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Original Article

Comparison of efficacy of Eflornithine and Nd:YAG laser in combination therapy versus Nd:YAG laser alone for treatment of idiopathic facial hirsutism

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Abstract

Objective To compare the efficacy of Eflornithine and Nd:YAG laser in combination therapy versus Nd:YAG laser alone in treating patients of idiopathic facial hirsutism.

Methods This randomized controlled trial was done from 9th April 2019 to 8th December 2019 in Dermatology department, Services Hospital, Lahore. Total 80 female with idiopathic hirsutism, 18-45 years of age, randomized into two groups. Group A was treated with combination therapy of Eflornithine and Nd:YAG laser and Group B was given Nd:YAG laser alone. The patients were followed at 4 weeks interval till 24 weeks to observe efficacy. Final assessment was done on the 8th visit (taking baseline at 0 and 24th week as final session). Hair counts were done in 1 cm^2 surface area of the treated area.

Results Both groups A and B had 40 patients each, from 18-45 years with mean age of 29.05±5.89 years. The mean ages of patients in group A and B was 29.10±6.03 and 29.03±5.82 years respectively. Majority of the patients 52 (65.0%) were between 18 to 30 years of age. Efficacy of Group A (Eflornithine and Nd:YAG laser) was seen in 37 (92.50%) patients while in Group B (Nd:YAG laser alone) was seen in 29 (72.50%) patients (p-value = 0.018).

Conclusion This study concluded that combination of eflornithine and Nd:YAG laser is more efficacious than that of Nd:YAG laser alone in treatment of idiopathic hirsutism.

Key words
Hirsutism; Eflornithine; Nd:YAG laser; Lasers hair removal; Aesthetic dermatology.

Introduction

Hirsutism is excess terminal hair growth in female occurring in a male-like distribution such as the beard, moustache and chest.[1] Androgens in excess either secreted by the ovaries or adrenal glands are the culprit. The ovarian causes for hyper androgenism are polycystic ovaries or ovarian tumors. Cushing's syndrome, androgen-producing tumors, and congenital adrenal hyperplasia occur there is increased production of androgens from adrenal glands. Nevertheless upto 20% of the patients suffer with idiopathic hirsutism with an unremarkable hormonal profile and normal ovarian function.[2] The problem is worldwide and approximately 4-11% of women are reported to be hirsute.[3] Studies have shown that excessive growth of hair in women leads to higher degree of psychiatric problems compared to the general population.[4]

When managing hirsuitism treatment of underlying cause is mandatory. Apart from that empirical therapies like physical hair removal

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through electrolysis or laser treatment are a must. In addition, many cases require hormonal therapy to normalize androgen production in many cases. Still the treatment options are limited with variable cure, cost and side effects. Temporary hair removal techniques like threading, shaving, waxing, depilatory creams and tweezing need continuous maintenance, although these are easily affordable. Sometimes they can cause skin irritation and follicle infection.[5] Laser hair removal ensures permanent hair removal. Working on the principal selective photothermolysis, lasers are designed to destroy undesirable hair follicles and to reduce hair shaft diameter without damaging the adjacent tissue.[6] The Nd:YAG laser due to its longer wave length, scatter less and penetrates deep into the darker skins and this property makes it ideal for terminal hair. When using shorter pulse durations with the Nd: YAG it is effective in finer hair with shorter thermal relaxation time.[7] A recent study done in Egypt showed 64.3% reduction in hair counts one month after 5 consecutive sessions a month apart.[8]

Eflornithine, also known as difluromethylornithine (DFMO) was originally invented as an anticancer medicine. It causes irreversible inhibition of ornithine decarboxylase enzyme which is related with extension of the anagen growth phase in hair cycle. It diminishes the growth rate of all types of hair. Eflornithine seems to be efficacious regardless of the cause of unwanted hair.[9] Hamzavi *et al.* compared eflornithine cream alongwith with laser treatment to Nd:YAG laser alone for terminal hair in women. At the end of 6 session combination of eflornithine and laser showed a complete hair removal of 93.5% of While success rate of 67.9% was achieved with placebo cream and laser.[10] Another Study by Smith *et al.* revealed superior results with eflornithine-treated sides after 34 weeks of treatment aided by Nd:YAG laser therapy to both sides of the face.[11]

Hirsutism is a common disorder in our society. We want to know whether combining eflornithine and Nd:YAG laser is more efficacious in hirsutism.

