

Comparison of Efficacy and Safety of Q-Switched Nd:Yag (532 nm) Laser Versus Cryotherapy in the Treatment of Solar Lentigines in Fitzpatrick Skin Type-Iv

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ABSTRACT

Background: Solar lentigines are brown macules appearing after excessive sun exposure with profound effect on the quality of life of patients.

Objectives: To compare the efficacy and safety of Q-switched Nd:YAG laser (532nm) and cryotherapy in the treatment of solar lentigines in Fitzpatrick skin type-IV.

Materials & Methods: It was a comparative interventional study carried out in Dermatology Department, KEMU/Mayo Hospital, Lahore from 18th December 2014 to 17th December 2015. 40 Patients with solar lentigines were randomly divided into two groups. Group A patients were treated with Q-switched Nd:YAG (532nm) laser and group B patients with cryotherapy. The new pigmentation severity index (PSI) score was calculated before and after the treatment to assess the treatment's efficacy. Safety was measured by recording number of side effects by each modality. The data were collected and analyzed.

Results: Out of 40 patients enrolled in the study, females (95%) out-numbered the males (5%). The percentage decrease in PSI revealed 55% (n=11) patients in category of clear improvement (91-100%) in Group A treated by Q-switched Nd:YAG (532) laser while in Group B treated by cryotherapy 5% (n=1) patients fell in clear category (91-100%), showing superior results with Q-switched laser. Both modalities showed significant reduction in lentigines and PSI score with minimal side effects with no statistical significance between the two groups.

Conclusion: It is concluded from our study that Q-switched Nd:YAG laser 532 nm is more efficacious and safe than cryotherapy while treating solar lentigines among skin type IV.

Keywords: Lentigines, Q-switched laser, Cryotherapy

INTRODUCTION

Lentigines characteristically appear as brown pigmented macules which become visible after acute or chronic sun exposure [1]. These are commonly seen in fair-skinned people [1]. The dorsal surfaces of the hands as well as the face are the common sites. They are further classified into simple lentigines, solar or actinic lentigines, ink spot and PUVA lentigines. The persistence of lentigo without UV stimulation clinically distinguishes it from freckles. The increase in melanocyte at the dermo-epidermal junction in a linear fashion is the histological characteristic of lentigo.

To improve pigmentary changes caused by UV light following therapeutic methods are used: topical agents and procedural remedies. Topical agents are hydroquinones, retinoids and combination of both modalities, while

procedural therapies include microdermabrasion, chemical peels, cryotherapy, intense pulsed light (IPL) and Q-switched (532nm) lasers [2].

Q-switched Nd:YAG (532nm) laser emits monochromatic

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light in the spectrum of 532 nm and has a proven efficacy in photodamaged pigmented lesions like solar lentigines with melanin as chromophore [3]. Q-switched technology spares the surrounding skin by delivering a flat top beam to target tissue with ultimate perfection. It is due to this Q-switched technology that the principle of selective photothermolysis is used on pigmented lesions, achieving the right clinical results without damaging the surrounding area [3].

In cryotherapy, a cold liquid is used to freeze leading to destruction of cells of the skin [4]. The procedure is considered as a standard therapy in the treatment of lentigines [1]. Cryotherapy can be used to destroy a variety of skin lesions such as lentigines, warts and actinic keratoses, and malignant lesions such as early basal cell and squamous cell carcinomas. The aim of cryotherapy is to freeze and destroy by coagulative necrosis targeting cutaneous lesions while preserving the surrounding skin [4].

In a study by Goldust et al. [5], cryotherapy was compared with 40% TCA chemical peel in solar lentigines and the result showed cryotherapy to be superior. Seirafi et al. [6] found pulsed dye laser therapy to be superior to cryotherapy with less side effects in dark skinned individuals. In a study by Todd et al. [7] Q-switched Nd:YAG (532 nm) laser was found to be more effective than cryotherapy in patients of solar lentigines. Another study conducted by Lee et al. [8] showed good results with Q-switched Nd:YAG (1064 nm) laser in facial lentiginosis. A study conducted in Pakistan by Rashid et al. [9] the Quasi-continuous Nd:YAG (532nm) laser found to be effective in the treatment of freckles and lentigines in Fitzpatrick skin type IV. There is need to compare cryotherapy or laser for treating solar lentigines for outcome. The objectives of this study were compare the efficacy and safety of Q-switched Nd:YAG 532nm laser and cryotherapy in the treatment of solar lentigines. It was thought to be helpful in improving patient care and quality of life in patients with solar lentigines in our skin types.

