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Evaluation of Topical Capislow Extract and Long Pulsed Nd-YAG Laser in the Treatment of Idiopathic Hirsutism

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Abstract

Introduction: Hirsutism is a condition that affects 10% of women worldwide. In many cultures, hirsutism is regarded as loss of femininity and can be psychologically traumatizing to the suffering females. The aim of the present study was to evaluate how topical capislow would affect or enhance the efficacy of laser hair removal.

Methods: A randomized, monoblinded, placebo controlled split face study of combined topical capislow and long pulsed Nd-YAG laser on one side of the face versus long pulsed Nd-YAG laser alone on the opposite side of the face. Laser sessions were done at 4 weeks interval for maximum seven sessions. Topical capislow and placebo were applied once daily from the day of the first laser session to the day of the last laser session. Patients were evaluated both subjectively and objectively in each laser session and for six months after the last laser session.

Results: Both treatment modalities were well tolerated and accepted with significantly better results in combined capislow and laser group versus laser alone.

Conclusion: Topical capislow can represent a safe and effective synergistic method for laser with faster results but this is a temporary effect retained only to the time of its application.

Keywords: Laser; Hair removal; Capislow; Nd-YAG.

Introduction

Hirsutism is excessive growth of terminal hair in androgen dependant skin areas. Hirsutism may result in response to elevated androgen levels and on the contrary it may result due to normal androgen levels however with increased sensitivity of the hair follicles.[1] It is a common clinical problem that affects a large percentage of women, particularly in the reproductive age.[2,3]

Lasers were introduced and developed for hair reduction to provide a safe, fast and consistent method to reduce hair. This method has achieved a worldwide acceptance for its effectivness.[4] Despite the effectiveness of this hair removal method, yet there are some limitations to consider when choosing laser and these include pain that could be incurred during the sessions, the need for repeating the sessions to achieve a satisfactory response and the possibility of causing either hyper or hypopigmentation and finally the relative higher cost of this method to traditional hair removal techniques. Moreover light or white colored hair is relatively laser hair removal resistant due to its shortage in melanin.[5]

Capislow extract (an extract from *Larrea divaricata* a shrub that grows in the desert) has been used as a topical hair retardant by inhibiting the anagen phase of hair growth. This is attributed to it high levels of nordihydroguaiaretic acid (NDGA) which has antiproliferative, anti-inflammatory, antioxidant, 5 α reductase enzyme inhibitor and ornithine decarboxylase enzyme inhibitor effects.[6-10]

Owing to the mentioned actions of capislow, the following study setting was designed to examine how much safe and effective is combining topical capislow cream and Nd-YAG laser for treating idiopathic hirsutism.

Methods

Forty-five female patients (skin type III-IV) with idiopathic facial hirsutism, age 18-42 years) were included in this study. They were recruited from the laser clinic and informed consent was obtained from all study participants. They were divided into 2 groups.

Group I (Capislow side): Included a split half face of all the included patients treated by combination of long pulsed Nd-YAG laser and topical capislow while group II (Vehicle side) included the same 45 patients with the

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opposite split side of the face treated with long pulsed Nd-YAG laser and placebo.

Only patients and subjects with preexisting facial hair of the dark type were recruited and subjected to photography. Exclusion criteria included patients with recent viral or bacterial active skin diseases, acne vulgaris, pregnant or lactating females, anyone with scar history as well as patients with hormonal conditions. Patients who completed recent laser or radiofrequency sessions in the 6 months before the study were excluded and those on isotretinoin or anticoagulant medications were dismissed from joining the study.

