Review Article

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Using a 308 nm excimer laser in the treatment of vitiligo

Excimer" laser 308nm no tratamento do vitiligo

ABSTRACT

Introduction: Vitiligo is an acquired idiopathic disorder characterized by hypochromic and achromic well-delimited macules. The 308 nm excimer laser can be used to treat this condition.

Objective: To analyze studies published in indexed medical journals on the use of the 308 nm excimer laser in the treatment of vitiligo.

Method: Adopting a qualitative approach, a survey of related articles from 2001 to 2009 was carried out using the Medline, Lilacs and Scielo databases.

Results: According to the literature review, the 308 nm excimer laser achieved positive results in the treatment of vitiligo. Recent lesions and those located on the face responded better than those located elsewhere. The extremities of the body were more difficult to treat using this method. The patient's age did not affect the outcome. On average, 11 sessions were necessary before the re-pigmentation started. Ideally, the laser application should be carried out from one to three times a week, with at least 48-hour intervals.

Conclusion: The 308 nm excimer laser is effective and safe in the treatment of vitiligo when compared to other treatment modalities. The results depend on the location and the timeline of the disorder.

Keywords: vitiligo; lasers, excimer; skin.

RESUMO

Introdução: O vitiligo é doença idiopática adquirida, caracterizada por manchas hipocrômicas e acrômicas bem delimitadas, sendo o Excimer Laser 308nm um dos possíveis tratamentos para essa dermatose.

Objetivo: Analisar estudos publicados em revistas indexadas sobre a utilização do Excimer Laser 308nm, no tratamento de vitiligo.

Método: Pela abordagem qualitativa, fez-se levantamento bibliográfico de artigos científicos relacionados ao tema no período de 2001 a 2009, nas bases de dados Medline, Lilacs e Scielo.

Resultados: Segundo essa revisão bibliográfica o Excimer Laser 308nm apresentou resultados positivos no tratamento de vitiligo. As lesões recentes e as localizadas na face respondem melhor do que as de outros locais. As extremidades são de resposta mais difícil. A idade do paciente não interfere no resultado. Em média, foram necessárias 11 sessões até o início da repigmentação. O ideal é que a aplicação seja feita uma a três vezes por semana, com intervalo nunca inferior a 48 horas.

Conclusão: O Excimer Laser no tratamento de vitiligo é efetivo e seguro quando comparado a outras modalidades de tratamento. O resultado depende da localização e do tempo da doença.

Palavras-chave: vitiligo; lasers de excimer; pele.

308nm Excimer laser to treat vitiligo

INTRODUÇÃO

Vitiligo is an idiopathic disorder characterized by the acquired loss of melanocytes, which results in hypochromic and achromic plaques in the skin and/or hair. The disorder can be induced by any stressful event and, from a clinical perspective, may present in localized areas of the body, in segments, in the mucous membranes or over large parts of the body. It occurs in 1 to 3% of the general population, and is evenly distributed across age, gender and racial groups. Its manifestation in association with autoimmune disorders, such as thyroid disorder, Addison's disease, diabetes mellitus, alopecia areata, and pernicious anaemia, has already been documented. 1,2

This dermatosis may cause psychological disorders, even causing the loss of one's social status in some societies. Patients often lack appropriate scientific information and emotional comfort; the clinical response, adherence to the treatment, and even resilience in face of possible therapeutic failures depend on a good physician-patient relationship. Considering the wide variety of medical treatments currently available, dermatologists must evaluate their patients in a holistic manner ^{2,3}.

The 308 nm excimer laser induces the migration of the melanocytes adjacent to the outer root sheath of normal hair follicles, of those on the borders of depigmented areas, and also of the intralesional residual ones, to repopulate the areas affected by vitiligo lesions. This is an effective device, approved by the Brazilian National Sanitary Surveillance Agency (ANVISA) to treat patients with vitiligo.

