

Treatment of melasma by a combination of intense pulsed light with advanced optimal pulse technology and human-like collagen repair dressing

A case series study

Juping Chen, MD, PhD^{a,*} , Jun Liu, MA, Jianhong Wu, BA

Abstract

To observe the efficacy and safety of a combination of intense pulsed light (IPL) with advanced optimal pulse technology (AOPT) and human-like collagen repair dressing in the treatment of melasma.

Ten patients with melasma were treated using IPL with AOPT once a month for a total of 8 times, and received the treatment of external human-like collagen repair dressing after each operation. The efficacy was evaluated with the modified Melasma Area Severity Index (mMASI) score and satisfaction score, respectively, before treatment, after each treatment and at 4 months after the end of the whole treatment course.

The melasma was significantly lightened in all 10 patients after 8 times of treatments. The mMASI score before treatment was (8.6 ± 3.8) points, which decreased significantly to (5.1 ± 2.7) points after 8 times of treatments, and there was a significant difference in mMASI score between before and after 8 times of treatments ($P = .001$). The mMASI score was (3.3 ± 2.2) points at 4 months after the end of whole treatment course, and there was no significant difference in mMASI score between after 8 times of treatments and 4 months after the end of whole treatment course ($P > .05$). The satisfaction score was (7.2 ± 1.4) points after 8 times of treatments and (7.1 ± 1.4) points at 4 months after the end of whole treatment course, there was no significant difference in satisfaction score between after 8 times of treatments and 4 months after the end of whole treatment course ($P > .05$).

A combination of IPL with AOPT and human-like collagen repair dressing can effectively decrease the severity of melasma, and is associated with a higher patient satisfaction score and a lower risk of relapse after discontinuation of treatment.

Abbreviations: AOPT = advanced optimal pulse technology, IBM = International Business Machines, IPL = intense pulsed light, mMASI = modified Melasma Area Severity Index, OPT = optimal pulse technology.

Keywords: advanced optimal pulse technology, human-like collagen repair dressing, intense pulsed light, melasma

1. Introduction

Melasma is a common, acquired, symmetric, and patchy hyper-melanosis and the disease most commonly occurs on parts zygomatica, forehead, and cheeks. It can occur in any human race, but it is more commonly seen in Asian and Hispanic people. Melasma affects both men and women, but it is more common in women, especially women of childbearing age.^[1,2] The patient's appearance, self-confidence, and quality of life are usually impaired, and its typical causative risk factors are family genetics, sun exposure, abnormalities in the endocrine system, oral contraceptives, cosmetics, drugs, and visceral diseases.^[3-6] Epidermal barrier destruction, inflammation, vascular changes, phagoaging, autophagy, non-ultraviolet light and oxidative stress may be associated with the pathogenesis of melasma.^[7-11] The study of Lee et al^[7] showed that the pigment index and erythema index in lesional skin are higher than those in the

surrounding normal skin in melasma patients, additionally, the integrity of the stratum corneum is impaired and barrier repair is delayed.

At present, melasma is largely managed by combined treatment that includes oral drugs, topical medication, and photo-electric therapy.^[12] Oral drugs such as tranexamic acid have some effect on melasma, but also have some potential risks such as spanomenorrhoea and thrombosis.^[13] Furthermore, topical drugs have some shortcomings such as inaccurate efficacy.^[14] Traditional intense pulsed light (IPL) and Q-switched lasers have some effects on melasma, but can also readily lead to melasma relapse.^[15,16] To treat pigment diseases, a single pulse or double pulse is generally used with a pulse width not exceeding 5 milliseconds. In order to reduce the epidermal irritations and postoperative relapse rate, a longer pulse width of more than 5 milliseconds is recommended. Optimal pulse technology (OPT) is a kind of IPL technology for achieving stable pulse energy

The patients have provided written informed consent for publication of this paper. The authors have no funding and conflicts of interest to disclose.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

^a Affiliated Hospital of Yangzhou University, Yangzhou, People's Republic of China.

* Correspondence: Juping Chen, Affiliated Hospital of Yangzhou University, Yangzhou 225009, People's Republic of China (e-mail: chen_juping@sina.com).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is

permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Chen J, Liu J, Wu J. Treatment of melasma by a combination of intense pulsed light with advanced optimal pulse technology and human-like collagen repair dressing: A case series study. *Medicine* 2022;101:31(e29492).

