Melasma and non-ablative (1540 nm) laser: a prospective study

Melasma e laser fracionado não ablativo (1540nm): um estudo prospectivo

Original Article

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ABSTRACT

Introduction: In 2006 the US Food and Drug Administration approved the use of fractional photothermolysis for the treatment of melasma.
Objectives: To evaluate the treatment of melasma patients with fractional photothermolysis.
Methods: Patients with a clinical diagnosis of melasma (n = 20) received three non-ablative laser sessions at 4-week intervals. The parameters used were: pulse = 15 ms, and progressively increasing energies in each session (8, 10 and 12 J). Results were evaluated using the Melasma Area and Severity Index and colorimetry analysis (with indices **ITA**, ***L, a, b***) at baseline and 4 weeks after the last session.
Results: Female patients (n = 18), with ages between 23 and 48 and Fitzpatrick phototypes from II to IV, completed the study. One patient did not complete both Melasma Area and Severity Index evaluations. There was a statistically significant decrease in the Severity Index ($p < 0.0001$, CI = 95%) and an average increase in the colorimetry indices **L** ($p = 0.0003$, CI = 95%) and **ITA** ($p = 0.0017$, CI = 95%), meaning a decrease in the pigmentation.
Conclusions: Fractional photothermolysis is a safe and effective option in the treatment of melasma, and should be considered an alternative to conventional methods.
Keywords: melanosis; lasers; colorimetry.

RESUMO

Introdução: *Diversos tratamentos têm sido propostos para o melasma porém todos com variáveis limitações. Em 2006 a FDA aprovou a fototermólise fracionada para o tratamento dessa dermatose.*
Objetivos: *Avaliar a evolução clínica, através de métodos objetivos, de pacientes com melasma tratadas isoladamente com a fototermólise fracionada.*
Métodos: *Estudo de intervenção terapêutica, aberto, prospectivo, de 20 pacientes com diagnóstico clínico de melasma. Os critérios de exclusão foram terapia hormonal, uso de retinoides orais, infecções cutâneas, gravidez e amamentação. Foram realizadas três sessões de laser fracionado não ablativo a intervalos de quatro semanas. Os parâmetros utilizados foram: Pulso = 15ms e energia crescente a cada sessão = 8 - 10 - 12J. Masi e colorimetria (com índices* ***ITA, L, a, b****) foram os parâmetros de avaliação utilizados antes do tratamento e quatro semanas após sua última sessão.*
Resultados: *Completaram o estudo 18 pacientes do sexo feminino com idade entre 23 e 48 anos e fototipos de II a IV (Fitzpatrick). Realizaram-se o Masi em 17 e a colorimetria nas 18 pacientes. Houve redução estatisticamente significante da escala Masi ($p < 0,0001$, IC95%) e aumento médio dos índices L ($p = 0,0003$, IC 95%) e* ***ITA*** *($p = 0,0017$, IC 95%) na colorimetria, traduzindo redução da pigmentação.*
Conclusões: *A fototermólise fracionada mostrou-se opção segura e eficaz para o tratamento do melasma, apontando para alternativa a se somar aos tratamentos convencionais.*
Palavras-chave: *melanose; lasers; colorimetria.*

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INTRODUCTION

Melasma is an acquired common, chronic hypermelanosis of indistinct etiology. It occurs in exposed areas of the skin, mainly in the frontal and malar areas, and is nine times more frequent in women than in men.[1,2] The condition is characterized by symmetrical brownish patches in all ethnicities, especially in individuals with high phototypes. Exposure to the sun, pregnancy and use of oral contraceptives have been significantly correlated to its etiopathogeny.[1,3]

Melasma is classified according to its clinical and histological characteristics. The pigment can be located in the epidermal or dermal layers, or both. Choice of treatment and the prognosis rely heavily on the classification of its characteristics. [1,3,4]

Several treatments focusing on several stages of the formation of melasma have been proposed. Among them are the inhibition of tyrosinase (hydroquinone, tretinoin, azelaic acid, kojic acid), the non-selective suppression of melanogenesis (topical corticosteroids), the inhibition of reactive species of oxygen (azelaic acid) and melanin removal (peels). Notwithstanding, each has limitations of varying degrees.[1]

