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ORIGINAL ARTICLE

Comparison of Efficacy of Nd-YAG Laser with Adjuvant Eflornithine Cream versus Nd-YAG Laser alone for the treatment of facial hirsutism in women

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ABSTRACT

Background: Hirsutism is an important array of clinical syndrome that ranges from various dermatological to gynecological concerns. This is characterized by growth terminal hairs in women in male-pattern.

Aim: To compare the efficacy of Nd-YAG laser with adjuvant eflornithine cream versus Nd-YAG laser treatment alone for facial hirsutism in women.

Methods: It was a Randomized Controlled Trial conducted in the Department of Dermatology, Shalamar Hospital, Lahore from 25th February, 2020 to 25th October, 2020. Sampling technique used was probability consecutive sampling. In this study female cases with age 18-40 years with Fitzpatrick type III-IV were enrolled having facial hirsutism for > 6 months and were randomly allocated in two groups A and B. In group A, cases were provided with eflornithine cream to apply on face after cleaning and drying in the form of a thin film only on the treatment area every night.

Results: A total 162 cases (81 in each group) were enrolled in this study. Mean age of the subjects in group B and A was 30.23±5.43 vs 30.94±4.88 years. Efficacy was observed in 64(79.01%) cases in group B managed with ND-Yag laser alone and 78(96.30%) cases in group A managed with ND-Yag laser along with Eflornithine with p=0.001. For age group 30-40 years efficacy in group B was 41(80.39%) cases and in all the 49(100%) cases in group A with p= 0.001.In cases with BMI up to 25 kg/m^2 efficacy in group B and A was observed in 44(88%) vs 49(100%) cases (p=0.03) and those with BMI more than this, this efficacy was found in 20(64.52%) and 29(90.63%) cases respectively with p=0.02.

Conclusion: Efficacy in facial hirsutism is significantly better in ND-Yag laser combined with Eflornithine as compared to ND-Yag laser alone and this difference is also significantly better for combination group in terms of age group 30-40 years, BMI up to 25mg/m^2 and in those with duration of complaint upto 2 years.

Keywords: Hirsutism, Efficacy, Eflornithine, Nd-YAG laser

INTRODUCTION

Hirsutism is defined as increased growth of terminal hair in women in a male pattern distribution over the body especially on face. In females, vellus hair are present on the skin which are fine, light coloured hairs but at puberty androgens act on hair follicles to convert them into coarse hyperpigmented terminal hair normally in axillae and groin region but acquire male pattern in case of hirsutism[1].

It is a common disorder affecting around 10% of women population in United States and in Northern Europe[2]. Although the disease itself is least likely associated with significant morbidity and mortality but it can significantly affects quality of life due to its cosmetic concern and may lead to psychological problems and social isolation[3].

Hirsutism may be idiopathic but in approximately 50% of cases it occurs as a result of some endocrine disorder in which androgen levels in the body get raised either due to ovarian or adrenal pathology[4]. Most common cause of hyperandrogenism is polycystic ovarian syndrome (PCOs). Engmann et al studied women of 18-40 years of age with PCOs and reported prevalence of hirsutism was 93.8% in Hispanic women while 86.8% in non-Hispanic women.[5] Other causes includes congenital adrenal hyperplasia, hypothyroidism, cushing syndrome or androgen secreting tumors[4]. Hence investigating the cause of disease with measurement of serum total and free testosterone levels, FSH, LH, TSH and progesterone levels along with ultrasound abdomen.

The prevalence of hirsutism is less in women of Caucasian, Ashkenazi Jews, East/Southeast Asian, and Native American ethnicity who have darker Fitzpatrick skin types[6]. The reason may be due to differences in the activity of 5-α reductase enzyme that cause local production of dihydrotestosterone in the skin[7].

Management of hirsutism includes various systemic drugs to correct underlying hyperandroginism alogwith skin directed therapies that act locally for reduction of hairs in a particular area. Prognosis is variable depending upon the etiology of disease[8].

Traditionally multiple techniques are being used to temporarily remove unwanted facial hairs like waxing, shaving, epilation and electrolysis etc. Incorporation of various energy based devices had shown a major breakthrough in the treatment of hirsutism for the last ten years. It includes Intense Pulsed Light (IPL) (550nm to 1200nn) and LASERs including Diode (810nm), Alexandride (755nm) and Nd-YAG (1064nm).[9] Laser therapy not only helps in gradual and to some extent permanent reduction in the terminal hairs it also helps in improving quality of life and aesthetic concerns of women[10]. But response is variable depending upon various factors and sometimes unpredictable and poor[9].