Received: 10 August 2021 / Received in final form: 11 April 2022 / Accepted: 5 May 2022

<http://dx.doi.org/10.1097/MD.00000000000029492>

output and avoiding energy attenuation. Under the condition of retaining all the advantages of the original IPL with OPT, the energy and width of each sub-pulse in the advanced optimal pulse technology (AOPT) can be customized and adjusted individually, which has the characteristics of achieving better treatment effect and fewer side effects. Due to the destruction of the skin barrier function in melasma, dry skin often occurs within a short time after photoelectric therapy, which can be treated by the application of skin barrier repair dressing. Human-like collagen is highly expressed by recombinant *Escherichia coli* BL21 containing a partial cDNA clone for human collagen mRNA. The human-like collagen repair dressing has moisturizing, film-forming, skin barrier repairing, and pigment lightening effects.^[17]

In this study, we first evaluated the effectiveness and safety of the combined use of IPL with AOPT and a topical human-like collagen repair dressing in the treatment of 10 melasma patients.

2. Methods

2.1. Participants

This is similar to a before-after study, so the ratio of the number of subjects in the control group to that in the treatment group was 1. The mean modified Melasma Area Severity Index (mMASI) score before treatment in the control group was 8.6 points, and the mean mMASI score after treatment in the treatment group was 3.0 points. The standard deviation of mMASI score in overall subjects was 4.0 points. The total sample size was 20. If the calculation parameter, 2-sided test and significance level ($\alpha = 0.05$) were selected, it was calculated that the power of test of the results was 0.891. The present case series included 10 melasma patients who were treated in the Laser Center of Affiliated Hospital of Yangzhou University between June 2017 and April 2019, including 9 female patients with an average age of (46.7 ± 5.2) years and 1 male patient with an age of 30 years. Fitzpatrick skin phototype: type III in 5 patients and type IV in 5 patients. Inclusion criteria: all 10 patients had melasma diagnosed independently by 2 senior dermatologists, and Wood's light examination was performed in all patients, of whom, 3 had mixed type of melasma and 7 had dermal type of melasma.^[18] Melasma lesions were located in centrofacial area in 5 patients and malar area in 5 patients (Table 1). Exclusion criteria: the patients with scars, severe diabetes, mental illness, active vitiligo and psoriasis, systemic lupus erythematosus and photo allergy, pregnant or lactating women, patients with high expectations for treatment, patients who were unwilling to perform sun protection and those who had been exposed to sunlight within a 4-week period were excluded. We obtained institutional approval for the use of this new clinical technology (No. 20170606). We explained the treatment plan in detail to the patients, and obtained their written consent before initiating the treatment.

2.2. Treatment protocol

First, we recorded the patients' medical histories in detail. Before each treatment, the patients washed their faces. We used

the same camera (Canon EOS700D, 18 megapixels, Canon Inc., Japan) in the same environment and at the same angle to capture and save images for every patient. The treatment efficacy was evaluated during the follow-up visit every month and at 4 months after the end of whole treatment course. All doctors and patients wore goggles during the treatment.

For performing IPL with AOPT in this study, M22 instrument produced by the American Scientific Medical Company (USA) was used, with a wavelength of 640 nm, an initial energy of about $5 \text{ J}\cdot\text{cm}^{-2}/5 \text{ J}\cdot\text{cm}^{-2}/5 \text{ J}\cdot\text{cm}^{-2}$, and a pulse width of 6.0 ms/6.0 ms/6.0 ms. The pulse width was changed to about 5.0 ms/5.0 ms/6.0 ms after 3 times of treatment. The energy was increased by 10% to 15% each time according to the context, and a total of 8 times of treatment were carried out at a frequency of once every month. Evaluation was performed before the initiation of treatment, after each treatment and at 4 months after the last treatment. Meanwhile, we asked the patients to apply the human-like collagen repair dressing and sunscreen evenly on their faces twice a day.

2.3. Clinical assessment

2.3.1. Treatment efficacy. All patients (10 patients, no patient was lost to follow up) were photographed before and after treatment. The images were compared between before and after the treatment. The skin lesions and subjective feelings of the patients were evaluated respectively by 2 doctors not involved in the treatment and the patients themselves. According to the changes in the affected area before and after treatment, the treatment efficacy was divided into 4 types: cured, markedly effective, effective, and ineffective. "Cured" indicates that the affected area was reduced by 90%. "Markedly effective" means that the color of the affected area was obviously lightened, and the pigmentation area was reduced by 60% to 89%. "Effective" implies that the color of the affected area was lightened, and the pigmentation area was reduced by 30% to 59%. "Ineffective" means that the color of the affected area was not lightened, and the pigmentation area was reduced by <30%. The total effectiveness rate was calculated as follows: (number of cured cases + number of markedly effective cases + number of effective cases)/total number of cases $\times 100\%$.^[19]

