Original Article

Treating melasma with (1540 nm) fractional non-ablative erbium laser: a pilot study

Estudo-piloto: tratamento de melasma com laser de Erbium fracionado não ablativo (1.540nm)

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ABSTRACT

Introduction: Melasma is a common pigmentary disorder. Notwithstanding, its treatment is frustrating, and slow to take effect. Although depigmenters still are the main treatment modality, lasers have recently emerged as an innovative option.
Objective: To preliminarily determine the effects of non-ablative photothermolysis on persistent melasma.
Methods: Ten patients with resistant melasma underwent three 1540 nm fractional non-ablative erbium laser sessions (with one month intervals), with a 15 mm spot size handpiece. No additional treatment was carried out 3 months before or after. The energy level used ranged from 8 to 15 mJ/MB, and the pulse duration was 15 ms. Responses were evaluated by both the researcher physician and the patients.
Results: Seven patients completed the study; three patients left due to side effects. The researching physician reported that the patients who completed the study obtained 50-75% improvement one month after the last session. The patient's analysis resulted 50-75% improvement for 5 patients, and 75-100% for the remaining two. The physician and the patients reported that the improvement was maintained at the 3-month follow-up visit.
Conclusions: Although the preliminary results were satisfactory, further, longer-term studies are necessary to establish more efficient protocols and to observe possible recurrences.
Keywords: melanosis; lasers; treatment outcome.

RESUMO

Introdução: *O melasma constitui desordem pigmentar frequente. Apesar disso, o tratamento é frustro, e a doença segue curso indolente. Despigmentantes ainda são a principal forma de tratamento. Recentemente, os lasers surgiram como nova opção.*
Objetivo: *Determinar de modo preliminar o efeito da fototermólise fracionada não ablativa no melasma resistente.*
Métodos: *Dez pacientes com melasma resistente foram selecionados. Realizaram-se três sessões, com intervalo mensal, de laser de Erbium fracionado não ablativo de 1.540nm, com ponteira de 15mm. Nenhum outro tratamento foi realizado nos três meses anteriores ou posteriores. A energia utilizada variou entre oito e 15mJ/MB. A duração de pulso foi de 15ms. As respostas foram avaliadas pelo médico pesquisador e pelos pacientes.*
Resultados: *Sete pacientes concluíram o estudo, tendo os outros três sido afastados devido a efeitos colaterais. Na opinião do médico examinador os sete obtiveram melhora de 50% a 75% um mês depois da última sessão. Para cinco pacientes a melhora em um mês variou de 50% a 75%, e para dois pacientes de 75% a 100%. As impressões prévias se mantiveram após três meses, tanto para o médico examinador quanto para os pacientes.*
Conclusões: *Apesar dos resultados preliminares satisfatórios, novos estudos tornam-se necessários, no intuito de estabelecer protocolos mais eficientes com seguimento de longo prazo, visando observar possíveis recidivas e eventuais rebotes.*
Palavras-chave: *melanose; lasers; resultado de tratamento.*

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INTRODUCTION

Melasma is characterized by a dysfunction in the pigment of the skin that results in hyperpigmentation on the face or, less frequently, on other areas of the body. The spots range in color from brown to grayish-brown.[1] Most cases occur in sun-exposed areas, and 90% of those with the condition are women.[2]

Newcomer and colleagues were the first to observe the high frequency of hyperpigmentation, especially in the face.[3] They highlighted the influence of the sun in triggering the initial appearance and recurrence of the disease, the absence of inflammation, the unpredictable development of the condition, and the lesions' resistance to treatment.4 Although melasma's etiopathogenesis remains inconclusive, several risk factors are described in addition to sun exposure: pregnancy, use of cosmetics or medicines, endocrine dysfunction, hormone therapy and stress.[1]

From a histological perspective, three pigmentation patterns are recognized: an epidermal type with pigment deposited in the basal and suprabasal layers, a dermal type in which macrophages containing melanin are deposited in the superficial and medium dermis, and a mixed type, which combines characteristics of both.[5]

Because of its refractory and recurrent nature, melasma is difficult to treat. Treatment objectives include preventing or reducing the severity of recurrence, with the fewest possible side effects.6 The principles of this therapy include UV protection, inhibiting the activity of melanocytes and melanin synthesis, and removing existing melanin granules.[7]

Several studies have recently tested non-ablative fractional photothermolysis as an option for treating melasma. Such devices use 1,440, 1,540, 1,550 and 1,565 nm laser beams. Due to its good absorption by water, its main indication is to stimulate the synthesis and remodelling of collagen. 8 These lasers have the following specific characteristics:

1 - The handpiece beams fractions of rays, which emit energy measured in millijoules.

