quasi-long pulsed laser combined with D-pigment cream in treatment of melasma

Le Thi Thu Hai*, Bui Thi Thu Phương*,
Nguyen Thi Hong Minh**

**108 Military Central Hospital,*
***National Hospital of Odonto-Stomalogy*

Summary

Objective: To evaluate the efficacy and safety of the dual toning laser of Nd:YAG 1064nm picosecond and quasi-long pulsed laser combined with D-pigment night cream in treatment of severe melasma. *Subject and method:* Twenty four Vietnamese females, mean age of 44.46 ± 8.04 years, Fitzpatrick skin type IV with the clinical diagnosis of dermal and mixed-type melasma were treated with 5 combination sessions of picosecond laser Nd:YAG 1064nm (Picoplus) with a spot size of 8mm, the energy of 0.65 - 0.8J/cm^2 and quasi-long pulsed mode laser (Clarity) with the duration of 0.35ms, the spot size of 15mm, the energy of 2.6J/cm^2, ICD (Intelligent Cool Device) off. Mild and transient erythema was the endpoint. Laser treatments were given every 4 weeks. All patients were applied with UVA/B sunscreen, SPF of at least 30 in daytime and D-pigment cream at night. Improvement was rated by mMASI at the baseline (first -T1) and after 5 sessions (sixth -T6). *Result:* The mean mMASI score of 24 patients at T1 was 11.10 ± 3.59 (min 6.0; max 22.4); after one month of 5th session, the mean mMASI score at T6 was reduced to 5.43 ± 2.18 (min 1.8 - max 11.0) (mMASI score reduced by a mean of 5.68 ± 2.36), achieving 51.06 ± 13.17% reduction. There were no unexpected side effects in any patients. *Conclusion:* Dual toning technique using 1064nm Nd:YAG picosecond and quasi-long pulsed laser combined with D-pigment cream at night was safe, effective and well-tolerated in treatment of patients with melasma. Further larger studies should be carried out with control to confirm the advantage of the method.

Keywords: Laser Nd:YAG, melasma, picosecond laser, quasi-long pulsed laser, rejuvenation.

1. Background

Melasma is an acquired, chronic hyperpigmentary disorder recognized by bilateral, light-to-dark brown maculae occurring in sun-exposed areas of skin, especially on the face. Most commonly observed in females in their thirties or forties and more with darker skin types, especially East Asians. It adversely affects the patients' self esteem and quality of life. The pathogenesis of melasma is very complicated and has not been fully elucidated so that the management of this condition remains challenging [1]. The laser and lightening cream treatment was applied for patients with dermal and mixed or refractory melasma. The low-fluence 1064nm Q-Switched Nd:YAG has been widely accepted for melasma treatment in Asia. This technique was referred to a term of "laser toning" with selective destroy of melanin-containing cell intact by photothermal effect. However, some recent articles have reported that unexpected mottled

***Received**: 2 August 2021, **Accepted:** 27 October 2021*
***Correspondence to:** Le Thi Thu Hai - The Laser and Cosmetic Department, the Center of Multidisciplinary Consultation and Treatment, 108 Military Central Hospital*
***Email:** lethuhai3009@gmail.com*

hypopigmentation (MH) and rebound hyperpigmentation (RH) remain because of heat accumulation. Over the past few years, picosecond pulsed laser system was introduced with shortening pulse duration to a billionth of a second to treat tattoo and benign hyperpigmentation including melasma. Picosecond laser pulses create a largely photomechanical effect on the targeted tissue, accompanied by a diminished photothermal effect. This allows more safety during treatment while Nd:YAG 1064nm picosecond laser (PSNY) may have the same or higher efficacy in decreasing the amount of melanin. To treat severe melasma, we decided to combine PSL toning at 1064nm to destroy the pigment-containing cell with Nd: YAG 1064nm quasi-long pulsed to improve the altered dermal environment of melasma through rejuvenation effects and D- pigment night cream to slow melanin synthesis and restrict its spread in the skin.

2. Subject and method

2.1. Subject

A total of 24 Vietnamese females with Fitzpatrick skin type IV, ages ranging from 33 to 66 years (mean 44.46 ± 8.04 years) with clinical diagnosis of severe dermal and mixed-type melasma were treated at the Laser and Cosmetic Department of the 108 Military Central Hospital from June 2019 to February 2020.

