Journal of Cosmetic and Laser Therapy

ISSN: 1476-4172 (Print) 1476-4180 (Online) Journal homepage: https://www.tandfonline.com/loi/ijcl20

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To cite this article: Faisal R. Ali, Raj Mallipeddi, Emma E. Craythorne, Nisith Sheth & Firas Al-Niaimi (2016) Our experience of carbon dioxide laser ablation of angiofibromas: Case series and literature review, Journal of Cosmetic and Laser Therapy, 18:7, 372-375, DOI: 10.1080/14764172.2016.1197403

To link to this article: https://doi.org/10.1080/14764172.2016.1197403

Accepted author version posted online: 22 Jun 2016.
Published online: 05 Aug 2016.

JOURNAL OF COSMETIC AND LASER THERAPY
2016, VOL. 18, NO. 7, 372–375
http://dx.doi.org/10.1080/14764172.2016.1197403

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REVIEW

Our experience of carbon dioxide laser ablation of angiofibromas: Case series and literature review

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ABSTRACT

Angiofibromas are one of the dermatological hallmarks of tuberous sclerosis. Various ablative treatments have been trialled and more recently topical rapamycin has been proposed. We present our experience of treatment of angiofibromas using carbon dioxide (CO_2) laser ablation and provide a timely literature review. Nine patients were retrospectively identified as being treated with CO_2 laser between 2009 and 2015. Three patients were male, six were female, median age at first treatment was 28 (range 15–49) years and the median number of treatments was two (range 1–17). Four of these patients could be contacted for a post-treatment telephone interview. All reported an improvement in appearance of angiofibromas following treatment and that they would recommend CO_2 laser ablation to others. Three of the four reported recurrence of some lesions following treatment. The only side effect reported by one patient was transient hyperpigmentation. CO_2 laser ablation appears to be a well-tolerated, efficacious treatment for angiofibromas with few long-term side effects.

ARTICLE HISTORY
Received 13 February 2016
Accepted 30 May 2016

KEYWORDS
Ablative laser; angiofibroma; carbon dioxide laser; tuberous sclerosis

Introduction

Tuberous sclerosis (TS) is an autosomal dominant genodermatosis with a myriad of cutaneous and extracutaneous manifestations. Multiple angiofibromas, skin-coloured or red papules typically distributed on the cheeks, chin and nose, are amongst the dermatological hallmarks of TS (1). Angiofibromas exhibit broad phenotypic heterogeneity. Whilst unproblematic when small, their propensity to enlarge may eventually cause obstruction of the nares, obscuration of the visual fields, pain and bleeding, as well as being aesthetically disfiguring (2). Various treatment modalities for angiofibromas have been proposed, including surgical excision, curettage, dermabrasion, electrocautery, topical rapamycin and laser ablation.

In our laser unit, following assessment in the outpatient clinic, patients are referred for a test patch of carbon dioxide (CO_2) laser ablation to a small area of affected skin. Anaesthesia is achieved locally either by application of Eutectic Mixture of Local Anaesthetic cream 45 minutes prior to treatment and/or through local injection of lidocaine mixed with adrenaline. The area is reassessed at three months, partly owing to the waiting times in our department, to gauge response to treatment, assessment for side effects and the patient's willingness to continue with the treatment.

We present our experience of the use of the ablative CO_2 laser, explore patient-reported outcomes and discuss the role of CO_2 laser in the treatment of angiofibromas.

Materials and methods

We identified all patients in our unit with angiofibromas treated with CO_2 laser in our centre between 2009 and 2015 and notes were retrospectively interrogated. Attempts were made to contact all patients in order to conduct a telephone interview.

The following questions were asked to the contacted patients:

1. Did the treatment work?
2. Did any lesions recur?
3. Did you notice any complications following treatment (such as scarring, hypopigmentation and hyperpigmentation)?
4. How satisfied were you with the treatment on a scale of 1 to 10? (1 is not satisfied at all and 10 is very satisfied)
5. Would you recommend the treatment to other patients?