2.3.2. mMASI score assessment. The severity of melasma was determined based on the mMASI score, which was calculated using the following formula:^[20]

$$0.3A(\text{lm})D(\text{lm}) + 0.3A(\text{rm})D(\text{rm}) \\ + 0.3A(\text{f})D(\text{f}) \\ + 0.1A(\text{c})D(\text{c})$$

In the above formula, A represents lesional area: when the cumulative lesional area is <10%, 1 point is assigned. 10% to 29%, 2 points. 30% to 49%, 3 points. 50% to 69%, 4 points. 70% to 89%, 5 points. $\geq 90\%$, 6 points. D represents color depth: none, 0; mild depth, 1; moderate depth, 2; obvious depth, 3; and severe depth, 4. lm indicates the left cheek, rm, the right cheek, f, the forehead, and c, the chin.

Table 1

Effectiveness rate of the combined use of IPL with AOPT and human-like collagen repair dressing.

	Total number of patients	Cured (cases)	Markedly effective (cases)	Effective (cases)	Ineffective (cases)	Total effectiveness rate (%)
After first treatment	10	0	0	0	10	0
After 5 times of treatment	10	0	2	5	3	70
After 8 times of treatment	10	0	6	4	0	100
At 4 mo after the end of whole treatment course	10	0	6	4	0	100

AOPT = advanced optimal pulse technology, IPL = intense pulsed light.

2.3.3. Satisfaction score assessment. The satisfaction score was assessed based on patient's self-evaluation and joint evaluation of the efficacy and side effects by the patients and evaluators, and ranged from 1 to 10 points, with 1 indicating "very dissatisfied" and 10 indicating "very satisfied."

2.4. Adverse events

Adverse reactions, including pain, burning, erythema, edema, pigmentation, depigmentation, scaling, and itching, were recorded after each visit.

2.5. Statistical analysis

We conducted all the statistical analyses using the SPSS19.0 software version (IBM International Business Machines, New York, NY). Measured data were expressed as mean \pm standard deviation. A paired *t* test was used to comparatively analyze the mMASI and satisfaction scores between before and after treatment. *P* values $<.05$ were considered to indicate statistical significance.

3. Results

3.1. Comparison of treatment efficacy

After 5 times of treatments, the treatment was markedly effective in 2 cases and effective in 5 cases, and the total effectiveness rate was 70%. After 8 times of treatments, the treatment was markedly effective in 6 cases and effective in the remaining 4 cases, and the total effectiveness rate was 100%. At 4 months after the end of the whole treatment course, the total effectiveness rate was maintained at 100% (Table 2).

3.2. Comparison of mMASI score between before and after treatment

The mMASI score was decreased respectively after 5 and 8 times of treatments and at 4 months after the end of the whole treatment course.

mMASI score before treatment was (8.6 ± 3.8) points, and it decreased significantly to (5.1 ± 2.7) points after 5 times of treatments ($t = 2.367, P < .05$) and remained significantly lower

than the pretreatment score after 8 times of treatments (mMASI score = $[3.0 \pm 1.8]$ points, $t = 4.194, P < .05$). Although the mMASI score after 8 times of treatments was lower than that after 5 times of treatments, the difference was not significant ($t = 2.074, P > .05$). The mMASI score was (3.3 ± 2.2) points at 4 months at the end of the whole treatment course, and it was not significantly different from that after 8 times of treatments ($t = -0.399, P > .05$; Fig. 1).

3.3. Comparison of satisfaction score between before and after treatment

The satisfaction score increased respectively after 8 times of treatments and at 4 months after the end of whole treatment courses.

The satisfaction score was (5.2 ± 0.8) points after 5 times of treatments and increased significantly to (7.2 ± 1.4) points after 8 times of treatments ($t = 3.939, P < .05$). The satisfaction score was (7.1 ± 1.4) points at 4 months after the end of whole treatment course, there was no significant difference in satisfaction score between after 8 times of treatments and 4 months after the end of whole treatment course ($t = 0.162, P > .05$; Fig. 2).

