Original Article

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Dermatology Section

A Prospective Interventional Study of Xanthelasma Palpebrarum Treated with Ultrapulse Carbon Dioxide Laser

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ABSTRACT

Introduction: Xanthelasma palpebrarum (XP) is the most common of all the xanthomas which presents as asymptomatic, often bilateral, soft, yellow, papules and plaques around the eyelids. Although, the lesions are benign, it is aesthetically upsetting. The surgical laser is the most effective treatment modality to this problem.

Aim: To evaluate the efficacy and safety of ultrapulse Carbon dioxide (CO_2) laser in XP in Indian patients.

Materials and Methods: It is a prospective, interventional study carried out for two years in which 29 patients with 61 XP lesions were part of the study. Ultrapulse CO_2 (Fraxis Duo laser; 10,600 nm) laser treatment was done in every patient for a single sitting. Statistical significance was calculated using Chi-square test using Statistical Packages for Social Sciences (SPSS) version 19.0. The p-value of 0.001 was considered statistically significant.

Results: A total number of 29 patients with 61 xanthelasma lesions were included in the study, of which 11 were males and 18 were females with an age range of 27-54 years. In the present study XP lesions were completely resolved in majority (54 lesions in 25 patients) of treated patients. No intraoperative complications were observed. Two patients showed hypopigmentation. There was neither scarring nor recurrence seen after six months follow-up.

Conclusion: Ultrapulse CO_2 laser is a safe and effective option of treatment for xanthelasma. It is considered as less painful procedure with fewer side effects and recurrences in the present study.

Keywords: Efficacy, Hypopigmentation, Xanthomas

INTRODUCTION

The XP is a disorder which presents with symmetrical soft, yellowish papules and plaques on the inner canthi of upper and lower lids [1]. It is one of the commonest xanthomas seen in dermatology practice that create aesthetic problem for patients. The exact cause of XP is not known, but factors such as hormonal, local and macrophage factors have been implicated in its pathogenesis. However, acetylated low density lipoproteins and macrophages with their scavenger receptor were newly described to be involved in the pathogenesis of XP [2]. Xanthelasma usually occurs in persons above fifty years. About 50% have dyslipidaemia (high low density lipoproteins cholesterol and triglyceride, low high density lipoproteins cholesterol and apolipoprotein A-1) [3].

There are various treatment modalities for XP that include surgical removal, electrocauterisation, chemical cauterisation with Trichloroacetic Acid (TCA), cryotherapy, blepharoplasty and laser ablation [4]. Various types of Light Amplification by Stimulated Emission of Radiation (laser) like CO_2 laser in different modes (continuous, ultrapulse [5], and superpulse [6], potassium titanyl phosphate (KTP) laser [7], Erbium-Doped: Yttrium Aluminium Garnet (Er:YAG) laser [4], 1450 nm diode laser [8], 1064 nm Q switched Neodymium-Doped:Yttrium Aluminum Garnet (Nd:YAG) [9] and fractional CO_2 laser [6,10] have been used. CO_2 laser is regarded as the gold-standard of all the ablative laser. The chromophore for CO_2 laser is water whose vaporisation within the cells results in nonselective thermal damage and ablation of skin layer by layer. The ultrapulsed CO_2 laser emit very short light pulses (600-900 µsec) with maximum peak energies (up to 500 mJ). It results in deepest penetration and narrow controlled thermal zone as the pulse duration which is short lies well beyond the thermal relaxation time of skin [5]. Its concept lies in giving a uniform treatment zone by the laser causing skin surface vaporisation but accelerated re-epithelialisation from undamaged hair follicles and other adnexal structures [11].

All laser treatment offers moderate to excellent clearance rates with less side effects. Very few studies have been done in XP treated with Ultrapulse laser with fewer number of subjects. Most of the studies in which XP was treated with ultrapulse CO_2 laser showed good efficacy and less side effects [5,12,13]. Thus the present study was aimed to evaluate the efficacy and safety of ultrapulse CO_2 laser in xanthelasma in Indian patients.

MATERIALS AND METHODS

A single centre, open label, non-randomised prospective interventional study was carried out in the Department of Dermatology, Venereology and Leprosy, Outpatient Department (OPD), Grant Government Medical College, Mumbai, Maharashtra, India, from January 2018 to January 2020 after obtaining the approval from Institutional Ethics Committee. Total sample size considered was 29 and subjects were selected using non probability convenience sampling technique.