Results and discussion

As detailed in Table 1, nine patients were identified in total, of whom three were male, six were female, median age at first treatment was 28 (range 15–49) years and the median number of treatments was two (range 1–17). Only one patient was not able to fully tolerate treatment under local anaesthetic and subsequently required laser ablation under general anaesthetic. Following CO_2 ablation, one patient subsequently underwent

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Table 1. Characteristics of patients with angiofibromas treated with carbon dioxide (CO_2) laser ablation.

Sex	Age at first treatment	Age at final treatment	Number of treatments	Site(s) of treatment	Note(s)
F	28	34	17	Cheeks, forehead, temple	Multiple treatments owing to number and size of lesions and patient preference
M	15	16	4	Nasolabial fold, upper cutaneous lip	
F	47	48	2	Nasal ala, cutaneous lip	
F	44	48	3	Cheek, nose, chin	
M	49	49	2	Nose, medial cheeks, chin, forehead	Previous treatment with CO_2 laser at another unit
F	20	20	2	Chin, upper cutaneous lip	
F	15	17	3	Forehead	
F	32	33	1	Nose, medial cheeks, chin, forehead	One treatment with CO_2 laser; two further treatments with pulsed dye laser
M	25	25	2	Nose, cheeks, chin	First treatment under local anaesthetic poorly tolerated; second treatment under general anaesthetic

pulsed dye laser (PDL) treatment for residual vascular, erythematous elements of angiofibromas. One patient had 17 treatments over many years, owing to a combination of the number and size of lesions and the patient's preference to have smaller regions treated over multiple visits.

Our approach is to use the UltraPulse CO_2 laser (Lumenis, Israel) in its computer pattern generator scanning ActiveFx handpiece, choosing the size and shape according to the individual lesion. We use a starting fluence between 100 and 150 mj according to anatomic location of the lesions and background skin colour. One or several passes are performed with wiping of the char in between until lesion flattening is achieved. We do not tend to ablate deeper than the level of the reticular dermis (Figure 1).

Four of the nine patients could be contacted by telephone following treatment. All reported that CO_2 laser ablation alleviated the angiofibromas and all would recommend the treatment to other patients. Three of the four reported some recurrence following treatment but to a much lower extent; the only complication reported by one patient was transient post-treatment hyperpigmentation that resolved after six months. Median satisfaction with treatment was 7.5 out of 10 (range 7–9).

Our results suggest that CO_2 laser ablation using topical and/or local infiltrative anaesthesia is well tolerated by the majority of patients and typically fewer than five treatments are needed. Multiple treatments were mainly required because in some patients different parts of the face were treated over a course of sessions. In those contacted following treatment, patients unanimously reported instant treatment success and that they would recommend CO_2 laser ablation to other patients. Whilst satisfaction with treatment was high and side effects of treatment were few, recurrence following treatment was reported in three of four cases, albeit at a much milder scale.

We acknowledge our study is limited by its retrospective nature, paucity of subjects and low response rate to the telephone survey. Whilst it is reassuring that patients did not report any adverse effects following treatment, and could therefore be assumed not to have long-lived symptoms, our study weakened by a lack of long-term independent clinical assessment of scarring, dyspigmentation and persistent erythema. Unfortunately, resource constraints and patient preference limited our capacity to recall patients for such review. Access for referral back to our department for further treatment is possible; none of the patients felt that the mild recurrence was to such an extent that necessitated further treatments.

Our study compares favourably with previous work. Papadavid and colleagues reported 29 patients with TS, all of whom were treated under general anaesthesia. Of 13 patients treated with the CO_2 laser as monotherapy for fibrous or protuberant angiofibromas, considerable long-term improvement was reported in ten patients; poor response with persistent hypertrophic scarring was observed in the three remaining patients. Twelve patients were treated with PDL for small erythematous or vascular angiofibromas with good effect. Four patients were treated with both PDL and CO_2 laser devices, three of whom demonstrated an excellent response (3). Another group reported treatment of three patients with angiofibromas with combination treatment of PDL and fractionated CO_2 laser, all performed under general anaesthetic (4). They reported significant improvement in erythema and texture of angiofibromas at follow-up (between three and ten months), with no side effects of scarring or pigmentary changes. Two of the three patients required subsequent treatments with the combination treatment. In our cases, eight of nine patients were treated using local anaesthesia (either topically applied or injected) and the need for general anaesthesia was avoided.