3.4. Typical cases

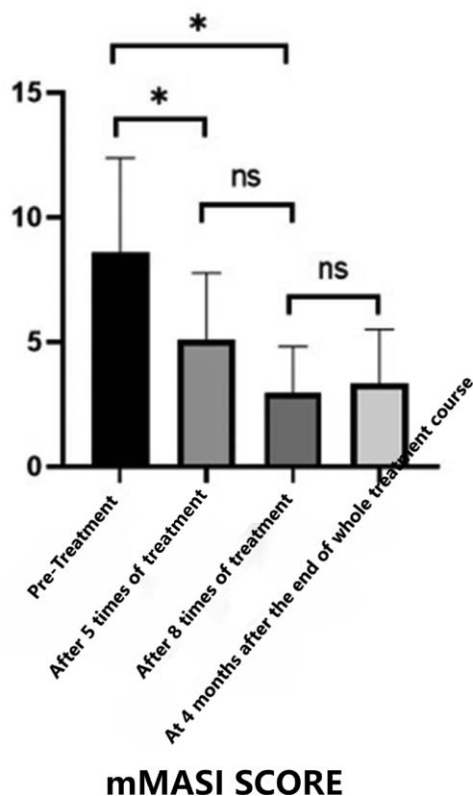
3.4.1. Patient 1. A 40-year-old Chinese woman presented with yellowish-brown macules on the left and right cheeks that had developed over the last 4 years (Fig. 3). She did not have a history of liver or kidney dysfunction, but she had a high level of stress at work. Fitzpatrick skin phototype: type III. Physical examination showed that yellow-brown macules occurred on both sides of the cheek and occupied 20% of the area of each cheek. The color depth was moderate, and telangiectasias could be seen on both cheeks. The patient was diagnosed with a mixed type of melasma. The mMASI score before treatment was 3.6 points. The M22 instrument was used for treatment, and the wavelength was set at 640 nm, with an initial pulse width of 6.0 ms/6.0 ms/7.0 ms and an initial energy of about 5 J-cm⁻²/5 J-cm⁻²/5 J-cm⁻². The patient was treated once a month for 8 months, and the mMASI and satisfaction scores were calculated before treatment, after each treatment, and at

Table 2

The demographic data of 10 patients.

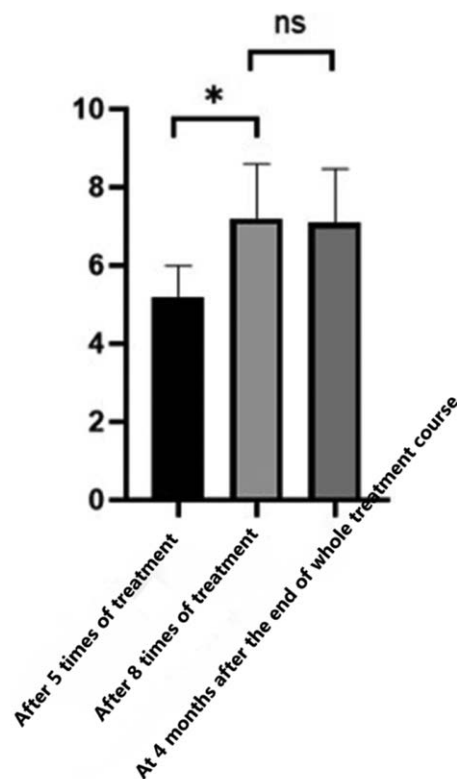
	Age (years old)	Fitzpatrick skin phototype	Type of melasma	Clinical type of melasma	Treatment times	Treatment parameters	The mMASI score before treatment	The mMASI score after whole treatment	The mMASI score after 4 mo of whole treatment
Patient 1	52	III	Mixed	Malar	8	The wavelength is 640 nm, the initial energy is about 5 J-cm ² /5 J-cm ² /5 J-cm ² , and the pulse width is 6.0 ms/6.0 ms/6.0 ms. After 3 treatments, the pulse width became about 5.0 ms/5.0 ms/6.0 ms. Increase the energy by 10%–15% each time according to the specific situation.	12	4.2	6.0
Patient 2	30	IV	Dermal	Malar	8		4.8	1.2	1.2
Patient 3	40	III	Mixed	Malar	8		5.4	1.2	1.2
Patient 4	52	IV	Dermal	Centrofascial	8		7.2	1.8	1.8
Patient 5	52	IV	Dermal	Centrofascial	8		9.0	4.8	4.8
Patient 6	44	III	Dermal	Malar	8		12	4.5	4.5
Patient 7	43	IV	Dermal	Centrofascial	8		14.4	6.0	6.0
Patient 8	51	III	Mixed	Centrofascial	8		12	3.6	5.4
Patient 9	46	III	Dermal	Malar	8		5.4	1.2	1.2
Patient 10	40	IV	Dermal	Centrofascial	8		3.6	1.2	1.2

mMASI = modified Melasma Area and Severity Index.



