

A Combination of Low-Fluence (1064 nm) Q-SNd: Yag Laser with Topical 2% Hydroquinone Cream v/s Topical 2% Hydroquinone Cream for Melasma in Indians-Randomised Controlled Trial

Dr. Snehal M. Navande¹, Dr. Amit Kelkar², Vidyadhar R. Sardesai³

Assistant Professor, Department of DVL, MIMER Medical College, Talegaon(D), Pune, India

Corresponding Author Email: [snehalnavande\[at\]gmail.com](mailto:snehalnavande[at]gmail.com)

Phone number: 7757996741

Associate Professor, Department of DVL, BVP Medical College, Pune, India

Email: [kelkaramit\[at\]rediffmail.com](mailto:kelkaramit[at]rediffmail.com)

Professor & HOD, Department of DVL, BVP Medical College, Pune, India

Email: [nitinsardesai22\[at\]gmail.com](mailto:nitinsardesai22[at]gmail.com)

Abstract: Context: Long term treatment, unpredictable results and recurrence necessitate search for new modalities of treatment of melasma. Aims: To compare the efficacy and side effect of combination (Q-S Nd-YAG laser + 2% hydroquinone cream) with topical 2% hydroquinone cream alone for melasma in Indians. Settings and Design: A prospective, comparative and interventional study with split face design randomized control study was conducted in the Dermatology Department of a Teaching hospital and a Tertiary Care Centre, in Pune for 18 months. Methods and Material: 30 patients with dermal or mixed-type melisma (Wood's Lamp examination) were enrolled for 10 weeks of study. One side of the face was treated with topical application of 2% hydroquinone cream alone and other side was treated with combination of 1,064-nm QS-Nd:YAG laser, 6-mm spot size, 1.5- to 1.7-J/cm² fluence for four sessions at 1-week intervals and topical application of 2% hydroquinone cream. Evaluation was done by standard digital clinical photographs and Modified MASI score taken at 0, 6 and 10 weeks. Results: 63.6% sides treated with a combination vs. 31.8% sides treated with topical cream alone reported improvement. The combination therapy was significantly more effective than the topical treatment alone as per Chi-Square test ($p=0.034$). During follow-up, eight of 22 patients developed rebound hyperpigmentation of melasma. Conclusion: The Combination therapy is more effective than the Topical treatment alone in treatment of dermal and mixed melisma. However, the Combination does not show sustained results and has undesirable side effects and hence needs to be used with caution.

Keywords: Q-Switched Nd-YAG laser, Melasma, Hydroquinone cream, Hyperpigmentation

Key Messages: Though Combination therapy of low- fluence (1064nm) Q-S Nd:YAG Laser and topical hydroquinone cream is more effective than topical hydroquinone cream alone, it needs to be advocated with caution considering the lack of sustained results and side effects.

1. Introduction

A blemish free skin is the desire of all human beings. Melasma is a common, acquired, symmetric hypermelanosis, characterized by irregular light to dark brown macules and patches commonly involving the cheeks, forehead, upper lip, nose, and chin and other extra facial sites like forearm, arms and neck. It affects individuals of all races and predominately affects women of childbearing age, especially those of Asian, Hispanic, African or Middle Eastern descent i.e., darker skin phenotypes (Fitzpatrick skin type IV-VI). Though topical application of 2% hydroquinone cream is the gold standard for treatment of Melasma, the long duration of treatment coupled with unpredictable results and recurrence are often frustrating and necessitate search for new modalities of treatment. Recently, many studies have reported the clinical effectiveness of laser toning with the Q-switched Nd- YAG laser for the treatment of melasma.^{1,2}

The present study was done to compare the effectiveness of combination of a Low- fluence Q switched Nd: YAG laser

(1064nm) and topical 2% hydroquinone with topical 2% hydroquinone cream used alone for the treatment of melasma in Indians.

Subjects and Methods

The prospective, comparative, hospital-based split-face randomized controlled trial study was carried out from September 2016 to March 2018 at a Teaching Hospital and Tertiary Care Centre after approval from the Institutional Ethics Committee. All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable Ethical Standards.