2 - The rays promote coagulation columns in the skin, keeping the skin's surface untouched, meaning that rays do not promote their ablation. The laser stimulates the reconstruction of the entire coagulated area in this column, in the dermoepidermal direction; this process begins a few hours after the procedure and lasts for 14 days. The collagen and the residues of pigment and vessels that have been coagulated are eliminated through the epidermis.[9]

3 - The penetration of the rays varies according to the fluence. The greater the energy released, the deeper the action, which allows the modulation of the desired result.[10]

4 - Although melanin and hemoglobin are not targeted by these lasers, some of the pigments and/or vessels coagulate when they come into contact with the laser's beam. Thus the laser indirectly causes the removal of superficial epidermal and dermal pigments and some small blood vessels.[11]

The most commonly used devices in Brazil are the 1,550 nm and 1,540 nm lasers, which are slightly different. The 1,540 nm laser (Erbium glass rod laser) releases rays in a static manner, as if "stamping" the skin, in pulses of 10-100 ms. There are two handpieces: one for more superficial penetration (15 mm) and another for deeper penetration (10 mm). The fluences used vary from 20-100 mJ/cm^2; high fluences cause an average thermal damage of 333 wide x 1 mm deep. The 1,550 nm (Erbium glass laser) dynamically releases rays through a tip that is moved over the skin to begin the treatment. This device automatically controls the rays' density and the width and depth of the coagulation columns.[11]

Since non-ablative fractional photothermolysis involves fewer side effects than ablative techniques (fractional or not), and because its action removes epidermal and dermal pigments, it is reasonable to assume that it would affect melasma. Therefore, we proposed using the non-ablative fractional photothermolysis 1,540 nm (Erbium glass rod laser) with the more superficial 15 mm tip in a pilot study.

METHODS

Ten melasma patients (nine women) with skin types II to VI were selected for this study (Table 1). Patients on hormone therapy were excluded. All were advised about the treatment's possible risks and benefits, and signed a free and informed term of consent. All study patients had melasma that was resistant to treatment (characterized by the type, number and length of previous treatments) (Table 2), and at the time of the study they had not undergone any therapy for at least three months. Patients were asked to specify which previous treatments they had undergone and drugs they had used from a list of common therapies (Table 2). All patients who enrolled in the study had already undergone some type of topical therapy for melasma; however they had never been treated with laser or intense pulsed light.

Topical anesthesia was carried out using anesthetic cream (25 mg/g lidocaine + 25 mg/g prilocaine) applied 30 minutes before, and systemic analgesia with 10 mg ketorolac tromethamine sublingually 15 minutes before. The entire face was treated (areas with and without patches.. Three sessions were administered at one-month intervals. The protocol is described in Table 3. After the treatment, 0.1% cream was applied to the patients' face, and subjects were given SPF 30 sunscreen for daily use up to three months after the last session.

Table 1: Patient demographics

Patients	sexo	Gender	Phototype
1	Male	35	IV
2	Female	26	III
3	Female	44	IV
4	Female	46	IV
5	Female	32	IV
6	Female	42	IV
7	Female	49	IV
8	Female	44	V
9	Female	31	II
10	Female	51	VI

Table 2 - Duration of the condition and previous treatments

Patient	Condition duration*	Previous treatments**
1	5	1, 3, 9, 10
2	4	1, 3, 9, 10
3	9	1, 3, 4, 9, 10
4	11	1, 3, 10
5	2	1, 3, 4, 9, 10
6	10	1, 3, 10
7	13	1, 3, 10
8	12	1, 3, 10
9	5	1, 3, 8, 9, 10
10	21	1, 3, 5, 6, 8, 9, 10

*In years
**1 = Retinoic acid; 2 = Laser or IPL; 3 = Hydroquinone; 4 = Azelaic acid 5 = Kojic acid; 6 = Phytic acid; 7 = Ursine grape extract (8 = Glycolic acid 9 = Peelings (of any type); 10 = Sunscreen; 11 = Other;

Patients were evaluated and photographed by the examining physician and responded to a questionnaire that included the following objective criteria of improvement (after one month and three months after the last session): up to 25%, 25-50%, 50-75% and 75-100%. Patients also reported their satisfaction about the treatment (very satisfied, satisfied, dissatisfied, very dissatisfied). The patient questionnaire also assessed the pain experienced during treatment, on a scale ranging from 0-10 (0=no pain, 5=moderate pain and 10=severe pain). One patient was photographed by a professional photographer for illustrative purposes, using the computer program Reveal Imager®(Canfield Imaging Systems, Fairfield, NJ, USA) which captures the distribution of melanin in the skin (Figures 1-2).

