

Melanin Index in Assessing the Treatment Efficacy of 1064 nm Q Switched Nd-Yag Laser in Nevus of Ota

Background: Q-switched neodymium-yttrium aluminium-garnet (Q switched Nd-Yag) laser has been used in the treatment of nevus of Ota in all skin types with variable success rate. Data with an objective assessment parameter to this laser treatment is lacking. **Objective:** To evaluate the utility of melanin index in assessing the treatment response and also determine the efficacy and safety of the Q-switched Nd-Yag laser (1064-nm) in the treatment of nevus of Ota in Fitzpatrick skin types IV and V. **Materials and Methods:** A total of 35 patients treated with Nd-Yag laser were studied. The objective improvement (pigment clearance) was determined by melanin index from two fixed points: A1, 2 cm below the pupil at the mid pupillary line (when the gaze is fixed); A2, the most prominent part of zygoma. The melanin index in these two areas was recorded as M1 and M2, respectively. The subjective clinical improvement was determined by the physician and the patient global assessment score. **Results:** The mean baseline melanin indices M1 and M2 were 59.54 ± 9.72 and 59.02 ± 9.16 , respectively. At the last visit the mean M1 and M2 decreased to 53.8 ± 8.55 ($P < 0.001$) and 54.13 ± 6.01 ($P < 0.001$), respectively. Patient and the physician global assessment score showed that 26 (74.3%) and 20 (57.14%) patients, respectively, had >50% pigment clearance. **Conclusion:** The melanin index, a simple non-invasive parameter is useful in assessing the treatment response more objectively. The 1064-nm Q-switched Nd-Yag laser offers good improvement in patients with nevus of Ota in darker skin types IV/V.

KEYWORDS: Nevus of Ota, melanin index, Fitzpatrick skin type IV and V

INTRODUCTION

Nevus of Ota is a dermal melanocytosis, which is characterised by bluish or greyish brown pigmentation affecting the areas innervated by the ophthalmic and maxillary division of the trigeminal nerve. Mucosal pigmentation may occur involving the conjunctiva, oral and nasal mucosae and tympanic membrane.^[1,2] In approximately 60% of the cases, the nevus is present at birth and in the remaining it develops during the first decade. It is common in Asians.^[1-12] It is a benign condition, but may cause impairment in the quality of life due to the cosmetic disfigurement. Various treatment

modalities have been used such as dermabrasion, cryotherapy, surgical removal and skin grafting. But the overall outcome with these therapeutic options is not satisfactory due to the inevitable side effects such as scarring, atrophy and pigmentary changes.^[6]

The Q-switched neodymium-yttrium aluminium-garnet (Q switched Nd-Yag) laser has been used in the treatment of nevus of Ota for more than two decades, with variable success. This laser emits a longer, near infrared ray of 1064 nm, which is capable of reaching the deeper dermis and destroying the dermal melanocytes of nevus of Ota, by selective photothermolysis.^[1,2] The treatment outcome with Q switched Nd-Yag laser may vary depending on the depth and density of the melanocytes in the dermis and also the skin types. In most of the published literature, the treatment outcome was assessed by the physician and patient's global assessment.^[1-4,6-12] This perception can vary from person to person and may not reflect the accurate clinical change. Also it will not help in generating the standard guidelines parameter

Access this article online	
Quick Response Code: 	Website: www.jcasonline.com
	DOI: 10.4103/0974-2077.123398

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(e.g. optimal fluence, number of sessions required, treatment intervals) in the laser treatment. Derma-spectrometer is a narrow band spectrophotometer that measures the quantity of melanin (melanin index) and oxy haemoglobin (erythema index) in the skin.^[12] The instrument has two light emitting diodes that emit green light centred at 635 nm for oxy haemoglobin and red light centred at 635 nm for melanin. After detecting the reflected light, photoelectric conversion in diodes proceeds and the values are expressed on the digital screen. The values correlate with the degree of redness (erythema index) and the pigmentation (melanin index). It is a very simple non-invasive device that can be used in assessing the laser treatment response in patients with nevus of Ota.^[13]

In this follow up study (on cases being managed routinely in our laser clinic), we evaluated the treatment efficacy of 1064-nm Q switched Nd-Yag laser by melanin index in nevus of Ota in patients with Fitzpatrick Skin types IV and V and also determined the efficacy and safety of the Q-switched Nd-Yag laser.

MATERIALS AND METHODS

Study period

April 2009 to October 2012.