Treatment Protocol

Selected patients were subjected to detailed history taking, complete clinical examination, laboratory and radiological investigations to exclude any cause of hirsutism other than the idiopathic type. Patients included in the study received sessions using the 1064 nm, long-pulsed Nd:YAG laser (Coolglide CV, Cutera, Brisbane, CA). On one split side of the face laser was done alone and laser was done in combination with topical capislow extract on the opposite side, every 4 weeks until 80% of hair reduction was achieved for a maximum 7 sessions. Protection of the epidermis was achieved using a chill tip in contact with the skin during laser firing. Topical 3% capislow extract in butylene glycol cream (No Hair Cream®, Mash Co. Pharmaceuticals, Egypt) was applied on one side of the face while topical placebo (butylene glycol base) was applied on the other side daily during the study period in a monoblinded manner. Patients were provided with anonymous tubes with two different colors (red and blue). The patients were asked to put on the red cream on one split side of the face and to apply the blue cream from the other tube to the other split half of the face. This was done throughout the whole study. They were applied once daily from the first session then during the study period. No laser session was delivered at a scheduled session if the hairs were apparent and visible by the naked eye. Follow up of the patients continued for up to six months after the last laser session.

Treatment Guidelines

Preoperative Care

Sun screen, bleaching cream, antivirals and antibiotics were used when needed. All hair removal modalities except shaving or chemical depilation were stopped 2-4 weeks before treatment and during the study period.

Technique

All makeup, skin creams or powders were removed. The treatment sessions were performed with the following parameters:

Wavelength (nm): 1064

Pulse duration (ms): 15-40

Energy range (J/cm^2): 30-45

Spot size (mm): 10.

Each side of the face received identical treatment parameters at every session where vaporization of hair shaft, perifollicular erythema and edema were set as immediate end point for the session provided. No other treatment regimen was utilized, and epidermal cooling was done by sapphire- hand piece.

Postoperative Care

Following the session, patients were advised to apply a mildly potent steroid cream (Mometasone furate) once daily for a maximum of 3 days to reduce the erythema and/ or perifollicular edema if it was markedly obvious in certain sensitive patients, while an antibiotic cream (fusidic acid) was indicated twice daily for maximum 5 days if only epidermal injury had occurred. The patients were advised to avoid picking or scratching the area lased and to use sunscreen with a sun protection factor of 50.

Evaluation

Patients were assessed at base line and at every session. The remaining assessments were carried out 1, 3 and 6 months after the last laser session. Side effects as, dyspigmentation, leucotrichia, paradoxical hypertrichosis, scarring and inflammations were recorded during each visit. Treatment efficacy was evaluated through serial photographs, hair counting (using 5 cm^2 transparent grid), and rate of hair regrowth per month. Independent global evaluations were done separately by blinded investigators and patients to evaluate hair quality and degree of skin hairiness (Table 1).

Punch biopsies (2 mm) were taken from the targeted sites bilaterally at base line, at post procedure week, the third and seventh sessions, and at the end of the study. Sections of hair samples were produced and H&E staining was performed.

Statistical Analysis

Analysis of the study as well as statistical interpretations were carried out with the Minitab statistical software using chi-square, *t* test (unpaired and paired) and Man-Whitney analyses. *P* value less than 0.05 was regarded and

Table 1. Investigator Assessment for Facial Hair Response in Comparison to the Baseline

Category	Description
Grade 0 No improvement/ worse	Either no decrease or increased visibility of terminal hair on the treated site. There could be darkening of skin of face
Grade 1 Improved	Clinically obvious decrease in the terminal hair visibility in each of the treated sites. Facial skin lightening
Grade 2 Marked improvement	Considerable decrease in visibility of terminal hair on the treated site. Only minimal darkening in appearance of facial skin.
Grade 3 Clear/ almost clear	Terminal hair not visible at the site of treatment. No change in facial skin color

accepted as statistically significant. Analysis of variance (ANOVA or F test) was used for comparison of more than 2 groups. The analysis was done by a professional statistician at our institute.

Results

Sixty-two patients were recruited for the study; 17 of them failed to complete the treatments and dropped out while 45 continued. All included patients were complaining from idiopathic hirsutism with a mean age (24 ± 8.6 years). They were classified into 2 groups according to the line of treatment.

All the included subjects in the study received long pulsed Nd YAG laser for 7 sessions along with topical application of either capislow on one side of the face group I or placebo on the other side group II. The topical treatment was stopped at the last session then the patients were followed up 1 month, 3 months and 6 months after respectively.

