Comparison of Q-Switched Nd:YAG LASER with 10% Azelaic Acid versus Fractional CO2 LASER with 10% Azelaic Acid in the treatment of Post Inflammatory Hyperpigmentation secondary to Acne

Sumedha Tirthani[1], Rajashekar Talari Srinivas[1], Suresh Kumar Kuppuswamy[1], Hanumanthayya Keloji[1], Vaishnavi Bindumalyam Venkatesh[1], Madhu Kiran Chandrashekar[1]

[1]*Department of Dermatology Venereology and Leprosy, Sri Devaraj Urs Medical College, Kolar, Karnataka,* India.

Corresponding Author: Dr. Rajashekar Talari Srinivas
*Department of Dermatology Venereology and Leprosy, Sri Devaraj Urs Medical College, Kolar, Karnataka, India.Phone: (+91) 9448316136, Email: yeshits@rediffmail.com

KEYWORDS
Post-inflammatory hyperpigmentation, Acne vulgaris, Q-switched Nd:YAGlaser, Fractional CO2 laser, Azelaic acid

ABSTRACT

Background:
Post inflammatory hyperpigmentation (PIH) secondary to acne is a common undesirable sequela following acne that leads to psychological distress and a sense of incomplete treatment among the patients with acne. Few studies have been done in regard to address this condition, and no definite treatment or clear ranking of treatment modalities is available as of yet.

Aims:
The aim of our study was to assess and compare the efficacy and safety of 1,064-nm Q-switched neodymium-doped yttrium aluminum garnet (QSNY) laser with 10% azelaic acid versus Fractional carbon dioxide (FCO2) laser with 10% azelaic acid in the treatment of post acne pigmentation.

Materials and Methods:
Seventy patients with PIH secondary to acne were recruited in this study. The patients were randomized into two groups, Group A and Group B, of thirty-five patients each. Patients in group A underwent QSNY laser, while Group B received FCO2 laser. 10% azelaic acid cream was administered to both groups. Both groups received a total of 5 treatment sessions, with 3 weeks interval between each setting. The efficacy and safety of both modalities were assessed using the quartile grading score(QGS), post acne hyperpigmentationindex(PAHPI), patient satisfaction score, and documentation of adverse effects.

Results:
At the end of five sessions, significant improvement in QGS, PAHPI and patient satisfaction ($P < 0.001$, respectively) was seen in both groups. The mean PAHPI significantly reduced after the third setting and was followed by drastic reduction in the following settings. However, significantly superior results were noted in Group A with respect to all assessments. Side effects noted were mild and transient, except two patients of Group B who developed further pigmentation over the treatment areas.

Conclusion:
This study shows that both QSNY laser and FCO2 laser can be used to treat post-acne pigmentation; however, QSNY laser should be preferred with respect to efficacy and safety, especially in the Indian population, owing to the higher risk of pigmentation following FCO2 laser.

INTRODUCTION

Postinflammatory hyperpigmentation (PIH) is a typical sequela seen in the Indian population following affliction by acne. Patients may experience significant psychological effects from PIH resulting in decreased quality of life

There is a rising concern regarding its treatment among the patients that initially present with acne but remain dissatisfied if the hyperpigmentation remains unaddressed.[1]

Due to higher epidermal melanin content in patients with darker phenotypes, treatment of post-acne hyperpigmentation can be achallenge. Numerous approaches to treating PIH have been proposed, such as topical keratolytics, retinoids, corticosteroids, and depigmenting agents, chemical peels; and several types of lasers.[2] Nevertheless, there is no clear ranking of these therapies or a proven consistently effective modality according to patient satisfaction and clinical effectiveness. Only a few studies on the treatment of acne-

induced PIH have been published to date. Due to paucity of literature in this regard, and with technological advances in aesthetic medicine, an updated quantitative comparative study is needed to aid in clinical decision-making.

