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ORIGINAL ARTICLE

Comparing Two Methods of Cryotherapy and Intense Pulsed Light with Triamcinolone Injection in the Treatment of Keloid and Hypertrophic Scars: A Clinical Trial

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Abstract
Objectives: Keloid and hypertrophic scars are abnormal manifestations of wounds that occur following skin injuries in the form of local proliferation of fibroblasts and increased production of collagen. There are several ways to cure these scars; treatment must be selected based on the nature of the scars. In this clinical trial, two methods—cryotherapy and intense pulsed light (IPL)—are compared in the treatment of scars, and the results are presented in terms of improvement level, complications, and patient satisfaction.
Methods: This clinical trial was conducted in southeastern Iran. The intervention group included scars that underwent the IPL method and the control group, which consisted of scars that were subjected to cryotherapy. In both methods, intralesional corticosteroid injection was administered. To select samples, the easy sampling method was used. To determine the expected outcomes, the criteria determined in the Vancouver scar scale were used. Data were analyzed using the Mix Model, chi-square test, and *t* test.
Results: In this study, 166 samples of keloid and hypertrophic scars were cured using two methods (Cryotherapy, 83; IPL, 83). The recovery rate was higher in the Cryotherapy group than in the IPL group ($p > 0.05$), and the incidence of complications was also higher in the Cryotherapy group (14.5% vs. 12%). Moreover, patients were more satisfied, although not significantly so, with the cryotherapy method ($p = 0.09$).
Conclusion: Both methods were highly successful in curing scars; participants were totally satisfied with both methods.

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1. Introduction

Keloid and hypertrophic scars are abnormal manifestations of wounds that occur following skin injuries in the form of local proliferation of fibroblasts and increased production of collagen. These scars often tend to occur in places that are under pressure, but some body organs such as the ear lobules, which are low-pressure areas, are also disposed to keloid scars [1,2].

Keloid and hypertrophic scars occur for different reasons including skin injuries, burns, surgery, injections (vaccine, tattoos) and dermatitis (acne vulgaris, bites) [3]. Among them, deep burns are reported to be the main cause of keloid scars [4]. Moreover, there are several reports of keloid manifestation during or after puberty and after menopause and also of occurrence or enlargement of keloid during pregnancy [5].

Several studies have reported that hypertrophic scars occur in 1.5−4.5% of the general public [2]. There are numerous ways to cure both scars [e.g., surgery, silicone coating, and compressing the scar to reduce the size of the lesion, interferon, bleomycin, and 5-fluorouracil (5-Fu) intralesional injection, corticosteroid intralesional injection, cryotherapy and intense pulsed light (IPL) with/without corticosteroid intralesional injection] [2,3,6−9]; methods must be selected based on the type and cause of scarring, recovery rate, recurrence rate, and complications.

Cryotherapy is one of the common methods used to cure scars. The recovery rate in scars treated with cryotherapy is reported to be 76%, with an average of 20 therapeutic sessions held once in 2 weeks [10]. Although this method is satisfactory in terms of recovery, its main shortcoming is the length of the treatment period. Studies have shown that IPL is better than cryotherapy; in addition to desirable recovery, IPL requires fewer therapeutic sessions to achieve good results, is more flexible, and can be used in different skin treatments [11]. Moreover, IPL treatment is not invasive and has few complications that can be relieved by cooling the location and using anesthetic creams. Making use of special sheets, we can prevent the skin around the lesion from being exposed to the sunlight [6].

In a study carried out by Erol et al [1] in 2008 on 109 patients (with hypertrophic scars) who were treated with IPL, clinical improvement in scar appearance was reported in 99.5% of patients. Myers et al [12] cured 107 patients with IPL; the recovery rate was 55% [7]. In a study by Han et al [13], clinical recovery was 100% with an average of 5.3 therapeutic sessions on 22 patients.

According to the researchers' experience, the prevalence of hypertrophic and keloid scars is relatively high in southeast Iran (Kerman), and the common method (cryotherapy) used in this regard is not satisfactory because of the long treatment period, lack of treatment completion, complications, and patient dissatisfaction. Thus, in this clinical trial researchers compared the overall recovery rate, recovery rate in terms of number of treatment sessions and features of scars, complications, and level of patient satisfaction; accordingly, several suggestions were proposed.