Considering a confidence level of 95% and confidence interval of 21 the number of patients in our study to achieve statistical significance was 22 as per the calculation by The Survey system[®] of Creative Research Systems. (<http://www.surveysystem.com/sscalc.htm#one>).

Volume 12 Issue 11, November 2023

www.ijsr.net

Licensed Under Creative Commons Attribution CC BY

30 patients newly detected with melasma and above 18 years of age and able to understand and provide informed consent were included in the study. Pregnant and lactating women were excluded from the study. After enrolment of patients in study, they were instructed to apply broad spectrum sunscreen with Sun Protection Factor of 30 on the face in morning and repeat application every 2-3 hrs along with the application of 2% hydroquinone cream to lesions on both sides of face at night for 10 weeks. After 2 weeks, one side of face was treated with low fluence 1064 nm Q-switch Nd:YAG Laser with spot size - 6mm, fluence : 1.5 – 1.7 J/cm² with two passes, for 4 sessions at 1 week interval. The other side of face (not treated with laser) was taken as control. The selection of side to be treated with laser was done by simple random sampling technique. Evaluation was made by standard digital clinical photographs taken at 0, 6 and 10 weeks. Evaluation of results of patient were made at 0, 6 and 10 weeks with Modified MASI score i.e.,mMSI (Modified Melasma severity index).

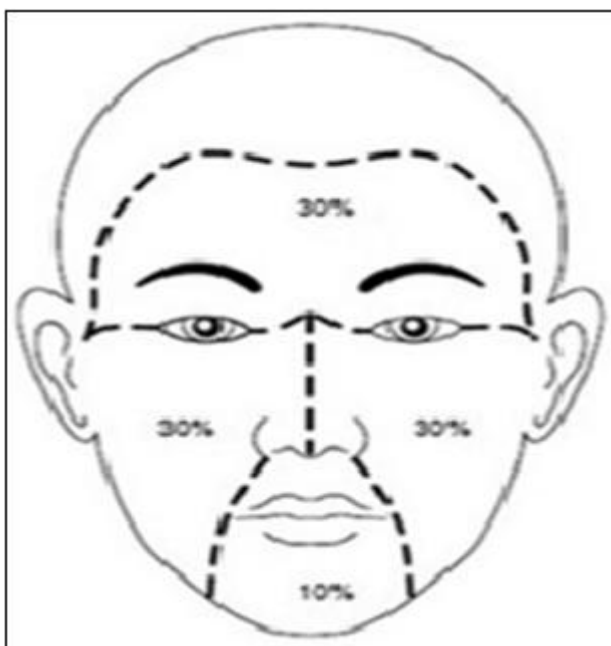
For modified MSI, the formula used is -
0.3

$A(f)D(f)+0.3A(Lm)D(Lm)+0.3A(Rm)D(Rm)+0.1A(c)D(c)$
where “A” stands for area of involvement, “D” darkness of pigmentation, “f” for forehead, “Lm” for left malar, “Rm” for right malar, and “c” for chin.

Darkness (D)	Area of involvement (A)
Score 0: No visible pigmentation	Score 0: no involvement
Score 1: Slight	Score 1: < 10 % area
Score 2: Mild	Score 2: 11-29%area
Score 3: Marked	Score 3: 30-39%area
Score 4: Severe	Score 4: 60-69%area
	Score 4: 70-89 %area
	Score 6: 90-100%area

Calculation of Area in mMSI Score

Forehead	30%
Right + Left Malar	30% + 30% = 60%
Chin	10%



Two blinded independent dermatologists of the Department and the treating dermatologist reviewed the clinical photographs to determine the degree of improvement and score the mMSI, as well as see for any complications.

Visual analogue scale (0-10) was used for assessment of degree of pain during laser procedure.

A Questionnaire with a 3-point grading system as ‘satisfied’, ‘somewhat satisfied’ and ‘dissatisfied’ was used to assess the patients’ subjective satisfaction with laser treatment.

