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Role of Pulsed Dye Laser With and Without Intralesional Corticosteroid Injections for Treatment of Hypertrophic Scars

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ABSTRACT

Hypertrophic scar formation remains notoriously difficult to eradicate because of the high recurrence rate and side effects after treatment. The universally accepted protocols that could be used for treatment of hypertrophic scars and the appropriate time to start intervention have not been determined. The present study was conducted to evaluate the effectiveness of flashlamp pulsed dye laser (FPDL, 585nm) alone and in combination with intralesional triamcinolone acetonamide (TAC) injections for early and late treatment of hypertrophic scars. Out of 24 patients, 26 linear hypertrophic scars at different body regions were treated into two equal groups. Patients initially presented with hypertrophic scars of a duration <6 months were treated by FPDL at group (I); whereas, patients initially presented with hypertrophic scars of a duration ≥6 months were treated by combined FPDL and intralesional TAC injections at group (II). All patients were followed up for 6 months after discontinuation of treatment. Different levels of statistically significant improvement ($p \leq 0.05$ at group I, as well as $p \leq 0.05$ and $p \leq 0.01$ at group II), as regard the subjective symptoms, scars' pliability, erythema analysis, and scars' height, have been elicited after treatment. However, no significant statistical change as regard scars' length and width has been observed after treatment in both groups. Clinical improvements after both treatment protocols seemed comparable. Despite of the proved importance of the concomitant use of intralesional TAC injections with FPDL to reduce scar bulk and symptoms during late treatment of hypertrophic scars at group (II), hypopigmentation and dermal atrophy are still encountered complications after intralesional corticosteroid injections. Accordingly, early treatment of hypertrophic scars with FPDL alone is suggested to achieve better response at fewer side effects, as well as it may also prevent scar hypertrophy in hypertrophic scar prone patients. However, lower FPDL fluence is still recommended to minimize the incidence of hyperpigmentation especially in relatively dark-skinned patients commonly seen among Egyptians.

INTRODUCTION

Hypertrophic scars affect 1.5-4.5% of the general population. The exact prevalence of hypertrophic scarring, particularly after burn injury, is unknown **[1]**. Hypertrophic scar formation remains difficult to eradicate because of the high recurrence rate and side effects after treatment **[2]**. Clinically, hypertrophic scars can be disfiguring functionally, aesthetically, or both. Hypertrophic scars develop as a result of alterations in the normal process of cutaneous wound healing. Hypertrophic scars are characterized by proliferation of dermal tissue with excessive deposition of fibroblast-derived extracellular matrix proteins, especially collagen parallel to the skin surface, over long periods, as well as by persistent inflammation and fibrosis. Unlike keloids that are characterized by invasion of the surrounding skin, hypertrophic scars remain within the confines of the original wound and increase in bulk by pushing out the wound margins rather than invasion **[3,4]**.

Despite of the disfigurement, symptoms and psychological impact associated with hypertrophic scars, as well as although different modalities could be used for treatment of hypertrophic scars, there is still no universally accepted treatment protocol. Accordingly, prevention of hypertrophic scars was reported to be the best mainstay strategy **[5]**. However, once a hypertrophic scar is present, there are many treatment modalities that could be used. Lasers, surgical excision, radiation therapy, silicone cream or gel application, cryosurgery, and intralesional injections of variable agents including triamcinolone acetonamide (TAC) and 5-fluorouracil, have all been used either alone or in various combinations with variable reported success rates **[6,7]**. The difficulty to assess the efficacy of existing treatment modalities was reported to be due to the limited numbers of controlled, comparative studies of the effectiveness of various treatment modalities in improving the appearance and/or symptoms of hypertrophic scars especially for new scars of less than 12 months' duration [3].

Various lasers are used to attempt hypertrophic scars improvement; however, inconsistent results have been reported **[3,4,8]**. Moreover, most previous studies investigated the use of lasers in patients with light skin phototypes; whereas, the use of

lasers for treatment of hypertrophic scars in dark-skinned patients is not well established **[9-11]**. Furthermore, the appropriate time to start treatment of hypertrophic scars has not been determined **[6,12,13]**.

