

Efficacy of combination of intralesional triamcinolone and pulsed dye laser (PDL) in keloid

Maryam Kkhalili, Saeedeh Farajzadeh*, Masoumah Rabbani**, Saman Mohammadi, Rezvan Amiri, Mahin Aflatoonian

Department of Dermatology, Kerman University of Medical Sciences, Iran.

* Pathology and Stem Cell Research Center, Kerman University of Medical Sciences, Iran.

** General Practitioner, Kerman University of Medical Sciences, Iran.

Abstract

Objective To evaluate efficacy of combination of intralesional triamcinolone with PDL in patients with keloid.

Methods This is a cross-sectional observational study on patients with keloid referring to Afzalipour hospital during five years. Efficacy of treatment was evaluated by physician's and patients' global assessment. PDL was done in monthly interval with single pulse, no overlapping, 5-10 mm spot size, 0.5-6 ms pulse duration and fluence of 6-10 j/cm². Intralesional triamcinolone was injected (0.1cc in each one cm², maximum 2cc) after laser with concentration from 10-40 mg/ml.

Results Eighty-two patients (range 2-65 years) with keloid were treated with mean number of 4.05±0.51 treatment sessions (range 2-10). Side effects included purpura, hyperpigmentation, blister, crust formation, persistent erythema and hypopigmentation. Patients were mainly satisfied or very satisfied (73.1%) and physician evaluation demonstrated more than 50% improvement in 70.7% of cases. There was no significant correlation between response rate with demographic features of the patients, site of the lesions or treatment protocol.

Conclusion In the current study, nearly third-quarter of the patients demonstrated more than 50% improvement and were satisfied or very satisfied with treatment results. Males, younger patients and lighter skin types showed better outcome. Furthermore, more number of treatment sessions and higher fluence accompanied with better results.

Key words

PDL; Keloid; Triamcinolone.

Introduction

Keloid results from increased synthesis and deposition of type I and III collagen fibers as well as decreased degeneration of collagen. Elevated level of cytokines including transforming growth factor (TGF)-β1 and TGF-β2 leads to reduced level of matrix

metalloproteinase (MMP) and increased level of tissue inhibitor metalloproteinase (TIMP) that eventually results in less collagen degeneration.¹⁻⁴ On the other hand, increased level of TGF-β1 and TGF-β2 leads to higher fibroblast activity and more collagen and extracellular matrix protein production (ECM). Furthermore, increased level of other cytokines and chemokines such as interleukin (IL)-1, IL-6, IL-15, IL-13, tumor necrosis factor (TNF-α), vascular endothelial growth factor (VEGF), connective tissue growth factor (CTGF) and platelet derived growth factor (PDGF) has an essential role in the pathogenesis of keloid.¹⁻⁴

Address for correspondence

Dr. MahinAflatoonian, Associate Professor,
Dermatology Department,
Afzalipour Hospital, Kerman Medical University,
Kerman, Iran. Post code: 761614111
Tel:09125987542
Email:maafatoonian@gmail.com

Keloid can lead to considerable physical restriction, symptoms such as pain and pruritus as well as serious cosmetic concern.¹⁻⁴ Currently, there are several treatment modalities [such as intralesional corticosteroid (IL CS), imiquimod, IL 5-fluorouracil (5-FU), bleomycin, occlusive dressing, cryotherapy, surgical excision and laser therapy] with variable rates of success and relapse.¹⁻⁴ IL CS is usually first-line of treatment and acts through inhibition of collagenase and increased degeneration of collagen fibers. It can lead to side effects such as atrophy, telangiectasia and depigmentation at injection site. Various types of ablative lasers including carbon dioxide (CO₂) and erbium-doped YAG (Er: YAG) and non-ablative lasers including PDL, intense pulsed light (IPL), neodymium-doped YAG (Nd: YAG laser) and Er: doped laser have been applied for the treatment of keloid.¹⁻⁴ In this study we decided to evaluate efficacy of combination of IL CS with PDL in patients with keloid.

Material and methods

This is a cross-sectional observational study on patients with keloid referring to laser ward of Afzalipour hospital for PDL during five years. Firstly, after obtaining informed consent from patients, demographic features (age, sex and skin type) and site of the lesions were recorded. Then, efficacy of treatment was evaluated by two dermatologists via photographs by digital camera (SX410IS, Canon, China) taken before and after each treatment session. Percentage of improvement was graded as poor (0-25% improvement), fair (26-50% improvement), good (51-75% improvement) and excellent (more than 75% improvement). At the end of the treatments, patients were asked about percentage of satisfaction of the treatment graded as very satisfied (more than 75% improvement), satisfied (51-75% improvement), slightly satisfied (26-50% improvement) and dissatisfied

(less than 26%). This proposal was approved by ethical code IR.KMU.AH.1398.120.