2. Materials and methods

This clinical trial was carried out in southeastern Iran in 2012−2013. The intervention group included scars that were treated using the IPL method with corticosteroid intralesional injection, and the control group consisted of scars that were treated using the cryotherapy method with corticosteroid intralesional injection. The inclusion criteria included all keloid or hypertrophic scars (scars with appearance of more than 1-year duration and scars that extend beyond the wound of margin) caused by trauma, surgery, burns, acne, and thermal or chemicals burns. The exclusion criteria included complications considered unacceptable by the patients.

Intervention in IPL (MED FLASH II; Manufacturer, Italy) was performed using 450−1,200 nm filters, 30−40 J/cm^2 fluence, pulse duration of 2.1−10 ms, and pulse delay of 10−40 ms. The normal skin around the lesion was protected by a covering (protection) device attached to the laser handle. In the control group, cryotherapy with liquid nitrogen was performed for 10 seconds on the lesion. In both methods, 1 mg/cm^2 triamcinolone acetonide injection mixed with lidocaine (50:50 ratio) was used. The interval between therapeutic sessions was 3 weeks with a maximum of eight treatment times.

The required sample size for each group was 73 patients. Because the participants were patients who were referred to the department of dermatology in Afzalipour Hospital in Kerman, Iran, simple sampling (census method) was used. As the study started, the first sample was allocated to the intervention group and the second sample to the control group; next, samples were allocated to both groups in the same manner.

This study was approved by the Ethics Committee of Kerman University of Medical Sciences with the code 91/140. Prior to the study, research conditions and treatment procedures were explained to all potential participants; individuals were included after they have provided written informed consent to participate in the study. Participants were also free to leave the study in every stage of the research. In addition, studies indicated that complications of the intervention method did not exceed those of the routine method (Cryotherapy). This investigation was designed as a single blind study. Neither evaluators nor patients knew what type of scar or which patient was allocated to the intervention or control groups. Details of all patients were recorded in a

form; to prevent exclusion of patients, some guidelines were suggested including suitable advice in the first session and telephone follow-ups.

To gather information, a checklist was designed; it included the variables of age, sex, scar occurrence age, length of scar, causes of scar, history of treatment, scar clinical status in terms of vascularity, pigmentation, pliability, height, clinical improvement, color improvement, scar height, and satisfaction of patients with the therapeutic methods. To determine the expected outcomes of the research (complete recovery rate, recovery rate in poor, average, good and excellent levels, recovery rate in terms of number of treatment sessions and complications), criteria determined in the Vancouver scar scale [10] were used. Also, to determine features of the lesion, the criteria proposed in a study by Erol et al [1] were used.

For classification of treatment results, recovery of up to 25% was considered poor; 26−50%, average; 51−75%, good; and more than 75%, excellent. Moreover, scars with 100% recovery were considered complete recovery.

SPSS ver. 20 (Chicago: SPSS Inc) was used to include and analyze data; data were analyzed using chi-square test and *t* test. It should be noted that the significance level of the test was considered equal to or less than 5%.

3. Results

In this study, 166 samples of colloid and hypertrophic scars were cured using two methods (Cryotherapy, 83; IPL, 83). The average age of participants in the Cryotherapy group and the IPL group was 30.9 ± 14.6 and 32.5 ± 18.4 years, respectively. According to the results of the *t* test, the differences were not statistically significant ($p = 0.5$). Most samples (72.3%) came from women.

Table 1 shows that distribution of samples is not statistically different in both Cryotherapy and IPL groups in terms of the place and cause of scars, vascularity, and pigmentation, whereas it is different in terms of other variables mentioned in the sample distribution table.