Accordingly, the present study was conducted to evaluate the effectiveness of flashlamp pulsed dye laser (FPDL, 585nm) alone and in combination with intralesional TAC injections for early and late treatment of hypertrophic scars.

PATIENTS AND METHODS

Twenty-four patients, of both sexes and different skin phototypes, with twenty-six linear hypertrophic scars at different body regions were included in the present study. All the enrolled scars did not heal to the patients' satisfaction. Keloid scars were excluded from the present study. Moreover, hypertrophic scars treated within the preceding 2 months were excluded from the present study. According to hypertrophic scars' durations at initial presentations, patients were classified into two equal groups. Patients initially presented with hypertrophic scars of a duration <6 months were treated by FPDL (585nm) at group (I); whereas, patients initially presented with hypertrophic scars of a duration ≥6 months were treated by combined FPDL and intralesional TAC injections at group (II). The objective of the treatment was to prevent or suppress hypertrophic scars' growth. Treatment was repeated at 4 weeks intervals till the objective goal was obtained or no further improvement could be achieved.

Group (I): Hypertrophic scars <6 months' duration:

Flashlamp pulsed dye laser (FPDL):

FPDL (585nm, Candela, SPTL-1 b Laser System, USA), at a fluence of 5-7 J/cm^2, pulse duration of 450μsec and spot sizes of 5 and 7mm, were used. Treatment was carried out with pulses overlapping of up to 10%. Before treatment, all laser safety measures were done and an occlusive dressing with EMLA cream for about an hour was applied. After treatment, topical antibiotic and sunscreen preparations were prescribed and avoidance of sun exposure was instructed.

Group (II): Hypertrophic scars ≥6 months' duration:

1- *Flashlamp pulsed dye laser (FPDL):*

It was used at the same laser parameters, instructions and precautions as were previously presented for group (I).

2- *Intralesional corticosteroid injections:*

Concomitant intralesional triamcinolone acetonamide (TAC) injections of (40mg/mL) in a total dose/injection of up to 40mg were carried out.

Evaluating parameters:

All patients were followed-up at 4 weeks-basis visits for 6 months after discontinuation of treatment. At each visit, scars were photographed and questionnaire was done addressing the subjective symptoms; namely pruritis, scar pain and burning sensation. Subjective symptoms were rated on a quartile scale from 1 (absent) to 4 (severe). Photography was obtained using digital camera (Panasonic, LUMIX DMC-FX 8, Matsushita Electric Industrial Co., Ltd., Japan). Lens aperture, exposure time, subject distance and room illumination were kept constant.

Caliber (Cynosure, USA) was used to measure scars' dimensions. Scars' pliability was rated according to the standard scale **[14]**. Scars' erythema was digitally analyzed using Adobe Photoshop 6.0 ME Software (Adobe System Incorporation, USA). The following equation was used to evaluate erythema clearance after treatment and to minimize the possible artifacts during photography.

Erythema clearance (%) =

$$(A - B \div A \times 100) - (C - D \div C \times 100)$$

A and B represent the numerical erythema values of identical areas of the scar at pre- and post-treatment photographs, respectively; whereas, C and D represent the numerical colour values of an identical area of normal skin at pre- and post-treatment photographs, respectively.

Statistical analysis:

Data are presented as numbers, percentages, mean values ± standard deviations and ranges. Results were statistically analyzed using ANOVA test and statistical significance was set at $p \leq 0.05$.

RESULTS

Table (1) summarizes patients' and scars' data. Regarding early treatment of scars at group (I), FPDL was used at a mean of 4.46±1.13 sessions (range, 4-6 sessions) at a fluence of 5.28±0.22J/cm^2 (range, 5-7J/cm^2). However, FPDL at a mean of 5.15±0.8 sessions (range, 4-7 sessions) and a mean fluence of 6.55±0.37J/cm^2 (range, 5-7J/cm^2), combined with intralesional TAC injections at a mean of 4.08±0.86 injections (range 3-5 sessions) and a mean dose of 35.67±5.33mg (range, 20-40mg /injection) were used for late treatment of scars at group (II).