METHODS

It was a comparative interventional study carried out in Dermatology Department Unit-II, KEMU/Mayo Hospital, Lahore, outpatient department, 18th December, 2014 to 17th December, 2015. Sample size was 40 cases (20 cases in each group), using 21% clearance rate with cryotherapy and 47% with Q-switched Nd:YAG 532 nm laser at 6 weeks [7]. using 95% confidence level, 5% level of significance and 80% power of study. Non-probability purposive sampling for patient selection and simple random sampling for group making by balloting was done.

Patients with solar lentigines on exposed parts (face and hands) of either gender with ages between 15-60 years old with Fitzpatrick skin types-IV were included in the study.

Pregnant or lactating females, patients with history of vitiligo, acne, herpes simplex, keloid, those who had taken any topical treatment in previous one month and laser or other physical therapy during last two months for lentigines and patients who had used systemic retinoids within previous 6 months were excluded. Patients with known photosensitivity or taking photosensitizing medications, with recent (4 weeks) sun tanning and history of intolerance to cold, urticaria due to cold, Raynaud's disease and allergy to cryotherapy were also not taken.

After approval from the ethical committee, forty patients with Fitzpatrick skin type-IV were enrolled in the study. Written informed consent was taken from the patients before enrollment. Detailed history and clinical examination was recorded on a predesigned proforma on the first visit. Twenty patients in group A were treated with Q-switched Nd:YAG laser (532 nm) and twenty patients in group B were treated with cryotherapy. Maximum of six treatment sessions were given at four weeks interval or till clearance within this period whichever was achieved first. Photographs of the patient were taken before and at each follow-up visit. Q-switched laser treatment parameters for this study were 532 nm wavelength, low fluence with 2-4 mm spot size, frequency of 1 Hz and pulse width of 10 ns from a distance of 4-5 cm. Machine specifications were as follows: Manufacturers: Weifang Huamei Electronics Co. Ltd., Model: HM-LT, Laser type : Q-switched Nd:YAG laser; Laser wavelength: 1064 nm & 532 nm. Laser personnel used protective goggles during treatment. For group B, cryotherapy was done with liquid nitrogen using cryospray (Premier Nitrosray Plus®-USA). The cryospray was applied for 3-5 s on each lesion from a distance of 1-1.5 cm with one freeze-thaw cycle. No anesthesia either local or systemic was used for both procedures. Patients were advised to avoid sun exposure and use sunblock cream of SPF 60 after treatment. Patients were followed up monthly for six months during treatment to record the efficacy and side effects of the treatment. The treatment response was assessed by comparing the new pigmentation area and severity index (PSI) on each visit.

Efficacy was measured by reduction in pigmentation at the end of 6 months of treatment. Treatment was said to be effective when the reduction in mean PSI score at the end of 6 months of treatment was >50%, and was said to be ineffective with mean score <50%.

Safety of either procedure was defined when it had no or minimal side effects. The treatment modality with minimum side effects like erythema, pain, hyperpigmentation or hypopigmentation, blistering, urticaria, acneiform eruption considered as safe and the procedure causing scarring considered as unsafe. Side effects were classified as mild, moderate and severe and calculated on the basis of number of patients having these side effects. Safety was measured by

recording number of side effects by each modality. The patients were further followed up for four weeks after completion of treatment to assess response and persistence of side effects. Data were collected on a well-designed proforma.

Assessment of the patient was clinical carried out by two qualified dermatologists as independent observers. Response of the patient to treatment (Q-switched laser 532 nm and cryotherapy) was graded by comparing the new pigmentation area and severity index (PSI) as follows:

New Pigmentation area and Severity index (PSI) [10]
 Area (the extent of pigmented lesions)
 0 = no involvement, 1 = less than 10% involvement, 2 = 10-29%, 3 = 30-49%, 4 = 50-69%, 5 = 70-89%, 6 = 90-100%
 Darkness
 0 = absent, 1 = slight, 2 = mild, 3 = marked, 4 = severe
 Density (number of pigmented lesions per unit area)
 0 = minimal, 1 = slight, 2 = mild, 3 = marked, 4 = maximum
 The values are added up to obtain PSI Score
 PSI Score (0-48) = (Darkness+Density) x Area
 Improvement rate at the time of evaluation (%) =
 PSI pretreatment - PSI posttreatment/PSI pretreatment x 100
 The criteria of assessment were defined as follows: Poor = 0%-25%, Fair = 26%-50%, Good = 51%-75%, Excellent = 76%-90%, Clear = 91%-100%.