Eflornithine is drug that irreversibly inhibits ornithine decarboxylase (ODC), an enzyme that catalyzes synthesis of

intracellular polyamines that stimulates growth of hair. A formulation of 13.9% cream is approved by FDA and it is found to be safe and effective in the treatment of hirsutism.[11] However the process is slow and long term treatment is required.

Combination of skin different directed therapies with or without systemic treatment is being practiced and evaluated by practitioners. This study is designed to evaluate whether topical eflornithine is helpful in enhancing the response of Nd-YAG LASER when given as an adjuvant therapy in the treatment of hirsutism or not.

The objective of the study was to compare the efficacy of Nd-YAG LASER with adjuvant eflornithine cream versus Nd-YAG LASER alone for the treatment of facial hirsutism in women.

Hypothesis: It was hypothesized that there was a difference in efficacy of Nd-YAG LASER with adjuvant eflornithine cream versus Nd-YAG LASER alone for the treatment of facial hirsutism in women. Eflornithine cream combined with Nd-YAG laser treatment versus laser treatment alone for facial hirsutism in women.

OPERATIONAL DEFINITIONS

Facial Hirsutism: Participants were labeled to have hirsutism if they had an excess terminal hair in women that occurs like male pattern involving face area.

Efficacy: It was defined as grade ≥2 improvement in comparison to the baseline (Annexure-I) after 6 months of therapy assessed by the researcher himself based on photographs.

PATIENTS AND METHODS

This randomized controlled trial was conducted in the Department of Dermatology, Shalamar Hospital, Lahore from 25th February, 2020 to 25th October, 2020. Sample size is 162 calculated alpha = 5% (two-sided) with power = 80%. While p1= 78%,[6] and p2= 93.33%,[4] where p1 is the expected proportion (efficacy) in population 1 and p2 is the expected proportion (efficacy) in population 2. 81 patients were in eflornithine cream combined with Nd-YAG laser or Group A while 81 patients were in Nd-YAG laser treatment alone group or Group B. Non-probability consecutive sampling technique was used.

Inclusion Criteria: Women with 18-40 years of age**,** Facial hirsutism as per operational definition for > 6 months **&** patients falling in Fitzpartrick skin type III-V

Exclusion Criteria: Patients having active viral or bacterial or fungal skin infection on treatment area, Patients with active acne vulgaris, Pregnant / lactating participants, Participants who had history of keloidal tendencies, Patients taking any hormonal therapy or having endocrine abnormalities, Patients who completed recent laser with in 6th month or electroepilator with in 2 month before starting of the study & those patients who lost to follow up were excluded from our study

Data collection and procedure: A total of 162 (81 in each group) cases with hirsutism participated in this study after taking approval from ethical review board of Shalamar hospital, Lahore. Informed consent was obtained from each participant. Basic demographics (age and duration of complaints) were recorded. Randomization was performed by lottery method. Names of both therapeutic regimens were mentioned separately on papers and sealed in envelopes. After taking consent, one envelope was randomly picked by the each participant to decide the treatment group. 81 patients were in eflornithine cream combined with Nd-YAG laser or Group A while 81 patients were in Nd-YAG laser treatment alone group or Group B.

In group A, cases were provided with eflornithine cream to apply on face after cleaning and drying in the form of a thin film only on the treatment area every night. The cases of both groups A and B were treated with Nd-YAG laser of 1064nm every month till 6th months with variable pulse and duration along with an air cooling system. All were instructed to not use any other topical medication during the whole period. Efficacy was defined as grade ≥ 2 in comparison to the baseline after 6 months of therapy.

Operational parameter of Nd-YAG laser were individually modified according to patients skin type and hair thickness and density keeping maximum fluence that was safe and well tolerated by the patient. Every case was evaluated before starting the treatment and at the time of every session. Further assessments were carried out at follow up at 3 months after completing the treatment. Photographs of each case were taken at start and end of treatment and at 3 month of follow up after completing the treatment. Efficacy was evaluated after final session at 6 months of treatment as per operational definition by researcher himself on especially designed proforma (Annexure-I)

Annex. I: Investigator assessment for facial hair response in comparison to the baseline

Category	Description
Grade 0 No improvement/worse	Minimal reduction or increased visibility of terminal hairs on the area treated. There may be increased pigmentation on face.
Grade 1 Improved	Clinically obvious reduction in the visibility of terminal hairs on the area treated. Facial skin lightening.
Grade 2 Marked improvement	Marked reduction in the visibility of terminal hairs on the area treated. Minimal increase in the pigmentation of face.
Grade 3 Clear/ almost clear	Terminal hairs hardly visible on the area treated. No change in colour of face

Data analysis: Data was analyzed using SPSS version (24.0). For qualitative variables like efficacy, frequency and percentage was calculated. For quantitative variables like age, BMI and duration of complaints, Mean ± SD was calculated. Chi-square test was used to evaluate and compare efficacy of both treatment groups taking p-value ≤0.05 as significant.