The number of sessions to reach 80% complete hair removal was less and statistically significant $P<0.001$ in the capislow group (mean ± SD = 4.15 ± 2.1) versus (mean ± SD = 6.21 ± 3.12) in the placebo group. Starting from the fifth session, the hair regression showed significant difference towards the capislow side with the most significance demonstrated at the seventh session (Table 2). The rate of hair regrowth was significantly lower at the capislow side starting from the third session onwards (Table 3).

Global evaluation carried out by investigators was significantly positive starting from the third treatment and up to one month following the last session (Tables 4 and 5). The degree of patient satisfaction paralleled that of the investigators and was significant from the third treatment onwards, and up to one month following the last session. At 3- and 6-month follow up intervals, patient evaluation to both modalities returned insignificant satisfaction suggesting a temporary and early improvement only (Table 6).

Only 2 cases (4.44%) in the (Capislow side) and 9 cases (20%) in the (Vehicle side) experienced complications. They included erythema, discomfort, burning sensation, hyperpigmentation, paradoxical hypertrichosis, leukotrichia and inflammation which were insignificant among both groups (Table 7).

Moreover, all the patients were screened for liver enzymes (SGPT & SGOT) and renal functions (serum creatinine),

Table 2. Comparison Between the 2 Sides Regarding Degree of Regression in Hair Number During the Study Period for About 7 Sessions

The Compared Sides	Points of Comparison				Total
	Hair Number				
	Ist Session	3rd Session	5th Session	7th Session	
Nd -YAG and capislow	34.17 ± 19.3	23.4 ± 14.7	18.3 ± 3.8	11.6 ± 2.8	21.86 ± 7.24
Nd-YAG and placebo	34.88 ± 20.1	27.9 ± 16.5	24.7 ± 8.5	19.36 ± 5.8	26.71 ± 4.25
P value	>0.05	>0.055	<0.05*	<0.05*	<0.05*

*Significant ($P<0.05$).

Table 3. Rate of Hair Regrowth During the Study Sessions

The Compared Sides	Points of Comparison				Total
	Hair Regrowth				
	Ist Session	3rd Session	5th Session	7th Session	
Nd -YAG and capislow	8.4 ± 3.5	5.41 ± 1.9	4.10 ± 3.4	1.74 ± 0.88	4.28 ± 2.5
Nd-YAG and placebo	8.16 ± 13.7	7.42 ± 3.2	6.11 ± 3.8	4.13 ± 2.1	6.87 ± 3.5
P value	>0.05	>0.055	<0.05*	<0.05*	<0.05*

*Significant ($P<0.05$).

Table 4. Comparison Between the 2 Sides Regarding the Global Score of Evaluation During the study Period

The Compared Sides		Points of Comparison				Difference
		Global Score of Evaluation				
		0	1	2	3	
Third session	Nd-YAG and capislow	-	21	24	-	$\chi^2=5.411$ *P* value = 0.59
	Nd-YAG and Placebo	9	24	12	-	
Fifth session	Nd-YAG and capislow	-	18	20	7	$\chi^2=20.24$ *P* value = 0.001*
	Nd-YAG and Placebo	6	28	8	-	
Seventh session	Nd-YAG and capislow	-	15	17	13	$\chi^2=15.72$ *P* value = 0.001*
	Nd-YAG and Placebo	-	24	12	9	

*Significant ($P<0.05$).

Table 5. Comparison Between the 2 Sides Regarding the Global Score of Evaluation During Followup

The Compared Sides		Points of Comparison: Global Score of Evaluation 0	1	2	3	Difference
One month after	Nd-YAG and capislow	-	15	17	13	$\chi^2=15.72$
	Nd-YAG and Placebo	-	24	12	9	*P* value = 0.001*
Three months after	Nd-YAG and capislow	-	19	17	9	$\chi^2=5.48$
	Nd-YAG and Placebo	-	24	15	6	*P* value = 0.73
Six months after	Nd-YAG and capislow	-	21	14	10	$\chi^2=6.35$
	Nd-YAG and Placebo	-	25	12	7	*P* value = 0.62

*Significant ($P<0.05$).