Inclusion criteria: Patients diagnosed as XP and aged 25-60 years of either gender and those willing to participate in the study and giving valid consent for the same were included in the study.

Exclusion criteria: Active infection at the treatment site, history of keloids/hypertrophic scars, treatment taken for last six months, pregnant and lactating females and patients with unrealistic expectations were excluded in this study.

Baseline Evaluation

After obtaining informed consent baseline evaluation was done. This comprised a detailed history regarding the duration, any systemic co-morbidities, such as diabetes mellitus, or hypertension, any concomitant drug use by the patient, and a history suggestive of keloid or hypertrophic scar. Female patient's status on pregnancy or lactation was also noted. A detailed clinical history, examination, and pretreatment clinical photographs were taken. The lesions of XP were examined for number, size, depth, and if it is unilateral or bilateral. The size of lesions was calculated using a measuring

tape. Biochemical investigation that is lipid profile was carried out for all patients.

Treatment Protocol

Treatment of all the lesions of XP was done with ultrapulse CO_2 laser (Fraxis duo CO_2 laser; 10,600 nm wavelength; pulse energy 500 mJ/impulse; pulse duration 600-900 µsec, spot size of 1.1-1.5 mm). The patients were asked to close their eyes and an assistant holds the eye shield for protection. With all aseptic precautions, the lesions were infiltrated with 2% xylocaine before the procedure. While the laser procedure is being done, the skin layers were curated and the evaporated skin is wiped off with moist gauze. Layer by layer, the lesion was subjected to laser light till bleeding points appeared. Topical antibiotic was applied immediately after the procedure and for next seven days. Patients were advised not to touch or remove the crust over the operated area. The patients were asked to follow-up for six months. Pre and post laser photographic documentation was done. Every patient was looked for complications like secondary infection, post inflammatory hypo or hyperpigmentation, scar and ectropion.

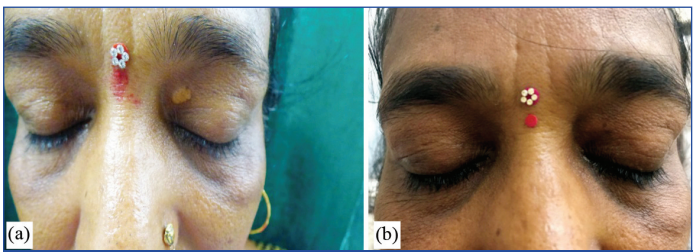
Evaluation: Flattening and complete disappearance of the lesion of XP was considered as efficacy. The efficacy was done by clinical evaluation by a dermatologist by looking at the pre-treatment and post-treatment photographs and evaluated by considering a complete response (cleared completely), a partial response (50-70% reduction in original diameter), and no response (<50% reduction in size).

STATISTICAL ANALYSIS

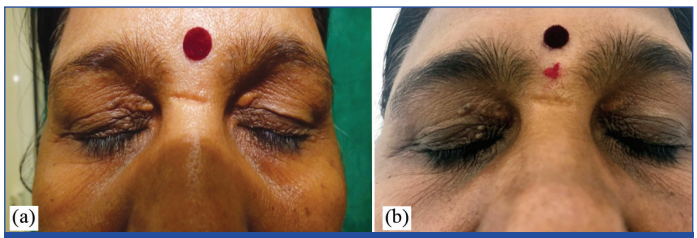
The collected data were entered and analysed using SPSS version 19.0. Frequencies and percentages were computed for qualitative variables like gender and efficacy. Mean±SD for continuous variables like age was calculated. Chi-square test was used to compare efficacy of treatment in both eyes. The p-value of 0.001 was considered statistically significant.