Low-fluence Q-switched Nd:YAG laser (LFQSNY) selectively destroys the melanin in melanophores, leaving thecells containing melanin undamaged. This results in safe depigmentation of pigmented spots. Furthermore, one of the main benefits is that since the epidermis is left intact, there is no downtime that interferes with patients' normal life.[1]

Fractional carbon dioxide (CO2) laser can be a very effective tool in PIH treatment by employing conservative laser settings and offering appropriate post-treatment care.[3] It creates micro-thermal zones (MTZs) that serve as a path for transepidermal elimination of melanin.[4] Fractional CO2 laser also enhances the penetration of topical treatments like azelaic acid, further boosting the treatment outcome in PIH cases.[3]

Azelaic acid (AZA) is a dicarboxylic acid derived from Pityrosporumovale. It acts as a topical depigmenting agent by affecting heavily pigmented melanocytes.[5]

The aim of this study is to evaluate and compare the efficacy of Q-Switched Nd:YAG LASER with 10% Azelaic Acid versus Fractional CO2 LASER with 10% azelaic Acid in the treatment of post inflammatory hyperpigmentation secondary to acne.

MATERIALS AND METHODS

Study Design

This study is a randomised controlled trial (RCT) hospital-based study, conducted in outpatient clinic of Dermatology, Venereology and Leprosy in R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar from May 2024 to October 2024 in patients with post inflammatory hyperpigmentation secondary to acne. The study protocol was approved by the institutional ethical committee. An informed consent for treatment, photography and necessity to follow up was taken before enrolment.

Patient characteristics

70 patients presenting with acne induced PIH, who had not received treatment for the same in the past 6 months were included. Exclusion criteria were patients on systemic isotretinoin or corticosteroids or photosensitive drugs, patients with a history of keloid formation, presenting with any connective tissue disease or systemic illness, immunocompromised patients, pregnant or lactating women and those not willing for study.

Patients were randomly divided into two groups, of 35 patients each, by computer generated block randomisation from www.randomization.com.

Treatment Protocols

Each patient received a total of 5 treatments, with the interval gap of 3 weeks, in each group.

For both groups, pre-procedural: A topical anaesthetic, containing a mixture of lidocaine- 2.5% w/w + prilocaine-2.5% w/w in a cream base was applied under occlusion for 1 hour on the treatment area. After satisfactory anaesthesia was achieved, the treatment area was cleaned with a mild cleanser.

Group A: Q-Switched Nd:YAG LASER with 10% Azelaic Acid

Eyes were protected with eye shields. 1,064 Q-switched Nd:Yag laser using parameters: 1.5-mm spot size, 2-Hz repetition rate, pulse width of 6 ns, and a fluence of 450 mJ was delivered, until target therapeutic appearance (endpoint) of perilesional erythema and fine hair whitening was achieved. 5 treatment sessions were given to each patient at 3-week intervals.

Group B: Fractional CO2 laser with 10% Azelaic Acid

Eyes were protected with eye shields. Fractional CO2 laser was then delivered after adjusting area of scanner according to the size of striae. One pass was administered per treatment site without overlapping. Fractional CO2 laser was performed using Dermaindia Futura RF 50 RF Excited CO2 Laser, using parameters as follows:

Power 20 W, Duration 1ms, distance 0.8, point energy 30mJ/cm2.

All Patients received Fractional CO2 laser for 5 settings with an interval of 3 weeks between each setting.

For both groups, post-procedural: Topical 10% Azelaic acid gel was applied immediately to the irradiated areas and continued once a day together with sunblock creams twice a day.

