Use of laser technologies and intense pulsed light in the treatment of exogenous ochronosis: a literature review

Uso de tecnologias a laser e luz intensa pulsada no tratamento da ochronose exógena: uma revisão da literatura

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ABSTRACT
Exogenous ochronosis is a cutaneous hyperpigmentation condition caused by the accumulation of substances derived from phenol on the skin or mucous membranes without affecting other tissues. It occurs mainly due to the use of bleaching agents, most frequently hydroquinone. The lesions are difficult to treat, being resistant to several approaches. Sometimes it’s necessary to use laser technologies or intense pulsed light to achieve some degree of improvement. The present work consists of a literature review of publications on these technologies in exogenous ochronosis from January 1990 to July 2020.

Keywords: Hyperpigmentation; Intense pulsed light therapy; Lasers; Ochronosis

RESUMO
A ochronose exógena é um quadro de hiperpigmentação cutânea por acúmulo de substâncias derivadas de fenol em pele ou mucosas, sem acometimento de outros tecidos. Ocorre, principalmente, por uso de clareadores, sendo mais frequente na hidroquinona como despigmentante. As lesões apresentam difícil tratamento, sendo resistentes a diversas abordagens. Por vezes, é necessário utilizar tecnologias com laser ou luz intensa pulsada para atingir algum grau de melhora. O presente trabalho realizou pesquisa bibliográfica na forma de revisão de literatura entre janeiro de 1990 e julho de 2020, organizando publicações acerca do uso destas tecnologias na ochronose exógena.

Palavras-chave: Hiperpigmentação; Lasers; Ochronose; Terapia de luz pulsada intensa
INTRODUCTION

Exogenous ochronosis (EO) is described as skin and mucous membranes hyperpigmentation caused by phenol-derived substances deposits, most commonly after the use of whitening creams containing hydroquinone, topical resorcinol, or intramuscular or oral antimalarials.1,2,5,6 Contrary to endogenous ochronosis, which arises from homogentisic acid deposition in soft areas and internal tissues, exogenous ochronosis does not affect these sites. EO is considered uncommon:7 it presents a moderate incidence in South Africa,8 with isolated reports in Asia, Africa, and Latin America in patients with Hispanic ancestry and high skin phototypes.7,8,9

Rudolph Virchow named EO in 1865.10,11 Findlay6 related the disease to the use of bleaching cream with hydroquinone in 1975, and Beddard and Plumtre12 associated it to with use of phenol to treat leg ulcers in 1912.12

A recent review of cases in the American literature showed a total of 39 reports of EO in the United States, from January 1983 to June 2020. Of these cases, 18 described the disease onset from the use of whitening creams, and, among these, 14 had hydroquinone in the composition. The concentrations ranged from 2% to 7.5%, with application time from two months to 30 years until the onset of the lesions.2,3,8

Clinically, EO presents as asymptomatic bluish-black or yellow-brown macules, or areas of hyperpigmentation in sun-exposed regions, such as the face, neck, back, extensor zones of the upper limbs, distal portions of the forearms, legs, and dorsum of hands or feet.13 At the histological level, the clinical picture is similar to that of endogenous ochronosis, but with no pigment accumulation in joints, bones, urine, other secretions, or tissues.14,15

For some authors, the condition occurs due to resistance of melanocytes to the effect of whitening agents, with consequent pigment leakage in the papillary dermis and accumulation of this pigment in fibroblasts, resulting in phenols presence in elastic fibers and their hyperchromia.4 Other authors argue that hydroquinone is oxidized to quinone forming hydroxylated indoles similar to melanin precursors.16 A third group believes that high hydroquinone concentrations stimulate melanocytes to produce more melanin.17 However, the most widely accepted theory is that hyperpigmentation results from homogentisic acid oxidase enzyme inhibition by hydroquinone, causing local homogentisic acid accumulation. The homogentisic acid then polymerizes, forming an ocher pigment in the papillary dermis, as occurs in other tissues in cases of endogenous ochronosis due to a primary structural defect of this enzyme.18

Exogenous ochronosis lesions observed in dermoscopy were initially described in 200819,20 as sites of blue-gray or brown to black, amorphous globules, with follicular obliteration areas. It contrasts with melanoma cases where dermoscopy demonstrates a pattern of reticular pigmentation, pseudonanet accentuation, and brownish granules and globules, sparing the follicles.21