Improvement of clinical status, improvement of color, and improvement of height were observed more in the cryotherapy method than in IPL; however, these differences are trivial and are not statistically significant. The average number of therapeutic sessions in IPL and Cryotherapy groups was 5.3 and 4.6, respectively. This difference is not statistically significant ($p = 0.05$). Complications in the Cryotherapy group exceeded those of the IPL group (14.5% vs. 12%). Moreover, satisfaction with cryotherapy was nonsignificantly higher compared with IPL ($p = 0.09$). Excellent response to treatment (recovery of more than 75%) was higher in Cryotherapy than in IPL ($p = 0.5$). It should be noted that the most common complication of both methods was hyperpigmentation (Table 2).

In Table 3, the rate of complete recovery was not statistically different in both methods in terms of sex. The highest recovery rate in the Cryotherapy group was in the age groups of below 10 and 21−40 years, respectively, whereas in the IPL group it was observed in the age groups of 11−20 and 21−40 years. The highest recovery rate in the Cryotherapy group was related to leg and hand scars, whereas it was related to arm and abdomen in the IPL method. The chest area had the lowest recovery rate (14.9% scars) in the Cryotherapy method. However, IPL could cure 76.5% of scars in this area. Concerning causes of scars, no significant difference was observed between both methods. Cryotherapy could treat 91.7% of scars caused by burns, whereas IPL cured only 50% of them. Furthermore, more purple vascularity scars were cured using cryotherapy than with IPL (92.3% vs. 53.8%).

Table 3 shows that the rate of complete recovery (treatment result) is not statistically significant in cryotherapy method in terms of scar clinical status concerning pigmentation ($p = 0.2$). However, these differences are significant ($p = 0.003$) in the IPL method. In the IPL method, response to treatment of hyperpigmentation scars is lower than that of other pigmentation scars (hypopigmentation and mixed). In terms of scar clinical status concerning pliability, the rate of complete recovery is statistically different in these two methods ($p < 0.001$); the response of both methods to yielding and supple scars was excellent. Moreover, response to treatment of contracture scars was better in IPL than in cryotherapy (50% vs. 0%) and cryotherapy was better in curing rope scars than the IPL method (100% vs. 0%). Response to treatment of scars with height of more than 5 mm was low in both methods (Cryotherapy, 50%; IPL, 43.2%). It should be noted that response to treatment—in terms of scar height—is statistically different in cryotherapy and IPL methods ($p = 0.007$ and $p < 0.001$, respectively).

4. Discussion

In this clinical trial, the efficiency of two methods—cryotherapy and IPL—along with corticosteroid injection was compared in curing keloid and hypertrophic scars. It was shown that both methods were highly successful in curing these scars, and the participants were completely satisfied with both methods. However, complications of cryotherapy exceeded those observed in IPL. The average number of therapeutic sessions in IPL was higher than the other method (although not at a very significant level).

In a study carried out by Kontes et al [14] on 83 patients who underwent the IPL + intra lesional corticosteroid (ILC) method in 2002, the recovery rate in all

Table 1. Comparison of demographic data and basic variables in the samples studied.

Variables		Cryotherapy *n* (%)	IPL *n* (%)	*p*
Sex	Male	13 (15.7)	33 (39.8)	< 0.001
	Female	70 (84.3)	50 (60.2)	
Age group	≤ 10	1 (1.2)	7 (8.4)	0.01
	11−20	20 (24.1)	17 (20.5)	
	21−40	44 (53)	46 (55.4)	
	41−60	14 (16.9)	4 (4.8)	
	≥ 61	4 (4.8)	9 (10.8)	
Member of overtaken	Chest	19 (22.9)	17 (20.5)	0.9
	Abdomen	7 (8.4)	6 (7.2)	
	Hand	12 (14.5)	14 (16.9)	
	Shoulder	17 (20.5)	14 (16.9)	
	Leg	7 (8.4)	7 (8.4)	
	Arm	21 (25.3)	25 (30.1)	
Cause of scarring	Surgery	11 (13.3)	12 (14.5)	0.1
	Acne	38 (45.8)	23 (27.7)	
	Trauma	22 (26.5)	32 (38.6)	
	Burn	12 (14.5)	16 (19.3)	
Vascularity	NL	0	0	0.8
	Pink	23 (27.7)	26 (31.3)	
	Red	47 (56.6)	44 (53)	
	Purple	13 (15.7)	13 (15.7)	
Pigmentation	NL	0	0	0.2
	Hypopigmentation	11 (13.3)	6 (7.2)	
	Mixed	40 (48.2)	36 (43.4)	
	Hyperpigmentation	32 (38.6)	41 (49.4)	
Pliability	NL	0	0	0.004
	Supple	4 (4.8)	1 (1.2)	
	Yielding	26 (31.3)	8 (9.6)	
	Firm	46 (55.4)	63 (75.9)	
	Contracture	4 (4.8)	4 (4.8)	
	Rope	3 (3.6)	7 (8.4)	
Height	Flat	0	0	0.01
	< 2 mm	28 (33.7)	16 (19.3)	
	2−5 mm	35 (42.2)	30 (36.1)	
	> 5 mm	20 (24.1)	37 (44.6)	
History of treatment	Yes	8 (9.6)	20 (24.1)	0.01
	No	75 (90.4)	63 (75.9)	
Total		83	83	—