Collected information was transferred to SPSS version 17.0 computer software and analyzed accordingly. Output was presented in the form of graphs and frequency tables. Mean, median and standard deviation were used to represent the quantitative variables and percentages for qualitative variables. Efficacy and safety were compared by using Wilcoxon-signed-ranks test and Chi-square test. Crohnback alpha was used to confirm inter-rater reliability of assessment. A p-value of ≤ 0.05 was considered as significant.

RESULTS

A total of 40 cases (20 in each group), out of which 38 were females with only 2 males completed the study. Mean age of the patients enrolled was 23.4 years in Group A and 25.20 years in Group B (Table 1), with mostly unmarried subjects in Group A and equal marital status in Group B. Regarding occupation in both groups, most of the subjects were students (48%), and rest of them being housewives, medical personnel and others. Mean facial area of involvement of the affected site in both groups was around 50% with mean of 6.3 years as duration of disease (Table 1).

Table 1. Comparison Of Age, Gender, Marital Status, Duration And Area (%) Involved In Both Study Groups.

	Group A Laser Treatment Group	Group B Cryotherapy Treatment Group	P value
Age (years)			
Mean	23.35 ± 7.58	25.20 ± 8.09	0.46
Minimum	12.00	14.00	
Maximum	46.00	50.00	
Gender			
Male	2	0	
Female	18	20	
Marital Status			
Married	5	10	
Unmarried	15	10	
Duration of disease (years)			
Mean	6.55 ± 5.11	5.95 ± 4.81	0.704
Minimum	1.00	1.00	
Maximum	15.00	20.00	
Area involved (%)			
Mean	53.25 ± 28.97	50.17 ± 31.39	0.76

Minimum	10.00	2.00	
Maximum	95	100	
Occupation			0.093
Housewife	3	8	
Doctors / Health	5	1	
Students	11	8	
Others	1	3	

Table 2. Comparison of Psi in Both Study Groups At Different Follow-up.

		Group-A Laser Treatment	Group-B Cryotherapy	Total	p-value
		Group	Treatment Group		
PSI baseline	Mean	27.20 ± 11.66	31.50 ± 13.33	29.35 ± 12.55	0.284
	Minimum	10.00	10.00	10.00	
	Maximum	48.00	48.00	48.00	
PSI at 1st visit (4 weeks)	Mean	18.40 ± 11.63	26.32 ± 11.60	22.36 ± 12.15	0.037
	Minimum	0.00	6.00	48.00	
	Maximum	40.00	.00	48.00	
PSI at 2nd visit (8 weeks)	Mean	12.50 ± 10.59	21.27 ± 14.04	16.88 ± 13.05	0.032
	Minimum	0.00	3.00	.00	
	Maximum	35.00	48.00	48.00	
PSI at 3rd visit (12 weeks)	Mean	10.05 ± 10.76	19.90 ±13.28	14.97 ± 12.93	0.014
	Minimum	0.00	3.00	.00	
	Maximum	40.00	48.00	48.00	
PSI at 4th visit (16 weeks)	Mean	7.10 ± 8.81	19.05 ± 13.10	13.07 ± 12.57	0.002
	Minimum	0.00	2.00	0.00	
	Maximum	35.00	48.00	48.00	
PSI at 5th visit (20 weeks)	Mean	6.35 ± 7.44	17.60 ± 12.49	11.97 ± 11.63	0.001
	Minimum	0.00	2.00	0.00	
	Maximum	24.00	48.00	48.00	
PSI at 6th visit (24 weeks)	Mean	5.95 ± 7.05	16.55 ± 12.45	11.25 ± 11.34	0.002
	Minimum	0.00	2.00	0.00	
	Maximum	24.00	48.00	48.00	
PSI at 7th visit (28 weeks)	Mean	5.55 ± 7.10	16.55 ± 12.45	11.05 ± 11.45	0.001
	Minimum	0.00	2.00	0.00	
	Maximum	24.00	48.00	48.00	

PSI = new pigmentation area and severity index (0-48)