Study patients

All patients with nevus of Ota, treated with 1064-nm Q switched Nd-YAG laser at our hospital were included. The diagnosis was based on the classical clinical criteria. Patients treated with lasers earlier or any other modalities were excluded. All the clinical details were recorded in a performa. Written Informed consent was obtained from all the patients and parents/guardians of younger patients.

Melanin index

Melanin index was measured by a Derma-spectrometer (Cortex technology, Denmark) at each visit. For uniformity, the readings were taken from two fixed points: A1, 2 cm below the pupil at the mid pupillary line (when the gaze is fixed); A2, the most prominent part of zygoma. The melanin index in these two areas was recorded as M1 and M2, respectively.

Photographic assessment

Clinical photographs were taken at each visit, by using the Nikon D 3000 camera (Nikon Corporation, Japan), under the constant camera, light and other settings. The clinical response of pigment clearance (assessment by comparing the final visit photograph to the baseline) to the laser treatment was graded by a dermatologist who was not involved in the study and also blinded to the laser details, on a scale of 1-5: Grade 1 – <25% pigment

lightening; Grade 2 - 26-50% pigment lightening; Grade 3 - 51-75% pigment lightening; Grade 4 - 76-95% pigment lightening; Grade 5 - > 95% pigment lightening. Patients also graded their assessment on a scale of 1-5.

Treatment protocol

For topical anaesthesia, EMLA cream (mixture of 2.5% lidocaine HCL and 2.5% prilocaine) was used. Patients were treated with 1064-nm Q switched Nd-YAG Laser (MedLite C6, Hoya Con Bio Inc., Fremont, CA, USA) with a spot size of 4 mm and energy ranging from 5 to 7 J/cm². The frequency used was 5 with a maximum of 5 passes. The therapeutic endpoint was immediate whitening and/or fine bleeding points. Laser sessions were continued at an interval of 6-10 weeks, till no further improvement was observed or a maximum of 12 sessions. During all treatment sessions, the eyes of the patients were protected by a silicone coated lead shield provided by the manufacturer. The clinical staff also wore the appropriate eye protection glasses supplied by the company. After each laser treatment, patients were advised about sun protection and the regular use of sunscreens. Topical ointment (a mixture of fluticasone and mupirocin) was advised for 2 days after each treatment session.

Side effects

At every visit, patients were assessed for any side effects such as hyperpigmentation, spotty hypo-pigmentation or any others.

Measurement of melanin index, clinical photography, laser treatment and monitoring of side effect profile were carried out by Gomathy Sethuraman (GS) in all the patients.

Statistical analysis

Quantitative data was presented as mean \pm SD. A generalised estimating equation (GEE) model was applied to see the trends of melanin and erythema indices over every laser session. The correspondence between the clinician assessment, the patient's global assessment and the change in the melanin index was assessed by comparing the average reduction in the melanin index score between the two categories of clinical improvement, that is, > 75% pigment reduction and < 75% pigment reduction, by Student's *t*-test. The timing of last clinical photograph (which was used for the clinical assessment scoring) corresponded with the final melanin index reading.

A *P* value of < 0.05 was considered as significant. All statistical analysis was implemented on Stata version 11.0.

RESULTS

A total of 35 patients (8 males and 27 females) were treated with Q switched Nd-YAG laser. Their age ranged from 11 to 32 years with a mean of 21.2 ± 5.1 years. All excepting one had unilateral nevus of Ota. In 16 patients, the nevus was confined to V2 distribution and in 18, it was present in both V1 and V2 areas of trigeminal nerve. Only one patient had isolated involvement of V1 area. All patients were Indians having a skin type of IV or V. The laser energy ranged from 5 to 7 J/cm² with a mean fluence of 5.84 ± 0.58. The average number of laser treatment sessions was 8.62 ± 2.00 (ranging from 6 to 12) and the average interval between the two successive laser sessions was 7.46 ± 0.92 weeks (ranging from 6 to 10 weeks).