Table 6. Comparison Between the 2 Sides Regarding the Degree of Patient Satisfaction During the Study Period

The Compared Sides		Points of Comparison: Degree of Patient Satisfaction No Improvement	Fair	Average	Very Good	Excellent	Difference
Third session	Nd-YAG and capislow	-	-	21	24	-	$\chi^2=4.18$
	Nd-YAG and placebo	8	4	32	1	-	*P* value = 0.58
Fifth session	Nd-YAG and capislow	-	-	17	19	9	$\chi^2=33.87$
	Nd-YAG and placebo	4	3	35	3	-	*P* value = 0.001S*
Seventh session	Nd-YAG and capislow	-	-	15	18	12	$\chi^2=22.60$
	Nd-YAG and placebo	-	6	28	5	3	*P* value = 0.002S*

*Significant ($P\leq0.05$).

Table 7. Comparison Between the 2 Treated Sides Regarding the Occurrence of Complications During the Study Period

The Compared Sides	Complication: Dyspigmentation	Whitening of Hair	Paradoxical Hypertrichosis	Scarring	Inflammation	Total
Nd -YAG and capislow	1	1	-	-	-	2
Nd-YAG and placebo	3	1	2	-	3	9
Difference	0.05	>0.05	>0.05	>0.05	>0.05	>0.05

for evaluation of topical capislow safety, at the beginning, during and at the end of the study and no discovered abnormalities were reported (Table 8).

Histological Evaluation

Biopsies taken from both study groups at base line, showed a normal hair structure. Histologically, at all post treatment sessions, the external root sheath appeared normal with mild focal disruption. Some hair shafts showed thinning and shriveling due to thermal injury whereas some specimens had no shaft due to atrophy following treatments. Some specimens showed incomplete and uneven disruption of the internal root sheath due to the thermal effect of treatment. Increased collagen deposition had been noted. All the previous changes were equally encountered in biopsies obtained from group I (Capislow side) and group II (Vehicle side) patients with an exceptional less inflammatory infiltrate in the capislow group (Figure 1).

Discussion

Hirsutism is a medical condition whose hallmark is excess growth of dark colored coarse hair in male like pattern. The condition affects 5% to 15% of females mostly during the child bearing period in androgen dependant sites.[11] Hirsutism represents a severe cosmetic disturbance and causes great social and psychological embarrassment including anxiety, social avoidance and confusion of gender identity.[12,13]

Idiopathic hirsutism is identified in 10%-15% of women who are apparently hirsute, with normal levels of serum androgen levels and normal ovulatory and hormonal functions.[14-16] In the present study, we aimed to evaluate whether the combination of physical "(long pulsed Nd-YAG laser) and pharmacological (topical capislow)" method would be superior to long pulsed Nd-YAG laser alone in the treatment of idiopathic hirsutism. Additionally, we assessed how safe and effective this combination is. To our knowledge, this represents the first study of its nature and was not carried out before in this study setting.

The synergistic significant effect of topical capislow and the Nd-YAG laser could be explained by the ability of capislow extract to slow terminal hair growth by inhibiting the anagen hair cycle phase. The extract contains high levels of nordihydroguaiaretic acid (NDGA) which has an antiproliferative, anti-inflammatory, 5 α reducase enzyme and ornithine decarboxylase enzyme inhibitory effects.[17]

Table 8. Evaluation of the Effect of the Topical Capislow on Liver Enzymes (SGPT, SGOT) at the First Session and at the Seventh Session

	Points of Comparison					
	SGPT (ALT) Alanine aminotransferase Normal =up to (7:56 U\L)			**SGOT (AST) Aspartate aminotransferase Normal = up to (5:40 U\L)**		
	Before Treatment	**After Treatment**	***P* value**	**Before Treatment**	**After Treatment**	***P* Value**
Treated patients	22.34 ± 3.24	23.12 ± 2.16	> 0.05	21.92 ± 4.29	21.65 ± 7.21	> 0.05

*Significant ($P \leq 0.05$).