Group A = Patients treated with Q-switched Nd:YAG laser

Group B = Patients treated with cryotherapy

PSI score of all the patients in Group A and Group B was calculated at baseline, at every visit and 4 weeks after the 6th treatment session. Data are presented in (Tables 2 and 3). Similarly, mean PSI score, mean decrease in PSI of Q-switched Nd:YAG laser and cryotherapy were calculated (Table 2 and Figure 1). Comparison of improvement with Q-switched Nd:YAG laser and cryotherapy (Table 3,

Figures 2-3), showed that (n=11) 55% in Group A and (n=1) 5% in Group B improved in clear category, while (n=2) 10% in Group A and (n=4) 20% in Group B responded poorly, p - value was calculated as 0.008 which showed a significant difference between the two groups (Table 3 and Figure 3).

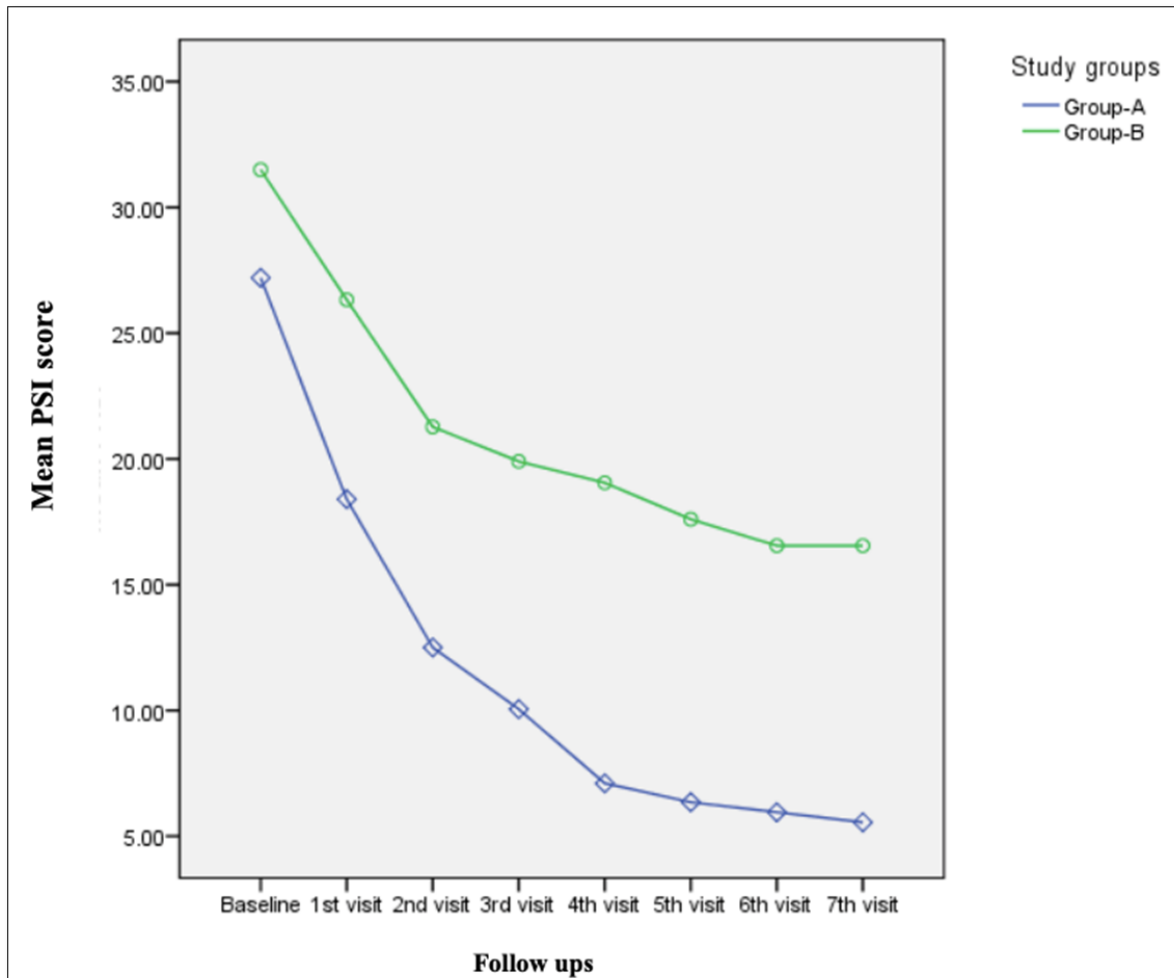


Figure 1. Comparison of Psi Score in both study groups at different intervals.