IPL = intense pulsed light; NL = normal.

patients was more than 75% and the lesion size reduction was more than 50% [14]; this is in line with the results of the present study. In another study conducted by Erol et al [1] in 2008, 109 patients with hypertrophic scars were treated with IPL; excellent response, moderate response, and poor response to treatment were 31.2%, 34%, and 9.1%, respectively. The efficiency of IPL in the treatment of scars was lower than its efficiency in the present study, which used IPL plus intralesional corticosteroid injection [1]. Han et al [13] cured 22 patients with keloid and hypertrophic scars caused by surgery using IPL in 2007; 100% of patients achieved clinical recovery. It was better than the results of our study. Myers et al [12] reported that the recovery rate of 107 patients who suffered from various skin disorders was 55% with the IPL method, which is significantly lower than that recorded in the present study. This difference can be attributed to the fact that Myers et al [12] did not use IPL and intralesional corticosteroid injection simultaneously.

Using cryosurgery plus intralesional corticosteroid injection, Boutli-Kasapidou et al [15] cured eight patients with keloid scars caused by surgery. Complete recovery and good recovery (50−75%) were 13% and 74%, respectively. Concerning the cryotherapy method, recovery at good level was 17% and 50% for scars

Table 2. Comparison of cure rate in samples studied.

Variables		Cryotherapy	IPL	*p*
Improvement of clinical (%)		91.5	89.3	0.5
Improvement of color (%)		91.5	89	0.4
Improvement of height (%)		91.4	89.3	0.5
Average number of treatment sessions (*n*)		4.6	5.3	0.05
Incidence of Complications (*n*/%)		12/14.5	10/12	0.4
Satisfaction of treatment method (%)		93.2	88.8	0.09
Kind of complications (*n*)	Telangiectasia	0	1	0.5
	Hyperpigmentation	7	7	
	Hypopigmentation	1	0	
	Atrophy	1	2	
	Erythema	2	0	
	Hyperpigmentation and ulcer	1	0	
Cure rate (%)	Weak	3.6	4.8	0.5
	Moderate	7.2	6	
	Good	8.4	15.7	
	Excellent	80.7	73.5	

IPL = intense pulsed light.

caused by acne and scars resulting from burns, respectively [15]; these are much lower than the results of our study (in our study, 78.9% of scars caused by acne and 91.7% of scars caused by burns recovered completely). In a study by Zouboulis et al [16] in 1992, 93 patients with keloid and hypertrophic scars were treated using cryosurgery without injection. Excellent recovery, good recovery, and treatment failure were 32.35%, 29%, and 9.75%, respectively [16]; the efficiency of cryotherapy was lower than that recorded in the present study. The desirable result observed in the present study can be attributed to the simultaneous use of cryotherapy and intralesional corticosteroid injections.

The results of a study by Layton et al [17], who treated 11 cases of colloid scars, showed that cryotherapy was effective in lesions with high vascularity [17]; this is in line with the results of the present study (pink). Moreover, Layton et al [17] showed that response to treatment of scars and lesions on the chest is less than the response to lesions in other areas, which is in contrast with our findings.