RESULTS

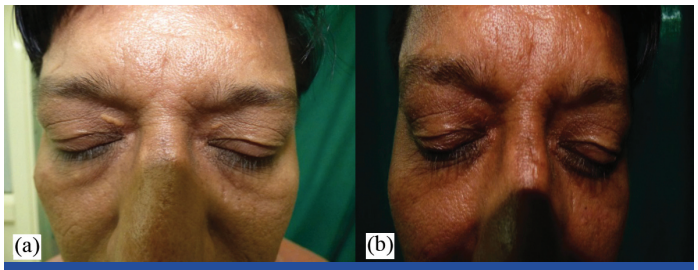
A total number of 29 patients with 61 xanthelasma lesions were treated with ultrapulse CO_2 laser. Of these, 11 were males and 18 were females and age range from 27-54 years. Of all the lesions, seven lesions were >1 cm^2 and 54 lesions were <1 cm^2. Six patients had multiple xanthelasma (more than two). None of the patient had diabetes mellitus, or hypertension, any concomitant drug use. None of the patients had keloids/ hypertrophic scars. None of the female patients were pregnant or lactating. Five patients (17.2%) had deranged lipid profile (cholesterol and triglycerides). Of these, 54 lesions of xanthelasma were cleared completely with single sessions of ultrapulse CO_2 laser [Table/Fig-1-4], while seven lesions required multiple sittings. Downtime was one week with crusted lesion. One patient had oedema over the operated lesions for three days which resolved with anti-inflammatory agents. There was no erythema or post inflammatory hyperpigmentation. There was hypopigmentation in two patients. All the patients were satisfied with the treatment. There were no complications (like haematoma, infection, bleeding, ectropion) encountered in any patient. There was no recurrence of lesion in any patient after six months.



[Table/Fig-1]: a) Pre laser image of XP seen on left eye lid; b) Post laser follow-up image.



[Table/Fig-2]: a) Pre laser image of XP seen on right and left eye lids; b) Post laser follow-up image.



[Table/Fig-3]: a) Pre laser image of XP seen on right eye lid; b) Post laser follow-up image.

Sr. No.	Age	Sex	Location	No. of Lesions	Size approx.	Lipid profile	Result
1	40	F	Upper eyelids	2	8×8 mm	Normal	Cleared
2	34	F	Upper eyelids	2	14×14 mm	Normal	Partial response
3	32	F	Upper eyelids	2	9×8 mm	Abnormal	Cleared
4	36	F	Upper eyelids	1	7×8 mm	Normal	Cleared
5	45	M	Upper eyelids	2	9×3 mm	Normal	Cleared
6	42	M	Upper eyelids	1	9×7 mm	Normal	Cleared
7	38	F	Upper and lower eyelids	3	22×11 mm	Normal	Partial response-2 Cleared -1
8	29	F	Upper eyelids	2	7×7 mm	Normal	Cleared
9	40	M	Upper eyelids	2	17×15 mm	Normal	Partial response
10	42	F	Upper eyelids	2	6×5 mm	Normal	Cleared
11	55	M	Upper eyelids	2	9×6 mm	Abnormal	Cleared
12	48	F	Upper eyelid	1	8×9 mm	Abnormal	Cleared
13	27	F	Upper eyelids	2	9×8 mm	Normal	Cleared
14	40	M	Upper and lower eyelids	3	7×6 mm	Normal	Cleared
15	33	F	Upper eyelid	1	8×9 mm	Normal	Cleared
16	48	F	Upper eyelids	2	6×9 mm	Normal	Cleared
17	45	F	Upper and lower eyelids	4	5×8 mm	Normal	Cleared
18	46	F	Upper eyelids	1	5×6 mm	Abnormal	Cleared
19	48	M	Upper eyelids	2	9×7 mm	Normal	Cleared
20	28	F	Upper eyelids	2	9×8 mm	Normal	Partial response-1 Cleared -1
21	43	F	Upper and lower eyelids	4	7×6 mm	Normal	Cleared

22	55	M	Upper and lower eyelids	3	7×4 mm	Normal	Cleared
23	31	F	Upper eyelids	2	9×4 mm	Normal	Cleared
24	39	M	Upper eyelids	2	8×7 mm	Normal	Cleared
25	34	M	Upper eyelids	2	9×6 mm	Abnormal	Cleared
26	39	M	Upper eyelids	2	9×8 mm	Normal	Cleared
27	42	M	Upper and lower eyelids	4	9×8 mm	Normal	Cleared
28	36	F	Lower eyelid	1	7×7 mm	Normal	Cleared
29	30	F	Upper eyelids	2	8×9 mm	Normal	Cleared

[Table/Fig-4]: Demographic details, pre and post-treatment details of 29 patients of the present study.
F: Female; M: Male; mm: millimeters.

DISCUSSION

The XP is an asymptomatic benign disorder, without any functional disturbances; in spite of that patient seek treatment for aesthetic reasons. The classical treatment for XP is surgical excision but it has its limitation. It may lead to scarring, ectropion and is not feasible for very extensive lesion and may not be repeatable for relapses [14].