Melanin index

The mean melanin indexes, M1 and M2 at baseline were 59.54 ± 9.72 and 59.02 ± 9.16, respectively. At final visit, the levels decreased significantly to 53.8 ± 8.55 (P < 0.001) and 54.07 ± 3.10 (P < 0.001), respectively [Figure 1]. GEE analysis showed that the average reduction of both M1 and M2 per laser session were -0.76 (95% CI: -0.97 to -0.56, P < 0.001) and -0.89 (95% CI: -1.06 to -0.74, P < 0.001), respectively. However, significant reduction of M1 and M2 compared with the baseline was evident from visit 6 and 5 (i.e. after the fifth and fourth laser session), respectively. The treatment response was compared between the speckled (n = 21) and confluent type (n = 14) of the nevus and it showed that the former responded earlier than the later type. The average visit wise reduction of M1 and M2 in the speckled type were -0.85 (95% CI: -1.16 to -0.54, P < 0.001) and -0.80 (95% CI: -1.02 to -0.58, P < 0.001), respectively, and in the confluent type it was -0.72 (95% CI: -0.99 to -0.45, P < 0.001) and -0.97 (95% CI: -1.23 to -0.72, P < 0.001), respectively. However, the earliest significant reduction in M1 was evident after the fourth laser treatment while in M2 it was evident after sixth laser sitting.

In Fitzpatrick’s skin type IV, the average pigment clearance of both M1 and M2 per laser visit were -0.80 (95% CI: -1.04 to -0.57, P < 0.001) and -0.87 (95% CI: -1.06 to -0.69, P < 0.001), respectively, while in skin type V the reduction were -0.52 (95% CI: -0.56 to -0.49, P < 0.001) and -1.13 (95% CI: -1.47 to -0.79, P < 0.001), respectively. In the skin type IV the significant reduction in the melanin index was evident after fifth laser sessions, whereas in skin type V it was seen after the fourth laser session.

Patient global assessment showed that overall 26 (74.3%) had > 50% pigment clearance from the baseline [Figures 2-5]. Seven patients (20%) had improvement of 25-50%, 15 patients (42.8%) had 50-75% improvement, 10 patients (28.6%) had 75-95% improvement and only

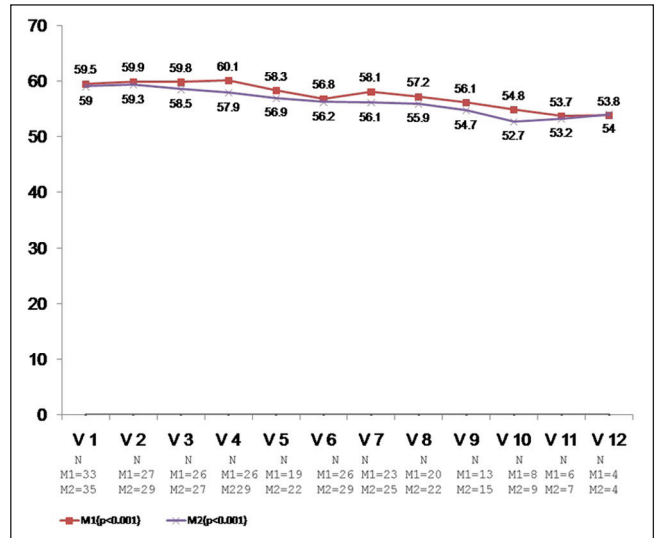


Figure 1: Shows the mean visit wise reduction in the Melanin indices M1 and M2, (V: Visit)



Figure 2: A1 Before laser treatment; A2 after laser treatment (>75% pigment clearance); B1 Before laser treatment; B2 after laser treatment (>75% pigment clearance)



Figure 3: C1 Before laser treatment; C2 after laser treatment (>75% pigment clearance); D1 Before laser treatment; D2 after laser treatment (>75% pigment clearance)

1 (2.9%) patient had >95% improvement.

Assessment done by the dermatologist blinded to the laser sessions and parameters, showed that 20 patients (57.1%) had > 50% improvement. Six patients (17.1%) had improvement of <25%, 9 patients (25.7%) had 25-50% improvement, 8 patients (22.9%) had 50-75% improvement, 11 patients (31.4%) had 75-95% improvement and only 1 (2.9%) patient had >95% improvement.

Correlation between the melanin index and global assessment scores

There was a significant correlation between the physician assessment scoring and the mean reduction in the melanin indexes, M1 and M2. With the physician’s score of >75% pigment clearance, the reduction in the melanin index was significantly higher as compared with < 75% pigment clearance (M1: 8.9 Vs 3.2 P = 0.03; M2: 11.4 Vs 3.4 P < 0.001) [Figure 6]. However, the reduction in the melanin index was not significant when it was compared with patient global assessment score (M1: 7.2 Vs 4.3 P = 0.36; M2: 7.8 Vs 5.4 P = 0.24).