PSI = new pigmentation area and severity index (0-48)

Group A: Laser Treatment Group

Group B: Cryotherapy Treatment Group

Regarding side effects, mostly mild pain was seen during the initial sessions in both groups, which subsequently reduced in the next sessions (Table 4). Mild to moderate itching was reported by few patients in both groups initially and it also reduced in the subsequent sessions. Erythema and swelling were also noticed in both groups which were transient and statistically insignificant.

Hyperpigmentation in Group A was seen in 25% (n=5) of patients, which was reduced to 15% (n=3) by the end of treatment. While in Group B 40% (n=8) suffered from hyperpigmentation and it did not resolve till the end of treatment sessions. Only one patient (5%) in Group A developed hypopigmentation which resolved after few weeks spontaneously.

Table 3. Comparison of final psi score in both study groups

		Study groups		Total
		Group-A Laser Treatment Group	Group-B Cryotherapy Treatment Group	
Final PSI score	Clear (91-100%)	11 (55.0%)	1 (5.0%)	12 (30.0%)
	Excellent (76-90%)	3 (15.0%)	3 (15.0%)	6 (15.0%)
	Good (51-75%)	2 (10.0%)	9 (45.0%)	11 (27.5%)
	Fair (26-50%)	2 (10.0%)	3 (15.0%)	5 (12.5%)
	Poor (0-25%)	2 (10.0%)	4 (20.0%)	6 (15.0%)
Total		20 (100.0%)	20 (100.0%)	40 (100.0%)

Chi-square test = 13.65
p-value = 0.008

Table 4. Side effects in both treatment groups.

	Group A Laser Treatment Group	Group B Cryotherapy Treatment Group
Pain	12 (60%)	7 (35%)
Erythema	9 (45%)	4 (20%)
Swelling	10 (50%)	4 (20%)
Itching	8 (40%)	5 (25%)
Hyperpigmentation	5 (25%)	8 (40%)
Hypopigmentation	1 (5%)	0
Scarring	0	0

Chi-square = 2.9917
p-value = 0.559

DISCUSSION

Solar lentigines are of cosmetic concern. Regardless of the etiology, these can cause mental trauma and emotional anguish. Lentigines have negative impact on quality of life of patients. Poor quality of patient’s life forces both the patient and physician to opt for expensive and even cumbersome therapies in order to get relief. Cryotherapy is an inexpensive and effective treatment for lentigines but the post-inflammatory hyperpigmentation or hypo-pigmentation limits its use in darker skin types. Lasers have a broader absorption spectrum (532-1064 nm) for melanin which is the

reason they are currently being used in the treatment of solar lentigines.

Our study was conducted to compare the efficacy of cryotherapy versus Q-switched Nd:YAG 532nm laser in the treatment of solar lentigines. Additionally, distribution of disease in various demographic features like age, gender, marital status, severity and duration were also identified. Globally used new pigmentation area and severity index (PSI) score was employed to assess the effect. This score was used because it is relatively comprehensive and self-explanatory, and it has been widely employed in other international studies as well [10]. Different other studies