Statistical Analysis

Quantitative data was presented with the help of Mean and Standard deviation. Comparison among the study groups was done with the help of unpaired t test as per results of normality test. Qualitative data was presented with the help of frequency and percentage table. Association among the study groups was assessed with the help of Fisher test, student ‘t’ test and Pearson’s Chi-Square test. ‘p’ value less than 0.05 was taken as significant.

2. Results

Patient demographics

Out of the 30 patients enrolled for the study, 22 patients followed up completely for 10 weeks of study while 8 patients were lost to follow up before completing 10 weeks. Hence data of 22 patients who completed treatment was used for analysis. The mean age of the patients was 34.73 years ± 8.05. The age wise distribution is shown in the Table 1. There was female preponderance of 86.4 %. The Male: Female ratio was 1: 6.3. The other patient demographics and clinical characteristics are given in Table 1.

Table 1: Baseline demographics and clinical characteristics

Variable	N	%	
Age	≤ 30 years	9	40.9
	31-40 years	5	22.7
	>40 years	8	36.4
Gender	Male n (%)	3	13.6
	Female (n) %	19	86.4
Occupation	Housewife	21	70
	Office Job	3	10
	Nursing staff	6	20
	Watchman	2	9.1
	Doctor	1	4.5
	Medical representative	1	4.5
	Student	1	4.5
	Indoor job	1	4.5
Family History	Yes	1	4.5
	No	21	95.5
Pregnancy Induced Melasma	Yes	11	50
	No	11	50
Sun Exposure	Yes	19	86.4
	No	3	13.6
Type of Melasma	Dermal	7	31.8
	Mixed	15	68.2
Laser Treated Side	Left	16	72.7
	Right	6	27.3

Subjective analysis: A higher number of patients from Combination Side reported improvement as compared to Topical Side (63.6% vs. 31.8%). The combination of low-fluence QS-Nd:YAG laser with topical 2% hydroquinone cream was more effective than the topical treatment alone as per Chi-Square test ($p=0.034$). (Fig 1 and 2)



0 weeks

6 weeks



10 weeks

Figure 1: Improvement on combination treatment side without post inflammatory hyperpigmentation.



6 weeks



10 weeks

Figure 2: Front view showing the difference between laser treated side (left) and topical control side (right)

Complications after Laser treatment: All the patients reported transient erythema after laser treatment (Fig 3) while 77.3% and 36.4% patients reported pain and post inflammatory hyperpigmentation (Fig 4) respectively. No patient had odema or hypopigmentation after laser treatment.



Figure 3: Erythema after laser treatment which subsided in 1-2 hours.



0 week



10 weeks

Figure 4: Both sides Post inflammatory hyper pigmentation observed at 10 weeks

31.8% patients were satisfied with laser treatment while 59.1% and 9.1% patients were dissatisfied and somewhat satisfied respectively with laser treatment. Out of the 14 patients who showed improvement on the combination treated side, 8 developed hyper pigmentation. 9.1% patients reported erythema after topical application.

Objective Analysis

In Combination Side, the mean Modified MASI Score i.e., Melasma severity index (mMSI) score at 0 weeks was 1.36 ± 0.51 which significantly decreased to 0.95 ± 0.45 ($p=0.001$) and 1.02 ± 0.50 ($p=0.009$) at 6 weeks and 10 weeks follow-up respectively. In Topical Side, the mean mMSI score at 0 weeks was 1.32 ± 0.53 which significantly decreased to 1.20 ± 0.53 ($p=0.036$) and 1.04 ± 0.65 ($p=0.042$) at 6 weeks and 10 weeks follow-up respectively, which showed the efficacy of both therapeutic regimens. However, the difference between the sides at 0 weeks (1.36 ± 0.51 vs. 1.32 ± 0.53 ; $p=0.796$), 6 weeks (0.95 ± 0.45 vs. 1.20 ± 0.53 ;

$p=0.106$) and 10 weeks (1.02 ± 0.50 vs. 1.04 ± 0.65 ; $p=0.909$) was comparable and statistically not significant as per Student t-test.