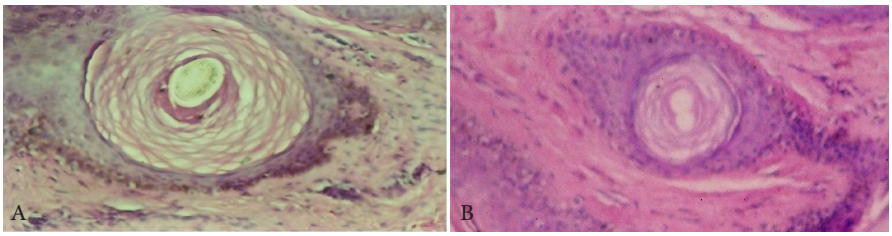

Figure 1. A cross section in the hair (H&E×250) after 5 sessions (**1A**) After Nd-YAG laser and placebo showing atrophy of outer and inner root sheaths with degeneration and rupture of focal areas of sheath, atrophy of hair shaft, inflammatory cellular infiltrate mainly lymphocytes and the dermis shows more collagen deposition. (**1B**) After Nd-YAG and capislow showing atrophy of the outer and inner root sheaths, atrophy of the hair shaft, minimal inflammatory cellular infiltrate and the dermis showing more collagen deposition.

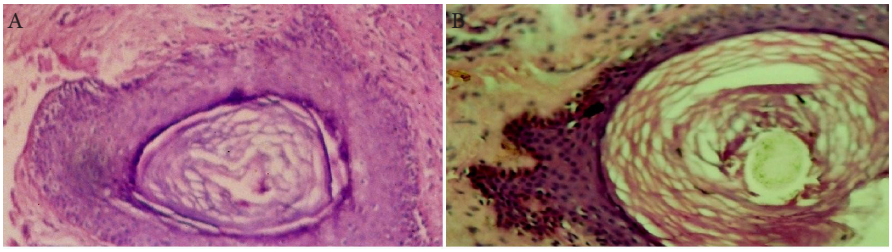

Figure 2. A cross section (H&E×200) after three months of follow up (2A) in the side treated with long pulsed Nd-YAG laser and placebo showing a more or less normal structure. (2B) in the side treated with long pulsed Nd-YAG laser and capislow with a more or less normal structure.

The inhibitory action of capislow extract on 5 α reductase enzyme is mediated by many natural and synthetic polyphenolic compounds including NDGA which is a highly more effective inhibitor of the type 1 than the type 2 isozyme of the 5 α reductase enzyme.[6] Moreover the anti-inflammatory effect of NDGA is attributed to its inhibition of the lipoxygenase and cycloxygenase enzymes that are involved in synthesis of leukotriens and prostaglandins respectively, which induce the anagen phase of hair growth.[18] In addition, NDGA is suspected to have reversible inhibitory action on the ornithine decarboxylase, enzyme involved in the production of the hair shaft by induction of the lipogenase inhibitor.[19]

Histologically, we demonstrated an insignificant difference between the 2 studied therapeutic lines except for minimal inflammatory infiltrate in the capislow treated side. Generally, there was hair shaft destruction with follicular damage and more collagen deposition but these effects were temporary and thought to be due to the thermal effect of laser, as specimens of hair at the end of the study showed a more or less normal hair structure. This means that in spite of the clinical synergistic effect of topical capislow to photoepilation, there were no additive effect at the histological level (Figure 2).

The present work agreed to the concept that topical capislow is effective, well tolerated and a safe therapy for hirsutism. We did not report any skin or systemic side effects from topical use of capislow. In spite the objection of some authors that NDGA has common hepatotoxic and less common nephrotoxic effects, the included patients were evaluated for liver enzymes (SGPT & SGOT) and renal functions (serum creatinine) before and throughout the treatment and it showed no impact. This is in accordance with Stickel et al,[20] who stated that NDGA is toxic only either in systemic large doses of 1.5 to 3 gm per day for no less than 6 months, or in prolonged topical use of concentrations no less than 5%, while the concentration used in this study was 3%.

Conclusion

Topical capislow can represent a safe and effective synergistic method for laser with faster results but this

is a temporary effect retained only to the time of its application.

Conflict of Interests

None.

Ethical Considerations

All subjects gave an informed consent to join this study. The study has been approved by the research ethics committee prior to study beginning.

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