Patients were asked to apply a thin layer of topical anesthesia (xylocain-p) on the lesion under occlusion for 30 minutes, and then washed off with water and soap. PDL (Synchro Vas-Q, DEKA M.E.L.A., Florence, Italy) was done in monthly interval with single pulse, no overlapping, 5-10 mm spot size, 0.5-6 ms pulse duration and fluence of 6-10 j/cm². In order to reduce pain, blister formation and hyperpigmentation, cooling air system and ice pack was applied on the treatment area during and after each laser therapy session. Intralesional triamcinolone was injected via 30 gauge needle (0.1cc one cm² apart, up to total of 2 cc) after PDL laser with concentration from 10 mg/ml to 40 mg/ml (depend on lesion thickness and site). In order to prevent infection, topical fusidic acid was applied on the site for 5 days. Patients were asked to avoid sun-exposure for the next two weeks, and to apply antisolar and emollient on the lesions.

Results

Eighty-two patients (64.6% female) with keloid were treated with combination of IL CS and PDL during five years. Mean age of the patients was 27.78±13.68 (range 2-65) years, and the majorities had skin type of III (57.3%). Lesions were mostly in torso (43.9%), and the remaining were in head and neck (35.4%) and extremities (20.7%). Mean number of sessions was 4.05±0.51 (range 2-10). Side effects including purpura, hyperpigmentation, blister, crust formation, persistent erythema and hypopigmentation were observed in 85.3%, 12.2%, 6.1%, 6.1%, and 1.2% and 1.2% of cases, respectively.

Patients were mainly satisfied or very satisfied (64.6% and 8.5%, respectively) and the rest

were slightly satisfied or dissatisfied (12.3% and 14.6%, respectively). Physician’s evaluation demonstrated excellent, good, fair and poor improvement in 14.6%, 56.1%, 17.1% and 12.2% of cases. There was no significant correlation between response rate with demographic features of the patients, site of the lesions or treatment protocol (**Table 1**).

Discussion

PDL works through selective photothermolysis, and destroys microvasculature supplying fibrous tissue, induces hypoxia and apoptosis of fibroblasts, also stimulates collagenolysis via down regulation of inflammatory mediators (TGF-β, VEGF, CTGF, IL-1, IL-6 and TNF-α) and up regulation of MMP-13.¹⁻⁶ It demonstrated better outcome compared to conventional

treatment modalities such as IL CS and silicone gel sheeting.⁷⁻⁹ Side effects generally are transient and tolerable.⁷⁻⁹ The current study demonstrated good-to-excellent improvement in 70.7% of cases with combination of IL CS (10-40 mg/cc) and PDL (2-10 treatment sessions). Furthermore, approximately 73% of the patients were satisfied or very satisfied with treatment results.

Previous studies used different device setting (wavelength 585-595 nm, fluence 3.5-9 j/cm2, pulse duration 0.25-40 ms) as monthly or bimonthly sessions for up to 12-18 treatment sessions. Good-to-excellent improvement was reported in 70-86.7% and 37.2%-80% of cases via physician global assessment and patients’ global assessment, respectively (**Table2**).⁵⁻¹¹

Table 1 Response rate based on demographic and site of the lesions.

