

## Research Article

### Comparison of the Effectiveness and Safety of Intense Pulsed Light (IPL) and Placebo Versus Intense Pulsed Light and Eflornithine in Idiopathic Facial Hirsutism

Fauzia Khalid Janjua<sup>1</sup>, Shehla Shaukat<sup>2</sup>, Amina Afzal<sup>3</sup>, Mahwish Zahoor<sup>4</sup>, Maryam Rafat<sup>5</sup>, Ghazala Butt<sup>6</sup>, Muhammad Nadeem<sup>7</sup>, Atif Hasnain Kazmi<sup>8</sup>

<sup>1</sup>Department of Dermatology, KEMU/ Mayo Hospital, Lahore.; <sup>2</sup>Department of Dermatology, KEMU/ Mayo Hospital, Lahore; <sup>3</sup>Department of Dermatology, KEMU/ Mayo Hospital, Lahore; <sup>4</sup>Department of Dermatology, KEMU/ Mayo Hospital, Lahore; <sup>5</sup>Department of Dermatology, KEMU/ Mayo Hospital, Lahore; <sup>6</sup>Department of Dermatology, KEMU/ Mayo Hospital, Lahore; <sup>7</sup>Department of Dermatology, FJMU/ Sir Ganga Ram Hospital, Lahore; <sup>8</sup>Department of Dermatology, University of Lahore, Lahore.

#### Abstract

**Background:** Hirsutism is a distressing condition among women and one of the major causes of depression.

**Objective:** To compare the effectiveness and safety of Eflornithine and Intense Pulsed Light versus Intense pulsed light and Placebo in idiopathic facial hirsutism.

**Methods:** In this randomized placebo-controlled trial, 40 female patients of >18 years, suffering from idiopathic facial hirsutism with Fitzpatrick skin type III and IV, were included. Two groups, A and B were made. A-Group (right side of all patients) was treated with Intense Pulsed Light (IPL) and placebo and Group B (left side of all patients) with Intense Pulsed Light (IPL) and Eflornithine. Six sessions (each with 4-week interval) were done for both treatment modalities. Before first session and 4 weeks after the last session photographs were taken and hair count and hair reduction were calculated.

**Results:** In Group A (Intense Pulsed Light (IPL) and Placebo) treated sites effectiveness of treatment was seen in 22 (55%) while in Group B (Intense Pulsed Light (IPL) and Eflornithine) treated sites effectiveness was seen in 35 (87.5%). This proved that efficacy of Group B treatment was higher than Group A ( $p$ -value=0.001). Earlier side effects like mild transient erythema, transient swelling and transient pain were seen with Intense Pulsed Light (IPL) in 100% of the patients and late side effects in both groups like folliculitis ( $p$ -value=0.692) and hyperpigmentation ( $p$ -value=0.064) were also recorded and compared.

**Conclusion:** Intense Pulsed Light (IPL) and Eflornithine combination is more successful than Intense Pulsed Light (IPL) and Placebo for the treatment of idiopathic facial hirsutism. Both treatments were equally safe.

**Corresponding Author** | Dr. Fauzia Khalid Janjua, Assistant Professor, Department of Dermatology Unit-II, KEMU/ Mayo Hospital, Lahore **Email:** drfauziajanjua@gmail.com

**Key Words:** Eflornithine, Intense pulsed light, Hirsutism.

#### Introduction

Hirsutism is the appearance of extra hair in females in the areas typically meant for male hair growth, for example upper lip, chin, mandibular

area and chest, resulting from enhanced androgen action on hair follicles. This enhanced androgenic effect may be because of increased level of circulatory sex hormones (endogenous or exogenous) or due to increased receptiveness of hair fol-

icles to normal levels of circulatory sex hormones.<sup>1</sup> It is a medical problem affecting 5-10% of females of childbearing age.<sup>2</sup>

Hirsutism has many underlying conditions including polycystic ovary syndrome, congenital adrenal hyperplasia, adrenal secreting tumors, medications, thyroid disorders and Cushing syndrome.<sup>3</sup> Idiopathic hirsutism is a diagnosis of exclusion which affects 50% of women with mild hirsutism. Such hirsute females have regular menstrual cycle, usual sized ovaries and no documentation of adrenal or ovarian carcinomas or dysfunction.<sup>4</sup> Notable insulin resistance was found in non-obese females with idiopathic hirsutism in a study which was conducted in 2009.<sup>5</sup>