Clinical Assessment of improvement
Assessment of efficacy and safety profile in both groups was done based on:
a) Quartile Grading Score
b) Post-AV hyperpigmentation index (PAHPI)
c) Assessment of patient satisfaction
d) Adverse effects assessment

- Participants underwent serial photography, keeping lighting and positioning identical, using iPhone 15 Pro, at baseline, before every setting and 3 months after last setting. The serial photographs were assessed independently by a blinded third observer at each sitting. A third observer graded the efficacy of the treatment modality based on the standardised digital photographs, by using a quartilegrading scale as follows;

a. 1 = poor (0–25% improvement)
b. 2 = mild (26–50% improvement)
c. 3 = moderate (51–75% improvement)
d. 4 = excellent (>76% improvement)

- Post-AV hyperpigmentation index (PAHPI) (Table 1)

Table 1: Post AV hyperpigmentation Index[6]

Weighted score (S)	**Size of median lesion**
2	<3mm
4	3-6mm
6	7-10mm
8	>10mm
Weighted score (I)	**Intensity of median lesion**
3	Slightly darker than surrounding skin
6	Moderately darker than surrounding skin
9	Significantly darker than surrounding skin
Weighted score (N)	**No. of lesions**
1	1–15
2	16–30
3	31–45
4	46–60
5	>60
Total postacne hyperpigmentation index = S + I + N; score range: 6–22.	

• Patient satisfaction was evaluated for degree of improvement as 'Poor', 'Fair', 'Good', 'Excellent'.

• Patients were also evaluated for the side effects, including pain, itching, erythema, and hyperpigmentation.

Statistical analysis

Data was entered into a Microsoft Excel Data Sheet, analysed using SPSS 27 version software. Categorical data was represented as frequencies and percentage. Continuous data was represented as mean and standard deviation or median and interquartile range. Paired t-test test was used as test of significance to compare the difference in clinical parameters across three groups. Chi square test was used to compare the side effects across three groups.

P value of <0.05 was considered as statistically significant.

RESULTS

A total of 70 patients participated in the study, 35 patients in each group, treated with Q-switched Nd:YAG Laser and Fractional CO2 LASER, respectively, followed by application of 10% azelaic Acid cream.

In our study, there were 57 female (81.4%) and 13 male (18.6%) patients, with a mean age of 24 years (age range of 18-29 years).

Efficacy evaluation

Quartile Grading Score by third blinded observer

Table 2: Comparison of Quartile Grading Score at the end of 5 treatment sessions between two groups

QGS Score	Group A	Group B	Total
1- Poor	0	2(5.7)	2(2.8)
2- Mild	5(14.2)	10(28.5)	
3- Moderate	19(54.2)		
4- Excellent	11(31.4)		
Total	35(100)	35(100)	

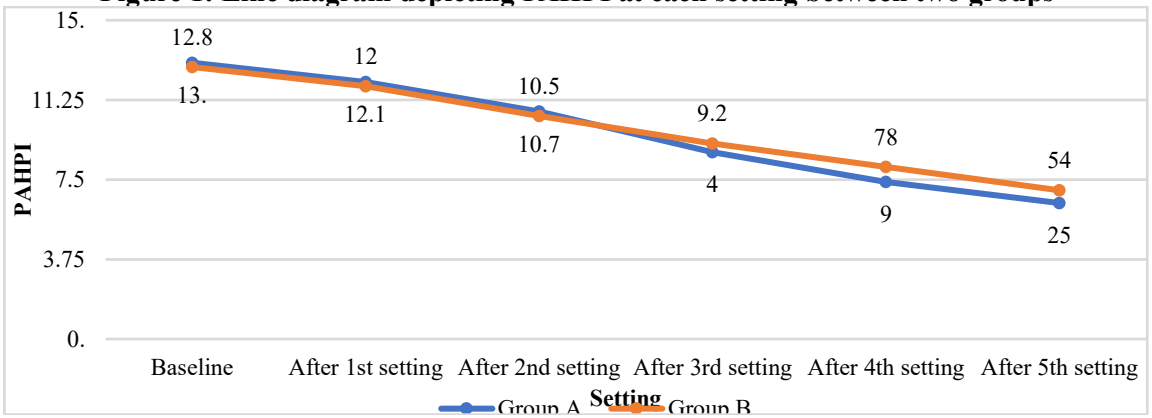
A significant improvement in Quartile Grading Score was seen in both the groups.