RESULTS

Only seven patients completed the study. One left after developing polymorphic light eruption. After being referred to a rheumatologist, a positive result was found for an anti-DNA antibody in addition to increased VHR; a lupus diagnosis had not been confirmed for this case at the time this paper was submitted, however the patient was being followed up. Two other patients presented blisters after the second session, and were treated with topical corticosteroids (0.05% clobetasol cream) combined with antibiotic (1% silver sulfadiazine), and 40 mg of prednisone orally for five days. Neither developed sequelae after six weeks, however they were dismissed from the study for not being 100% cured of their side effects before the third session four weeks later. Of the seven patients who completed the study, six were women. The average duration of the condition for each participant is shown in Table 2; their ages and phototypes are listed in Table 1.

The observed side effects – in addition to second-degree burns and polymorphic light eruption in the three patients who were dismissed from the study – were limited to mild erythema that lasted two to four days in patients who completed the study. In those seven cases, rough skin (corresponding to very small crusts) was observed five days after the session in areas exposed to the fractional rays. Those crusts fell off spontaneously during the subsequent week; all patients presented a normal appearance eight days after the session.

The pain scale used by the patients is in Table 4. It is important to note that both patients who were dismissed from the study as a result of second-degree burns had the highest phototypes in the study (phototypes V and VI), which might explain their reaction to the treatment. All patients who completed the treatment returned to work the day after the sessions.

One month after the last treatment session, two patients rated their improvement at 75-100% (very satisfied), and five at 50-75% (satisfied) (Table 7). According to the observer physician, the improvement reached 50-75% for all seven patients who completed the study. Three months after the last session, the impressions remained the same for both the examiner physician and the patients (Tables 4 to 6). It is important to note that although the characteristics "better texture" and "skin quality" were not evaluated by the examiner physician, the patients sporadically reported these results.

DISCUSSION

Nouri in 1999 12 and Angsuwarangsee in 2003 13 documented the treatment of melasma with CO_2 and Q-switched Alexandrite laser, with satisfactory results. The therapy's principle was to mechanically remove the accumulated pigment through photothermolysis. Nevertheless, probably due to the aggressiveness of ablative therapy – and its possible side effects – this method did not become a popular treatment option for melasma. With the description of fractional photothermolysis by Manstein in 2004,[14] a new possibility arose to remove pigmentation through photothermolysis more safely and with fewer side effects. The creation of necrosis columns in the skin that eliminate excess pigmentation and preserve healthy skin allows faster recovery times than previous therapies.

Table 3 - Protocol used in the treatment of melasma (with 15 mm tip)m)

Phototype	Fluence (mJ/mB)	Pulse duration (ms)	Passes	Overlap
I -III	15	15	3-4	50%-20%
IV	13-15	15	3	40%-20%
V	11-14	15	3	20%-20%
VI	8-12	15	2	Sem overlap

Table 4: Patient reported improvement (n = 7)

Patient reported improvement *	1 mês**	3 meses**
até 25%	0	0
25%-50%	0	0
50%-75%	5	5
75%-100%	2	2

*Patients' analysis
** Number of patients (n=7)

Table 5: Clinician reported improvement (n = 7)

Clinician reported improvement	1 month	3 months
até 25%	0	0
25%-50%	0	0
50%-75%	7	7
75%-100%	0	0

*Patients' analysis
** Number of patients (n=7)

Table 6: Satisfaction index (n = 7)

Satisfaction index	1 month*	3 months*
Dissatisfied	0	0
Somewhat satisfied	0	0
Satisfied	5	5
Very satisfied	2	2

** Number de patients (n=7)

Table 7: Patient reported pain scale

Pain scale *	Pain rating 0 -10*
1	6
2	8
3	10
4	8
5	8
6	7
7	9

* 0 = none; 5 = moderate; 10 = intense

The rays' fractioning can occur in higher wavelengths (10,600 nm or 2,940 nm, in CO_2 and Erbium, respectively) – which involves the ablation of the epidermis – or in lower wavelengths, without the ablation of the epidermis. A fractional non-ablative Erbium laser, with a wavelength of 1,540 nm, was used in this study.

Few studies have evaluated the benefits of that therapy. The vast majority focuses on the Fraxel 1,550 nm Erbium laser (Reliant Technologies, USA), the first platform approved by the US Food and Drug Administration (FDA) for treating melasma. In 2005 Fitzpatrick reported a pilot study 2 that found significant improvement, using photographic documentation, when treating melasma with this device. In 2005, Rokhsar 15 also evaluated the efficacy of this platform in 10 patients through subjective impressions, reporting an improvement ranging from 75-100%. In 2007, Naito 16 analyzed melasma's response to the Fraxel laser using digital photography, with improvements in excess of 50%.