At the histological level, the lesions show collagen fibers with a yellow-brownish color in a “banana shape”, degradation of these fibers, and formation of colloid milium amid an inflammatory infiltrate with plasma cells, histiocytes, and multinucleated giant cells in the development of the lesions.16,22

In 1979, Dogliotti and Leibowitz classified the clinical stages of exogenous ochronosis into stage I (lesions with erythema and some pigmentation); stage II (injuries presenting hyperpigmentation, hyperpigmented colloid milium, atrophy); and stage III (presence of papulonodular eruptive elements in a lesion with stage II features plus inflammatory characteristics in more recent wounds that are less pronounced in older injuries).23 In 1986, Phillips et al. classified ochronosis as mild, moderate, and severe in a series of 395 cases in patients assessed by the Dermatology Service of a hospital in Johannesburg, South Africa, during one year. Only lesions with altered skin hyperpigmentation and hypertrophy were considered as mild; presence of hyperchromic papules was the standard for moderate degree; and lesions with hyperchromic caviar-like papules, coalescent in plaques, were deemed as severe.8 In a third classification, in 1989, Hardwick et al. considered five grades of presentation: grade 1 comprised lesions with hyperchromic macules; grade 2, with macules and micropapules; grade 3 included injuries with darkened deposits and larger papules; grade 4, with colloid milium of 1 mm or more; and grade 5 encompassed lesions with keloid nodules and hyperchromic cysts.24

According to the European Society of Laser Dermatology (ESLD), the exogenous ochronosis treatment is challenging, with unpredictable results, often below expectations. The use of photoprotection becomes a relevant element in the initial approach by slowing the progression of the lesions and preventing the emergence of new hyperpigmented areas.15 Some cases achieved a partial response with topical retinoic and glycolic acid in low concentrations and oral use of tetracycline in papular presentations or with sarcoidosis-like lesions.25 In a recent review on the use of these technologies, the ESLD recommends such therapies associated with multiple laser technologies sessions, combining fractional ablative modalities such as CO2 or Erbium 2940nm with Q-Switched 1064nm for better and faster results.26,27

The present study reviews publications containing a therapeutic approach to exogenous ochronosis conditions using laser technologies or intense pulsed light, demonstrating the described protocols and results obtained from 1990 to July 2020.

METHODS

Four databases were searched from June 15 to August 5, 2020: Embase, MEDLINE/Pubmed, LILACS, and Cochrane Library. The selected languages were English, Spanish, and Portuguese. In the first stage, the keywords used were chronicus, exogenous ochronosis, ocronose, and ocronosis. They generated a total of 1,377 results in the Embase platform, 978 in the MEDLINE/Pubmed, 32 in the LILACS, and 16 results in the Cochrane Library platform.
After this stage, the terms treatment, therapy, tratamiento, tratamiento, efficacy, upade laser and intense pulsed light were included in the search. The results with crossings between these keywords obtained 79 results in the Embase platform, 19 in the MEDLINE/Pubmed, two in the LILACS, and one result in the Cochrane Library platform. Considering the objectives of the review, we selected studies that cited the use of laser technologies and intense pulsed light to treat exogenous ochronosis conditions published from January 1990 to July 2020.

Thus, the selection criteria were scientific articles on exogenous ochronosis regardless of its cause, approached with the use of laser or intense pulsed light at some point in the therapy. Studies on other pathologies, other ochronosis forms, or other therapies that did not address the use of lasers or intense pulsed light were excluded. The entire method of research and selection of articles containing the terms described was repeated by a secondary researcher, following the same methodology, generating the same data and articles.

RESULTS

Among several therapeutic modalities, lasers are considered excellent options to treat hyperpigmented lesions, promoting selective photothermolysis of pigments. The most used lasers for this purpose are Q-Switched Ruby (QSRL), Q-Switched Alexandrite 755nm, Q-Switched Nd:YAG 1064nm, Q-Switched Nd:YAG 532nm, picosecond lasers, and intense pulsed light with specific filters. Technologies such as non-ablative Erbium–Glass 1550nm laser, ablative Erbium:YAG 2940nm, CO₂ laser 10600nm, and Thulium laser 1927nm use water as a chromophore and can be alternatives both in pigments vaporization and in facilitating depigmenting agents penetration. In 2015, a review on therapeutic modalities in exogenous ochronosis cases was published. The main technologies used for this purpose were Q-Switched Ruby (694nm), Q-Switched Alexandrite (755nm), Q-Switched Nd:YAG (1064nm), CO₂ lasers, and intense pulsed light. Only recently the picosecond laser was also reported as an option for treating hyperpigmented lesions (Table 1).