Exclusion criteria included skin lesions in the treated, pregnancy or breastfeeding, photosensitivity, usage of oral contraceptive pills, hormone replacement, topical bleaching or chemical peeling within one month.

Patients were informed of the study procedures, risks, benefits, potential complications, and side-effects. Informed consent was obtained prior to treatment.

2.2. Method

Laser treatment

The first part of the treatment was picotoning using 1064 nm Nd:YAG (Pico Plus, Lutronic, Korea) with the parameters of 8mm spot size, 0.65 - 0.8J/cm^2 energy based on skin type and severity of pigmentation and 10Hz pulse repetition. Two to three passes were applied over the entire hyperpigmentation area of the face with 20 - 30% overlap. The clinical endpoint was immediate lightening of hair or very mild erythema without petechiae. A cooling pack was applied for 2 minutes. Following immediately by long pulsed Nd:YAG (Clarity, Lutronic, Korea) with a spot size of 15mm, 0.35ms, and 2.6J/cm^2, 10Hz pulse repetition and cooling off. 3 - 4 passes were applied to stack pulses (painting motion technique) until the expected endpoint with mild erythema on the whole face. After that, an infrared thermometer measurement of the facial patient's skin was performed to ensure the surface temperature reaching to 40 - 42° Celsius. A cooling pack was applied following the dual toning session for 2 minutes, and patients were able to return immediately to their usual daily activities. Patients were instructed to daily apply UVA/B sunscreen with an SPF of at least 30 on daytime and D-pigment cream with the ingredients of melanyde, retinaldehyde and pretocophenyl at night. The patients received combination treatment every 4 weeks for total of 5 sessions. Any possible complications and side-effects (petechiae, acute urticaria, post-inflammatory hypopigmentation, and hyperpigmentation) were recorded.

Assessment

The improvement was assessed by two blinded independent dermatologists who reviewed the clinical photography at baseline (first treatment - T1) and after the 5th session (sixth treatment - T6) using mMASI score (Modified melasma area and severity index).

The mMASI as well as the physician's global assessment (PGA) were scored at baseline and one month after the final treatment. Unlike the original MASI, mMASI does not take homogeneity into consideration and is calculated as mMASI = 0.3 A(f) D(f) + 0.3 A(lm) D(lm) + 0.3 A(rm) D(rm) + 0.1 A(c) D (c), where A is the area of involvement (0 - 6 points: 0 = absent, 1 < 10%, 2 = 10% - 29%, 3 = 30% - 49%, 4 =

50% - 69%, 5 = 70% - 89%, and 6 = 90% - 100%) and D is the pigment darkness (0-4 points: 0 = absent, 1 = slight, 2 = mild, 3 = marked, and 4 = severe). PGA (physician global assessment) assessed the results of treatment based on the improvement of mMASI by 2 dermatologists (0 - 5, 0 = worsening or no improvement, 1 = poor (1 - 25%), 2 = fair (26 -50%), 3 = good (51 - 75%), and 4 = excellent (76 - 100%).

PtGA (patient global assessment) was evaluated based on the patient's self-assessment about the lightening after treatment (0 - 4; 0 = no change or worse (≤ 0%), 1 = poor; slight lightening (1 - 25%), 2 = fair; moderate lightening (26 - 50%), 3 = good; marked lightening (51 - 75%), 4 = excellent; near-normal skin (76 - 100%).

We also used VAS (visual analog scale) to measure the participants' satisfaction about their skin quality (0 = no satisfaction and 10 = highest satisfaction); 1 - 3 = mildly satisfied, 4 - 7 = moderately satisfied, 8 - 10 = very satisfied.

Statistical analysis was performed using SPSS® 21.0 software package. Descriptive statistics were presented as mean ± standard deviation. The p value less than 0.05 was defined as significant difference.