Stratification for effect modifiers with like age, BMI and duration of complain was performed and post-stratification was done by applying chi-square chart to check whether these variables can modify affect the efficacy of both treatment groups. A p-value of ≤0.05 was considered statistically significant.

RESULTS

There were total 162 cases (81 in each group). Mean age of the subjects in group B and A was 30.23±5.43 vs 30.94±4.88 years (table 1). Mean duration of complain was 1.37±1.04 vs 1.42±1.07 years as shown table 1. There were 51 (62.97%) cases in group B with age 30-40 years and 40(60.49%) in group A with same age group (table 1).

Efficacy was observed in 64(79.01%) cases in group B managed with ND-Yag laser alone and 78 (96.30%) cases in group A managed with ND-Yag laser along with Eflornithine with p= 0.001 as shown in table 1. In terms of age group 18-29 years efficacy was observed in 23(76.67%) vs 29(90.63%) in group B and A respectively with p= 0.17 (table 2). For age group 30-40 years efficacy in group B was 41 (80.39%) cases and in all the 49(100%) cases in group A with p= 0.001 (table

2).In cases with BMI upto 25 kg/m^2 efficacy in group B and A was observed in 44(88%) vs 49(100%) cases (p= 0.03) and those with BMI more than this, this efficacy was found in 20(64.52%) and 29(90.63%) cases respectively with p= 0.02 as displayed in table 2. Efficacy was significantly better in group A, where this was seen in 30(90.91%) cases as compared to 19(57.58%) cases in group B with duration of complain more than 2 years with p= 0.004 as in table 2

Table-1: Comparison of age, duration of complaints and efficacy between groups

Age (in years)	**Group B**	**Group A**
Mean	30.23	30.94
Std. Deviation	5.43	4.88
Minimum	18	18
Maximum	40	40
Duration of complain (in years)		
Mean	1.37	1.42
Std. Deviation	1.04	1.07
Minimum	1	1
Maximum	4	5
Efficacy p-value (0.001)		
Yes	64 (79.01%)	78 (96.30%)
No	17 (20.99%)	3 (3.70%)

Table 2: Efficacy between groups in regard to stratification of age, BMI & Duration of Complaints

		Efficacy	**GROUP**		**Total**	**p-value**
			B (n= 30)	**A (n= 32)**		
Age	18-29	Yes	23 (76.67%)	29 (90.63%)	52	0.17
		No	7 (23.33%)	3 (9.37%)	10	
	30-40	Yes	41 (80.39%)	49 (100%)	90	0.001
		No	10 (19.61%)	0 (0%)	10	0.03
BMI	Upto 25 kg/m^2	Yes	44 (88%)	49 (100%)	93	
		No	6 (12%)	0 (0%)	6	
	>25 kg/m^2	Yes	20 (64.52%)	29 (90.63%)	49	0.02
		No	11 (35.48%)	3 (9.37%)	14	
Duration	Upto 2 years	Yes	45 (93.75%)	48 (100%)	93	0.004
		No	3 (6.25%)	0 (0%)	3	
	>2 years	Yes	19 (57.58%)	30 (90.91%)	49	
		No	14 (42.42%)	3 (9.09%)	17	
Age	18-29	Yes	23 (76.67%)	29 (90.63%)	52	0.17
		No	7 (23.33%)	3 (9.37%)	10	
	30-40	Yes	41 (80.39%)	49 (100%)	90	0.001
		No	10 (19.61%)	0 (0%)	10	0.03
BMI	Upto 25 kg/m^2	Yes	44 (88%)	49 (100%)	93	
		No	6 (12%)	0 (0%)	6	
	>25 kg/m^2	Yes	20 (64.52%)	29 (90.63%)	49	0.02
		No	11 (35.48%)	3 (9.37%)	14	
Duration	Upto 2 years	Yes	45 (93.75%)	48 (100%)	93	0.004
		No	3 (6.25%)	0 (0%)	3	
	>2 years	Yes	19 (57.58%)	30 (90.91%)	49	
		No	14 (42.42%)	3 (9.09%)	17	

DISCUSSION

Hirsutism is excess growth of terminal hair in women in a male pattern distribution over the body especially on face. It is a common disorder affecting around 10% of women population in United States and in Northern Europe.[2] The disease can significantly affects quality of life due to its cosmetic concern and may lead to psychological problems and social isolation[3]. Management of hirsutism includes various systemic drugs to correct underlying hyperandroginism alogwith skin directed therapies that act locally for reduction of hairs in a particular area. Prognosis is variable depending upon the etiology of disease[8]. Eflornithine cream is the FDA approved topical treatment for the treatment of this condition but the treatment is continuous with delayed response.[11] Invention of lasers had been a major breakthrough in the treatment of hirsutism[9].

