



The use of ablative lasers in the treatment of facial melasma*

O uso de lasers ablativos no tratamento do melasma facial

Orlando Oliveira de Morais¹
Márcia Carolline dos Santos Sousa²
Izelda Maria Carvalho Costa⁴

Érica Freitas Lima Lemos²
Ciro Martins Gomes³
Carmen Déa Ribeiro de Paula⁵

Abstract: Melasma represents a pigmentary disorder that is difficult to treat. This study aims to broadly review the use of ablative lasers (Er:YAG and CO₂) in the treatment of melasma, presenting the level of evidence of studies published to date. A total of 75 patients were enrolled in four case series studies (n=39), one controlled clinical trial (n=6) and one randomized controlled clinical trial (n=30). Studies on the Er:YAG laser showed better results with the use of short square-shaped pulses, which determined low rates of post-inflammatory hyperpigmentation and long-lasting maintenance of results. Likewise, studies on the CO₂ laser proved the benefits of short pulse duration along with low-density energy. Post-treatment maintenance with the use of antipigmenting creams was necessary and effective to sustain long-term results. Ablative lasers may represent another useful and effective tool against melasma. Postinflammatory hyperpigmentation and difficulty in sustaining long-term results still represent the main limitations to a broader use of ablative lasers. Based on actual evidence, the use of this technology should be restricted to patients with recalcitrant disease. Further studies will help establish optimal laser parameters and treatment regimens.

Keywords: Carbon dioxide; Erbium; Laser therapy; Lasers, gas; Melanosis

Resumo: O melasma representa desordem pigmentar de difícil tratamento. O presente estudo tem como propósito apresentar ampla revisão da literatura acerca do uso de laser ablativos (Er:YAG e CO₂) no tratamento do melasma, estabelecendo o nível de evidência dos estudos publicados até o instante. Um total de 75 pacientes foram envolvidos entre quatro séries de casos (n=39), um ensaio clínico controlado (n=6) e um ensaio clínico controlado e randomizado (n=30). Os estudos acerca do laser de Er:YAG demonstraram melhores resultados com o uso de pulsos de forma quadrada, os quais determinaram menores taxas de hiperpigmentação pós-inflamatória. Ademais, os estudos com laser de CO₂ também demonstraram benefício no uso de pulsos curtos com baixa densidade de energia. O uso de cremes despigmentantes no período pós-tratamento se mostrou necessária e efetiva na manutenção de resultados à longo prazo. Os lasers ablativos, por conseguinte, podem representar ferramenta efetiva e de grande utilidade no manejo do melasma. Entretanto, hiperpigmentação pós-inflamatória e dificuldade na manutenção de resultados à longo prazo parecem representar as principais limitações atuais ao seu amplo uso. Por conseguinte, com base nas atuais evidências, o uso de tais tecnologias ainda deve ser restrita à casos de doença recalcitrante. Novos estudos ainda são necessários para o estabelecimento de parâmetros e regimes ideais de tratamento.

Palavras-chave: Dióxido de carbono; Erbio; Lasers de gás; Melanose; Terapia a laser

Received on 15.05.2012.

Approved by the Advisory Board and accepted for publication on 25.06.2012.

* Work conducted at the Department of Dermatology, University Hospital of Brasília - University of Brasília (HUB-UnB) - Brasília (DF), Brazil.

Conflict of interest: None

Financial Support: None

¹ MD - MSc. Student - Postgraduate Program in Health Sciences - University of Brasília (UnB) - Brasília (DF), Brazil.

² MD Student - University of Brasília - Brasília (DF), Brazil.

³ MD - Residency Program preceptor in Dermatology - University of Brasília - Brasília (DF), Brazil.

⁴ PhD - Adjunct professor of Dermatology - University of Brasília - Brasília (DF), Brazil.

⁵ PhD - Residency Program preceptor in Dermatology - University of Brasília - Brasília (DF), Brazil.

INTRODUCTION

Melasma is a common acquired symmetric cutaneous hypermelanosis that represents a disruption of the skin pigmentary system. It affects mainly Asian and Latin women most frequently aged 30 to 55 years. Lesions are often light brown to blackish macules of irregular but sharp borders. They mainly affect areas chronically exposed to sun light like the cheeks, forehead, temples, upper lip and chin. Many factors have been linked to the appearance and worsening of melasma, although pregnancy, use of contraceptive pills and exposure to UV radiation are frequently reported.^{1,2}