In 1990, Diven et al. reported a case of exogenous ochronosis in the face of a 53-year-old African-American woman treated with dermabrasion and CO₂ laser. It resulted in the first description of the use of laser technologies to approach ochronosis. After using 2% hydroquinone cream for two to three months, the patient had progressive darkening of the area. Approach attempts with tretinoin 0.025% topical gel, cryotherapy, and peeling with TCA 50% did not achieve improvement. Therefore, we opted for dermabrasion of the whole face, followed by CO₂ 3-6W application in defocused irradiation mode in the periorcular regions, nose, and forehead, obtaining satisfactory results.

Ten years later, Kramer et al. reported an exogenous ochronosis case treated with laser technology in bilateral zygo-
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Case</th>
<th>Causal factors</th>
<th>Treatment</th>
<th>Protocol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Diven et al.</td>
<td>Woman, 53 years old, African American</td>
<td>Topical hydroquinone 2% during 2-3 months</td>
<td>Dermabrasion across the face and CO2 laser (3-6W) in periocular, nasal, and forehead regions</td>
<td>One session each</td>
<td>Satisfactory whitening of areas</td>
</tr>
<tr>
<td>2000</td>
<td>Kramer et al.</td>
<td>Woman, 50 years old, Hispanic origin</td>
<td>Topical hydroquinone 2% during 30 years</td>
<td>Q-Switched Ruby Laser 694 nm (7 J/cm²) 5mm spot-size</td>
<td>One application</td>
<td>Whitening of the hyperpigmented area</td>
</tr>
<tr>
<td>2004</td>
<td>Bellew and Alster</td>
<td>Woman, 47 years old, African American</td>
<td>Face whitening creams during several months (unspecified usage time)</td>
<td>Q-Switched Alexandrite laser 755nm initial fluency 7.0 J/cm² and final fluency 8.0 J/cm² (mean of 7.8 J/cm²)</td>
<td>6 sessions</td>
<td>Significant lightening of hyperchromias</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Man, 46 years old, Indigenous origin</td>
<td>One year using whitening cream containing hydroquinone</td>
<td>Q-Switched Alexandrite laser 755nm initial fluency 6.0 J/cm² and final fluency 7.0 J/cm² (mean of 6.9 J/cm²)</td>
<td>4 sessions</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>Huerta Brogeras and Sánchez Vieira</td>
<td>Woman, 70 years old</td>
<td>Topical hydroquinone 2% during 6 months</td>
<td>Q-Switched Nd-YAG laser 1064 nm</td>
<td>Still in progress until the date of publication</td>
<td>Treatment not completed until the publication date</td>
</tr>
<tr>
<td>2008</td>
<td>Charlin et al.</td>
<td>Woman, 56 years old, skin phototype V</td>
<td>Topical hydroquinone 6% (unspecified usage time)</td>
<td>Q-Switched Nd-YAG laser 1046 nm (parameters used not described)</td>
<td>Not reported</td>
<td>No improvement in condition</td>
</tr>
<tr>
<td>2010</td>
<td>Gil et al.</td>
<td>Woman, 56 years old, skin phototype V</td>
<td>Whitening cream with 2% to 3% hydroquinone and 2% oxybenzone for several (unspecified usage time)</td>
<td>Intense Pulsed Light 645 nm, 6 milliseconds, 20-22 J/cm²</td>
<td>6 sessions</td>
<td>Moderate whitening of lesions</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Depigmenting cream with 4% kojic acid and 0.2% salicylic acid</td>
<td>2 months of use</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>França et al.</td>
<td>Woman, 40 years old</td>
<td>Topical hydroquinone for 8 years (non-detailed concentration)</td>
<td>Q-Switched Nd:YAG Laser 1064mm 4mm spot at 2.9-3.05 J/cm² fluency</td>
<td>4 sessions</td>
<td>No satisfactory response with Q-Switched</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ultrapulsed CO₂ laser 5W</td>
<td>6 sessions</td>
<td>Nd:YAG laser 1064mm, partial response with ultrapulsed CO₂ laser, and resolution of lesions with IPL, microdermabrasion and peelings</td>
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<tr>
<td></td>