The study shows that Quartile grading score was higher in Group A than in Group B with significant difference (p value<0.05).

85.6% patients in Group A showed 'moderate' to 'excellent' improvement while 14.2% patients had only 'mild' improvement. No patient in this group reported 'poor' result. In Group B, 65.7% patient had 'moderate' to 'excellent' improvement, 28.5% had 'mild' and 2(5.7%) patients showed 'poor' results. (Table 2)

Post AV Hyperpigmentation Index (PAHPI)

Figure 1: Line diagram depicting PAHPI at each setting between two groups



There was a statistically significant reduction in Post AV Hyperpigmentation Index (PAHPI) in both groups after 3 treatment sessions which improved further in following sessions. At completion of 5 sessions the

mean PAHPI reduced by 50.8%, from 13 to 6.4 in Group A. While in Group B, a reduction of, 45.3%, from 12.8 to 7 was noted. (Figure 1)

Patient Satisfaction

Table 3: Comparison of Patient satisfaction score between two groups

	Group A	Group B	Total
Poor	1(2.8)		4(5.7)
Fair	7(20)		
Good	18(51.4)		
Excellent	9(25.7)		
Total	35(100)		

In Group A, 27 (77.1%) patients reported 'good' to 'excellent' improvement, 7(20%) had 'fair' improvement while 1 (2.8%) patient had 'poor' improvement. 17(48.5%) patients reported 'good' to 'excellent' improvement in Group B, while 15(42.8%) had 'fair', and 3(8.5%) 'poor' improvement. (Table 3)

Side effects

Table 4: Comparison of Side effects between two groups

Side effects	Group A (n=35)	Group B (n=35)
Erythema	9(25.7)	
Pain	2(5.7)	10(28)
Itching	2(5.7)	
Transient pigmentation	1(2.8)	
Worsening of Hyperpigmentation	0(0)	2

Erythema, pain, itching, hypopigmentation and accentuation of hyperpigmentation were the sides effects noted, which were more in Group B (Table 4). Majority of the side effects seen like erythema, pain, itching were minimal and transient, which resolved spontaneously after a few days. 2(5.7%) patients in Group B had worsening of hyperpigmentation in the treated site.

Group A: Q-switched Nd:YAG Laser with 10% Azelaic Acid gel

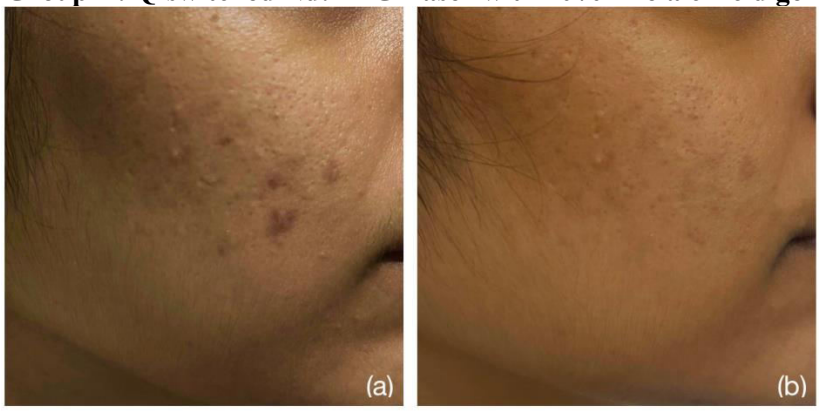


Figure 2:

(a) Baseline presentation of a patient with Post acne hyperpigmentation
(b) After 5 sessions of QSNY laser with 10% Azelaic acid - significant reduction in post acne hyperpigmentation

Figure 3:

(a) Baseline presentation of a patient with Post acne hyperpigmentation
(b) After 5 sessions of QSNY laser with 10% Azelaic acid - significant reduction in post acne hyperpigmentation