Hypothesis

There is a difference in efficacy of Eflornithine and Nd:YAG laser in combination therapy versus Nd:YAG laser alone in treating patients of idiopathic facial hirsutism

Method

It was a randomized controlled trial conducted in department of Dermatology, Services Hospital, Lahore from 9th April 2019 to 8th December 2019. Total 80 patients enrolled on basis of Non-probability, consecutive sampling who fulfilled the inclusion criteria after giving written informed consent suffering from ***Idiopathic Hirsutism*****:** defined as a female patient with moderate to severe hirsutism involving chin, upper lip and areas of side of face according to Ferriman and Gallwey score ≥8 without any medical causes of hirsutism. Patients with idiopathic facial hirsutism as per-operational definition. Age 18–45 year with Fitzpatrick skin type 4 and 5 having brown/ black terminal hairs. While patients having hypertrichosis, active cutaneous infections in the treatment area, taking retinoids or hypersensitive to eflornithine were excluded. Patients were randomly allocated into group A and B. Patients in group A (Eflornithine+Laser) were treated with Nd:YAG laser and eflornithine. ***Nd:YAG laser***: GentleYAG machine with specifications machine with following specification used of pulse duration 10ms, 230 VAC, single phase, 16 A having wavelength of 1064nm and frequency of 50/60 Hz. ***Eflornithine:*** As eflornithine

hydrochloride is a cream containing 13.9% (1.3mg/gm) of eflornithine hydrochloride monohydrate (150mg/gm) manufactured from Biogen Pharma. While in Group B patients were treated with Nd:YAG laser only. In group A patient's (Eflornithine + Laser) affected site was treated with Nd:YAG laser afterwards, eflornithine cream was prescribed to be applied two times a day. Every patient was treated with Nd:YAG laser at 4 weeks interval for 6 visits. Final assessment was done 4 weeks after the 6th visit. Hair counts were done in $1cm^2$ surface area of treated area. Patients were instructed to wash the area properly. To avoid any laser pulses overlapping and skipping of the treatment areas, the area was marked. According to the patient's response the fluence was increased with constant wavelength duration and wavelength. All the readings and findings on proforma for each patient were noted. Photographs of the patient were taken prior to beginning of treatment, and at four weeks after the last session. Improvement during each visit was judged by comparing the hair counts on both sides of unshaved area of face before each session and photograph of patient was taken. Efficacy was considered as fifty percent hair reduction from the baseline after 6 treatment sessions was considered as efficacious. Reduction was measured by difference in hair count on baseline visit and that after 4 weeks of last session. Patient was enquired about expected side effects (pain, itching, tingling, burning, blister formation, swelling, scarring) of given treatment and was managed accordingly. All the information was entered in a structured questionnaire. Effect modifiers like age, skin type were addressed through stratification of data. All the data was entered and analyzed using SPSS-23. Mean and standard deviation for the age and duration of disease were calculated. Frequencies and percentage were calculated for the categorical variables like skin type and efficacy (yes/no). Efficacy was compared in both groups and chi-square test was applied for comparison of efficacy at level of significance of 0.05.

Results

In this study the age range was from 18-45 years with mean age of 29.05±5.89 years. The mean age of patients in group A was 29.10±6.03 years and in group B was 29.03±5.82 years. Majority of the patients 52 (65.0%) were between 18 to 30 years of age as shown in **Table 1**. Mean duration of disease was 5.44±2.11 months **(Table 2)**. **Table 3** has shown the percentage of patients according to skin type.

Table 1 Age distribution for both groups (n=80).

Age (years)	*Group A (n=40)*		*Group B (n=40)*		*Total (n=80)*	
	No. of patients	*%age*	*No. of patients*	*%age*	*No. of patients*	*%age*
18-30	25	62.50	27	67.50	52	65.0
31-45	15	37.50	13	32.50	28	35.0
Mean ± SD	29.10 ± 6.03		29.03 ± 5.82		29.05 ± 5.89	

Table 2 Percentage of patients according to duration of disease (n=80).

Duration of disease	*Group A (n=40)*		*Group B (n=40)*		*Total (n=80)*	
(months)	*No. of patients*	*%age*	*No. of patients*	*%age*	*No. of patients*	*%age*
≤6 months	24	60.0	24	60.0	48	60.0
>6 months	16	40.0	16	40.0	32	40.0
Mean ± SD	5.63 ± 2.16		5.38 ± 2.01		5.44 ± 2.11	

Table 3 Percentage of patients according to skin type (n=80).