In 2006, the US Food and Drug Administration approved fractional photothermolysis for the treatment of melasma.4 Photothermolysis generates microscopic zones of thermal damage or Microscopic Treatment Zones (MTZ), surrounded by normal tissue, in the dermis and epidermis.4,-,7 Histologically, the homogenization of the dermal matrix and the formation of microscopic areas of epidermal necrosis take place, causing the elimination of the basal layer's pigment. This process validates the mechanism for which fractional photothermolysis is seen as a promising modality in the treatment of melasma.[6,7]

METHODS

A prospective and open study of a therapeutic intervention was carried out with individuals living in the city of Mogí das Cruzes, in the State of São Paulo, Brazil. Female patients (n = 20) clinically diagnosed with melasma were selected. The patients signed the term of free and informed consent, and the study complied with the recommendations of the Declaration of Helsinki 2000. The exclusion criteria were: use of hormonal therapy or oral retinoids, cutaneous infections, pregnancy and breast-feeding.

The patients were instructed to apply only SPF 30 sunscreen, four times per day. Three non-ablative Starlux® laser (Palomar; Burlington, Massachusetts, USA) sessions were carried out with the 1540 nm nozzle and 15 mm handpiece, at 4-week intervals.

The parameters used included: 15 ms pulse and increasing energy in each session (8, 10 and 12 J); there was one pass of the device, with 50% and 20% overlaps in the horizontal and vertical directions, respectively. Patients were instructed to use hydrocortisone cream (Therasona®; Theraskin, São Paulo, Brasil) 3 times a day during the 3 days following the sessions.

The following parameters were evaluated immediately before treatment and 4 weeks after the last session: Melasma Area and Severity Index (MASI) score and colorimetry (using the CR300 device Granotec® Curitiba, Parana, Brasil), with the collection of measurements in 3 different areas – right malar, left malar and inside the right arm as a control.

The MASI score takes into account the sum of the indices of the Frontal (F), Right Malar (RM), Left Malar (LM) and Mentonian (M) areas. These indices have an identical mathematical formula for the first 3 regions (0.3x (D + H)xA) and a slightly different one for the mentum (0.1x (D + H)xA). Below are the meanings of the variables and the values that can be clinically attributed to them:

A = Area
1: < 10%
2: 10-30%
3: 30-50%
4: 50-70%
5: 70-90%
6: 90-100%

D = Darkness (hyperpigmentation)
1: almost invisible
2: mild
3: moderate
4: intense

H = Homogeneity
0: normal skin
1:mild symptoms
2: patches smaller than 1.5 cm
3: patches larger than 2 cm
4: skin with no clear areas

In a simplified notation:
MASI = (Forehead + RM + LM) + mentum
MASI = 3x [0.3 (D + H) A] + 0.1 (D + H) A

The colorimeter provides 3 variables (***L, a, b***) that are coordinates of a three-dimensional axis, where:

L refers to luminosity, ranging from 0 (black) to 100 (white)

a indicates the grade of erythema and

b designates the color variation between blue and yellow

The ITA index (arctg [(L -50) /b)] x180/3.1416), which measures the pigmentation of the skin (where smaller values indicate darker skin and greater values, fairer skin) was also calculated. The results were used in a statistical analysis that employed the following methods:

(a) MASI: paired test of the mean values of the differences between scores calculated before and after treatment

(b) Colorimetry: linear models with repeated measures

Table 1: MASI scores statistics before and after treatment

Application	N	Average	Standard deviation	Median	Min	Max
Before	17	18.5	9.29	18.5	3.8	38.7
After	17	5.3	4.2	4.7	1	15.3
Difference	17	-13.2	10.32	-12.9	-36.6	4.7

RESULTS

Female patients (n = 18), aged between 23 and 48 (average 33), phototypes II to IV (Fitzpatrick classification) completed the study. The MASI score was calculated for 17 patients and colorimetry for 18. The reduction in MASI scores after treatment was significant when compared to baseline ($p < 0.0001$, with a confidence interval – CI – of 95%) (Table 1).

There was a significant average increase in the ITA scale ($p = 0.0017$, 95% CI, Table 2), as well as the L component ($p = 0.0003$, 95% CI, Table 3).Theer was a decline in the b component scores , tending from the yellow to the blue ($p = 0.0166$, Table 4), while the a component did not present a statistically significant change ($p = 0.2479$, 95% CI). The pictures illustrate the treatment progress of 3 patients; before treatment is shown on the left, and 4 weeks after the last session on the right (Figures 1, 2 and 3).