Group B: Fractional CO2 Laser with 10% Azelaic Acid gel

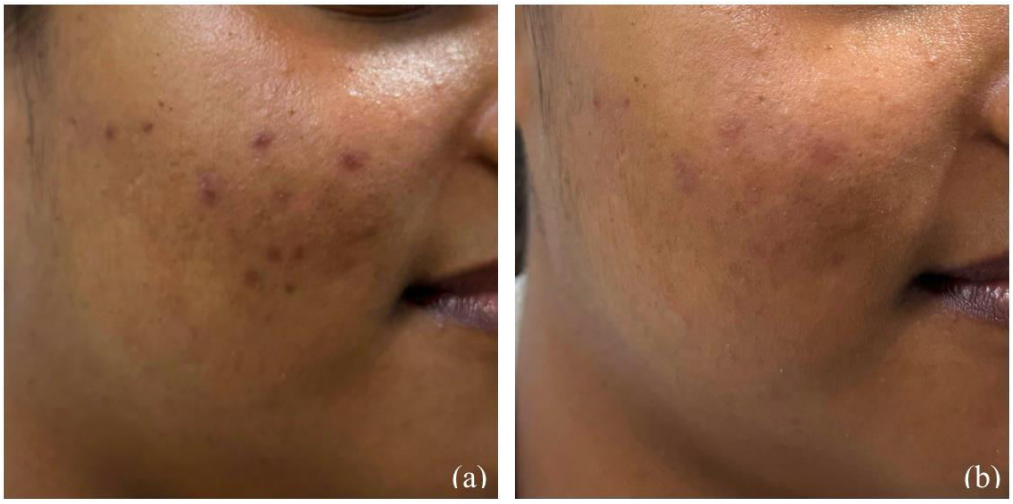


Figure 4:

a) Baseline presentation of a patient with Post acne hyperpigmentation
b) After 5 sessions of Fractional CO2 Laser with 10% Azelaic acid - good reduction in post acne hyperpigmentation

Figure 5:

a) Baseline presentation of a patient with Post acne hyperpigmentation
b) After 5 sessions of Fractional CO2 Laser with 10% Azelaic acid - good reduction in post acne hyperpigmentation

DISCUSSION

Post-inflammatory hyperpigmentation (PIH) is a consequence of various inflammatory skin conditions. Among these conditions, acne stands out as the most common trigger for PIH.

A combination of factors plays a role in its development, which makes PIH a common and challenging consequence of acne.

This study aimed to compare the efficacy of Q-Switched Nd:YAG Laser combined with 10% azelaic acid versus Fractional CO2 Laser with 10% azelaic acid in treating post-inflammatory hyperpigmentation (PIH) secondary to acne. Both modalities were demonstrated to be effective in improving post inflammatory hyperpigmentation. However,Nd:YAG laser with 10% azelaic acid appeared to be superior in improving PIH toward the end of study in contrast to the other arm.

In our study, a higher proportion of female patients was noted, with a Male to Female ratio of 1:4.3.

The age of patients enrolled in our study ranged from 18 to 29 years with a mean of 24 years. This is in accordance with the study done by Zawar et al[7], where similar gender and age ratios were seen. The female preponderance in early adults with PIH secondary to acne may be due to higher prevalence of acne in this age group, and also signifies the higher cosmetic concern in this group.

On evaluation of Quartile Grading Score in our study, 85.6% of patients in Group A achieved moderate to excellent improvement, compared to 65.7% in Group B.

The study by Cho et al[8] reported 55.6% patients with moderate to marked improvement with QS Nd:YAG Laser. Katz et al[3] and Oram et al[9] have reported case reports with successful treatment of PIH with Fractional thermolysis.

The higher efficacy observed in the Q-Switched Nd:YAG Laser group may be attributed to its mechanism of action, which targets melanin deposits more directly through high-energy pulses that fragment pigment particles.[1] This can lead to faster clearance of pigmented lesions compared to the more superficial skin remodeling effects seen with Fractional CO2 LASER.