CARACTERISTICS OF 308NM EXCIMER LASER DEVICE

The excimer laser emits a xenon and chlorine gas based 308 nm wavelength The light beam is transmitted by an articulated arm. The spot size varies from 4 to 30 mm in diameter, depending on the equipment model. The UV radiation is conveyed to the hand piece through a flexible optic fiber cable or a liquid core optical fiber cable. The hand piece emits the UV radiation in the form of a circular beam with an area of 1 to 10 cm2. These technical specifications provide two main advantages of this laser type when compared to conventional phototherapy 4-13: 1) it is possible to direct the light beam selectively to treat specific areas, thus preserving the healthy skin and limiting the unattractive hyperpigmentation adjacent to the lesion that is commonly seen in other forms of phototherapy (Figure 1); and 2) the articulated arm makes it easier to reach usually difficult areas, such as skin folds and mucous membranes (Figure 2).

The objective of this review paper was to analyze studies published in indexed medical journals on the use of the 308 nm excimer laser in the treatment of vitiligo.



Figure 1 - Excimer laser (XTRAC®, Photomedex, Pennsylvania, USA) is applied to damaged skin only; the healthy skin surrounding the lesion is protected



Figure 2 - The Xtrac* hand piece is flexible, articulated, and has an area of 4cm²

METHODS

Search strategy

A qualitative bibliographical survey was conducted using three databases (Medline, Lilacs and Scielo) on the theme of vitiligo and its treatment with 308 nm excimer laser. The 26 analyzed articles were published in English, between 2001 and 2009.

RESULTS

One of the first reports on the use of 308 nm excimer laser in the treatment of vitiligo was made by Baltas et al. 14 Since then, several studies have demonstrated its efficacy in repigmenting vitiligo plaques. 15-21 Al-Otaibi et al. 16 have appropriately translated the reality of the treatment with excimer laser. Five patients abandoned the treatment. Lesions on the hands and feet had a weaker response. On average, 11 sessions were necessary to start the repigmenting process. Skin type and duration of the disorder were relevant factors in patient response to treatment. The shorter the duration of the disorder, the better the results. However, that correlation was not statistically significant when evaluated by the Spearman's rank correlation coefficient (p=0.08). No significant correlation was verified between the patients' ages and their response to the treatment (p=0.392; Spearman's rank correlation coefficient). Although the objective assessment of the results showed only a discreet improvement, patients were satisfied with the laser treatment in general. In that study it was pointed out that vitiligo lesions could be effectively treated with 308 nm excimer laser two or three times a week. A treatment program of three sessions per week as found to be the most effective, especially in the first six weeks of therapy (Table 1), yet there were a greater number

Chart 1 - Data on the location of the lesion and response to the treatment Patient number gender phototype Location* **Duration of the disorder** Maximum dose improvement age (years) (months) (mj/cm²) % F k, df F F 100,400 fa an Μ fa, d 200, 1400 fa, ap, dh 150,700 M F fis, k, df F fi F dh, df F fa.k 150, 1450 F fa dh, df 200,900 M F t, l F fa, ap F fa, I, df 100,700 F a.t Μ a, dh, l M fa, t, d 500, 3300 Μ fa, t, d 50,800,1100 M e, k, fis, l M fa M fa, k 100, 1100 F fa 250,800 M fa, t M fa F e, dh e, dh, df, fa, k 150,850 F fa Μ dh, df

Source: Al-Otaibi et al. (2009)16.

of side effects observed. The highest grade of general repigmenting occurred after 12 weeks of treatment, in the group treated three times per week. (Table 1)

Of the lesions on the face and trunk, which were exposed to ultraviolet (UV) radiation, a 75% repigmentation rate was found in 41% of the patients analyzed. It is important to note that the laser-induced repigmentation persisted, in most of the cases described by Al-Otaibi et al., for the 12 months of follow up. Nonetheless, the authors also noted that the efficacy of the treatment, evaluated at the beginning of the repigmentation, ultimately depended on the number of treatment sessions. Those findings confirm that 308 nm excimer laser therapy is a viable alternative to current UV treatment of vitiligo.