The 1,540 nm Starlux (Palomar, USA) was the second platform to be authorized by the FDA for treating melasma. In 2011, Steiner[17] wrote about this laser in a study involving 18 patients analyzed using colorimetric analysis and the Melasma Area Severity Index (MASI); the four-week follow-up showed a reduction in pigmentation. The present study, which consisted of subjective and photographic analyses using the same platform, followed up the patients for three months after the last

Figure 1 - Patient before and 3 months after treatment

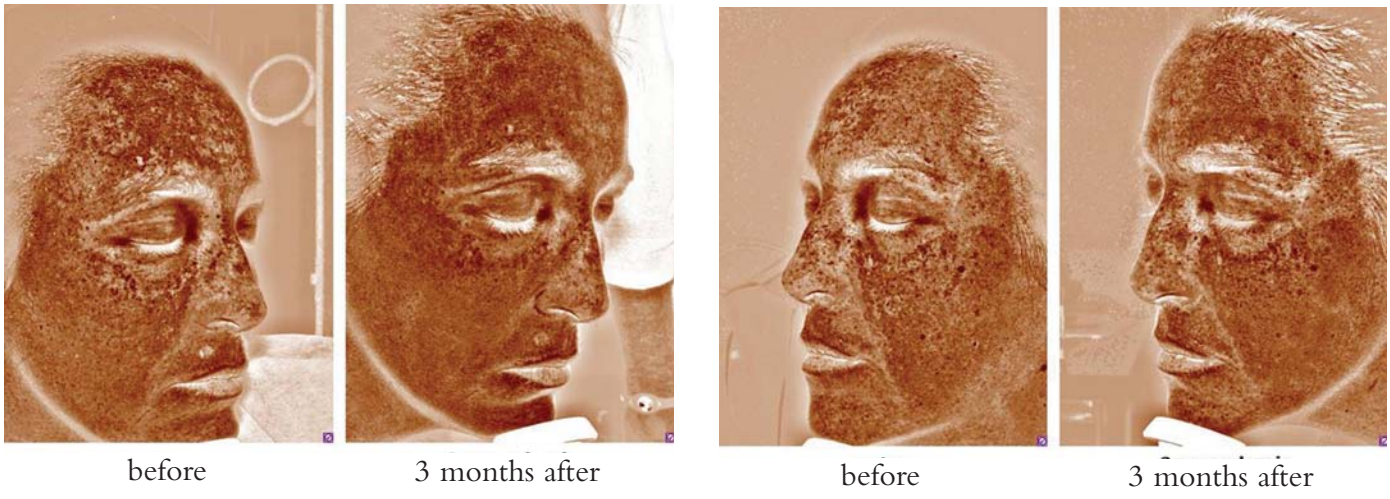

Figura 2 - antes e 3 meses após o tratamento com o programa Reveal®

session; the maintenance of the results was verified. In general, both the patients and the evaluator physician rated the improvement above 50%.

Lee's study 18 used the 1,550 nm technology and monitored 25 women for 24 weeks. Improvement, measured by a melanin quantitative index using a narrow-band reflectance spectrophotometer, dropped from 60-52%, while the MASI went from 7.6 to 6.2. Those findings provide support for rating this method as effective as an isolated treatment over a reasonable time horizon, outperforming our three-month follow-up with sustained results.

In the present study, the protocol used for patients was slightly more aggressive than that recommended by the manufacturer for treating melasma, yet it used energy levels considered safe for phototypes V and VI (according to the manual supplied by the manufacturer). Yet that statement proved to be false in the patient sample, in light of the side effects they experienced. No biopsy, dermoscopy or Wood light examinations were performed to determine the depth of the lesions. If that information had been available, the protocol could have been adjusted for each case, which may have optimized results. The second-degree burn cases in two patients demonstrate the need for individualized treatment plans and for dermatologists to work together to establish protocols to supplement those supplied by the manufacturer.

The polymorphic eruption case that presented an increase in the anti-DNA VHS positivity, suggesting a possible lupus diagnosis, reinforces the importance of carefully analyzing patients' medical histories and emphasizes the need for dermatologists to be able to expertly operate such devices. These are the professionals who are able to recognize important diagnoses that could go unnoticed by other specialist physicians or non-medical operators, possibly placing patients at risk.

In spite of the sublingual and topical anesthesia, the procedure was considered rather painful by the treated patients, which suggests the need to evaluate other forms of sedation or anesthesia. Nevertheless, the results were quite satisfactory in this preliminary analysis. The examiner physician concluded that the patients' melasma became lighter after treatment and made the stains appear more homogeneous and begin to merge with the normal skin, leading to the visual improvementdescribed. This treatment was proven to be considerably safer than ablative CO_2 laser, which can lead to sequelae ranging from hypochromia to scars.

It is also possible that this laser therapy can result in more improvement if combined with bleaching compounds including hydroquinone. Combining action mechanisms in the treatment of melasma is the correct approach to achieve better results. Our impression is that, in spite of its likely effectiveness as an isolated therapy, laser is potentially classified as an adjuvant therapy in the treatment of melasma. ●

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