3. Discussion

Melasma is a very common skin disorder among Indians. It imposes a major psychological and emotional burden on patients and affects their quality of life. The treatment options are limited and show unsatisfactory results because of frequent incomplete remission, recurrence and risk of treatment related complications. In present study, the efficacy of QS Nd:YAG laser + topical hydroquinone cream is compared with topical hydroquinone cream alone.

In the present study, majority of the patients (40.9%) were in the age group of ≤ 30 years and the mean age of the patients was 34.73 ± 8.05 years. The average age of melasma patients was 33.45 years in a study by Achar A *et al.*³, compared to 42.3 years, reported in a study from Singapore. As average age group is 3rd decade, hormonal changes, pregnancy, oral contraceptives, outdoor work (sun exposure) play important role in this age group.

There was a female preponderance (86.4%) with the male: female ratio being 1: 6.3. This is similar to the data reported by Tehranchinia Z *et al.*⁴ and Zamanian A *et al.*⁵ Female preponderance is seen because of hormonal changes during menstrual cycle, pregnancy and menopause, intake of oral contraceptive pills. The association of use of cosmetics with melasma was reported by Grime PE.⁶ Women are likely to be more conscious and apprehensive about their skin condition and it may also contribute enhanced percent of females seeking treatment.

In our study, 45.5% patients were housewives while 18.2% patients had office job. 9.1% patients each were from nursing staff and watchman while 4.5% patient each was doctor, medical representative, student and had indoor job. This is consistent with the study of Tehranchinia Z *et al.*⁴ In general, outdoor working class such as farmers, labourers and persons pursuing recreational activities like playing cricket or swimming are exposed to sun for prolonged period and prone to development of melasma whereas in our study most of the housewives developed melasma. In India, the sun is bright for most of the year. Housewives are greatly exposed to the sun during grocery shopping and dropping their children to school, which is one of the major etiological factors of melisma.⁷

In our study only 4.5% patients had a family history of melasma, whereas Tehranchinia Z *et al.*⁴ and Achar A *et al.*³ reported a family history of about 50 % and 33 % respectively.

In the present study 50% patients had pregnancy induced melasma. Melasma usually begins in 3rd trimester of gestation and regresses in postpartum. However, the persistent type of melasma may persist in 10% of the patients whereas the transient type disappears within one year of cessation of hormonal stimuli like pregnancy or oral contraceptive pills.⁸

Exposure to the sun triggered melasma in 86.4% patients in our study. UV Radiation is one of the primary culprits in pathogenesis of melasma, highlighting the role of sun-avoidance and sun protection in the management of melasma. In Indian scenario, sunscreens are used less frequently and, in less quantity, due to cost and compliance. Broad spectrum UVA, UVB protective sunscreen with physical block like Zinc oxide or titanium oxide is the mainstay of treatment along with optimum use -restricting outdoor activities during peak hours of ultraviolet exposure, using umbrellas, scarves, wearing protective clothing such as palluos worn by women in India.

In present study 31.8% patients had dermal melasma while 68.2% patients had mixed melasma but no patient had pure epidermal melasma. Epidermal melasma which appears light brown improves with topical therapy whereas dermal melasma appears dark brown or bluish is recurrent, recalcitrant and refractory where lasers can be a promising modality of treatment.

The combination of low-fluence QS-Nd:YAG laser with topical 2% hydroquinone cream was significantly more effective than the topical treatment alone as per Chi-Square test ($p=0.034$). Patient's photographic evidence and patient's satisfaction score showed improvement at 6th week on combination treated side with significant decrease in pigmentation ($p<0.05$) which is statistically significant. Wattanakrai P *et al.*⁹ noted similar observations in their study.