Hirsutism reflects a deviation from the normal female hair pattern. It causes significant cosmetic stigmatization.<sup>6</sup> It is an extremely distressing condition for females which eventually creates a negativity and depression in their social life. The aim of medical treatment of this condition is to decrease or arrest the extra hair growth and upgrade the external image of the patient, so creating positivity and happiness in her life.<sup>7</sup>

Non-permanent hair removal techniques are shaving, waxing, depilatory creams and tweezing. They are comfortable and low-cost techniques in order to remove unwanted hair but demand maintenance and can cause skin irritation and follicle infection.<sup>8</sup>

As the above mentioned methods result in temporary hair removal, there was a dire need of a rapid and permanent hair removal technique. Intense Pulsed Light (IPL) is a nonlaser filtered flash lamp device.<sup>9</sup> IPL emits a polychromatic light of multiple wavelengths (420-1200nm). The cutoff filters are used to narrow down the light spectrum to target the desired chromophores.<sup>9</sup> Furthermore, as compared to laser, IPL treatment is cheap & economical. So we can use IPL on patients who are non-affording.<sup>10</sup>

A preliminary study was done in order to see efficacy of IPL for hair removal in India. IPL was found to be safe and effective for hair removal.<sup>11</sup> A study for the treatment of facial hirsutism was done on 25 women, in which one side of face was treated with

electrolysis and other side with IPL. By visual analogue scales, patient satisfaction rates were noted, which showed better response with IPL than electrolysis.<sup>12</sup>

Eflornithine inhibits the ornithine decarboxylase enzyme irreversibly, an enzyme related with extension of the hair growth phase (anagen). It diminishes the growth rate of all types of hair. Eflornithine seems to be efficacious regardless of the cause of unwanted hair. Eflornithine, also known as diflur-methylornithine (DFMO), was manufactured in 1970 as an anticancer medicine. It also slows unwanted facial hair growth in hirsute females. This side effect got accepted in US in the year 2001.<sup>13</sup>

Hirsutism is becoming extremely prevalent in our community day by day. Few studies of this kind has been done previously in Pakistan. The purpose of this study was to observe and confirm the effects of eflornithine which is used less frequently in Pakistan among the darker skin types in the treatment of hirsutism. Therefore, this study was planned to add to the evidence based management of hirsutism.

## Methods

This randomized placebo-controlled trial was conducted at Dermatology Department, KEMU/ Mayo Hospital, Lahore. Sample size of 40 cases with 80 facial sides (40 facial sides in each group) was taken by using 90% power of test, 5% level of significance and by taking expected percentage of effectiveness with the use of IPL+Placebo as 67.9% and with the use IPL+Eflornithine as 93.5% respectively<sup>14</sup> by using purposive, non-probability consecutive sampling technique.

Female having idiopathic facial hirsutism, Ferriman & Gallwey score  $\geq 8$ , age 18 years or above, with Fitzpatrick skin type III & IV were included in the study. Patients who have already been treated for hirsutism in the past 6 months, patients taking oral retinoids within the last 6 months, immunodeficiency (Drugs/ Disorders), evidence of dermatological conditions like photosensitivity, inflammatory, pre-cancerous/ cancerous skin conditions on face were excluded. Pregnancy or lactation, sensitivity to

eflornithine or IPL (Photosensitivity), female with hormonal imbalance were also excluded. To diagnose any hormonal imbalance, following tests were done; Prolactin, Serum Luteinizing Hormone (LH), Testosterone, Follicle Stimulating Hormone (FSH), and Triiodothyronine (T3), Thyroxin (T4), Thyroid Stimulating Hormone (TSH), Dehydroepiandrosteronesulfate (DHEA-S) & abdomen-opelvic ultrasound (for the evaluation of adrenals and ovaries). Patients with idiopathic hirsutism were included. According to the operational definitions fifty percent hair reduction from the baseline at four weeks after 6 treatment sessions was considered as effective. Safety of both treatment modalities was determined by comparing the frequency of various side effects (immediate and delayed) throughout the treatment sessions and 4 weeks after 6th session. Modality with minimum side effects was considered as safe.