3. Result

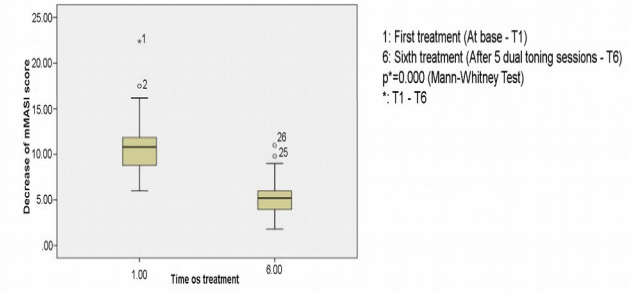

Figure 1. Average of mMASI improvement after 5 sessions of dual toning combined D-pigment cream treatments

The median mMASI score of 24 patients at baseline was 10.80 ±3.59 (mean 11.1, min 6.0; max 22.4); after the 5th dual toning combined D-pigment session, the median mMASI was reduced to 5.20 ± 2.18 (mean 5.425, min 1.8 – max 11.0) representing a 51.06 ± 13.17% reduction in mMASI score.

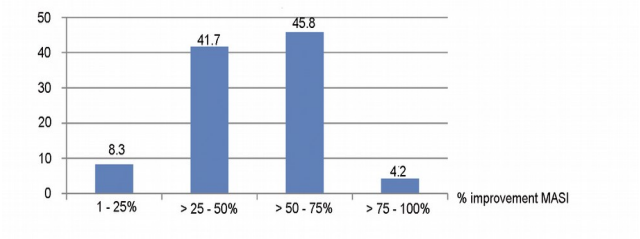

Figure 2. Ratio % improvement mMASI after 5 sessions on PGA

On PGA, the percentages of patients showed excellent, good, fair and poor results were 4.2%, 45.8%, 41.7% and 8.3%, respectively.

Table 1. PtGA (about lightening)

PtGA	n (%)	Mean ± Std
No change or worse	3 (12.5%)	31.25 ± 18.49
Slight lightening (poor) 1 - 25% improvement	4 (16.7%)	
Moderate lightening (fair) 26 - 50% improvement	15 (62.5%)	
Mark lightening (good) 51 - 75% improvement	2 (8.3%)	
Near normal skin (excellent) 76 - 100% improvement	0 (0%)	
Total	***24 (100%)***	

On PtGA, the percentages of patients showed excellent, good, fair, poor improvement and no change or worse were 0%, 8.3%, 62.5%, 16.7% and 12.5% respectively.

Table 2. VAS about skin quality

10 — 0

Very satisfactory — Unsatisfactory

VAS	Level of satisfaction	%	Mean ± Std (Min - Max)
1 - 3	Mildly satisfied	4.2	

4 - 7	Moderately satisfied	83.3	5.25 ± 1.327 (3 - 8)
8 - 10	Very satisfied	12.5	

The mean VAS about skin quality (pore size, wrinkles, skin roughness, skin laxity) after 5 treatments was 5.25 ± 1.327 with distribution 4.2% mildly, 83.3% moderately, 12.5% very satisfied.

All patients had no adverse or unexpected side effects. Erythema after laser treatment was mild and transient for 30 minutes to 2 hours. No patient reported excess pain during dual toning treatment.

4. Discussion

Goldberg et al [2] first suggested the concept of "laser toning" whereby multiple passes with a low fluence Q-switched laser. Laser toning at 1064nm has deeper penetrating properties and safety in pigmented skin so that it has been accepted as a new method of melasma treatment in Asia. The mechanism of action is known as "subcellular selective photothermolysis" because of minimal damage to the melanocytes, but it can destroy the melanosomes and melanin granules within melanocytes and keratocytes keeping the cell membrane and nucleus intact, thus avoiding cell death. The long dendritic processes of hyperactive melanocytes are cutoff (dendrectomy) and there is functional downregulation of melanocytes. There were various studies to confirm these findings such as a study by Kim et al [3] investigating histopathology of eight Korean women treated with laser toning or Mun et al [4] showed the 3D structure of melanocyte and ultrastructure of melanosome affected by laser toning. However, the more aggressive laser toning with high fluence and number of passes with short intervals are performed, the more risk of excessive cumulative energy may occur Nowadays, laser picotoning creates a largely optical breakdown with plasma formation and shock wave generation leading to photo disruption instead of simply heating. Some authors believe that applying a picosecond laser to treat melasma should achieve better result compared to QSNY so that it may well have the same or higher efficacy in decreasing the amount of melanin. However, melasma in the Asian skin type can remain refractory to laser toning. Since 2017, in our department, all melasma patients were treated with picotoning Nd:YAG combined with whitening night cream. A proportion of 5% to 10% of patients with severe melasma did not respond to either picotoning laser combined or topical cream (data not shown). So we decided to combine picotoning, quasi-long pulsed Nd:YAG 1064nm and topical cream to treat patients in this study. The quasi-long pulse 1064nm Nd:YAG laser is known as the laser for non-ablative skin rejuvenation via collagen remodeling and neocollagenesis. Furthermore, it also promotes wound healing by inducing heat shock protein and transforming growth factor beta, and by reducing the levels of the proinflammatory cytokine interleukin-8 [6]. Thus, quasi-long pulse Nd:YAG does not directly destroy melanosomes but might improve the altered dermal environment of melasma.