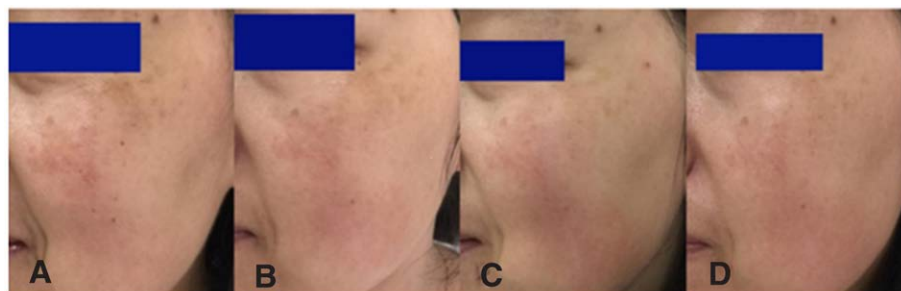
mMASI SCORE

Figure 1. Comparison of MASI score between before and after the combined application of IPL with AOPT and a skin barrier repair agent. The MASI score was evaluated before treatment, after each treatment, and at 4 mo after the end of the whole treatment course. Measured data were expressed as mean ± standard deviation. A paired *t* test was used to analyze the MASI score, *P* values <.05 were considered to indicate statistical significance. AOPT = advanced optimal pulse technology, IPL = intense pulsed light, MASI = Melasma Area Severity Index, mMASI = modified Melasma Area Severity Index.



Satisfaction SCORE

Figure 2. Comparison of satisfaction score between before and after the combined application of IPL with AOPT and a skin barrier repair agent. The satisfaction score was evaluated after each treatment, and 4 mo after the end of the whole treatment course. Measured data were expressed as mean ± standard deviation. A paired *t* test was used to analyze the satisfaction score, *P* values <.05 were considered to indicate statistical significance. AOPT = advanced optimal pulse technology, IPL = intense pulsed light.



(A) Left side. Pre-Treatment
 (B) Left side. After 5 times of treatment, the treatment efficacy was effective.
 (C) Left side. After 8 times of treatment, the treatment efficacy was markedly effective.
 (D) Left side. At 4 months after the end of whole treatment course, the treatment efficacy was still markedly effective.

Figure 3. Photographs of a typical case of melasma treated by the combined application of IPL with AOPT and a skin barrier repair agent. The M22/AOPT instrument was used, with a wavelength of 640 nm, an initial pulse width of 6.0ms/6.0ms/7.0ms and an initial energy of about 5 J·cm⁻²/5 J·cm⁻²/5 J·cm⁻². After 2 courses, the pigmentation became lighter and the overall skin tone was brightened, we adjusted the pulse width to 5.0ms/6.0ms/6.0ms and the energy to 6 J·cm⁻²/5 J·cm⁻²/5 J·cm⁻². After 3 more courses under the adjusted parameters (ie, after a total of 5 times of treatments), the pulse width was further adjusted to 5.0ms/5.0ms/5.0ms and the energy to 6 J·cm⁻²/6 J·cm⁻²/6 J·cm⁻². AOPT = advanced optimal pulse technology, IPL = intense pulsed light.

4 months after the end of the whole treatment course. The patient was advised to perform sun protection, use the topical human-like collagen repair dressing, and avoid any intense activity that could cause fatigue. After 2 treatment courses, the pigmentation became lighter and the overall skin tone was brightened, we adjusted the pulse width to 5.0 ms/6.0 ms/6.0 ms and the energy to 6 J·cm⁻²/5 J·cm⁻²/5 J·cm⁻². After 3 more times

of treatment under the adjusted parameters (ie, after a total of 5 times of treatments), the affected area was significantly lightened, the area of melasma lesions was decreased by about 57%, the telangiectasia was reduced, the mMASI score was lowered to 2.4 points, and the satisfaction score was 6 points. The pulse width was further adjusted to 5.0 ms/5.0 ms/5.0 ms and the energy to 6 J·cm⁻²/6 J·cm⁻²/6 J·cm⁻². After the

completion of 8 times of treatments under these conditions, the telangiectasia was reduced further, the skin tone of the affected area was lighter, the area of melasma lesions was decreased by about 75%, the mMASI score was lowered to 1.2 points, and the satisfaction score was increased to 8 points. At 4 months after the end of the whole treatment course, the area of melasma lesions was not increased, the mMASI score was still 1.2 points and the satisfaction score also remained 8 points (Fig. 3).