Side effects

Ten patients developed side effects with an average fluence of 6.75 J/cm² and average visit of 7.8. Eight patients developed spotty hypopigmentation [Figure 4] and two patients developed hyperpigmentation. In all these cases, the pigmentary changes have improved significantly over a period of time. The longest follow-up period is 24 months.

Improvement %	Patient assessment %	Physician assessment %
<25	2 (5.7)	6 (17.1)
26-50	7 (20)	9 (25.7)
51-75	15 (42.8)	8 (22.9)
76-95	10 (28.6)	11 (31.4)
>95	1 (2.9)	1 (2.9)

DISCUSSION

Nevus of Ota is a cosmetically disfiguring dermal melanocytosis. Q switched Nd-Yag laser has been used in the treatment of nevus of Ota with variable success rate. Most of the studies have been done in Fitzpatrick’s skin types II and III and the recommended laser fluence ranges from 4.5 to 12 J/cm².^[3-8] About 10 laser treatment sessions are required to achieve a considerable cosmetic outcome. There are few studies on Indian skin types, which have shown a cosmetic improvement of 50-60% at a fluence ranging from 2.5 to 8 J/cm². The number of sessions varied from 5 to 15.^[9-12] There are also few reports on Fitzpatrick’s skin types V and VI, which have shown significant pigment clearance.^[1,2]

In most of the published literature the treatment



Figure 4: E1 before Laser treatment E2: after laser treatment (>50% pigment clearance along with spotty hypo pigmentation)



Figure 5: Bilateral Nevus of Ota F1 and F3: Before laser treatment; F2 and F4 after laser treatment (50-75% pigment clearance)

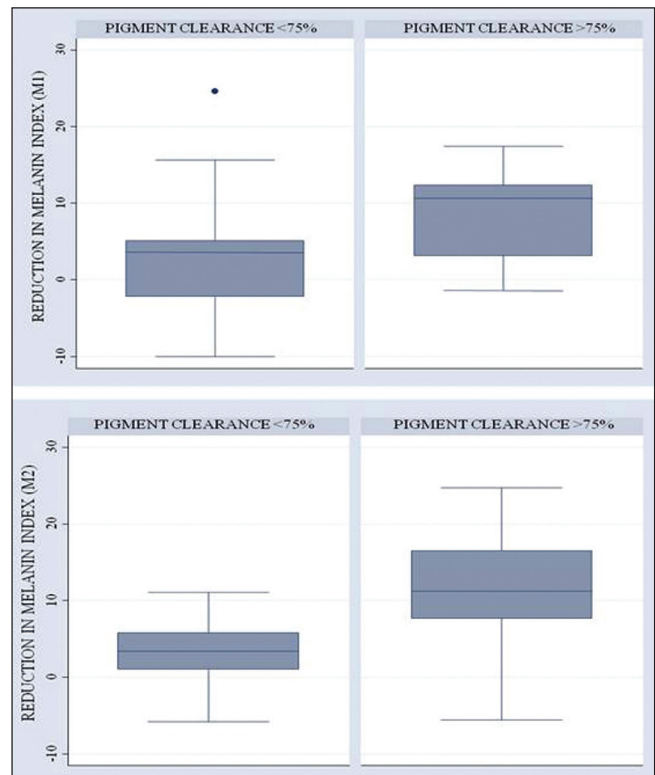


Figure 6: Box plots showing the reduction in melanin indices in the two groups of clinical improvement (<75% pigment clearance Vs >75% pigment clearance)

outcome was primarily evaluated by assessment of serial photographs that lacks uniformity and has lot of subjective variation.^[1,4,6-12] It may not reflect the actual treatment response. Hence there is a need of a good objective parameter to evaluate the pigment reduction after laser treatment in nevus of Ota. To quantify the pigment clearing or fading response, an estimate of dermal melanin fraction, that is, the melanin index is an ideal parameter which can be measured by Deraspectrometer.^[13] In a recent retrospective study from Taiwan, the authors have compared the efficacy of Q switched Ruby laser with that of Q switched Nd Yag laser on 94 patients of Nevus of Ota. The mean melanin index in both the groups showed excellent results.^[8] The present study in the darker skin types of IV/V suggests that the melanin index is an useful objective parameter. It has shown a significant reduction trend in both the infra orbital (M1) and Zygomatic area (M2). Also it has correlated well with the physician assessment scoring. Significant improvement was noticed after a minimum of four laser sessions.