In our study, there were 24 patients (mean age 44.46 ± 8.04 years) with median mMASI at baseline was 10.80 ± 3.59 (mean 11.1, min 6.0 - max 22.4); after 5 dual toning sessions combined with D-pigment daily night cream, the median mMASI was 5.20 ± 2.18 (mean 5.425, min 1.8-max 11.0), with p=0.000 (<0.05) (Mann-Whitney Test) (Figure 1). Our data showed that after five sessions using dual toning technique, the median mMASI score was improved by 5.60 ± 2.36 (51.06 ± 13.17%). In addition, all patients had significantly improvement of skin quality. The improvement of mMASI in our study is higher than that in the study of Choi CP et al when treating 360 Korean melasma patients with 10 sessions with one week interval with QS Nd:YAG toning (n = 177) or for dual toning (n = 183). The index mMASI in the dual toning group was reduced from the baseline 5.96 ± 1.81 to 3.6 dropping about 39.6%. The improvement in our study was also more than that in the study of Choi YJ (2017) [7]. In another study, the result showed that the efficacy and safety of a picosecond laser with dual-

wavelengths (1064nm and 595nm) combined with topical 2% hydroquinone with 5 sessions of picosecond laser weekly, the improvement was less than 50% by mean of mMASI). More over, in the study of Wang YJ et al [8] the improvement was 38% in the decrease of MASI score from 10.6 ± 4.4 to 6.6 ± 3.2 after 5 weekly treatments of picosecond alexandrite laser with one week interval.

On PGA, the percentages of patients with excellent, good, fair and poor improvement were 4.2%, 45.8, 41.7%, 8.3%, respectively (Figure 2). The distribution of PGA in our study demonstrated the enhanced improvement compared to that in Chalermthai et al (2017) [9]. They weekly treated 30 patients with dermal and mixed type melasma by using picosecond 1064nm. At 4 weeks after enrollment, mMASI-50 (50% or greater improvement from the baseline) after 4 treatments was 33% and after 8 treatments was 70%. Kang et al (2011) [10] weekly treated 30 females with melasma with dual mode of low fluence Q-switched and long-pulsed Nd:YAG laser for a total of 10 - 12 treatments, the result showed that after the final session, there was 10%, 30% and 26.7% of patients with excellent, good and fair improvement, respectively. Choi JE et al [11] weekly treated 40 patients with melasma using QSNY at low fluence for a median of 10 sessions (range 5 - 15), the result showed 2.5% patients with excellent, 35% with good, 37.5% with fair improvement based on PGA.