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<td>Intense Pulsed Light (IPL) 36J - 10 ms with microdermabrasion and peeling with 5% hydroquinone, 5% retinoic acid, and 14% salicylic acid</td>
<td>1 session</td>
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<td></td>
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<td></td>
<td>Intense Pulsed Light (IPL) 36J - 10 ms and peeling with 20% trichloroacetic acid (TCA)</td>
<td>3 sessions</td>
<td></td>
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<tr>
<td>2013</td>
<td>Kanechorn-Na-Ayuthaya et al.</td>
<td>Woman, 67 years old, skin phototype V</td>
<td>Whitening creams during long periods without to specify (unspecified usage time)</td>
<td>Q-Switched Nd:YAG laser 1064nm at 1.9-2.2 J/cm² fluency and fractional CO₂ laser</td>
<td>3 sessions + 1 session</td>
<td>Significant improvement with important whitening</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Woman, 58 years old, skin phototype III</td>
<td></td>
<td>Q-Switched Nd:YAG laser 1064nm at initial 1.9 J/cm² fluency and fractional CO₂ laser</td>
<td>3 sessions + 1 session</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Woman, 66 years old, skin phototype IV</td>
<td></td>
<td>Pulse-Dye Laser, Q-switched Nd:YAG laser 1064 nm, and fractional CO₂ laser</td>
<td>2 sessions + 1 session</td>
<td></td>
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<tr>
<td>Year</td>
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<td>2013</td>
<td>Tan</td>
<td>Six women, from 37 to 69 years old</td>
<td>Whitening creams</td>
<td>Q-Switched Nd:YAG laser 1064nm at 1.2 J/cm² fluency in hyperpigmented areas of exogenous ochronosis and melasma</td>
<td>8 sessions + 16 sessions</td>
<td>Two showed relevant improvement, four showed mild improvement.</td>
</tr>
<tr>
<td>2014</td>
<td>Liu et al.</td>
<td>Woman, 50 years old, skin phototype IV</td>
<td>Whitening creams for long periods often with hydroquinone (unspecified usage time)</td>
<td>Q-Switched Nd:YAG laser 1064nm at 6-9 J/cm² fluency</td>
<td>6 sessions</td>
<td>No improvement</td>
</tr>
<tr>
<td>2014</td>
<td>Lee and Weiss</td>
<td>Woman, 48 years old</td>
<td>Whitening cream (unspecified usage time)</td>
<td>Intense Pulsed Light in 570 nm waves at 12 J/cm² fluency and 15 milliseconds pulse</td>
<td>Total of sessions not reported</td>
<td>Whitening of the hyperpigmented area</td>
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<tr>
<td>2015</td>
<td>Ko et al.</td>
<td>Woman, 50 years old</td>
<td>Whitening cream with 4% hydroquinone</td>
<td>Q-Switched Nd:YAG laser 1064nm at 5.3 J/cm² fluency in left zygomatic region</td>
<td>2 sessions</td>
<td>Therapeutic failure with worsening of the hyperchromic areas</td>
</tr>
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<td>2016</td>
<td>Carvalho et al.</td>
<td>Woman, 46 years old, skin phototype V</td>
<td>Topical hydroquinone 4% during 5 years</td>
<td>Fractional CO₂ laser with 120μm tip, 120μJ, and 150 points stitches per cm²</td>
<td>12 sessions</td>
<td>Significant improvement</td>
</tr>
<tr>
<td>2018</td>
<td>Méndez Baca et al.</td>
<td>Woman, 55 years old, skin phototype IV</td>
<td>Whitening cream containing hydroquinone for 5 years (the concentration was not specified)</td>
<td>Non-Ablative Fractional picosecond laser 1064nm and 532nm at initial fluency of 1.30 and 0.18 J/cm² with an increase of 0.20/0.02 J/cm² at each application up to a maximum fluency of 2.9/0.30 J/cm²</td>
<td>9 sessions</td>
<td>Improvement in skin color and appearance</td>
</tr>
<tr>
<td>2019</td>
<td>Lee et al.</td>
<td>Woman, 66 years old</td>
<td>Not described</td>
<td>CO₂ and Q-Switched Nd:YAG Lasers in the same session with no description of the parameters used</td>
<td>3 sessions</td>
<td>Lost to follow-up due to no response to therapy</td>
</tr>
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</table>