1- Response to treatment according to location

Hofer et al. 17 observed some degree of repigmentation in

67% of their patients after 30 sessions. Their study indicates good therapeutic results in the face and trunk. In the limbs, results were more promising in arms and legs and less effective in elbows and knees. Consistent with other authors' findings, lesions in the hands and feet presented the worst results; the reasons for the variation in results according to the location of the lesions are not known. Hofer A et al ¹⁷ consider the hypothesis that there are fewer melanocytes to proliferate and disseminate in the perifollicular epidermis in areas with a low density of capillary growth.

Kwang-Ho et al. ²¹ comment on the therapeutic efficacy of the initial doses in different areas to be treated according to the table below. (Table 2)

Among the factors that can influence the clinical response to the treatment, the location of the lesions seems to play a crucial role. In their study, Taneja et al. ⁹ identified a minimum of

^{*} ap = armpit, a = arm, e = elbow, dh = dorsum of the hand, df = dorsum of the foot, fi = fingers, fa = face, g = genitalia,

k = knee, I = legs, fis = fist, t = trunk

Chart 2 - Initial doses by area				
Treatment areas	Initial dose (mj/cm²)			
Face, neck	100-150			
Trunk	200-250			
Extremities	250-300			
Articulations	300-500			

Source: Kwang-Ho et al. 21

75% repigmentation in all lesions located on the face, as opposed to 0% on the hands and feet. Ostovari et al. ¹⁸ showed a statistically significant difference in the results obtained in UVB-resistant areas (extremities and bone prominences) and other UVB-sensitive areas, where repigmenting rates were much higher. In their prospective study on Asians, Al-Otaibi et al. ¹⁶ confirmed that the 308 nm excimer laser is effective in treating localized vitiligo; 66% of patients presented more than 25% repigmenting after 25 sessions.

2- Response to treatment according to frequency of sessions

Hofer et al. ¹⁷ evaluated the ideal frequency of 308 nm excimer laser treatment in patients with vitiligo. The results concluded that vitiligo can be treated effectively with excimer laser one, two or three times a week. Although two or three treatments per week seems to trigger the repigmentation more precociously in the vitiligo patches, the start of the repigmenting process ultimately depends on the total number of treatments. In order to obtain a satisfactory degree of repigmentation, it can

be necessary to continue treatment for more than 12 weeks, particularly with once or twice weekly sessions (Table 1).

3- Duration of long-term repigmenting

It is difficult to know whether the repigmentation will remain stable over the course of time, given the lack or short duration of follow-up studies. Eposito et al. ¹⁰ verified the absence of depigmentation one year after the end of the sessions. Hofer et al. ¹⁷ reported that approximately 15% of new hypopigmentation occurred from one to three years after the end of treatment. The tolerance to the treatment is very good, and side effects are limited to erythema and rare blisters. Taneja et al. ⁹ and Baltas et al. ¹⁴ report that excimer laser treatment also seems to lead to effective aesthetic results in the long term, with patients obtaining more than 75% of repigmentation.

4- Phototype and lesion area

Hadi et al. ²⁰ conducted a retrospective review of medical records of 97 patients with stable chronic vitiligo (a total of 221 lesions) who were treated with 308 nm X and Cl excimer laser. They found that 50.6% of the patients presented pigmentation of 75% or more; 25.5% obtained 100% pigmentation; and 64.3% had 50% or more pigmentation. Patients with phototypes III-VI skins and

facial lesions reacted better to the treatment, as did small to medium lesions with durations of three years or less. Lesions in the face presented the best results.

DISCUSSION

The reduction in the proliferation of T lymphocytes, caused by the cellular apoptosis due to damages inflicted on the deoxyribonucleic acid (DNA), seems to be one of the most important effects of UVB phototherapy. It has already been demonstrated that 308 nm is the most efficient wavelength to damage lymphocyte DNA ²². The sufficient dose to induce apoptosis in 50% of T lymphocytes is 95 mJ/cm2 with the 308 nm excimer laser, as compared to 320 mJ/cm2 when using the narrow band UVB ²³. Similar levels of apoptosis-based depletion of T lymphocytes after treatment with 308 nm monochromatic excimer laser were already described in the psoriasis.²³