Despite the fact that melasma is one of the most common reasons for women to seek dermatological care, only a small number of drugs and procedures to treat this disorder has been launched in the market in the last decade. Conventional treatments usually fail to induce long-term remission, as is commonly seen with the use of first-line therapies such as Kligman's formula.^{3,4} This fact has prompted the search for innovative treatments to manage the disease. It is the case of non-ablative fractioned lasers, which have been established to treat melasma after initial positive results by Rokhs & Fitzpatrick (2005). These results were later reproduced by others.⁵⁻⁸

Ablative lasers have also been sporadically used by many professionals to treat melasma, although there is a lack of scientific data supporting this indication. The exact mechanism of action of both ablative and non-ablative lasers is also unknown, although many have been hypothesized.⁹

Therefore, the objective of this study is to present a review of available data from the medical literature about the use of resurfacing ablative fractioned lasers (CO2 and Er:YAG) to treat melasma. We also attempt to define the actual level of evidence for their use.

METHODS

A broad search for original studies was made on Pubmed, Scielo, LILACS (Latin America and Caribbean) and DOAJ (Directory of Open Access Journals) databases. The search was done by crossing the primary key-words "melasma" and "chloasma" with the secondary terms "Carbon Dioxide Laser" and "Erbium Doped Yttrium Aluminum Garnet Laser", as specified by Medical Subject Headings (MeSH). Once retrieved, all the studies were evaluated by one of the authors for selection of only primary clinical studies (case report/series, case control studies and clinical trials) developed with human subjects about the treatment of melasma. Studies were then discussed and classified according to their level of evidence as proposed by the Oxford Centre for Evidence-Based Medicine.¹⁰

RESULTS

After an individual review of all the studies retrieved, only six studies met the selection criteria and were included for discussion. A total of 75 patients were enrolled in the studies and were distributed among four case/series studies (CS, $n=39$), one controlled clinical trial (CCT, $n=6$) and one randomized controlled clinical trial (RCCT, $n=30$).¹¹⁻¹⁶ Three studies analyzed the CO2 laser, two analyzed the Er:YAG laser, and the other investigated the Q-switched alexandrite (QSAL) laser, although one of them involved the use of CO2 laser.¹¹⁻¹⁶ The study by Nouri et al. (1999) was also compiled as a case series study given both its small sample and small area treated, which did not allow for statistical analysis or generalizability of results.¹¹

Nouri et al. (1999) first published a pilot study about the use of CO2 laser to treat melasma.¹¹ Eight patients with Fitzpatrick skin prototype (FSP) IV to VI with dermal melasma were pretreated with Kligman's formula from day 1 to 14. Subjects were then randomly assigned to receive treatment in a melasma spot area of 1cm². One group was treated with CO2 laser alone, whereas the other group received combination therapy (first pass CO2 laser, followed by a second pass with QSAL). The authors stated that the combination laser was highly effective since treatment determined complete resolution inside the area treated and maintenance of results at 24-week follow-up. Level of evidence: IV.

A split-face study designed by Angsuwangsang et al. (2000) evaluated the efficacy of QSAL laser isolated and in combination with CO2 laser to treat facial melasma.¹⁵ Six female Thai patients with FSP II to V and refractory melasma participated in the study. Only facial sides receiving combined therapy showed statistically-improved maintenance in both Melasma Area Severity Index (MASI) and Melanin Index (MI), measured by reflectance spectrometry, at 6 months follow-up ($p=0.02$ for both); however, statistical analysis failed to show significant differences between treatments at that time ($p=0.08$), formerly a reflection of the small sample studied. On the other hand, patients with FSP IV and V showed transient postinflammatory hyperpigmentation in both sides treated. Level of evidence: III.

Trelles et al. (2010) developed the most recent randomized controlled clinical trial available in the literature comparing CO2 laser with traditional Kligman's formula.¹⁶ Thirty female patients with melasma, mean age of 38 years, FSP II-IV, were randomly allocated to three groups. Group A received post-procedure treatment for 15 days with Kligman's formula followed by maintenance topical cream program (hydroquinone 2%, kojic acid, glycolic acid);

group B, only CO₂ laser fractional resurfacing using high power, fixed pulse width and low frequency; and group C, both laser and maintenance topical cream program. Subjects of all three groups received pre-intervention treatment with antipigmenting topical cream for a period of 16 days. The satisfaction index and overall efficacy in groups A, B and C were 100% at month one in all groups, but progressively decreased in further assessments, except for group C, in which better scores were maintained throughout. MASI score was assessed by blinded evaluators using standard photographs. It showed a statistically significant improvement in group C compared to A and B at six and 12 months follow-up ($p < .001$, for both). The study presented a suitable methodology regarding randomization, blinding and appropriate control group. Level of evidence: II.