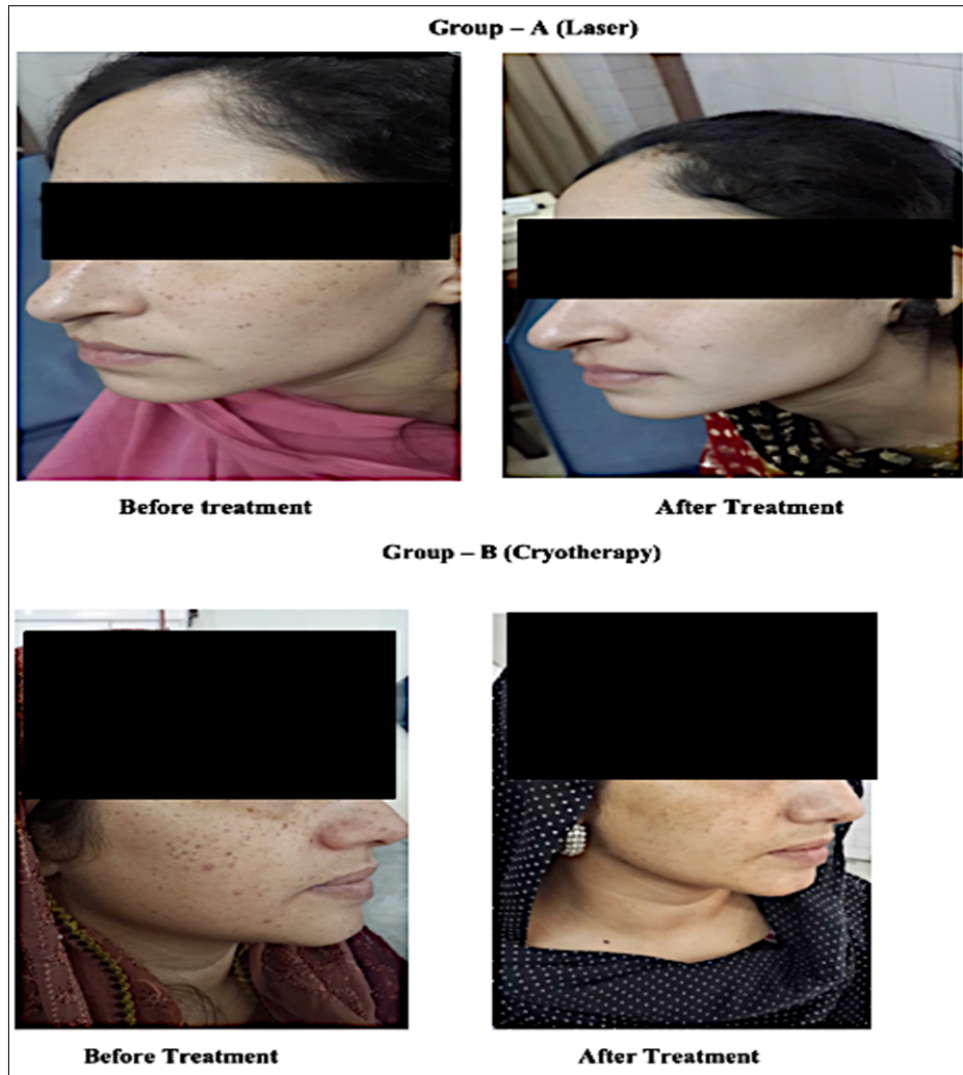


Figure 2. Comparison of before and after treatment of both groups.

assessing effects of treatment in patients with lentiginos have used scores other than PSI. The reason we used this tool was because of its ease of use and being less time consuming.

The mean age of patients was 23 (12-46) years in Group A and 25 (14-50) years in Group B in our study, which does not correlate with the study by Wang et al. and Seirafi et al. in which mean age was 45 years and 51 years respectively [6,10]. The reason for early presentation of solar lentiginos in our set up is probably excessive sun exposure and lack of sun protection and use of sunscreens.

According to the gender in Group-A there were 2 male and 18 female patients. While in Group-B there were 20 female patients. The number of female patients enrolled in our study was higher which correlates with the studies conducted by Sairafi et al. and Wang et al. [6,10]. It indicates that females

suffer from solar lentiginos in a greater proportion as compared to males. It could also be due to the fact that females are more conscious of their appearances and consult early.

Most of the patients in our study were unmarried and students by profession. A study conducted by Kavak et al. [11] found that truck drivers had increased number of solar lentiginos on the window side of the face which showed that occupation is one of the factors aggravating or inducing solar lentiginos. The reason for more students presenting to us could be due to the fact that our setting is near many educational institutions so more students were enrolled.

In Group-A and in Group-B mean duration of disease was 6.5 years and 5.9 years, respectively. The mean duration was 10-15 years in the study by Wang et al. [10]. Sun exposure,