Based on PtGA, 0% of patients showed excellent improvement, 8.3% of patients showed good, 62.5% of patients showed fair and 16.7% of patients showed poor. Especially, there was low percentage (12.5%) of patients had no change or worse condition (Table 1). The distribution of our PtGA was less effective than that of Gokalp et al (2016) [12], in which 11.8% of patients was excellent, 47% of patients was good, 29.4% of patients was fair, 5.9% of patients was poor and 5.9% of patients had no change or worse condition). This situation might be due to the severe mMASI score at baseline in our study (11.10 ± 3.59 vs 6.71 ± 3.31). Additionally, in non-ablative laser treatment, degeneration of collagen fibers requires temperatures of 55 - 65° Celsius in the dermis, which is equal to 40 - 42° Celsius on the skin surface. In our study, we used an infrared thermometer to measure the temperature on the skin surface following laser treatment. It is theorized that laser-induced subthreshold injury to the dermis and/or vasculature results in a wound repair response, stimulation of fibroblast activity, and collagen reformation. Therefore after dual toning with the 1064nm Nd:YAG picosecond and quasi-long pulse laser combined whitening daily night cream, not only improved the lightening of melasma but also improved general skin quality including reduced pore size, skin roughness, skin laxity and disappearance of the fine periocular lines. The mean VAS after 5 treatments was 5.29 ± 1.398 (min 3, max 8), in which the distribution was 4.2% with mildly satisfied, 83.3% with moderately satisfied and 12.5% with very satisfied (Table 2). Almost all patients assessed VAS based on the percentage of skin quality improvements, more improvement more satisfactory. These figures compare with Steven's study involving long pulsed 1064nm results that showed -35.8% fine wrinkles, -22.3% coarse wrinkles, -26.4% roughness, -25.5% uneven pigmentation, -36.3% skin laxity, and -40.6% overall improvement (base on decreases in Fitzpatrick Scale scores) [13]. Patients in our study measured their's satisfaction about overall improvement rather than individual metrics (including reduced pore size, skin roughness, skin laxity and disappearance of the fine periocular lines). They reported that the most common site of improvement was the nasolabial fold, perhaps because it is most noticeable.

Besides, the interval between treatments also plays an important role. Wattanakrai et al suggested that to minimize complications, the use of too many (more than 5 approaching up to 10 treatments) or too frequent (every week) laser toning sessions should be discouraged. Although picotoning laser has reduced the thermal effects, the skin still needs time to recover and eliminate pigmentation so we

decided to use the dual toning technique with longer intervals.

We considered that further increasing the number of treatment sessions may show a better effect because mMASI continuously reduces follow the next sessions. We will assess the next session and follow–up longer.

5. Conclusion

Dual toning of Nd:YAG picosecond laser and microsecond pulsed laser combined with D-pigment daily night cream may represent a good solution for severe Asian melasma patients, achieving both whitenings together with skin rejuvenation. The approach is effective, side-effect free, well-tolerated and minimally invasive with no downtime for the patient. However, larger controlled studies should be applied to confirm the benefit of the method.

References

1. Passeron T (2013) *Melasma pathogenesis and influencing factors - an overview of the latest research*. European Academy of Dermatology and Venereology 27(1): 5-6.
2. Goldberg D, Metzler C (1999) *Skin resurfacing utilizing a low-fluence Nd:YAG laser.* J Cutan Laser Ther 1(1): 23-27.
3. Kim JE, Chang SE, Yeo UC et al (2013) *Histopathological study of the treatment of melasma lesions using a low-fluence Q-switched 1064-nm neodymium:yttrium-aluminium-garnet laser.* Clin Exp Dermatol 38(2): 167-171.
4. Mun JY, Jeong SY, Kim JH et al (2011) *A low fluence Q-switched Nd:YAG laser modifies the 3D structure of melanocyte and ultrastructure of melanosome by subcellular-selective photothermolysis.* J Electron Microsc (Tokyo) 60(1): 11-18.
5. Park YW, Yeo UC (2015) *Mottled hypopigmentation from laser toning in the treatment of melasma: A catastrophic or manageable complication?.* Med Lasers 4: 45-50.
6. Choi CP, Yim SM, Seo SH et al (2015) *Retrospective analysis of melasma treatment using a dual mode of low-fluence Q-switched and long-pulse Nd:YAG laser vs. low-fluence Q-switched Nd:YAG laser monotherapy.* Journal of Cosmetic and Laser Therapy 17(1): 2-8.
7. Choi YJ, Nam JH (2017) *Efficacy and safety of a novel picosecond laser using combination of 1 064 and 595nm on patients with melasma: A prospective, randomized, multicenter, split-face, 2% hydroquinone cream-controlled clinical trial.* Lasers Surg Med 49(10): 899-907.
8. Wang YJ, Lin ET, Chen YT et al (2020) *Prospective randomized controlled trial comparing treatment efficacy and tolerance of picosecond alexandrite laser with a diffractive lens array and triple combination cream in female asian patients with melasma.* J Eur Acad Dermatol Venereol 34(3): 624-632.
9. Chalermchai T, Rummaneethorn P (2018) *Effects of a fractional picosecond 1,064 nm laser for the treatment of dermal and mixed type melasma*. J Cosmet Laser Ther 20(3): 134-139.
10. Kang Hy, Kim Jh, Goo Bc (2011) *The dual toning technique for melasma treatment with the 1064 nm Nd: YAG laser: A preliminary study.* Laser therapy 20(3): 189-194.
11. Choi JE, Lee DW, Seo SH et al (2018) *Low-fluence Q-switched nd:YAG laser for the treatment of melasma in Asian patients*. J Cosmet Dermatol 17(1053-1058).
12. Gokalp H, Akkaya AD, Oram Y (2016) *Long-term results in low-fluence 1064-nm Q-Switched Nd:YAG laser for melasma: Is it effective?* J Cosmet Dermatol 15(4): 420-426.
13. Dayan SH, Vartanian AJ, Menaker G et al (2003) *Nonablative laser resurfacing using the long-pulse (1064-nm) Nd:YAG laser.* Arch Facial Plast Surg 5(4): 310-315.