Gil et al., in 2010, reported a case of exogenous ochronosis in a 63-year-old woman, with skin phototype V, developed after using a whitening cream with 2% to 3% hydroquinone and 2% oxybenzone for several years, without specifying the duration of use. The diagnosis was confirmed histologically by the presence of yellow-brown material deposits in the papillary and medial dermis. She was treated with intense pulsed light 645nm, six milliseconds, 20-22J/cm², associated with depigmenting cream with 4% kojic acid and 0.2% salicylic acid. Moderate lightening of the lesions was achieved after two months of topical use and six sessions of intense pulsed light.41

Also in 2010, França et al. described an exogenous ochronosis case in a 40-year-old woman with hyperchromic macules and papules in the malar region and a history of topical hydroquinone use for eight years (the study did not describe the concentration). A histopathological examination revealed yellow-brown filaments in the papillary dermis, and investigation of deposits in other tissues was negative, ruling out an endogenous picture. In this report, the approach started with four sessions of Q-Switched Nd:YAG 1064nm laser, 4 mm spot, and 2.9-3.05 J/cm² fluency, without satisfactory response. Then, the authors opted for six sessions of ultrapulsed CO₂ laser, with one-month interval between each session, at 5W fluency, reaching some response. Finally, intense pulsed light (IPL) 36 J-10 ms was associated with the therapy, applied to the malar area, followed by microdermabrasion and chemical peeling with 5% hydroquinone, 5% retinoic acid, and 14% salicylic acid. The lesions resolved only after three more sessions, with intervals of 30 days of intense pulsed light (IPL) 36 J-10 ms and trichloroacetic acid (ATA) 20% peeling.13
Kanechorn-Na-Ayuthaya et al., in 2013, assessed the use of the combination of Q-Switched Nd:YAG and fractional CO2 laser to treat exogenous ochronosis. They applied these modalities in three cases. The first was a 67-year-old woman, skin phototype V, with a history of face melasma for 28 years and use of whitening cream for long periods (the time has not been determined), presenting darkening of the malar and zygomatic areas.

She received three sessions of Q-Switched Nd:YAG 1064nm at 1.9-2.2 J/cm² fluency and one session of fractional CO2 laser, totaling four months of applications. The second patient was a 58-year-old woman, skin phototype III, with a history of recalcitrant melasma for 28 years and long-term use of hydroquinone bleaching cream, presenting hyperchromia in the temporal, malar, eyelid, and peribulbar regions. For the treatment, she also received three applications of Q-Switched Nd:YAG 1064nm laser every 30 days, with an initial fluency of 1.9 J/cm² progressively increasing in multiple passes until the appearance of petechiae or purpura. After the third application, a CO2 laser was performed only once at the end of four months of treatment. Three months later, pulse-dye laser was applied for telangiectasias in the areas. The third case described was a 66-year-old woman, skin phototype IV, with a history of melasma for 20 years. She used whitening creams and complaint of bilateral darkening of the malar region. In this case, a Q-Switched Nd:YAG laser 1064nm was used in two sessions with a 30-day interval, resulting in purpura after each application. Fractioned CO2 laser was performed after the second Q-Switched session. All the cases showed significant skin improvement, with lightening of hyperchromic lesions and skin rejuvenation with enhancement of telangiectasias.

In the same year, Tan described six cases of exogenous ochronosis successfully treated after sessions of Q-Switched Nd:YAG 1064nm. Six women aged between 37 and 69 years, with a history of melasma and the use of whitening creams, two of them containing hydroquinone, presented hyperchromia in the application areas. The diagnosis was confirmed with histopathological examination, and the conditions were classified according to the ochronosis staging method described by Dogliotti and Leibowitz: stage I, lesions with erythema and some pigmentation; stage II, lesions with hyperpigmentation, hyperpigmented colloid milium, and atrophy; and stage III, papulonodular eruptive elements in a lesion with stage II characteristics. Four of the patients had stage I EO; one, stage II; and one, stage III. The cases were treated with a Q-Switched Nd:YAG 1064nm laser at 1.2 J/cm² fluency, 8 mm spot size, in four passes in the hyperpigmented areas, which included lesions of exogenous ochronosis and melasma. Subsequently, only areas considered as having exogenous ochronosis received new applications at 4-6 J/cm² fluency, 4 mm spot size, with two or three applications in stacks in each macula until the appearance of erythema or petechiae. Stage II and III patients showed significant improvement in areas of exogenous ochronosis after eight and 16 sessions, respectively. Nevertheless, stage I patients had no resolution of the lesions, but slight improvement in color after treatment.