Drawbacks of treating vitiligo with a 308 nm excimer laser include considerably high purchase and maintenance costs and an inability to treat more than 20% of the skin's surface due to the size of the device's spots. These factors should be taken into consideration when evaluating treatment options. The use of a monochromatic 308 nm wavelength offers photobiological effects that are theoretically superior to those of the narrow band UVB. ²²⁻²⁴ It is important to highlight that although the DNA of the T lymphocytes is one of the main targets for the UVB, in lower degrees it can also reach the keratinocytes inside the epidermis cells, and the fibroblasts in the dermis cells. Inflammatory reactions can also be present.

The mechanism of action of the excimer laser in treating vitiligo is more complex than the simple inducement of the migration of melanocytes triggered by the phototherapy itself. An important factor seems to be stimulating the migration and proliferation of melanocytes, starting from genitor niches in the hair follicles. This stimulation is caused by the direct action of the UVB on the melanocytes and the action of the cytokines secreted by the keratinocytes.

Table 1 - Treatment results by weekly frequency								
	Treatment frequency							
Beginning of the vitiligo repigmenting	Once a week		Twice a week		Three times a week			
Within 3 weeks	-		-		15%	(92/13)		
Within 6 weeks	8%	(1/13)	23%	(3/13)	62%	(8/13)		
Within 12 weeks	46%	(6/13)	62%	(8/13)	69%	(9/13)		

Source: Hofer et al. (2005)13.

Patient age at the onset of vitiligo, gender, and associated disorders are not directly correlated with treatment outcomes; the duration of the condition and its location on the body determine the success of various treatments. ²⁴ Early reports indicate that the 308 nm UV radiation generated by the X and Cl (xenon and chlorine) excimer laser is a promising option in the treatment of localized vitiligo. ²⁵ This treatment modality, with light amplification by stimulated emission of radiation (laser), stimulates follicular repigmentation and can lead to cosmetically satisfactory results ²⁶.

Selective phototherapy devices, such as the X and Cl excimer laser, allow the application of high intensity radiation to the affected skin only, thus protecting the normal skin from damage caused by UVB. In addition, parts of the body that are difficult to access using traditional sources of UV radiation can be treated with these more selective equipments.

The specific photobiological effects (such as the immunomodulatory effect, action in the antigen presentation cells, pigmentation, and carcinogenic effects) of this treatment are not yet known. A carcinogenic risk is possible, based on experimental studies and on the knowledge of narrow band UVB-based phototherapy. Yet no cases of cancer induced by 308 nm excimer laser have been identified to date. Recent data on the immunological sources of vitiligo suggest that UVB prompts an immunosuppressant response during treatment. ²⁵

Finally, the 308 nm excimer laser differs from the lamps used in conventional phototherapy by emitting photons in an intense and discontinuous way (60 nanoseconds pulse; distal pulse energy – 4.6 mJ/cm²).

CONCLUSION

The 308 nm excimer laser helps eliminate a great part of the inflammatory cells (T lymphocytes) that cause vitiligo, and stimulates the migration of melanocytes from the hair follicles outer root sheath to the epidermis. The applications are painless. The duration of the treatment and the number of sessions depend on the extent and amount of lesions. Lesions on the face display the best results, while hands, feet and fingers are more difficult to treat.

According to reports, the 308 nm excimer laser is highly effective in the treatment of vitiligo macules, with a small number of sessions during a relatively short period of time. Results show that vitiligo can be treated from 1 to 3 times per week, with more frequent treatments resulting in faster repigmentation. Additionally, this method only delivers UV radiation to the affected areas, preserving the adjacent healthy skin and reducing the risk of cutaneous aging and cancer. Localized phototherapy with 308 nm excimer laser can be conducted in areas that are inaccessible with conventional devices. This therapy is indicated for patients with less than 20% of the body affected by the disorder. Narrow-band UVB phototherapy should be indicated for larger areas.

With many treatment options available, the dermatologist must evaluate his or her patient holistically, especially when the disorder and its consequences can have emotional impacts and influence the patient's quality of life.

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