In the present study, efficacy was observed in 64 (79.01%) cases in group B managed with ND-Yag laser alone and 78 (96.30%) cases in group A managed with ND-Yag laser along with Eflornithine with p= 0.001which was statistically significant. These results were comparable with the findings of the studies done in the past where combination therapy has shown better results as compare to single therapy. According to a study done by Smith SR, et al[12] they have shown that efficacy was 78% when patients were treated with NdYAG laser combined with adjuvant eflornithine cream which is slightly less as compared to our study. The difference may due to the reason that sample size in this study was small i.e 44 as compared to our study[12]. Similarly a study done by Hamzavi et al[13] have reported that efficacy of combination therapy using laser with topical eflornithine was 93.5% as compared to 67.9% in the patients treated with laser and topical placebo. However he has used alexandrite laser (755nm) for hair treatment as compared to Nd-YAG laser which was used in our study[13]. Similarly in a single-case study done by Ganger[14] it has been reported that topical eflornithine can enhance the efficacy of hair removal when given in combination with diode laser (800nn)[14]. The differences of laser types used in these studies can be explained by the fact that efficacy of different lasers is based on skin type of population. So far Nd-YAG has shown to be most suitable for Asian population[15].

The sample size in our study was 161 which was fairly large as compared to similar other studies like one done by Smith et al,[12] in which the sample size was 44 and one done by Hamzavi et al,[13] in which 35 patients participated in the study. The large sample of the sutudy strengthens the results of our study showing benefits of eflornithine in enhancing the response of laser therapies. Most of the participants of our study were in the age group of 30 – 40 years, further this age group showed better efficacy as well. The age range is similar with most of the other studies e.g., a study done by Vissing et al[16] included females of age 20-40 years in which he evaluated and compared the efficacy of eflornithine combined with laser

and laser alone for treatment of facial hirsutism. The reason behind this is the fact that facial hirsutism is most troublesome in post pubertal and reproductive age group due to hormonal changes and abnormalities in this period and its effect on quality of life is relatively more adverse as compared to post menopausal women.[17] In another study by Shrimal A, et al. has shown that efficacy was 93.33% with Nd-YAG laser versus Intense Pulse Light (IPL)-755 in treatment for facial hirsutism in women. They further described that the efficacy was higher and seen in nearly 100% of the cases with Nd Yag laser group in their cases with age upto than 40 year. This was also in line with present study but the cut off values used were slightly different. In the present study for age group 30-40 years efficacy in group B was 41 (80.39%) cases and in all the 49(100%) cases in group A[18]. In this study better response was shown in patients with BMI upto 25 mg/m^2 i.e. 100% in combined group as compared to those with BMI >25mg/m^2. i.e., 90.3%. This may be explained by the fact that high BMI and obesity is associated with underlying hormonal problems especially polycystic ovaries and increased hirsutism. In these patients additional systemic drug therapies and weight reduction are required to correct underlying hormonal abnormalities for better response of laser hair reduction.[19] Data regarding BMI as a confounder is not found in other studies. In this study slightly better response was seen in patients with duration of disease upto 2 years (100%) as compared to duration of more than 2 years (91%) in combined group. This variable is also not considered in most of the similar studies.

There were few limitations of this study as this study didn't compare efficacy of eflornithine with other laser techniques which have also shown variable efficacy and furthermore, this study didn't look for the side effect profiles associated with both procedures keeping in mind for patient's concerns. However no difference in side effects was observed in both groups.

However, this had many strengthening points as well, like large sample size, and this study compared a modality of drug combined with laser that has shown promising results confabulated it against a number of variables about which limited local data is published to date.

CONCLSUION

Efficacy in facial hirsutism is significantly better in ND-Yag laser combined with Eflornithine as compared to ND-Yag laser alone and this difference is also significantly better for combination group in terms of age group 30-40 years, BMI upto 25 mg/m^2 in those with duration of complain for upto 2 years. Hence topical eflornithine may be a safe adjuvant drug used to enhance the effect of different lasers.