A report of the case of a 59-year old woman with melasma treated with CO₂ laser was also recently published by Neeley et al. (2010).¹² The patient had FSP V and a refractory malar dermal melasma. She had been irresponsive to previous 17 sessions of non-ablative fractional lasers (1320, 1440 and 1550nm) as well as to topical treatment. The patient underwent seven sessions of CO₂ laser over a period of 10 months, with a reasonable improvement in skin pigmentation and texture. No follow-up comments were presented by the authors. Level of evidence: IV.

No controlled clinical trial about the treatment of melasma with Er:YAG laser has been found in the literature. However, a well-conducted case series study was developed by Wanitphakdeedecha et al. (2009) in Thailand. The study involved 20 female patients with epidermal melasma.¹³ All the patients were treated monthly for a total of two treatments with an Er:YAG laser set at square pulse parameters. This measure aimed to minimize nonspecific heating of the surrounding tissues by avoiding the slow rise and the longer fall of laser pulse power commonly observed in conventional laser technology platforms. The patients were evaluated by MI measurement and were also clinically evaluated using a visual analog scale and MASI scoring system at baseline and 1, 2, and 4 months postoperative. Both MI and MASI score showed significant improvement at 2-month, but not at 1- and 4-month follow-up visits ($p > 0.05$). Furthermore, clinical improvement assessed by blinded dermatologists showed that only 15% of patients sustained improvement greater than 50% after 4 months of follow-up. Level of evidence: III.

Another recent case series study using Er:YAG laser was developed by Manaloto et al. (2009).¹⁴ Ten female patients with FPS II to V presenting with facial melasma unresponsive to previous therapy of bleaching creams and chemical peels were selected to receive

full-face skin resurfacing with Er:YAG laser. No pre-intervention treatment was offered to the patients. There was marked improvement of melasma immediately after the laser procedure; however, between 3 and 6 weeks postoperative, all patients exhibited post-inflammatory hyperpigmentation demanding intervention with daily use of 20% azelaic acid and glycolic acid peels biweekly. At six months postoperative, universal clinical improvement of pigmentation was observed as well as reduction in MASI and melanin reflectance spectrometry measurements ($p = .027$). Level of evidence: III.

A summary of laser parameters and side effects reported in the studies is presented in table 1.¹¹⁻¹⁶

DISCUSSION

It is known that skin affected by melasma contains more active epidermal melanocytes. These cells produce a higher number of mature dendritic melanosomes transferring them to keratinocytes, which ultimately leads to skin hyperpigmentation.^{2,3} The distribution of melanin pigments in the skin layers is an important factor related to the success or failure of melasma treatment. This is particularly important in cases of mixed melasma, in which removal of dermal pigment has been found to be strongly difficult with standard therapies.^{2,3}

Ablative lasers, by targeting water, can indirectly reduce melanin deposits from both the epidermis and dermis. Due to tissue vaporization, the number of abnormal epidermal melanocytes and melanin content are reduced, as probably occurs with the amount of melanin deposited into dermal melanophages occasionally reached by laser beams. Also, during the healing process, the epidermis is regenerated from the appendiceal units; therefore, it is believed that the inward migration of new melanocytes to the epidermis is unable to produce localized areas of hyperpigmentation.^{11,15} Nevertheless, a challenge still remains. Reducing residual thermal damage, which represents the mainstay for the development of postinflammatory hyperpigmentation commonly observed after ablative laser treatments, is difficult.^{11,15} Pulses shorter than thermal relaxing time of the epidermis are important to minimize this risk.¹⁶

Initial studies on the use of CO₂ laser to treat melasma were developed using non-fractional technology and showed a high rate (50%) of postinflammatory hyperpigmentation.^{11,15} In the same studies, combined treatment with QSAL targeting dermal melanin was found to increase treatment efficacy,^{11,15} but controversially failed to prevent postinflammatory hyperpigmentation.¹⁵ These poor results were quite discouraging as many years passed until the development of new studies addressing the issue.