Regarding the results of treatment, Table (2) summarizes the evaluating parameters for each group before treatment, as well as 6 months' period of follow up after treatment including; the improvement of the subjective symptoms, scars' pliability scale, erythema analysis and scars' dimensions. The percentages of erythema clearance after treatment were found to be 44.72%±10.36% and 62%±12.53% at statistical significances of $p \leq 0.05$ and $p \leq 0.01$ for groups (I and II), respectively. Hyperpigmentation was the only complication after early treatment of scars at group (I). It was elicited in only 2 scars (15.38%). However, after late treatment of scars at group (II); hyperpigmentation was elicited in 5 scars (38.46%) and hypopigmentation and dermal atrophy were observed in 2 scars (15.38%), for each.

Figs. (1,2) (A,B) show patients at groups (I and II, respectively) with hypertrophic scars before treatment and 6 months' period of follow-up after treatment, respectively.

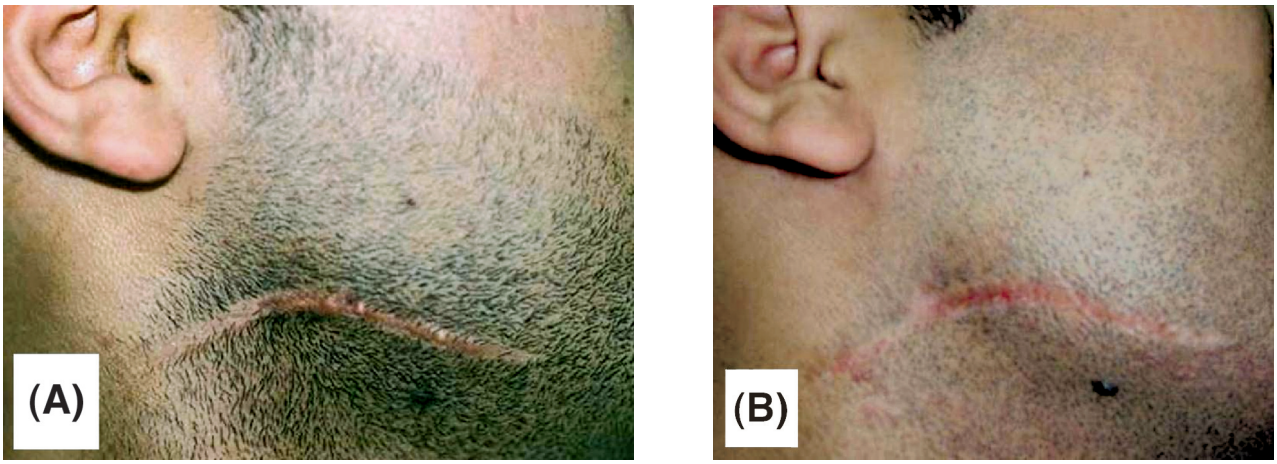

Fig. (1): Right lateral view for a patient at group (I) with hypertrophic scar treated by FPDL; (A) before treatment and (B) 6 months' period of follow-up after treatment.