Variables		Percentage of improvement				P. Value	
		Excellent N (%)	Good N (%)	Fair N (%)	Poor N (%)		
Sex	Male	5 (17.2)	16 (55.2)	5 (17.2)	3 (10.4)	0.9	
	Female	7 (13.2)	30 (56.6)	9 (17)	7 (13.2)		
Age (Year)	0-10	4 (40)	4 (40)	2 (20)	0 (0)	0.5	
	11-20	1 (5)	14 (70)	3 (15)	2 (10)		
	21-30	3 (11.5)	14 (53.9)	5 (19.3)	4 (15.3)		
	31-40	3 (20)	6 (40)	3 (20)	3 (20)		
	51-60	0 (0)	4 (66.8)	1 (16.6)	1 (16.6)		
	61-70	0 (0)	3 (100)	0 (0)	0 (0)		
	71-80	1 (50)	1 (50)	0 (0)	0 (0)		
Site	Head & neck	8 (27.6)	15 (51.7)	4 (13.8)	2 (6.9)	0.5	
	Trunk	3 (8.3)	20 (55.6)	6 (16.7)	7 (19.4)		
	Extremities	1 (5.8)	11 (64.8)	4 (23.6)	1 (5.8)		
Skin type	II	6 (30)	9 (45)	4 (20)	1 (5)	0.2	
	III	4 (8.5)	28 (59.5)	9 (19.1)	6 (12.9)		
	IV	2 (13.3)	9 (60)	1 (6.6)	3 (20.1)		
Treatment sessions	<3	4 (9.3)	26 (60.5)	10 (23.2)	3 (7)	.473	
	4-6	3 (13.1)	13 (56.5)	2 (8.7)	5 (21.7)		
	7-10	5 (31.3)	7 (43.7)	2 (12.5)	2 (12.5)		
Device setting	Fluence (J/cm ²)	6	3 (12.5)	15 (62.5)	4 (16.7)	2 (8.3)	.985
		7	5 (15.2)	18 (54.5)	6 (18.2)	4 (12.1)	
		10	4 (16)	13 (52)	4 (16)	4 (16)	
	Spot size (mm)	5	2 (15.4)	10 (76.9)	1 (7.7)	0 (0)	0.506
		7	1 (16.7)	4 (66.7)	1 (16.7)	0 (0)	
		10	9 (14.3)	32 (50.8)	12 (19.1)	10 (15.8)	
Pulse duration (ms)	0.5	8 (14.3)	34 (60.7)	12 (21.4)	2 (3.6)	0.786	
	1.5	4 (23.5)	11 (64.8)	2 (11.7)	0 (0)		
	6	0 (0)	1 (11.2)	0 (0)	8 (88.8)		

Table 2 Comparison of the results of this study with other studies in patients with keloid.

Reference	Number/ sex	Age (y)	Site	FST	Device setting	Physician Evaluation (% improvement)	Patients Evaluation (% improvement)	S/E (%)	Number of sessions/interval	Adjuvant therapy
This study	29 M 53 F	27.78±13.68 (2-65)	H&N Trunk Ext	II III IV	WL:595 nm; Spot:10 mm PD: 0.5 ms F:5-10 J/cm ²	0-25%:12.2 26-50%:17.1 51-75%:56.1 76-100%:14.6	Vs: 8.5 S: 64.6 SS: 12.3 DS: 14.6	Purpura (85.3) Hyperpigmentation (12.2) Blister (6.1) Crust (6.1) Erythema (1.2) Hypopigmentation (1.2)	4.05 ± 0.51 (2-5) monthly	ILT
Yang (2012) [5]	14 F 12 M	26.35±6.50 (20-40)	Trunk	III IV	WL: 595 nm Spot:7 mm PD: 1.5 ms F:10 J/cm ²	Mean improvement: 20.85%	NS	Blister (22.2) PIH (48.15)	3 Every 3-4 w	NS
Kuo (2004) [6]	18 F 12 M	32 (12-60)	H&N Ext Trunk	NS	WL: 585 nm SPOT: PD: F: J/cm ²	51-100: 86.7	NS	NS	1-11	NS
Omranifard (2007) [8]	31 F 9 M	27 (10-35)	H&N	III	WL: 585 nm; Spot: 5 mm PD: 1.5 ms; F:7-9 J/cm ²	51-100%: 70	>50%:65%	No	3-12 Monthly	NS
Asilian (2006) [9]	9 M 11 F	25.5±13 (5-70)	H&N Trunk Ext	NS	WL: 585 nm Spot: 5 mm PD: 250 μs F: 5-7.5 J/cm ²	0-25%:10 26-50%:20 51-75%:55 76-100%:15	0-25%: 10 26-50%: 15 51-75%: 55 76-100%:20	Purpura	3 monthly	ILT 5-FU
Cannarozzo (2015) [10]	33M 26 F	37.5	H&N Trunk	I II III IV	WL: 585 nm Spot:12 mm PD:0.5-1.5 ms F:6-7J/cm ²	0-25%: 5.08 26-50%: 20.4 51-75%: 25.4 76-100%:49.1	VS: 62.7 S:30.5 SS: 6.7	Hypopigmentation (3.4) PIH (11.8)	6-8 monthly	No
Stephanides (2011) [11]	41 M 51 F	NS	H&N Trunk	NS	WL: 595 nm Spot:7 PD:1.5 F:4-15 J/cm ²	0-50%:23.2 51-75%:59.6 76-100%:17.2	VAS score: 7-8	Atrophy (3.03) Erythema (3.03) Discomfort (3.03)	8-12 Every 6-8 w	ILT