Belmar and colleagues reported 23 patients with angiofibromas ablated by CO_2 laser, of whom the initial response was maintained in 30% of patients, but recurrence was noted in the majority, in keeping with our findings. In their study, angiofibromas in younger patients were noted to recur sooner in comparison to older patients. They did not report patient satisfaction with treatment or comment upon the anaesthesia required (5).

Bittencourt and colleagues reported CO_2 laser ablation of angiofibromas in ten patients with follow-up at 6, 12 and 24 months (6). Outcomes were assessed by blinded clinicians and by patients themselves. Whilst eight of the ten patients rated their treatment as good or excellent at 24 months, only two were judged by the blinded assessors to have sustained a good or excellent response, three patients had good or excellent initial response with partial deterioration by 24 months and five patients had a range of early results with poor response (high recurrence rate) at 24 months. Two patients had persisting post-treatment hypopigmentation. These findings

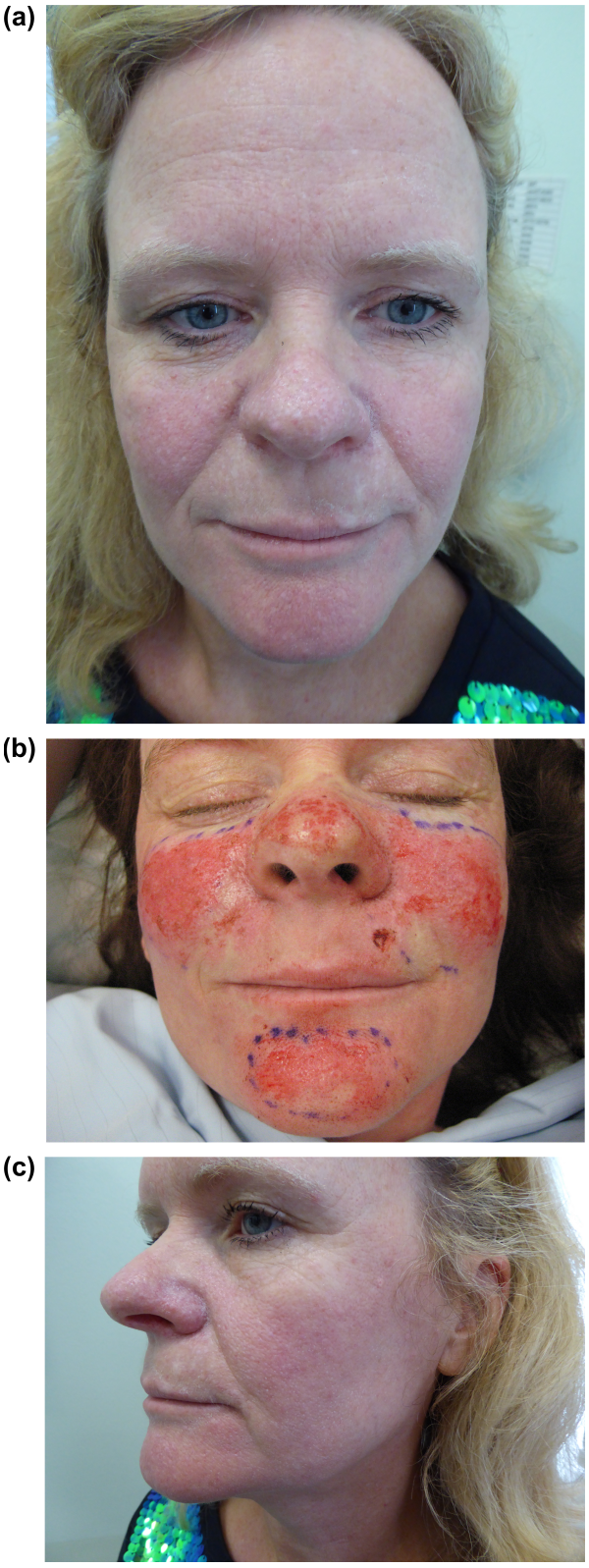

Figure 1. Angiofibromas before (a), during (b) and post treatment (c).