After approval from the ethical committee of KEMU, the study was carried out. Informed consent was taken from the patients. History and clinical examination was recorded on the first visit. It was a split-face study of 40 patients, who presented to the Dermatology Department, KEMU/ Mayo Hospital, Lahore. Immediately before treatment, patient was instructed to wash the area properly. Cooling transparent gel was applied over desired area before treating with IPL. To avoid any laser pulses overlapping and skipping of the treatment areas, the area was marked with white pencil. Skin type was selected according to Fitzpatrick scale. According to the patient's response the fluence was increased with constant pulse duration & wavelength. All the readings and findings for each patient were noted. Treatment results were compared over the chin area only. Patient's right side of chin was treated with IPL & placebo (Group-A) and left half of chin was treated with IPL & eflornithine (Group-B). A separate bottle was used for eflornithine and placebo (white petroleum jelly), the red one contained eflonithine while the green one contained the placebo. Patient was instructed to stop all temporary hair removing methods at least four weeks before treatment to allow

the hair growth cycle to return to normal. Every patient was instructed to apply placebo on the right half of chin (Group-A) and eflornithine cream on the left half of chin (Group-B) twice daily. Every patient was treated with IPL at 4-week interval for 6 visits. Final assessment was done 4 weeks after the 6th visit. Hair counts were done in 1cm<sup>2</sup> surface area on both halves of chin. Photographs of the patient were taken prior to beginning of treatment, and at four weeks after the last session. Patient was enquired about expected side effects (pain, itching, tingling, burning, blister formation, swelling, scarring) of given treatment. Improvement during each visit was judged by comparing the hair counts on both sides of chin just before each shave with the baseline photograph of patient.

Data was analysed in SPSS version 20.0. Mean±SD was calculated for numerical variables like age, average number of terminal hair and percentage hair reduction at first presentation and at the end of six sessions. Frequencies and percentages were calculated for categorical variables efficacy. Chi-square test was applied to compare the effectiveness. Independent sample t-test was applied to see the difference between the groups. A p-value of  $\geq 0.05$  was taken as significant.

## Results

In our study, mean age of the patients was 24.40 ±4.35 years. Minimum and maximum age of patients was 18 and 37 years respectively.

In Group-A, mean hair count before treatment was 14.57±2.69. Minimum and maximum number of hair in this group was 8 and 20. While in Group-B, mean hair count before treatment was 14.57±2.71. Minimum number of hair and maximum number of hair in this group was the same as that of in Group-A. **(Table-1)**

In Group-A mean hair count after treatment was 7.47±1.82. Minimum and maximum number of hair in this group was 4 and 12. While in Group-B, mean hair count after treatment was 5.00±2.06. Minimum

number of hair and maximum number of hair in this group was 2 and 10 respectively. (Table-1)

When both treatment groups were compared for hair count after treatment, it was observed that mean hair count in Group-B was low as compared to that of Group-A showing more reduction in hair on the side where IPL plus Eflornithine was applied. Statistically speaking, the difference in hair count in both treatment groups after treatment was significant. i.e. ( $p\text{-value}=0.000$  (Table-1).

In Group-A, mean percentage of hair reduction after treatment was  $47.79\pm 13.14$  and in Group-B mean percentage of hair reduction was  $65.40\pm 13.49$ . According to p-value, mean hair reduction was statistically different in both treatment groups. Group-B had more hair reduction after treatment as compared to that of Group-A ( $p\text{-value}=0.000$ ) (Table-2).

In Group-A, effectiveness of treatment was seen in 22 (55%) patients while in Group-B it was seen in 35 (87.5%) patients. According to p-value, statistically significant association was present in treatment groups. It can be clearly seen that effectiveness of Group-B treatment was high as compared to that of Group-A ( $p\text{-value}=0.001$ ) (Table-2).

All patients in Group-A and B had immediate erythema which did not last longer than 48 hours. None of the patients in both treatment groups had itching. All patients in A Group and in B-Group experienced swelling. In Group-A, and in Group-B, 30 patients had immediate pain. Regarding delayed side effects, 3 patients in Group-A and 4 patients in Group-B had folliculitis. 4 patients in Group-B had pigmentary changes. None of the patients in both treatment groups had scarring.

**Table 1:** Comparison of Hair count Pre-treatment and Post-Treatment in both study Groups

	Group-A	Group-B	Total
<b>n</b>	40	40	80
<b>Mean</b>			
<b>Pre-Treatment</b>	14.57±2.69	14.57±2.71	14.57±2.68
<b>Mean</b>			
<b>Post-Treatment</b>	7.47±1.82	5.00±2.06	6.23±2.30

**Group-A= IPL+P**

**Group-B= IPL+E**

**p- value=0.0000**

**Table 2:** Comparison of Hair Count Reduction Percentage in Both Study Groups

	Group-A	Group-B	
	Mean ± SD	Mean ± SD	p-value
<b>Reduction in Hair (%)</b>	47.79±13.14	65.40±13.49	<b>0.000*</b>
<b>Effectiveness</b>	22/40 (55%)	35/40 (87.5%)	<b>0.001**</b>