Skin type	*Group A (n=40)*		*Group B (n=40)*		*Total (n=80)*	
	No. of patients	*%age*	*No. of patients*	*%age*	*No. of patients*	*%age*
4	20	50.0	21	52.50	41	51.25
5	20	50.0	19	47.50	39	48.75

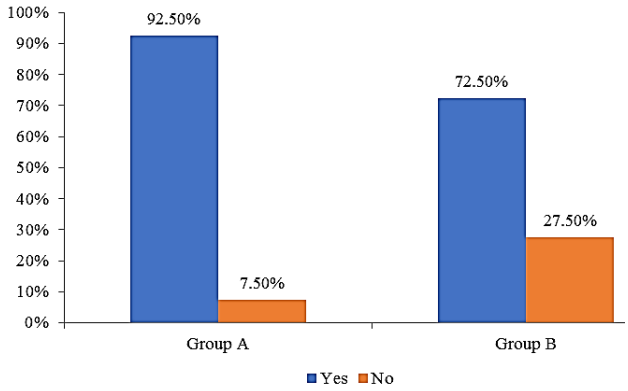

Figure 1 Comparison of efficacy in both groups.

Efficacy of Group A (Eflornithine and Nd:YAG laser) was seen in 37 (92.50%) patients while in Group B (Nd:YAG laser alone) was seen in 29 (72.50%) patients as shown in **Figure 1** (p-value=0.018). Stratification of efficacy with respect to age groups and duration of disease is shown in **Table 4**.

Discussion

We have conducted this study to compare the efficacy of Eflornithine and Nd:YAG laser in combination therapy versus Nd:YAG laser alone in treating patients of idiopathic facial hirsutism.

In this study the age range was from 18-45 years with mean age of 29.05±5.89 years. The mean age of patients in group A was 29.10±6.03 years and in group B was 29.03±5.82 years. The mean age of patients in our study was 29.05±5.89 years which was very much comparable with Hamzavi I *et al;* who had a mean age of 30 years. On the other hand, Battle EF *et al;*[16] had found much larger mean age i.e. 33 years, in his study compared to our study. In our study, we took patients having skin type Fitzpatrick IV and V was similar to the study done by Rachna Mittal *et al;* in india which showed results inferior to ours. As they used only laser modality for the treatment of hirsutism with the efficacy of 57% (as compared to ours of 92.5%). Our study has better results because both laser and eflornithine were used in our study as compared to Rachna Mitt *et al.*[7] study in which only laser was used.

Study done by Elizabeth L. *et al.*[16] in Washington DC took patients having skin type Fitzpatrick I-VI after 6 months of treatment of Nd;YAG laser, achieved mean hair reduction of 41% to 46% on the face. Meanwhile our efficacy was 92.50% with Fitzpatrick skin type IV and V which is more laser treatment.

Another study done by Smith *et al.*[11] was conducted which compared the efficacy and safety of eflornithine with placebo cream while laser therapy was given to both groups for unwanted hair. A total of 54 women with Fitzpatrick skin types I–IV, wanting their facial hair removal, were randomized and treated with either combination modality for 34 weeks. Laser modalities used were either long-pulsed Nd:YAG or alexandrite laser was performed.

Table 4 Stratification of efficacy with respect to age groups, duration of disease and skin type.

	Group A (n=40)		*Group B (n=40)*		*p-value*
	Efficacy		*Efficacy*		
	Yes	*No*	*Yes*	*No*	
Age groups					
18-30	24	01	18	09	0.007
31-45	13	02	11	02	0.877
Duration of disease					
≤6 months	23	01	15	09	0.004
>6 months	14	02	14	02	1.000
Skin type					
IV	18	02	15	06	0.134
V	19	01	14	05	0.065

A more significant improvement with lesser hair growth from weeks 6 to 22 was noted in the eflornithine group. Subjective evaluation revealed a superior improvement in lip and chin areas in eflornithine cream. Over all this combination lead to better patient satisfaction. The second study, by Hamzavi *et al;*[10] has also shown the results which are very similar to our study results . In their study, at the final follow up 75% of patients reported a greater improvement with eflornithine combination therapy. A complete hair removal was achieved in 94% of patients who underwent eflornithine and laser treatment in comparison to a 68% of patients reporting improvement in placebo and laser group. Response was sustained through week 34 in eflornithine laser group. There were no significant side effects noted in either groups.[10]

The present study is first of its kind in local population and adds to the limited research evidence on the topic. In the present study, combination therapy with topical eflornithine and Nd;YAG laser was found extremely effective in patients of idiopathic facial hirsutism. Side effects observed immediately after the procedure in a few patients includes mild erythema and swelling which subsides in one to three days. No major side effect was observed in any patient which also advocate the safety for its preferred use in future practice.

A very strong limitation to the present study was that we followed the patients for a limited time period of 6 months. We also did not compare the results with other treatment modalities in practice which could have enabled selection of more appropriate treatment. Such a study is highly recommended in future research.

Conclusion

We recommend that combination of Eflornithine and Nd:YAG laser should be used as a first line therapy in the treatment of idiopathic hirsutism to achieve desirable results and extended use of eflornithine after successful laser therapy will minimize the chances of recurrence and less frequent maintenance Nd:YAG laser sessions.

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