The side effects of laser treatment observed in our study are comparable to the studies of Tehranchinia Z *et al.*⁴, Wattanakrai P *et al.*⁹ and Zamanian A *et al.*⁵

In the present study only 31.8% were satisfied with laser treatment while 59.1% were dissatisfied and 9.1% patients were somewhat satisfied with laser treatment. This is concordant to the studies of Tehranchinia Z *et al.*⁴ and Wattanakrai P *et al.*⁹ While undergoing laser treatment patients feel that laser will work as a magic wand since they have spent a lot, their expectations are always high and they expect that results will be excellent. So, the patient should be counselled about the results which may be subtle and unpredictable and vary from patient to patient.

In the present study, the mean of Modified MASI Score i.e., Melasma severity index (mMSI) score decreased at 6 weeks and 10 weeks in the topical side only, whereas in the combination side, the mMSI decreased at 6 weeks from the baseline but again increased at 10 weeks. Majority of patients showed improvement as long as they were on laser treatment till 6th week. Between the 6th to 10th weeks hyperpigmentation developed and there was no much difference between the two groups. Also, the difference between the sides at 0 weeks, 6 weeks and 10 weeks ($p=0.909$) was comparable and statistically not significant as per Student t-test. Lasers, although showing initial promise, could not produce sustained results and produced side effects warranting their judicious use, hence the results have to be interpreted cautiously.

4. Conclusion

In the present study the following conclusions were noted:

- 1) Topical hydroquinone used alone is not very effective in treatment of melasma.
- 2) The combination of low-fluence QS-Nd:YAG laser with topical 2% hydroquinone cream is more effective than the topical treatment alone in treatment of dermal and mixed melasma at the end of 6 weeks. However, the combination doesn't show sustained results in the long term in some patients.
- 3) The side effects of combination treatment (laser + topicals) for melasma were more than topical hydroquinone alone.

Source(s) of support: None

Presentation at a meeting: No

Conflicting Interest: None

References

- [1] Kim T, Cho SB, Oh SH. Punctate leucoderma after 1064 nm Q-switched neodymium-doped yttrium aluminum garnet lasers with low-fluence therapy: is it melanocytopenic or melanopenic? *Dermatol Surg.* 2010; 36: 1790-1797
- [2] Na SY, Cho S, Lee JH. Better clinical results with long term benefits in melasma patients. *J Dermatolog Treat.* 2013 Apr; 24(2):112-8.
- [3] Achar A, Rathi SK. Melasma: a clinico-epidemiological study of 312 cases. *Indian J Dermatol.* 2011;56(4):380–382. doi: 10.4103/0019-5154.84722
- [4] Tehranchinia Z, Saghi B, Rahimi H. Evaluation of Therapeutic Efficacy and Safety of Tranexamic Acid Local Infiltration in Combination with Topical 4% Hydroquinone Cream Compared to Topical 4% Hydroquinone Cream Alone in Patients with Melasma: A Split-Face Study. *Dermatol Res Pract.*2018;2018: 8350317. Published online 2018 Jul 2 doi: 10.1155/2018/8350317
- [5] Zamanian A, Behrangi E, Ghafarpour GH et al. Effect of Hydroquinone Plus Neodymium-Doped Yttrium Aluminium Garnet Laser With and Without CO2 Fractional Laser on Resistant Dermal Melasma, *J Skin Stem Cell.* 2015 ;2(2):e30290.
- [6] Grimes PE. Melasma. Etiologic and therapeutic considerations. *Arch Dermatol.* 1995;131(12):1453-7.
- [7] Yalamanchili, R; Shastry, V ;Betkerur, J. Clinico-epidemiological Study and Quality of Life Assessment in Melasma. *Indian J Dermatol* 2015; 60 : 519.
- [8] Senthilkumaran M, Kanwar A. Pigmentary Changes in Pregnancy. In Lahiri K, Chatterjee M, Sarkar R. *Pigmentary Disorders- A Comprehensive Compendium.* 1st ed. New Delhi: Jaypee Brothers Medical Publishers; 2014. p. 210-274.
- [9] Wattanakrai P, Mornchan R, Eimpunth S. Low-fluence Qswitched neodymium-doped yttrium aluminum garnet (1,064 nm) laser for the treatment of facial melasma in Asians. *Dermatol Surg.* 2010, 36:76–87.