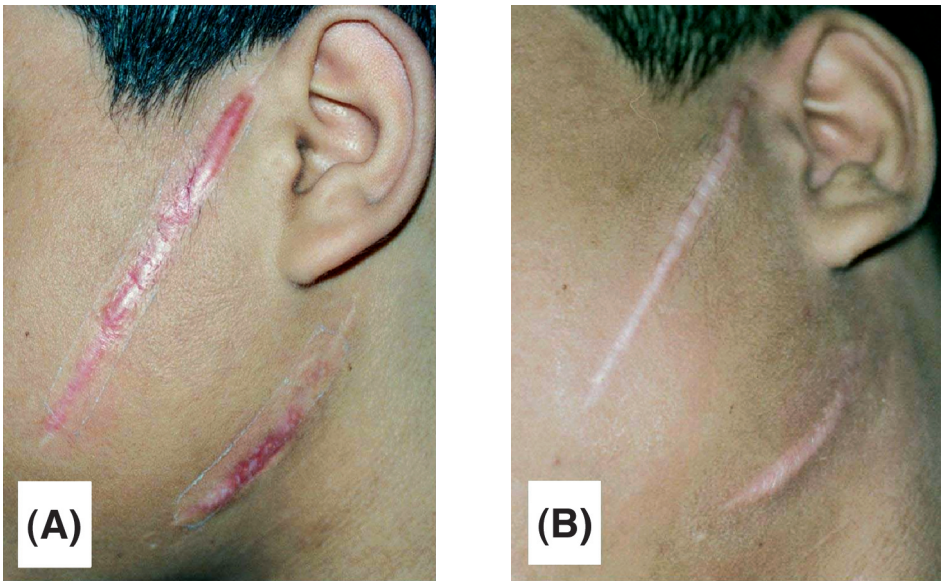

Fig. (2): Left lateral view for a patient at group (II) with hypertrophic scars treated by combined FPDL and intralesional TAC injections; (A) before treatment and (B) 6 months' period of follow-up after treatment.

Table (1): Patients' and scars' data before starting treatment. Data are presented as numbers (%), mean values ± standard deviations and ranges.

Clinical data	All patients (n=24)	Group (I) (n=12 pts)	Group (II) (n=12 pts)
Sex:			
Male	14 (58.33%)	8 (66.67%)	6 (50%)
Female	10 (41.67%)	4 (33.33%)	6 (50%)
Age (Yrs)	22.50±15.89 (4-42)	21.25±10.79 (4-38)	29.75±12.23 (14-42)
Skin phototype:			
II	2 (8.33%)	2 (16.67%)	–
III	9 (37.5%)	6 (50%)	3 (25%)
IV	10 (41.67%)	4 (33.33%)	6 (50%)
V	3 (12.5%)	–	3 (25%)
Number of hypertrophic scars	26	13	13
Locations:			
Head and neck	18 (69.23%)	12 (92.31%)	6 (46.15%)
Trunk	3 (11.54%)	–	3 (23.08%)
Extremities	5 (19.23%)	1 (7.69%)	4 (30.77%)
Scar duration (months)	9.58±7.59 (2-18)	3.83±1.07 (2-5)	12.33±5.57 (6-18)
Occurrence:			
De novo	14 (53.85%)	6 (46.15%)	8 (61.54%)
Recurrent	12 (46.15%)	7 (53.85%)	5 (38.46%)
Previous treatment:			
Surgical excision	8 (30.77%)	5 (38.46%)	3 (23.08%)
Intralesional corticosteroid injection	4 (15.39%)	1 (7.69%)	3 (23.08%)
Silicone gel sheeting	7 (26.92%)	3 (23.08%)	4 (30.77%)

Table (2): Evaluating parameters for each group before treatment and 6 months' period of follow-up after treatment. Data are presented as numbers (%), mean values ± standard deviations and ranges. Note: N.S. means not statistically significant.

Evaluating parameters	Group (I) (n=13 Hypertrophic scars)			Group (II) (n=13 Hypertrophic scars)		
	Before Treatment	After Treatment	*p* Value	Before Treatment	After Treatment	*p* Value
Subjective symptoms:						
1 (absent)	–	–		–	–	
2 (mild)	3 (23.08%)	9 (69.23%)	≤0.05	–	5 (38.46%)	≤0.05
3 (moderate)	10 (76.92%)	4 (30.77%)		6 (46.15%)	8 (61.54%)	
4 (severe)	–	–		7 (53.85%)	–	
Scars' pliability scale:						
1	–	1 (7.69%)		–	2 (15.38%)	
2	2 (15.38%)	5 (38.46%)		–	4 (30.77%)	
3	8 (61.54%)	7 (53.85%)	≤0.05	4 (30.77%)	7 (53.85%)	≤0.01
4	3 (23.08%)	–		9 (69.23%)	–	
5	–	–		–	–	
Erythema analysis	204.82±43.67 (238-153)	163.5±24.8 (181-127)	≤0.05	212.56±53.17 (244-165)	132.7±16.2 (161-110)	≤0.01
Scars' dimensions:						
Length (mm)	52±30.07 (20-100)	51.22±27.42 (20-100)	N.S.	52.69±30.24 (20-120)	51.66±31.79 (20-120)	N.S.
Width (mm)	8.62±3.55 (5-12)	9.15±2.39 (5-14)	N.S.	12.46±4.14 (5-16)	13.36±3.57 (5-18)	N.S.
Height (mm)	3.77±2.17 (3-5)	1.06±0.24 (0-2)	≤0.05	5.46±2.13 (5-7)	1.48±1.06 (0-3)	≤0.01