Ultrapulse CO_2 laser is a mode with great outcome, fewer side effects and less downtime. In a study it has been shown have shown that by a single ultrapulsed CO_2 laser treatment of 250 mJ impulses results in the ablation of skin upto 60 µm depth. A second laser application will further ablate to a depth of ~130 µm; a further abalation will lead to thermal destruction of skin structures to the extent of 316 µm, so that the ultrapulsed CO_2 laser does an accurate and proper ablation of skin layers. Because of this accurate and superficial effect, there is less damage to delicate deeper structures, thereby limiting the occurrence of scarring and pigmentary changes. This property helps in controlled ablation of xanthelasma lesion with minimal adverse effects [5]. In this study, most of the lesions of XP were cleared completely in one sitting except in few patients which may be because of the larger size and depth of the lesions. There were no side effect in any patients except hypopigmentation in two patients.

In a large case series of 23 patients with 52 xanthelasma by Raulin C et al., in 1999, concluded that ultrapulse CO_2 laser is an effective and safe therapeutic option with no scarring, minimal side effects and a recurrence rate of 13% at 10 months [5]. In another case series of 10 patients with 20 lesions by Pathania V and Chatterjee M showed complete removal in single session with less side effects and 20% recurrence rate [12]. A study by Goel K et al., comparing the efficacy of 30% TCA and ultrapulse CO_2 laser in XP concluded that both are good options for mild lesions, but laser is a better modality for severe lesions while there is recurrence with both [13]. Similar results were found in present study, however there was no recurrence of lesions in any patient which may be because of short follow-up period. Hence, long term follow-up is required to get an accurate result. Also, most of the patients from the present study were below 50 years of age and there was dyslipidaemia in only 17% of patients in contrast to the literature where XP is common after the age of 50 years with dyslipidaemia in 50% patients. This may be because of younger population affected where exact cause is not clear.

Other treatment options for XP are topical TCA, cryotherapy, Er:YAG laser, Q-switched Nd:YAG laser, argon laser, KTP laser, pulsed dye laser, Diode laser and fractional CO_2 laser. Topical TCA for XP is considered to be more effective for smaller lesions, but requires multiple sittings leading to post inflammatory pigmentation and scarring and recurrences ranging between 25% and 39% [15]. A gentle liquid nitrogen cryotherapy can be used for xanthelasma owing to the ease of application and less side effects [16]. Mannino G et al., stated that Er:YAG laser is an ablative laser that has a smaller thermal coagulation zone as compared to CO_2 laser which has been used effectively in XP with no scarring or pigmentation, [17]. Karsai S et al., suggested that Q-switched Nd:YAG (532 nm and 1064 nm) laser cannot be approved for the treatment of XP as most of patients showed poor or no clearance [18]. Argon laser is a simple, effective, and safe method of treatment for small lesions of XP as it has short penetration depths but major disadvantage being significant recurrence rate [19]. KTP laser is safe and highly effective for XP, but frequent treatments are required to maintain the desired results and avoid recurrence [20]. While pulsed dye lasers are effective in early vascular lesions, they fare poorly in xanthelasmas. Diode lasers causes photothermal destruction of sebaceous glands in the mid-dermis and thus have been tried and showed efficacy in XP [15]. The comparably high recurrence rate seems to be a classical characteristic of XP regardless of the mode of treatment which depends on factors such as depth, size, and extent of the lesion. Thus, it is necessary to have a standardised scoring system to compare various studies. In a nutshell, almost all the lasers require multiple sessions with varying rates of clearance and recurrence of lesions. Thus, with the advantages of a single treatment session, fewer side effects and low rates of recurrence by ultrapulse CO_2 laser as compared to contemporary conventional treatments, ultrapulse CO_2 laser can be the best therapeutic option in treatment of XP.

Limitation(s)

The exact recurrence rate in the present study could not be calculated because of short follow-up period. So, long term follow-up is required to assess it. Also, the modality of ultrapulse laser was not compared with any other modality to know the exact efficacy was another limitation of this study.

CONCLUSION(S)

Ultrapulse CO_2 laser is a safe and effective treatment of XP in the delicate periorbital area, advantages being no side effects and fewer recurrences. CO_2 laser being outpatient procedure will reduce patient's anxiety that is related to surgical intervention.

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