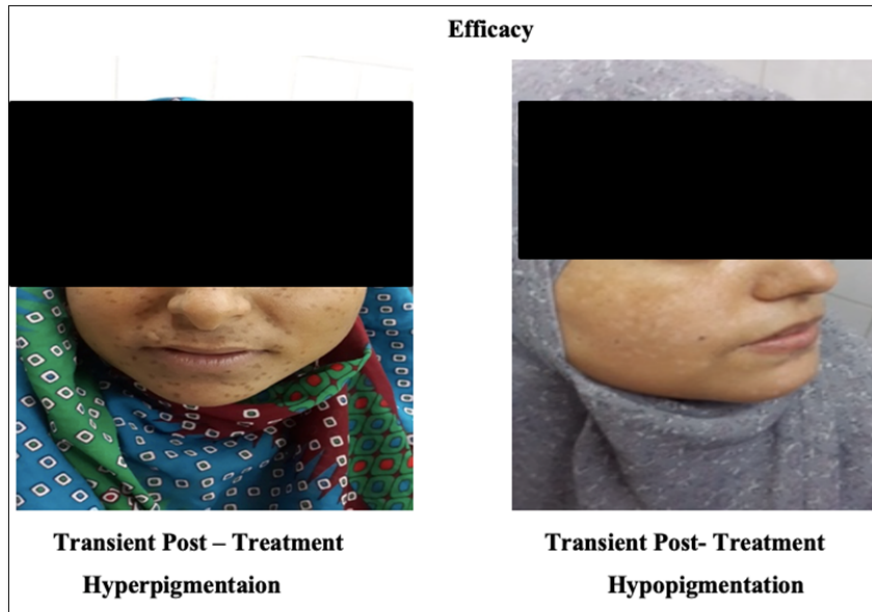


Figure 3. Comparison of efficacy.

lack of sun protection and perhaps some genetic and racial differences in our population is the reason for shorter duration of disease.

For assessing the treatment response in patients, new PSI score was used. This score has already been performed in a study by Wang et al. [10] and reliable results are achieved. Thus using this scale, it was seen that majority of patients suffered from higher PSI scores in our study compared to Wang et al where lower PSI scores were noted. Higher PSI was probably due to lack of education regarding sun protection in our society.

The effect of treatment was studied in our study by comparing the PSI score at baseline and at the end of study. The improvement was seen in both groups from the first visit with significant result. In the subsequent visits the results continued to be statistically significant. The treatment was found to be more efficacious in 55% patients in Group A patients who were treated with laser (p-value = 0.008). Similar results have been observed in clinical studies conducted by Lee et al., Rashid et al., Wang et al. and Kim et al. in which Q-switched lasers were found to be superior modality [8-10, 12]. Lee et al. reported that 50% patients achieved excellent results and 50% showed good improvement with low-fluence Q-switched 1064 Nd: YAG laser. In the study by Rashid et al. 80% patients achieved more than 50% improvement with Quasi-continuous frequency doubled Nd:YAG laser therapy.

We compared both treatment modalities at the end of our study and found that 55% had complete clearance of lentigenes with Q-switched Nd:YAG laser and 45% showed

partial clearance with cryotherapy. A statistically significant improvement was seen with laser therapy (0.008). Similar results were seen in the study by Todd et al. in which 60% patients improved with Nd:YAG laser and 24% with cryotherapy [7].

Different side effects were seen in both treatment groups during follow-up period. The side effects mainly reported were transient pain, erythema, swelling and pruritus. Hyper and hypopigmentation were also noted as late onset side effects. The hypopigmentation was temporary and patients recovered after a few months of withholding the treatment though hyperpigmentation persisted in some patients during follow up period. None of the patients in both groups had acneiform eruption and or any other type of side effects as a result of treatment. Similar results were observed in the study conducted by Todd et al [7]. In the study by Lee et al. 20% patients developed hypopigmentation, similarly, 25% reported hypopigmentation and 10% hyperpigmentation in a study by Rashid et al. [8, 9]. In a study by Wang et al. [10], 47% patients developed hypopigmentation and 10% patients developed hyperpigmentation in patients treated with Q-switched Alexandrite laser. Whereas in our study 25% patients developed hyperpigmentation and 5% developed hypopigmentation which was not statistically significant. The difference in hyperpigmentation as a side effect could be due to different types of Q-switched lasers and parameters used in both studies. Among the cryotherapy group, 40% patients developed hyperpigmentation and none had hypopigmentation in our study. It is comparable to the study by Seirafi et al. in which 36% patients experienced hyperpigmentation after cryotherapy [6].

Limitations of our study are a smaller sample size and the skin types in which the treatments were used. A larger sample size and inclusion of other skin types could probably take care of these weaknesses in our study.

Both treatment modalities are available in Pakistan but laser treatment though more efficacious is expensive. Further studies with higher sample size and longer duration of follow-ups should be done to see the resolution of pigmentary side effects or recurrence of disease.

CONCLUSION

In our study Q-switched Nd:YAG laser was found to be more efficacious and safe than cryotherapy in the treatment of solar lentigines among Fitzpatrick skin type-IV.

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