**NOTE**

(\*): Independent sample t-test was applied to see the difference between groups

(\*\*): Chi-Square test was used to see the significance of efficacy

**Table 3:** Frequency of Side Effects in Both Study Groups

	Group-A	Group-B	Total
N	40	40	80
Erythema	40	40	80
Pain	40	40	80
Swelling	40	40	80
Itching	0	0	0
Folliculitis*	3	4	7
Pigmentary change**	0	4	4
Scarring	0	0	0

**Group-A= IPL+P**

**Group-B= IPL+E**

\*Chi-Square=0.156, p-value=0.692

\*\*Chi-Square=3.408, p-value=0.064

### Discussion:

Hirsutism can be associated with significant psychosocial consequences that negatively affect patient's quality of life. Asian skin has high epidermal melanin content and is more prone to epidermal injuries and adverse pigmentary reactions. Therefore, the management of dark skin phenotypes remains problematic. In the management of hirsutism, the central goals are realistic treatment response expectations, providing emotional support and patient education regarding hirsutism.<sup>14</sup> Several pharmacological therapies are effective in reducing hirsutism.<sup>15</sup> For considerable improvement, pharmacological treatment can take up to 3-6 months.<sup>16</sup> US Food and Drug Administration (FDA) has approved the use of eflornithine in reducing hair by topical route.<sup>17</sup> Eflornithine has been found to be effective in reducing the hair growth by the in vivo study of Kumar et al.<sup>18</sup> This drug has proven to be highly effective in other national and international studies also.<sup>17-20</sup>

In our study the mean age of patients was 24 years. The study conducted by Faria et al. on hirsutism, recorded the mean age as 24.5 years which is same as ours.<sup>10</sup> The mean ages of patients in the study conducted by Hamzavi et al. and Vissing et al. were 40 and 37 years respectively.<sup>14-19</sup> The disparity could be due to the cultural differences as young age marriages are more common in our culture and

women are more conscious of their appearance in this age. So they present earlier in the hospital.

Scoring system used in our study was Ferriman Gallwey score system, which had been used in other national Tabinda et al. and international studies Fattah et al. for hirsutism.<sup>21,5</sup> In our study hair reduction was assessed before the start of laser treatment and 4 weeks after the last laser session. In this study the percentage hair count reduction in Group-A was 47.79% while in Group-B was 65.40%. The difference in percentage reduction of hair count was 17.71%. In studies by Hamzavi et al. and Vissing et al. the percentage reduction was 17% and this is comparable to our study.<sup>14-19</sup> In the study by Shrimal et al. the average hair reduction after last session of IPL was 71.1%.<sup>22</sup>

The effectiveness of treatment in Group-A (IPL + Placebo) was 55% while in Group-B (IPL + Eflornithine) was 87.5%, It can be clearly seen that effectiveness of Group-B treatment was high in comparison with Group-A. While in study conducted by Hamzavi et al. the HRE in group-A treated by Alexandrite laser plus Placebo combination was 67.9% and in Group-B treated with Alexandrite laser plus Eflornithine cream combination was 93.3%.<sup>14</sup> Hamzavi's study showed better results than our study. The difference in results of both studies may be because of different Fitzpatrick skin types and the use of laser in the study by Hamzavi for hair removal while we used IPL device.

In our study, we also noted the side effects experienced by the patients. These were of immediate and delayed type. Among the immediate ones were erythema, swelling, and pain in all patients and pruritus in few of them. While the delayed side effects were hyperpigmentation and folliculitis in few patients. The results were comparable with studies by Hamzavi et al.<sup>14</sup>, Vissing et al.<sup>19</sup> and Zahoor et al.,<sup>23</sup> they reported similar immediate side effects while acne was noted in eflornithine treated side in the study by Vissing et al.<sup>19</sup> Regarding delayed side effects observed in our study, folliculitis was seen in 3 patients of Group-A and 4 patients of Group-B respectively. In our study, scarring was not found in any patient. Hamzavi's study also had the similar results. Shrimal et al. in their study noted erythema in 50%, perifollicular edema in 16.67% and hyperpigmentation in 38.89%, none showed

folliculitis.<sup>14,22</sup> The disparity could have been due to different parameters used for the treatment by IPL.