In 2014, Liu et al. reported an exogenous ochronosis case in a 50-year-old woman, skin phototype IV, with a history of hyperchromic macules in malar areas. She was treated with whitening creams for long periods, often with hydroquinone, in different concentrations, which had been darkening for one year of the description, even with adequate photoprotection. The dermoscopy showed areas with sparse blue-gray dots and globules, and homogeneous follicular ostia obliteration. Histological examination revealed dilated and basophilic collagen fibers, fragmented and with ocher pigmentation. Exogenous ochronosis was classified as Dogliotti stage II, and the patient received six sessions of Q-Switched Nd:YAG 1064nm laser with 6-9 J/cm² fluency, with no improvement.

Also in 2014, Lee and Weiss presented an exogenous ochronosis case in a 48-year-old woman, after years of using a bleaching cream for facial dyschromia. Intense pulsed light in waves of 570nm was used for the treatment, at 12 J/cm² fluency, 15 milliseconds pulse, with sessions every six weeks, without description of the total number of sessions. The authors observed whitening of the maculae since the first application. The following year, Ko and Wang reported exogenous ochronosis in a 50-year-old woman after using a whitening cream containing 4% hydroquinone. Therapeutic response test was performed using Q-Switched Nd:YAG laser 1064nm at 5.3 J/cm² fluency, 3 mm spot size, in the left zygomatic region, and Q-Switched Alexandrite laser 755nm at 8.5 J/cm² fluency, 3 mm spot size, in the right zygomatic region. After two applications with a 5-week interval, both areas showed darkening, indicating therapeutic failure.

In 2016, Carvalho et al. described ochronosis lesions like hyperchromic papules and macules on the forehead, nasal dorsum, and malar regions of a 46-year-old woman, skin phototype V, using topical 4% hydroquinone for five years to treat melasma on the face. After ruling out endogenous ochronosis due to the absence of pigmentary deposits in other tissues, joint pain, and urinalysis alterations, the application of fractional CO2 laser was started on the entire face, using a 120 mm tip, 120 mJ energy, and 150 points per cm² density, in monthly sessions for one year, totaling 12 applications and reaching significant improvement of the condition.

Méndez Baca et al., in 2018, depicted the case of a 55-year-old woman, skin phototype IV, with exogenous ochronosis lesions in the bilateral malar region, reporting the appearance of blue-gray macules in the area after applying bleaching cream containing hydroquinone for five years to treat hyperpigmented lesions. The condition had been previously approached with intense pulsed light associated with depigmenting agents with 4% hydroquinone, kojic acid, phytic acid, ferulic acid, citric acid, as well as topical pimecrolimus and sunscreens, without improvement. It was then decided to use a fractionated non-ablative picosecond laser 1064nm and 532nm, at an initial 1.30-0.18 J/cm² fluency, with an increase of 0.20/0.02 J/cm² each session, up to a maximum 2.9/0.30 J/cm² fluency. The sessions...
occurred every two months, with applications until obtaining uniform facial erythema. After nine sessions, there was an improvement in skin color and texture.\textsuperscript{47}

In 2019, Lee et al. reported an exogenous ochronosis case in a 66-year-old woman with hyperpigmented perilarbial and scleral lesions for one year. Skin lesions were treated with CO\textsubscript{2} laser and Q-Switched Nd:YAG in the same session, without description of the parameters used. After three applications, the patient was lost to follow-up due to lack of response.\textsuperscript{48}

**CONCLUSION**

Despite the extensive use of hydroquinone bleaching agents in Dermatology, reports of exogenous ochronosis are infrequent. The difficulty in treating hyperchromic lesions reinforces the need for multiple therapeutic approaches to reach satisfactory results. In this context, the use of lasers or light therapies can be a promising alternative. However, there are several types of technologies used without a specific protocol.

The vast majority of studies on the topic refer to isolated cases of the use of lasers or different light technologies, without respecting standardization both in the clinical evaluation of the response and in the selected modalities. The need for population studies considering a larger number of cases, assessment standardization, exogenous ochronosis lesions and treatment classification, becomes, therefore, crucial for further clarification.

**REFERENCES**

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Study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.