TABLE 1: Summary of studies about the treatment of facial melasma with ablative lasers showing laser features applied and side effects reported

Study	Study Type and Groups	Laser features	Side effects
Nouri et al., 1999 ¹¹	RCCT* ^a CO2 laser (<i>n</i> =4) ^b CO2 laser plus QSAL (<i>n</i> =4)	^{a,b} CO2 laser (Coherent, Palo Alto, CA) – 0.3J/cm ² ; 950ms pulse duration ^b QSAL (manufacturer not reported) – 6J/cm ²	^a Postinflammatory hyperpigmentation peripheral to the treated area (<i>n</i> =2)
Angsuwarangsee et al., 2003 ¹⁵	CCT ^a QSAL (<i>n</i> =6 facial sides) ^b QSAL plus CO2 (<i>n</i> =6 facial sides)	^{a,b} QSAL (Accolade, Cynosure, Chemsford, UK) – 5-7J/cm ² , 60ns pulse duration, 3mm spot size, 5Hz ^b CO2 laser (Ultrapulse 5000C, Coherent, Palo Alto, CA) – 60W, 0.3-0.35J/cm ² , 950ms pulse duration, density: 5-6; 8mm spot size or 5W, 0.3J/cm ² , 950ms pulse duration, 3mm spot size, collimated handpiece	^b Contact dermatitis (<i>n</i> =1) – resolution with topical steroid use but determined hyperpigmentation ^b Transient hypopigmentation (<i>n</i> =1) – spontaneous gradual recovery within 6 months ^{a,b} Postinflammatory hyperpigmentation (<i>n</i> =3) – started 2-4 weeks post-treatment and began to fade away at 3-month follow-up
Neely et al., 2010 ¹²	CS ^a CO2 laser (<i>n</i> =1)	^a CO2 laser (Affirm, Cynosure, Westford, MA, USA) – 15-20W, 250-600µm spot pitch, 400-600ms pulse duration	Not known
Trelles et al., 2010 ¹⁶	RCCT ^a Kligman's formula plus TT2 cream (<i>n</i> =10) ^b CO2 laser (<i>n</i> =10) ^c CO2 laser plus TT2 cream (<i>n</i> =10)	^{b,c} CO2 laser (Ultrapulse Active FX, Lumenis, Yokneam, Israel) – 7.5W, 150mJ (11.3J/cm ²), 350ms pulse duration, 50Hz	^{a,b,c} Absence of complications either after CO2 laser procedure or after long-term use of antipigmenting ingredients
Manaloto et al., 2009 ¹⁴	CS ^a Er:YAG (<i>n</i> =10)	^a Er:YAG (Continuum Biomedical, Dublin, CA) – 1-1.5J (5.1-7.6J/cm ²), 5mm collimated spot, 8Hz	^a Postinflammatory hyperpigmentation three to six weeks after procedure (<i>n</i> =10) – resolved spontaneously
Wanitphakdeedecha et al., 2009 ¹³	CS ^a VSP Er:YAG (<i>n</i> =20)	^a VSP Er:YAG (Fidelis M320A, Fotona, Ljubljana, Slovenia) – 160mJ (0.4J/cm ²), 300µs pulse duration, 7mm spot size, 10Hz	^a Postinflammatory hyperpigmentation (<i>n</i> =3) – cleared spontaneously within 2 weeks; ^a Acneiform eruption (<i>n</i> =2) – treated satisfactorily with clindamycin and adapalene

CCT – controlled clinical trial

RCCT – randomized controlled clinical trial.

CS – case report/series

a, b, c – study groups and respective laser features and side effects* – both small sample and area of treatment (1cm²) limited strength of study

Ultimately, a new study was developed in 2010 using fractional CO₂ laser, a technology that is already well established for skin resurfacing treatments. Trelles et al. opted to use high power energy (150mJ/pulse) combined with short pulse duration (350ms) and low-density energy (11.3J/cm²) in order to minimize residual thermal damage which could trigger pigmentation rebound.¹⁶ This approach promoted deep but narrow non-selective ablation zones also capable of reaching dermal melanophages. The results of the combination therapy group (laser and antipigmenting cream) were quite impressive, with maintenance of improvement after a 12-month follow-up. These data, along with the poor results obtained by the laser-only group, reinforce the major role of antipigmenting cream in preventing recurrence of melasma. In fact, its use was considered mandatory by the authors.¹⁶

The same principle of minimizing residual thermal damage was used by Wanitphakdeedecha et al. when studying the use of Er:YAG laser to treat melasma. The short square-shaped pulse (300µs) produced more controlled heating and minimized post-inflammatory hyperpigmentation when compared to conventional short-pulsed Er:YAG.^{13,14} The mechanism

of action proposed by the authors involved ablation depth limited to the epidermis, probably eliminating excess epidermal melanin as well as stimulating epidermal turnover.¹³ However, even such superficial ablation wasn't enough to reduce post-inflammatory hyperpigmentation.