### Conclusion:

IPL & Eflornithine combination is more effective than IPL & placebo combination in the treatment of idiopathic facial hirsutism. Both treatments are equally safe.

Both the treatment modalities including IPL and Eflornithine are available in Pakistan. In this study IPL plus Eflornithine combination proved to be safe, beneficial and cost effective. The combination therapy will have an impact on the therapeutic practices employed for our skin types in hirsutism.

**Ethical Approval:** Given

**Conflict of Interest:** The authors declare no conflict of interest

**Funding Source:** None

### References:

- Messenger AG, Sinclair RD, Farrant P, de Berker DAR. Acquired disorders of hair. In: Rook's Textbook of Dermatology, 9th edn. Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, eds. Wiley-Blackwell, 2016.
- Fanta M. Hirsutismus [Hirsutism]. Ceska Gynecol. 2017;82(3):237-242.
- Matheson E, Bain J. Hirsutism in Women. Am Fam Physician. 2019;100(3):168-175.
- Mihailidis J, Dermesropian R, Taxel P, Luthra P, Grant-Kels JM. Endocrine evaluation of hirsutism. Int J Womens Dermatol. 2017;3(1):6-10.
- Abdel Fattah NS, Darwish YW. Is there a role for insulin resistance in non-obese patients with idiopathic hirsutism? Br J Dermatol. 2009;160(5):1011-1015.
- Ettler J. Hirsutism - etiopathogenesis, diagnostics and treatment. Cas Lek Cesk. 2017;156(3):133-136.
- Lumachi F, Basso S. Medical Treatment of Hirsutism. Curr Med Chem. 2010;17(23):2530-2538.
- Wanitphakdeedecha R, Alster TS. Physical means of treating unwanted hair. Dermatol Ther. 2008;21(5):392-401.
- Husain Z, Alster T. The role of lasers and intense pulsed light technology in dermatology. Clin Cosmet Invest Dermatol. 2016;9(2):29-40.
- Asad F, Hameed S, Khusrhid K. Efficacy and safety of intense pulsed light in idiopathic hirsutism. Ann KEMU. 2010;16(1):24-26.
- Mohan S, Basheerahmed P, Priyavathani R, Nellainayagam G. New intense pulse light with square pulse technology for hirsutism in Indian patient: a pilot study. J Cosmet Laser Ther. 2012;14(1):14-17.
- Harris K, Ferguson, Hills S. A comparative study of hair removal at an NHS hospital; luminette IPL ver Electrolysis. J Dermatolog Treat. 2012;25(2):169-173.
- Shapiro J, Lui H. Treatment for Unwanted Facial Hair. Skin Ther Lett. 2005;10(10):1-4.
- Hamzavi I, Tan E, Shapiro J, Lui M. A randomized bilateral vehicle-controlled study of eflornithine cream combined with laser treatment versus laser treatment alone for facial hirsutism in women. J Am Acad Dermatol. 2007;57(1):54-59.
- Harrison S. Update on the management of hirsutism. Cleve Clin J Med. 2010;7(12):388-398.
- Barrionuevo P, Nabhan M, Altayar O. Treatment Options for Hirsutism: A Systematic Review and Network Meta-Analysis. J Clin Endocrinol Metab. 2018;103(4):1258-1264.
- Mofid A, Seyyed-Alinaghi SA, Zandieh S, Yazdani T. Hirsutism. Int J Clin Pract. 2008;62(7):433-443.
- Kumar A, Naguib YW, Shi YC, Cui Z. A method to improve the efficacy of topical eflornithine hydrochloride cream. Drug Deliv. 2016;23(5):1495-1501.
- 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. J Eur Acad Dermatol Venereol. 2016;30(2):314-319.
- Shehzad T, Iqbal F, Iqbal N. A randomized study of eflornithine cream combined with intense pulsed light versus intense pulsed light treatment alone for hirsutism in women. J Pak Assoc Dermatol. 2018;28(4):482-484.
- Baig T, Aman S, Nadeem M, Kazmi AH. Quality of life in patients of hirsutism. J Pak Assoc Dermatol. 2014;24(3):217-223.
- 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. J Cutan Aesthet Surg. 2017;10(1):40-44.
- Zahoor H, Noor SM, Paracha MM. Combination of Intense Pulse Light and Topical Eflornithine Therapy versus Intense Pulse Light Therapy alone in the Treatment of Idiopathic Facial Hirsutism: A Randomized Controlled Trial. J Pak Med Assoc. 2019;69(7):930-933.