Abbreviations: Y, year; S/E, side effects; M, male; F, female; H&N, head and neck; Ext, extremity; WL, wavelength; PD, pulse duration; F, fluence; VS, very satisfied; S, satisfied; SS, slightly satisfied; DS, dissatisfied; ILT; intralesional triamcinolone; PIH; post inflammatory hyperpigmentation; NS, not stated; VAS, visual analogue scale; 5-FU, 5-fluorouracil;

Combination of PDL with traditional treatment modalities optimized treatment efficacy and reduced unwanted side effects due to reduced treatment sessions and employing of lower fluence. Stephanides *et al.* showed moderate-to-excellent improvement in keloid with monotherapy of PDL versus combined PDL and IL CS during 12-14 and 4-5 treatment sessions, respectively.¹¹ Likewise, Asilian *et al.* showed better efficacy with combined IL CS, IL 5-FU and PDL compared to combined IL CS and IL 5-FU (70% and 40%, respectively).⁹ Stephanides *et al.* evaluated efficacy of combination of IL CS (10-40mg/cc) and PDL (8-12 treatment sessions) on 99 patients with keloid. They reported good-to-excellent improvement (76.8%) and high patients satisfaction (mean visual analogue score of 7.5) that was nearly compatible with this study. Side effects including atrophy, erythema and discomfort were reported in small number of the patients.¹¹ In the current study, patients did not have atrophy or any serious complication. Hyperpigmentation and blister were observed in ten and five patients, respectively that disappeared after a few days to weeks. Persistent erythema and hypopigmentation each were reported only in one patient that resolved eventually after a couple of days to weeks. Cannarozzo *et al.* evaluated efficacy of PDL (6-8 monthly treatment sessions) as monotherapy on 59 patients with keloid. They reported good-to-excellent improvement in nearly three-quarter of cases. Furthermore, more than ninety percent of the patients were satisfied or very satisfied with the result.¹⁰

In the current study, males had slightly better outcome than females. Furthermore, younger patients (up to 40 years old) and lighter skin types demonstrated better treatment efficacy compared to older patients and darker skin phototypes. Also, face lesions showed better response compared to trunk and limb lesions. Nouri *et al.* showed better response in face,

shoulder and arm lesions compared to trunk lesions.¹² In contrast, Kuo *et al.* revealed no association between site of lesions and response rate.⁶ Stephanied *et al.* reported slightly better treatment efficacy in males compared to females.¹¹ Other studies showed better response in females and patients with lighter skin type.^{7,13}

In this study, the highest percentage of excellent improvement was achieved with more treatment sessions and higher fluence (10 mj/cm² compared to 5 mj/cm²). The highest excellent improvement observed with pulse duration of 1.5 ms and spot size of 7 mm. However, there was no statistically significant correlation between treatment outcome with demographic features, site of involvement or treatment protocol. Previous studies showed conflicting results regarding impact of device setting on treatment efficacy. Two studies showed better results with lower pulse duration (0.5 ms) compared to higher ones (40 ms).^{12,14} They explained it due to smaller diameter of vasculature in keloid that requires less pulse duration in order to concentrate heat on vessels more efficiently that leads to better outcome. Two other studies reported that applying higher fluence (10-16 j/cm² compared to 3 j/cm²) leads to more reduction in TGF-B and as a result higher collagen degeneration with better outcome.^{6,15} In contrast, Manuskiatti *et al.* revealed no significant correlation between fluence and treatment efficacy.¹⁶ Kue at al indicated better treatment efficacy with more treatment sessions; percentage of good-to-excellent improvement were 50% and 79% in patients with more than six treatment sessions compared to those who received less than six sessions, respectively.⁶ Other studies confirmed better outcome with higher treatment sessions. Manuskiatti *et al.* showed fair improvement with 3-6 treatment sessions,^{14,16} while other studies demonstrated good-to-excellent improvement with more than three treatment sessions.^{10,17}

The main limitations of this study were lack of objective methods for evaluation (length, width, height, pliability and vascularity) of keloid, and observational uncontrolled design of study.

Conclusion

In the current study nearly third-quarter of the patients demonstrated more than 50% improvement and were satisfied or very satisfied with treatment results. Although males, younger patients and lighter skin types showed better outcome, however the result was not statistically significant. Furthermore, higher treatment sessions and fluence accompanied with better results, but the difference was not significant.

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