CONCLUSION

Both Er:YAG and CO₂ lasers have already been studied in the treatment of facial melasma, although only a small number of patients were enrolled in clinical trials. To date, studies have shown that short pulses along with low-density energy seem to be rational parameters to target melasma because they limit residual thermal damage and the risk of post-inflammatory hyperpigmentation. Both Er:YAG and CO₂ laser were safe to treat patients even with high skin phototypes. High rates of post-inflammatory hyperpigmentation were adequately targeted with the use of antipigmenting agents, which makes them mandatory. No final conclusions can be made about the advantages between Er:YAG and CO₂ laser, since no study has directly compared them. Further studies are necessary to better establish optimal laser parameters and treatment regimens. □

REFERENCES

1. Tamega AD, Miot LD, Bonfietti C, Gige TC, Marques ME, Miot HA. Clinical patterns and epidemiological characteristics of facial melasma in Brazilian women. *J Eur Acad Dermatol Venereol*. 2012. [Epub ahead of print]
2. Miot LDB, Miot HA, Silva MG, Marques MEA. Fisiopatologia do melasma. *An Bras Dermatol*. 2009;84:623-35.
3. Gupta AK, Gover MD, Nouri K, Taylor S. The treatment of melasma: a review of clinical trials. *J Am Acad Dermatol*. 2006; 55:1048-65.
4. Cestari T, Arellano I, Hessel D, Ortonne JP; Latin American Pigmentary Disorders Academy. Melasma in Latin America: options for therapy and treatment algorithm. *J Eur Acad Dermatol Venereol*. 2009;23:760-72.
5. Goel A, Krupashankar DS, Aurangabadkar S, Nischal KC, Omprakash HM, Mysore V. Fractional lasers in dermatology- current status and recommendations. *Indian J Dermatol Venereol Leprol*. 2011;77:369-79.
6. Tannous SZ, Astner S. Utilizing fractional resurfacing in the treatment of therapy resistant melasma. *J Cosmet Laser Ther*. 2005;7:39-43.
7. Rokhsar CK, Fitzpatrick RE. The treatment of melasma with fractional photothermolysis: A Pilot study. *Dermatol Surg*. 2005;31:1645-50.
8. Goldberg DJ, Berlin AL, Phelps R. Histologic and ultrastructural analysis of melasma after fractional resurfacing. *Lasers Surg Med*. 2008;40:134-8.
9. Manstein D, Herron GS, Sink RK, Tanner H, Anderson RR. Fractional photothermolysis: A new concept for cutaneous remodeling using microscopic patterns of thermal injury. *Lasers Surg Med*. 2004;34:426-38.
10. Cebm.net [Internet]. OCEBM Levels of Evidence Working Group. The Oxford 2011 Levels of Evidence. Oxford Centre for Evidence-Based Medicine. [cited 2012 May 28]. Available from: <http://www.cebm.net/index.aspx?o=5653>.
11. Trelles MA, Velez M, Gold MH. The treatment of melasma with topical creams alone, CO₂ fractional ablative resurfacing alone, or a combination of the two: a comparative study. *J Drugs Dermatol*. 2010; 9:315-22.
12. Manaloto RM, Alster T. Erbium:YAG laser resurfacing for refractory melasma. *Dermatol Surg*. 1999; 25:121-3.
13. Nouri K, Bowes L, Chartier T, Romagosa R, Spencer J. Combination treatment of melasma with pulsed CO₂ laser followed by Q-switched alexandrite laser: a pilot study. *Dermatol Surg*. 1999;25:494-7.
14. Neeley MR, Pearce FB, Collawn SS. Successful treatment of malar dermal melasma with a fractional ablative CO₂ laser in a patient with type V skin. *J Cosmet Laser Ther*. 2010;12:258-60.
15. Wanitphakdeedecha R, Manuskiatti W, Siriphukpong S, Chen TM. Treatment of melasma using variable square pulse Er:YAG laser resurfacing. *Dermatol Surg*. 2009;35:475-81.
16. Angsuwarangsee S, Polnikorn N. Combined ultrapulse CO₂ laser and Q-switched alexandrite laser compared with Q-switched alexandrite laser alone for refractory melasma: split-face design. *Dermatol Surg*. 2003;29:59-64.

MAILING ADDRESS:

Orlando Morais
Hospital Universitário de Brasília (HUB - UnB) -
Serviço de Dermatologia - SGAN 604/605.
Avenida L2 Norte - Brasília
70910-900 - Distrito Federal - DF
Brazil
Phone/Fax: +55(61)99162339; 3448-5415.
E-mail: orlando.unb@gmail.com

How to cite this article: Morais OO, Lemos EFL, Sousa MCS, Gomes CM, Costa IMC, Paula CDR. The use of ablative lasers in the treatment of facial melasma. *An Bras Dermatol*. 2013;88(2):238-42.