3.4.2. Patient 2. A 43-year-old Chinese woman presented with a yellowish-brown rash on the cheek that had developed for 3 years and aggravated over 2 months (Fig. 4). The patient developed yellow-brown macules on both sides of the face in the past 3 years that had worsened after 2 months of traveling without the application of sun protection lotion. The patient had irregular menstruation with a small amount of menstrual discharge. The patient denied a history of liver or kidney dysfunction. Fitzpatrick skin phototype: type IV. Physical examination: The patient had a large area of symmetrical yellow-brown macules on the face, which covered 73% of each side of face with a high color depth, and the patient was diagnosed with a dermal type of melasma. The mMASI score before treatment was 14.4 points. We used the M22 instrument at a wavelength of 640 nm, with an initial pulse width of 6.0 ms/6.0 ms/7.0 ms and initial energy of 5 J·cm⁻²/5 J·cm⁻²/5 J·cm⁻². The patient received a total of 8 times of treatment, and the mMASI and satisfaction scores were calculated before treatment, after each treatment, and at 4 months after the end of whole treatment course. The patient was advised to apply sun protection lotion and a topical human-like collagen repair dressing. After 3 times of treatment, the pigmentation became lighter and the overall skin tone was brightened, we adjusted the pulse width to 6.0 ms/6.0 ms/6.0 ms and the energy to 6 J·cm⁻²/6 J·cm⁻²/5 J·cm⁻². After 2 more times of treatment with the adjusted parameters (ie, after a total of 5 times of treatment), the affected area was significantly lightened, the area of melasma lesions was decreased by about 80%, the mMASI score was reduced to 9.0 points, and the satisfaction score was 6 points. Thereafter, we adjusted the pulse width again to 5.0 ms/6.0 ms/5.0 ms and the energy to 7 J·cm⁻²/7 J·cm⁻²/6 J·cm⁻². The area of melasma lesions was decreased by about 88% after 8 times of treatments, the complexion appeared lighter, the mMASI score dropped to 6 points, and the satisfaction score rose to 9 points. At 4 months after the end of whole treatment course, the area of melasma lesions was not increased, the mMASI score and the satisfaction score were still 6 and 9 points, respectively (Fig. 4).

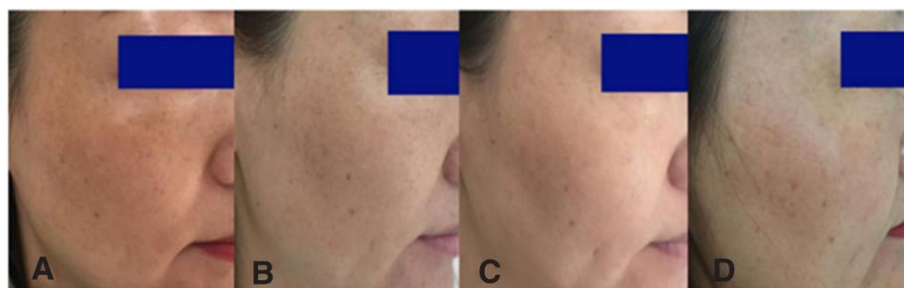
3.5. Side effects

None of the patients in this case series reported experiencing any discomfort during the treatment. The patients reported feeling warm during the treatment, without any burning, tingling, scaling or itching sensations.

4. Discussion

Melasma is a common skin condition that is prone to relapse and difficult to treat. It occurs more frequently in women than in men, and affects their appearance and self-confidence. Some studies have shown that melasma lesions are associated not only with an increase in the amount of epidermal pigment but also with changes of photoaging in the dermal tissue.^[8,9] Furthermore, current studies have discovered molecular and genetic changes related to photoaging in melasma lesions. For example, the vascular endothelial cells promote pigment production via secreting endothelin-1, additionally, the blood vessels abnormally proliferate in melasma lesions.^[11,21] These findings indicate that photoaging plays an important role in the development of melasma. The treatment of melasma is mainly combined treatment that includes oral drugs, topical medication, and photoelectric therapy, of which, the photoelectric therapy is a very effective method. Because photoaging plays an important role in the occurrence of melasma, the parameters similar to those for the treatment of skin photoaging should be selected when the photoelectric therapy of melasma was performed.

Many studies have shown that IPL, Q-switched laser or combined treatment is effective in treating melasma to some extent, but is associated with pigmentation, depigmentation, easy relapse and low patient satisfaction.^[15,16] In 1 study, Li used IPL to treat 89 Chinese patients with melasma,^[15] according to skin type, she treated epidermal type melasma using a 560/590 nm filter and double pulse, and treated mixed-type melasma using a 590/615/640 nm filter and 3 pulses, with a pulse width of 3 to 4 milliseconds, delay time of 25 to 40 milliseconds and energy of 13 to 17 J/cm², evaluation was performed after each treatment and at 3 months after the last treatment. The result showed all patients experienced moderate pain, with a hyperpigmentation incidence of 3.37%, and 72 patients had mild desquamation that lasted for 7 to 10 days. In another study, Vachiramon^[16] compared the efficacy of a single application of Q-switched 1064-nm low-energy laser with that of combined application of Q-switched 1064-nm low-energy laser and IPL in the treatment of melasma for 3 months, and found that both treatment methods were effective, but the efficacy of the combined treatment was better than that of the single treatment. However, the patients treated with both treatment methods reported melasma