Transient side effects such as oedema, crusting, erythema and burning or pain lasting for few days after the laser session was observed in most of the patients as reported earlier.^[1,2,9-12] The other side effects are spotty hypo pigmentation (seen in 22.8%, 8/35) and hyperpigmentation (seen in 5.7%, 2/35), which are more or less similar to earlier published studies in darker skin types.^[1,2]

In conclusion, the 1064-nm Q switched Nd Yag laser offers good improvement in nevus of Ota among Fitzpatrick skin type IV and V. The melanin index is a good objective tool in assessing the laser treatment response in nevus of Ota. A minimum of four laser treatment sessions are required to see a significant pigment reduction. Based on our experience we suggest the following laser parameters for the Indian skin types: Fluence 5-7 J/cm²; spot size 4 mm; treatment interval 6-8 weeks; frequency 5 with (a maximum of) 5 passes or immediate whitening. The ideal starting energy level is 5 J/cm², but after six treatments, the increase in the fluence level should be done cautiously with close monitoring for any side effects. The side effects of pigmentary changes are reversible, which improve over a period of time.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge Vamsi Krishna Y and Aditi Jha for their help in the data collection including the photographs.

REFERENCES

1. Fusade T, Lafaye S, Laubach JH. Nevus of Ota in Dark Skin — An Uncommon but Treatable Entity. *Laser Surg Med* 2011;43:960-4.
2. Landau MJ, Kalner IV, Goldberg LH, Roy GG, Friedman PM. Treatment of Nevus of Ota in Fitzpatrick Skin Type VI With the 1064-nm QS Nd:YAG laser. *Laser Surg Med* 2011;43:65-7.
3. Kunachak S, Leelaudomlipi P. Q-switched Nd:YAG Laser Therapy of Acquired Bilateral Nevus of Ota-like maculae: A Long Term Follow-Up. *Laser Surg Med* 2000;26:376-9.
4. Chan HH, Lam LK, Wong DSY, Leung RSC, Ying SY, Lai CF, et al. Nevus of Ota: A New Classification Based On THE Response to Laser Treatment. *Laser surg* 2001;28:267-72.
5. Chang JC, Kou CS. Comparing the effectiveness of Q-switched Ruby laser treatment with that of Q-switched Nd:YAG laser for oculodermal melanosis (Nevus of Ota). *J Plast Reconstr Aesth Surg* 2011;64:339-45.
6. Cho SB, Park SJ, Kim MJ, Bu TS. Treatment of acquired bilateral nevus of Ota-like macules (Hori's nevus) using 1064-nm Q-switched Nd:YAG laser with low fluence. *Int J of Dermatol* 2009;48:1308-12.
7. Lee WJ, Han SS, Chang SE, Lee MW, Choi JH, Moon KC, Koh JK. Q-switched Nd:YAG Laser Therapy of Acquired Bilateral Nevus of Ota-like macules. *Ann Dermatol* 2009;21:255-60.
8. Kim SD, Kim SW, Huh CH, Suh DH, Eun HC. Changes of biophysical properties of skin measured by non invasive techniques after Q-switched Nd:YAG laser therapy in patients with nevus of Ota. *Skin Res Technol* 2001;7:262-71.
9. Omprakash HM. Treatment of nevus of Ota by Q-switched, frequency doubled, Nd:Yag laser. *Indian J Dermatol Venereol Leprol* 2002;68:94-5.
10. Aurangabadkar S. QY AG5 Q-switched Nd:Yag Laser Treatment of Nevus of Ota: An Indian study of 50 Patients. *J Cutan Aesthet Surg* 2008;1:80-4.
11. Kar Hk, Gupta L. 1064 nm Q-switched Nd: YAG laser treatment of nevus of Ota; an Indian open label prospective study of 50 patients. *Indian J Dermatol Venereol Leprol* 2011;77:565-70.
12. Sekar S, Kuruville M, Pai HS. Nevus of Ota: A series of 15 cases. *Indian J Dermatol Venereol Leprol* 2008;74:125-7.
13. Diffey BL, Oliver RJ, Farr PM. A portable instrument for quantifying erythema induced by ultraviolet radiation. *Brit J Dermatol* 1984;111:663-72.

How to cite this article: Sethuraman G, Sharma VK, Sreenivas V. Melanin index in assessing the treatment efficacy of 1064 nm Q switched Nd-Yag laser in nevus of Ota. *J Cutan Aesthet Surg* 2013;6:189-93.

Source of Support: Nil. **Conflict of Interest:** None declared.