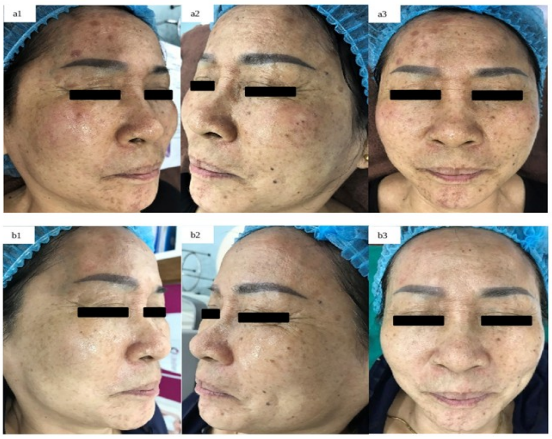

Figure 3. Clinical finding in a 66 year-old female patient (patient No1). (a1), (a2), (a3): baseline condition mMASI 22.4; (b1), (b2), (b3): After 5 sessions dual pico toning PSNY and LPNY with mMASI 9.8 (reduced 56.3%)

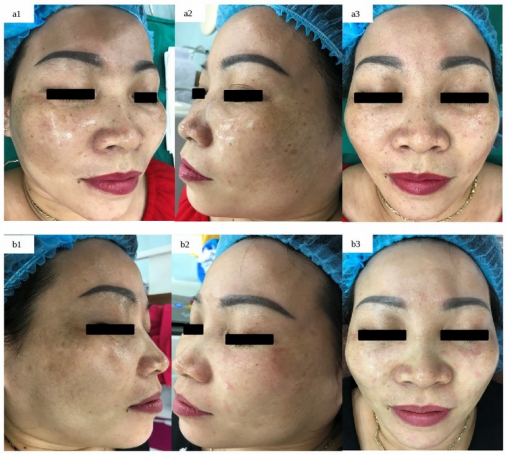

Figure 4. Clinical finding in a 39 year-old female patient (patient No11). (a1), (a2), (a3): baseline condition mMASI 10.8; (b1), (b2), (b3): After 5 sessions dual pico toning PSNY and LPNY with mMASI 4.8 (reduced 55.6%)

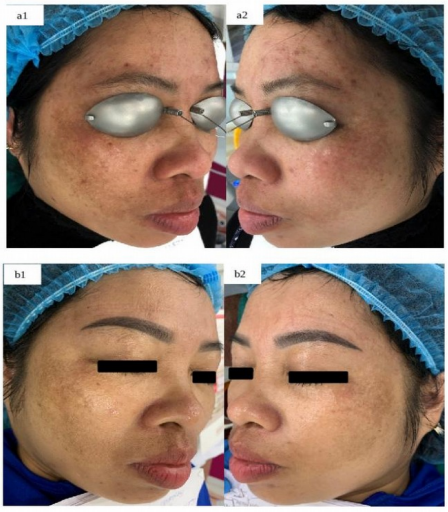

Figure 5. Clinical finding in a 46 year-old female patient (patient No21). (a1), (a2): baseline condition mMASI 16.2; (b1), (b2): After 5 sessions dual pico toning PSNY and LPNY with mMASI 6.6 (reduced 59.3%)