REFRENCES

1. Hawryluk EB, English III JC. Female adolescent hair disorders. Journal of pediatric and adolescent gynecology. 2009 Aug 1;22(4):271-81.
2. Escobar-Morreale HF, Carmina E, Dewailly D, Gambineri A, Kelestimur F, Moghetti P, Pugeat M, Qiao J, Wijeyaratne CN, Witchel SF, Norman RJ. Epidemiology, diagnosis and management of hirsutism: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome Society. Human reproduction update. 2012 Mar 1;18(2):146-70.
3. Ekbäck M, Wijma K, Benzein E. "It is always on my mind": Women's experiences of their bodies when living with hirsutism. Health care for women international. 2009 Apr 27;30(5):358-72.
4. Malik LM, Khursheed K, Haroon TS, Malik MA. An aetiological study of moderate to severe hirsutism. Pakistan Journal of Medical Sciences. 2007 Apr 1;23(2):167.
5. Engmann L, Jin S, Sun F, Legro RS, Polotsky AJ, Hansen KR, Coutifaris C, Diamond MP, Eisenberg E, Zhang H, Santoro N. Racial and ethnic differences in the polycystic ovary syndrome metabolic phenotype. American journal of obstetrics and gynecology. 2017 May 1;216(5):493-e1.
6. Afifi L, Saeed L, Pasch LA, Huddleston HG, Cedars MI, Zane LT, Shinkai K. Association of ethnicity, Fitzpatrick skin type, and hirsutism: A retrospective cross-sectional study of women with polycystic ovarian syndrome. International journal of women's dermatology. 2017 Mar 1;3(1):37-43.
7. Willis SK, Mathew HM, Wise LA, Hatch EE, Wesselink AK, Rothman KJ, Mahalingaiah S. Menstrual patterns and self-reported hirsutism as assessed via the modified Ferriman-Gallwey scale: a cross-sectional study. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2020 May 1;248:137-43.
8. Martin KA, Chang RJ, Ehrmann DA, Ibanez L, Lobo RA, Rosenfield RL, Shapiro J, Montori VM, Swiglo BA. Evaluation and treatment of hirsutism in premenopausal women: an endocrine society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2008 Apr 1;93(4):1105-20.
9. Bhat YJ, Bashir S, Nabi N, Hassan I. Laser treatment in hirsutism: an update. Dermatology practical & conceptual. 2020;10(2).
10. Alizadeh N, Ayyoubi S, Naghipour M, Hassanzadeh R, Mohtasham-Amiri Z, Zaresharifi S, Nejad KG. Can laser treatment improve quality of life of hirsute women?. International journal of women's health. 2017;9:777.
11. Jobanputra KS, Rajpal AV, Nagpur NG. Focus-Eflornithine. Indian journal of dermatology, venereology and leprology. 2007 Sep 1;73(5):365-6.
12. Smith SR, Piacquadio DJ, Beger B, Littler C. Eflornithine cream combined with laser therapy in the management of unwanted facial hair growth in women: a randomized trial. Dermatologic surgery. 2006 Oct;32(10):1237-43.
13. Hamzavi I, Tan E, Shapiro J, Lui H. A randomized bilateral vehicle-controlled study of eflornithine cream combined with laser treatment versus laser treatment alone for facial hirsutism in women. Journal of the American Academy of Dermatology. 2007 Jul 1;57(1):54-9.
14. Ganger LK, Hamzavi IH. Excess salt and pepper hair treated with a combination of laser hair removal and topical eflornithine HCl. Journal of drugs in dermatology: JDD. 2006 Jun 1;5(6):544-5.
15. Battle Jr EF, Hobbs LM. Laser- assisted hair removal for darker skin types. Dermatologic therapy. 2004 Jun;17(2):177-83.
16. Vissing AC, Taudorf EH, Haak CS, Philipsen PA, Haedersdal M. Adjuvant eflornithine to maintain IPL- induced hair reduction in women with facial hirsutism: a randomized controlled trial. Journal of the European Academy of Dermatology and Venereology. 2016 Feb;30(2):314-9.
17. Barnard L, Ferriday D, Guenther N, Strauss B, Balen AH, Dye L. Quality of life and psychological well being in polycystic ovary syndrome. Human reproduction. 2007 Aug 1;22(8):2279-86.
18. Shrimal A, Sardar S, Roychoudhury S, Sarkar S. Long-pulsed Nd: YAG laser and intense pulse light-755 nm for idiopathic facial hirsutism: A comparative study. Journal of cutaneous and aesthetic surgery. 2017 Jan;10(1):40.
19. Neubronner SA, Indran IR, Chan YH, Thu AW, Yong EL. Effect of body mass index (BMI) on phenotypic features of polycystic ovary syndrome (PCOS) in Singapore women: a prospective cross-sectional study. BMC Women's Health. 2021 Dec;21(1):1-2.