(A) Right side. Pre-Treatment
 (B) Right side. After 5 times of treatment, the treatment efficacy was markedly effective.
 (C) Right side. After 8 times of treatment, the treatment efficacy was markedly effective.
 (D) Right side. At 4 months after the end of whole treatment course, the treatment efficacy was still markedly effective.

Figure 4. Photographs of a typical case of melasma treated by the combined application of IPL with AOPT and a skin barrier repair agent. The M22/AOPT instrument was used with a wavelength of 640 nm, an initial pulse width of 6.0 ms/6.0 ms/7.0 ms and initial energy of 5 J·cm⁻²/5 J·cm⁻²/5 J·cm⁻². After 3 treatment courses, we adjusted the pulse width to 6.0 ms/6.0 ms/6.0 ms and the energy to 6 J·cm⁻²/6 J·cm⁻²/5 J·cm⁻². After 5 times of treatments, we adjusted the pulse width to 5.0 ms/6.0 ms/5.0 ms and the energy to 7 J·cm⁻²/7 J·cm⁻²/6 J·cm⁻². AOPT = advanced optimal pulse technology, IPL = intense pulsed light.

recurrence to some extent: the patients receiving combined treatment had a recurrence rate of 33%, and those receiving single treatment had a recurrence rate of 11%. In our study, we have investigated the effect of IPL with AOPT in the treatment of melasma in 10 patients, 8 times of treatments were administered at a frequency of once every month, mMASI and satisfaction scores were evaluated before the initiation of treatment, after each treatment, and at 4 months after the end of the whole treatment course. The findings indicate a high effectiveness rate that was maintained for up to 4 months after end of the whole treatment course.

The current OPT not only achieves uniform output of IPL pulse energy and makes treatment more gentle and safer, but also has the advantage of the continuous multiple pulse technology. The new generation of AOPT retains all the advantages of the original OPT, the energy and pulse width of each sub-pulse can be adjusted separately according to the condition, so it has a lighter epidermal response, less pain and better effect. We treated 10 melasma patients using IPL combined with AOPT, which showed a high effectiveness rate that was maintained for up to 4 months after the end of whole treatment course, without melasma recurrence.

Skin with melasma is very sensitive to sunlight and heat stimulation, therefore, the melasma must be treated with caution to avoid skin irritation, this is why we investigated the IPL with AOPT in the present study. Additionally, we chose a wavelength of 640 nm, which is known to be effective against pigmentation, moreover, it has a smaller irritation on the epidermis. The pulse width refers to the time span over which the light actually acts on the tissue, if the pulse width is short, the energy is too concentrated on the epidermis, and thus the epidermis will absorb too much energy, which can result in pigmentation and recurrence of the melasma, additionally, the extended pulse width is also conducive to the contraction of blood vessels. Therefore, for the treatment of these 10 patients, we chose a wavelength of 640 nm, and selected a lower energy and a longer pulse width, with an initial width of 6.0 ms/6.0 ms/6.0 ms and energy of 5 J·cm²/5 J·cm²/5 J·cm². We gradually increased the energy and shortened the pulse width after the skin texture was improved. Our research results showed that the mMASI score decreased significantly after treatment, the skin qualities of the patients were improved, and the satisfaction score was higher. After the whole treatment course was completed, the mMASI score did not increase significantly and the melasma relapse did not occur. The patients did not experience pain or discomfort during the entire treatment process.

Many studies have shown that damage to the skin barrier occurs in patients with melasma.^[7] Additionally, photoelectric therapy also has a certain impact on the skin barrier over the short treatment period, so it is necessary to use a postoperative barrier repair agent. Human-like collagen repair dressings have moisturizing, film-forming and repairing effects, and can lighten pigmentation,^[17] it can also repair the skin barrier caused by melasma and the photoelectric therapy. After each treatment, we asked patients to apply this human-like collagen repair dressing combined with sunscreen twice a day. This is one of the reasons for no recurrence till 4 months after the end of whole treatment course.

The main limitations of our study were the small sample size and the short observation time. In addition, this was a single-center study, in which, there was no control group, and no objective data evaluation was performed. In the future, more randomized control studies across multiple centers and with a large sample size need to be conducted to confirm these findings. Nonetheless, the present study clearly shows that a combination

of IPL with AOPT and a barrier repair agent has a definite effect in the treatment of melasma and does not result in relapse once the treatment is discontinued.