DISCUSSION

According to the fractional photothermolysis' theoretical model, the destruction of the pigment in the dermis – mainly in the epidermis – is the main method of improving melasma. The dermal material is incorporated into the microepidermic necrotic remains and is expelled through the horny layer. [5]

Nonetheless, the improvement was only partial in this study, as can be observed in the digital pictures. Other authors who carried out the same type of evaluation, such as Vasily,[8] also found only partial improvement. Using Starlux® (Palomar; Burlington, Massachusetts, USA), in 4 sessions with a 15 mm handpiece, 4 passes and a 50% overlap, he achieved a lightening f 40-50% that was maintained for 3 months. Naito[4] used a Fraxel laser (Reliant Technologies; San Diego, California, USA) in 3 to 4 sessions, with a 6 to 8 mJ/MTZ fluence, 250 MTZ/cm^2, and total energy varying from 550 to 2,820 mJ, achieving a maximum improvement of 50%. Such outcomes can be attributed to a series of factors, such as the participation of other physiopathogenic mechanisms that suffer individual interferences, the prevalence of dermal melasma or the need for a greater number of sessions. Tannous[5] suggests that this development should be compared in different phototypes.

Although the MASI is subject to the evaluator's interpretation, from a clinical point of view the MASI score and colorimetry parameters describe improvement, to allow greater objectivity than clinical inspection alone. In the present study, a single dermatologist calculated the patients' MASI scores before and after treatment, increasing the reliability of the scores. On the other hand, colorimetry can involve measurement errors, given that each point of the patch presents a set of indices with specific values. In order to minimize inconsistencies, two points were marked in the malar patch (one on the right and one on the left). Each point was measured 3 times (yielding significantly similar values), and the arithmetic mean was used in the analyses.

L and ITA are the most important colorimetry indices, for they measure melanic pigmentation. Both presented statistically significant improvement. As this type of laser does not influence vascularization, the expectation that index a would not change was confirmed.

Rokhsar[3] used the patient reported outcomes – which most of the times were aligned (9/10) with those of the 2 evaluator physicians – as the evaluation method in a study with

Table 2: ITA averages estimated using the least squares method

Application	Estimated average	Standard error	Degrees of freedom	T Value	Pr > |t|	95% CI
Before	11.79	2.15	33	5.47	<0.001	[7.41; 16.18]
After	17.66	2.15	33	8.2	<0.001	[13.28; 22.05]
Difference	5.87	1.72	33	3.42	0.0017	[2.37; 9.36]

Table 3: *L* component averages estimated using the least squares method

Application	Estimated average	Standard error	Degrees of freedom	T Value	Pr > |t|	95% CI
Before	53.4	0.58	33	91.42	<0.001	[52.2; 54.5]
After	55.1	0.58	33	94.42	<0.001	[53.9; 56.3]
Difference	1.75	0.44	33	3.99	0.0003	[0.86; 2.64]

Table 4: *b* component averages estimated using the least squares method

Application	Estimated average	Standard error	Degrees of freedom	T Value	Pr > |t|	95% CI
Before	26.08	0.29	33	54.83	<0.001	[15.49; 16.68]
After	15.35	0.29	33	52.33	<0.001	[14.75; 15.95]
Difference	-0.73	0.28	33	-2.52	0.0166	[-1.32; -0.14]

Figuras 1, 2 e 3 - evolução do tratamento com laser fracionado em melasma

10 female patients. There was an improvement of 75-100% in 6 patients, 3 months after the last session using the Fraxel laser device (4 to 6 sessions with 1- to 2-week intervals; 1,535 nm and 1550 nm; 6 to 12 mJ/MTZ; 2,000 to 3,500 MTZ/cm^2). However, the subjectivity of this evaluation method impedes an objective assessment of the treatment's effectiveness.

Although there was an improvement that lasted for a period of 4 weeks after the last treatment session, studies with a longer follow-up period describe the tendency of aggravation of dyschromia over time if no additional sessions or combined treatments are carried out. Lee 5 observed clinical improvement in 60% of patients after 4 weeks. Using the melanin quantitative index, obtained using a narrow-band reflectance spectrophotometer, that figure fell to 52% after 24 weeks. In this study, the MASI index average decreased from 7.6 (pre-treatment) to 6.2 (24 weeks after the 4th session), suggesting that the treatment can still be effective even 6 months after a series of 4 sessions.

CONCLUSION

Fractional photothermolysis, evaluated in this study as an isolated method of treating melasma, was shown to be a safe and effective option that significantly reduced melanic pigmentation. Therefore, it could become an alternative treatment method for this condition. ●

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