are in keeping with our own, suggesting a high degree of patient satisfaction with treatment and early initial successful treatment in the majority of patients but a high degree of recurrence.

Fioramonti and colleagues reported 13 patients with TS treated with a combination of laser devices with two treatments with the erbium-doped yttrium aluminium garnet (Er:YAG) laser at zero and three months to ablate protuberant angiofibromas, followed by PDL at six months for vascular components with final CO_2 resurfacing at 12 months (four treatments with laser devices in total). All procedures were performed using topical anaesthetic cream, as in the majority of our patients. 12 of the 13 patients were independently deemed to exhibit improvement six months following the final CO_2 resurfacing (2). In our series, one could observe that improvement in lesions may be achieved in many cases with fewer than four treatments using the CO_2 laser.

Another study reported one patient with extensive nodular angiofibromas, who underwent two sessions of UltraPulse CO_2 laser ablation under general anaesthesia, during which the lesions were ablated to the level of the upper reticular dermis. Recurrence of papules was noted at three years requiring a further treatment with the same modality (7).

In recent years, the ability of topical rapamycin (also known as sirolimus), an inhibitor of mammalian target of rapamycin pathway, to downregulate angiogenesis and growth signalling has also been exploited to help flatten angiofibromas (8). Since the incidental noting of regression of angiofibromas in an organ transplant recipient taking systemic rapamycin, various topical agents containing rapamycin have been trialled in patients with angiofibromas. Topical rapamycin appears to be well tolerated and safe and efficacious in 94% of patients reported to date (8). Formulations previously reported have been manufactured with various drug concentrations (0.003 to 1%) and an array of vehicles including creams, gels, ointments and solutions. However, commercially available preparations of rapamycin are not yet available; there is no consensus as to how to manufacture the topical formulation and the treatment remains off-licence. Furthermore, long-term efficacy data are not yet available. Whether topical treatment needs to be continued indefinitely is yet to be established and direct comparisons with other treatment modalities (including ablative laser devices) have not yet been performed.

Some groups have already explored the possibility of combining ablative treatments with topical rapamycin. In a 26-year-old female for whom CO_2 laser was reported to have effected 'minimal improvement' ten years previously, a combination of ablative fractional resurfacing upon papular lesions, followed by twice daily 0.2% rapamycin ointment, resulted in flattening of lesions, which was maintained at three months following treatment (9).

Park and colleagues explored this paradigm further, treating four patients with combinations of topical rapamycin (starting concentration 0.1% ointment) and CO_2 laser ablation of larger papules (10). The authors suggested that topical rapamycin (twice daily initially, three times weekly as maintenance) could be used in childhood (when invasive treatments are best avoided where possible), and would be most effective for lesions less than 4 mm in diameter and as an adjunct to CO_2 ablation. For adults with angiofibromas greater than 4 mm in diameter, topical rapamycin was less likely to be effective, and CO_2 laser ablation in combination with rapamycin would be more effective (8).

From our experience, we propose CO_2 laser ablation for angiofibromas as a well-tolerated procedure that can be

performed using topical or local anaesthetic agents with relatively few treatment sessions. Our patient survey suggests a high degree of patient satisfaction and few adverse side effects, but potentially a high degree of recurrence. Long-term data and comparative studies relating to all treatment modalities for angiofibromas are sparse, including laser devices and topical rapamycin. As such information becomes available, we may be able to better define the future integration of topical rapamycin with ablative laser technologies to optimise patient outcomes.

Funding

No funding was received for this work

Declaration of interest

The authors declare no conflicts of interest.

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