DISCUSSION

Although the basis of hypertrophic scar formation has not been fully delineated, an imbalance between matrix degradation and collagen biosynthesis resulting into excess collagen accumulation in the wound has been postulated. Normally, fibroblasts construct new extracellular matrix, initiate collagen synthesis, and provide wound edge tension along contractile proteins; actin and desmin. On the other hand, hypertrophic scar-derived fibroblasts produce increased amount of collagen per cell compared with normal fibroblasts **[3,4]**. Accordingly, the suppression of overwhelming and uncontrolled fibroblast activity in hypertrophic scars may be an essential approach during treatment of this abnormal wound healing. However, hypertrophic scar formation remains a difficult problem to eradicate. This is not only due to the high recurrence rate; where 46.15% of the scars in the present study were recurrent, but due to the incidence of side effects associated with treatment as well **[2]**.

The effectiveness of FPDL treatment of hypertrophic scars is hypothesized to be mediated to the selective photothermolytic effect of FPDL on scars' microvasculature with consequent wound ischaemia **[15]**. Moreover, the improvement in skin texture of scars treated with FPDL was found to be an interesting observation that adds a significant favorable outcome. This textural improvement is suggested to be due to collagen remodeling, the same concept for the improvement seen with FPDL treatment of photoaged skin **[16]**. Despite of the effectiveness of FPDL treatment of hypertrophic scars, three debatable issues should be concerned namely; the appropriate laser fluence to be used, the frequency of the treatment sessions and the appropriate time to start treatment.

First; regarding the appropriate fluence to be used, the fluence-dependent inhibition of hypertrophic scar formation after FPDL treatment was reported to be proportional to the used fluence **[4,15]**. This was clearly elicited in the present study where a relatively lower fluence (5.28±0.22J/cm^2) was needed for early treatment of less bulky scars at group (I) compared with the higher fluence (6.55±0.37J/cm^2) used for late treatment of more bulky scars at group (II). On the contrary, others observed no significant difference in the treatment results with the used fluences **[17,18]**; however, a concept toward better responses and fewer side effects with lower FPDL fluence was observed **[3]**.

Second; regarding the frequency of treatment sessions, Wittenberg et al. **[4]**, reported that there was no clinical improvement with 4 FPDL (585nm) sessions. In contrast, Goldman and Fitzpatrick **[17]** reported the reverse. This positive result is confirmed in the present study, where flattening of the scars at both groups was observed about as early as the 16th week after FPDL treatment (4 weeks after the 4th treatment session). Moreover, higher rate of scar flattening was elicited after more than two FPDL treatment sessions. Accordingly, multiple and sequential FPDL treatment sessions are essential to achieve better clinical outcome. However, it was still observed that late treatment of bulky scars at group (II) needed more frequent FPDL sessions (5.15±0.8) compared with the less frequent sessions (4.46±1.13) needed for early treatment of less bulky scars at group (I).