References

- [1] Arya L, Bagadia J, Bhat Y, et al. Clinical and epidemiologic features of melasma: a multicentric cross-sectional study from India. *Int J Dermatol*. 2019;58:1305–10.
- [2] Betkerur J, Shastry V, Yalamanchili R. Clinico-epidemiological study and quality of life assessment in melasma. *Indian J Dermatol*. 2015;60:519.
- [3] Bernerd F, Del BS, Duval C. Clinical and biological characterization of skin pigmentation diversity and its consequences on UV impact. *Int J Mol Sci*. 2018;19:2668.
- [4] Ortonne JP, Arellano I, Berneburg M, et al. A global survey of the role of ultraviolet radiation and hormonal influences in the development of melasma. *J Eur Acad Dermatol Venereol*. 2009;23:1254–62.
- [5] Hwang YJ, Kwon SH, Lee SK, et al. Heterogeneous pathology of melasma and its clinical implications. *Int J Mol Sci*. 2016;17:824.
- [6] Alamdari MI, Ardabili NS, Danesh MA, et al. Evaluation of the serum zinc level in adult patients with melasma: is there a relationship with serum zinc deficiency and melasma? *J Cosmet Dermatol*. 2018;17:417–22.
- [7] Ha J, Kang HY, Lee DJ, et al. Defective barrier function in melasma skin. *J Eur Acad Dermatol Venereol*. 2012;26:1533–7.
- [8] Castaneda-Cazares JP, Hernández-Barrera R, Moncada B, et al. Solar elastosis and presence of mast cells as key features in the pathogenesis of melasma. *Clin Exp Dermatol*. 2008;33:305–8.
- [9] Castaneda-Cázares JP, Fuentes-Ahumada C, Moncada B, et al. Histochemical and immunohistochemical study in melasma: evidence of damage in the basal membrane. *Am J Dermatopathol*. 2011;33:291–5.
- [10] Kang HY, Ortonne JP. What should be considered in treatment of melasma. *Ann Dermatol*. 2010;22:373–8.
- [11] Kim EH, Kang HY, Kim YC, et al. The vascular characteristics of melasma. *J Dermatol Sci*. 2007;46:111–6.
- [12] Elbuluk N, Ogbechie-Godec OA. Melasma: an up-to-date comprehensive review. *Dermatol Ther (Heidelb)*. 2017;7:305–18.
- [13] Cho SH, Kim HJ, Kim HS, et al. Efficacy and safety of tranexamic acid in melasma: a meta-analysis and systematic review. *Acta Derm Venereol*. 2017;97:776–81.
- [14] Atefi N, Dalvand B, Ghassemi M, et al. Therapeutic effects of topical tranexamic acid in comparison with hydroquinone in treatment of women with melasma. *Dermatol Ther (Heidelb)*. 2017;7:417–24.
- [15] Chen HD, Chen JZS, Dong G, et al. Efficacy and safety of intense pulsed light in treatment of melasma in Chinese patients. *Dermatol Surg*. 2008;34:693–700, 700–701.
- [16] Sirithanabadeekul P, Sahawatwong S, Vachiramon V. Low-fluence Q-switched Nd: YAG 1064-nm laser and intense pulsed light for the treatment of melasma. *J Eur Acad Dermatol Venereol*. 2015;29:1339–46.
- [17] Fan D, Li X, Liu Y, et al. A novel smart injectable hydrogel prepared by microbial transglutaminase and human-like collagen: its characterization and biocompatibility. *Mater Sci Eng C Mater Biol Appl*. 2016;68:317–26.
- [18] Sanchez NP, Pathak MA, Sato S, et al. Melasma: a clinical, light microscopic, ultrastructural, and immunofluorescence study. *J Am Acad Dermatol*. 1981;4:698–710.
- [19] Dua R, Ghunawat S, Garg VK, et al. Role of broad-spectrum sunscreen alone in the improvement of melasma area severity index (MASI) and melasma quality of life index in melasma. *J Cosmet Dermatol*. 2019;18:1066–73.
- [20] Abou-Taleb DAE, Ibrahim AK, Youssef EM, et al. Reliability, validity, and sensitivity to change over time of the modified melasma area and severity index score. *J Dermatol Surg*. 2017;43:210–7.
- [21] Ambrosetti D, Bahadoran P, Ballotti R, et al. Endothelial cells promote pigmentation through endothelin receptor B activation. *J Invest Dermatol*. 2015;135:3096–104.