The higher Quartile Grading Score in Group A indicates that Q-Switched Nd:YAG Laser gives not only a greater reduction in pigmentation, but also a more favourable overall treatment outcome, making it a valuable option in clinical practice for treating PIH.

In our study, the mean Post AV hyperpigmentation Index (PAHPI) at baseline was 13 in Group A and 12.8 in Group B. This is in accordance with the by Shucheng H[5] where baseline PAHPI was 13 in a group of patients treated with 15% Azelaic Acid gel. In a study by How K et al[10], the mean baseline PAHPI was 10 and 11 for two groups treated with peels for treatment of Postacne hyperpigmentation.

Although both groups demonstrated significant improvement, the Q-Switched Nd:YAG Laser group exhibited a higher mean reduction in hyperpigmentation.

Group A, receiving Q-Switched Nd:YAG LASER with 10% azelaic acid gel, showed a mean reduction of 50.8%, while Group B, treated with Fractional CO2 LASER with 10% azelaic acid gel, experienced a 45.3% reduction, at the end of 5 treatment sessions. These results are comparable with the studies by Kim et al[1] where good response was seen with QSNY in 65% patients, and Tawfic et al[11] where 34.5% improvement in PAHPI was noted with FCO2 Laser.

The results in our study indicate that both modalities significantly reduced the Post Acne Hyperpigmentation Index (PAHPI) after three treatment sessions, with further improvement observed after five sessions. The reduction in PAHPI highlights the effectiveness of both Q-Switched Nd:YAG Laser and Fractional CO2 LASER treatments in managing PIH.

The heat generated by the Fractional CO2 laser helps to break down excess melanin in the skin, which is responsible for the dark patches associated with PIH. This can lead to a gradual lightening of the hyperpigmented areas. By removing the outer layers of damaged skin, the FCO2 laser helps to exfoliate the skin and improve its texture. This resurfacing effect can lead to a more even skin tone and reduction in the visibility of PIH.[12]

Regarding the Patient satisfaction, the distribution of patient-reported outcomes further supports this conclusion. In Group A, a significant majority (77.1%) reported 'good' to 'excellent' improvement, contrasting with only 48.5% in Group B. This is in accordance with the study by Zawar et al[7], where 76.7% patients noticed good to excellent improvement with QS Nd:YAG Laser. In a study by Tawfic et al[11], 73% patients with PIH treated with Fractional CO2 LASER reported excellent response.

This suggests that patients treated with Q-Switched Nd:YAG Laser are more likely to perceive their results positively, which is an important consideration in the context of treatment satisfaction and compliance.

Side effects such as erythema, pain and itching occurred in both groups, but were few and transient in nature. QSNY laser is often associated with confetti-like hypopigmentation or punctateleukoderma. In our study, one patient developed hypopigmented macules which resolved spontaneously. Similar transient hypopigmentation was seen in a patient in the study done by Zawar et al[7].

In our study, two cases treated with FCO2 laser developed further pigmentation over treated areas, which persisted in two months of follow up. Hyperpigmentation with FCO2 laser is more commonly reported in Fitzpatrick phototypes IV and V and results from dermal inflammation. However, most cases resolve over a few months.[13]

Limitations

There was no long term follow up, as patients discontinued visits after resolution of symptoms. Therefore, further studies with long term follow-ups to assess permanence of effects with these treatment modalities in PIH secondary to acne, are required.

CONCLUSION

In conclusion, this study highlights the superior efficacy of Q-Switched Nd:YAG Laser with 10% azelaic acid over Fractional CO2 Laser with the same adjunctive treatment in reducing post-inflammatory hyperpigmentation secondary to acne. The significant improvements in Quartile Grading Scores, PAHPI and patient-reported outcomes reinforce the utility of Q-Switched Nd:YAG LASER as a preferred option for clinicians treating PIH.

DECLARATIONS

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Conflicts of interest: None
Ethical Approval: Received (SDUAHER/KLR/R&D/CEC/S/PG/14/2024-25)

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