Third; regarding the appropriate time to start treatment and because of the natural history of the proposed spontaneous improvement of hypertrophic scars during the first 6-12 months after injury, the evaluation of early treatment of hypertrophic scars may be difficult **[3]**. However, hypertrophic scars younger than 12 months were still included in the present study for few reasons. First, it was hypothesized that if any hypertrophic scars were to improve with FPDL treatment, it would be the younger, erythematous scars. Second, it was hypothesized that early FPDL treatment would prevent hypertrophic scars from getting worse. Finally, many studies have reported the use of FPDL for early treatment of hypertrophic scars younger than 6 months duration starting even on the day of suture removal **[6,9,12,13]**, as well as for late treatment of hypertrophic scars of more than 6 months' duration **[3]**.

All intralesional formulas have shown comparable results in hypertrophic scar flattening. They have been suggested to have higher effectiveness than laser treatment **[3]**. The role of intralesional corticosteroid injections for treatment of hypertrophic scars has been well-established. The suppression mechanisms of intralesional corticosteroid injection on wound healing include; first, the interruption of the inflammatory cell migration and phagocytosis. Second, it induces vasoconstriction resulting into deprivation of oxygen and nutrients in the wound. Third, it has an anti-mitotic activity on fibroblasts and keratinocytes **[2,3]**. Collectively, intralesional corticosteroid injection was reported to produce objective improvements in hypertrophic scar volume and symptoms especially for those scars of more than 6 months' duration **[1-3]**. Accordingly, it was considered in the present study for late treatment of more bulky scars at group (II) rather than less bulky scars at group (I).

Triamcinolone acetonamide (TAC) is the most commonly used corticosteroid for treatment of hypertrophic scars. Although intralesional TAC injection has shown clinical efficacy, the results have been uncertain and frequently associated with many side effects including; pigmentary changes, and dermal atrophy **[19-21]**. Theoretically, the combination therapy is supposed to be of value in order to achieve better results and to minimize the associated complications. However, there is a debate about the effectiveness of the combined treatment of FPDL and intralesional TAC injections **[2,3]**. Recently, others reported the effectiveness of this combination **[19,21]**. Similarly, different levels of statistically significant clinical improvements ($p \leq 0.05$ and $p \leq 0.01$) have been elicited after combined FPDL and intralesional TAC injections for late treatment of scars at group (II). However, despite of the proved importance of the concomitant use of intralesional TAC injections with FPDL to reduce scar bulk and symptoms during late treatment of hypertrophic scars at group (II), hypopigmentation and dermal atrophy are still encountered complications after intralesional corticosteroid injections.

Finally, it was frequently reported that high melanin in dark-skinned patients; as it is commonly seen among Egyptians, is a competitive chromophore to haemoglobin during FPDL treatment **[9-11]**. Accordingly, more frequent sessions of FPDL at higher fluence were found to be needed for effective treatment especially for late treatment of more bulky scars at group (II) rather than early treatment of less bulky scars at group (I). However, this could explain; meanwhile, the inevitable higher incidence of hyperpigmentation (38.46%) after late treatment of scars at group (II) compared with the lower incidence of hyperpigmentation (15.38%) after early treatment of scars at group (I).

Conclusion:

FPDL alone and its combination with intralesional TAC injections are effective modalities that could be used for early and late treatment of hypertrophic scars, respectively. Clinical improvements after both treatment protocols seemed comparable. Different levels of statistically significant improvements ($p \leq 0.05$ at group I, as well as $p \leq 0.05$ and $p \leq 0.01$ at group II), regarding the subjective symptoms, scars' pliability, erythema analysis and scars' height, have been elicited after treatment. However, no significant statistical change was observed as regard scars' length and width after treatment in both groups. Despite of the proved importance of the concomitant use of intralesional TAC injections with FPDL to reduce scar bulk and symptoms during late treatment of hypertrophic scars at group (II), hypopigmentation and dermal atrophy are still encountered complications. Accordingly, early treatment of hypertrophic scars with FPDL alone is suggested to achieve better response at fewer side effects, as well as it may also prevent scar hypertrophy in hypertrophic scar prone patients. However, lower FPDL fluence is still recommended to minimize the incidence of hyperpigmentation especially in relatively dark-skinned patients commonly seen among Egyptians.

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