In a study by Atiyeh [18] in 2007, the recovery rate was 51−74% after two times of treatment with cryotherapy, and the most common complications of cryotherapy were hypopigmentation, skin atrophy, and hyperpigmentation [18]. It was shown in a study conducted by Kelly [19] that cryotherapy with intralesional corticosteroids injection resulted in the recovery of 84% of patients; however, some patients complained about pain, slow recovery, and hypopigmentation [19]. In Zouboulis et al's study [20], the rate of recovery in scars was 75% using cryotherapy plus intralesional injection. However, hypopigmentation was observed in 12% of patients, and local necrosis, edema, and wound infection were observed in a few patients [20]. In a study carried out by Bloemen et al [10], the recovery rate of 76% (from scars) was at a good level, in which the treatment consisted of cryotherapy plus intralesional corticosteroids injection. Nevertheless, several complications such as skin atrophy, hypopigmentation, and telangiectasia were observed [10].

In his study, Erol et al [1] treated 109 patients with hypertrophic scars using IPL without injection; three patients reported purpura and one patient reported hyperpigmentation. However, no purpura was observed in our research. In their study, Kontes et al [14] observed blisters and crust following IPL plus injection, whereas no blisters and crust were observed in our study. In the study by Manuskiatti and Fitzpatrick [21], complications of intralesional steroid injection (e.g., hypopigmentation, telangiectasia, and atrophy) were reported in 50% of treated lesions; hyperpigmentation was the most common complication in our study, which used intralesional injection in both methods. Myers et al [12] used IPL to cure 107 patients with skin disorders. Of this total, six patients reported several complications; in addition to erythema and minor discomfort, one participant reported blister, one reported vesicol, and two reported edema. In our study, no erythema, blister, or vesicol was observed in treatment with IPL.

Shaffer et al [22] stated that the objective of treating scars depended on the beauty needs of patients and their disabilities. They also mentioned that in spite of the efficiency of cryotherapy in removing keloid scars, its side effects—especially hypopigmentation—must be taken into account. Generally, curing keloid and hypertrophic scars is controversial and has largely no fixed protocol. So far, various methods (including silicon sheets, surgery, surgery with radiation therapy, intradermal injections of interferon alpha, PDL laser, 5-Fu

Table 3. Comparison of complete cure in the samples studied.

Variables		Cryotherapy		IPL	
		N (%)	*p*	*N* (%)	*p*
Sex	Male	11 (84.6)	0.3	29 (87.9)	0.06
	Female	56 (80)		31 (62)	
Age group (y)	≤ 10	1 (100)	0.05	2 (28.6)	< 0.001
	11–20	15 (75)		17 (100)	
	21–40	39 (88.6)		33 (71.7)	
	41–60	8 (57.1)		2 (50)	
	≥ 61	4 (100)		6 (66.7)	
Member of overtaken	Chest	10 (14.9)	0.04	13 (76.5)	0.001
	Abdomen	6 (85.7)		5 (83.3)	
	Hand	11 (91.7)		7 (50)	
	Shoulder	15 (88.2)		9 (64.3)	
	Leg	7 (100)		3 (42.9)	
	Arm	18 (85.7)		23 (92)	
Cause of scarring	Surgery	7 (63.6)	0.3	8 (66.7)	0.08
	Acne	30 (78.9)		17 (73.9)	
	Trauma	19 (86.4)		27 (84.4)	
	Burn	11 (91.7)		8 (50)	
Vascularity	NL	—	0.2	—	0.02
	Pink	21 (91.3)		24 (92.3)	
	Red	34 (72.3)		29 (65.9)	
	Purple	12 (92.3)		7 (53.8)	
Pigmentation	NL	—	0.2	—	0.003
	Hypopigmentation	11 (100)		5 (83.3)	
	Mixed	34 (85)		31 (86.1)	
	Hyperpigmentation	22 (68.8)		24 (58.5)	
Pliability	NL	—	< 0.001	—	< 0.001
	Supple	4 (100)		1 (100)	
	Yielding	23 (88.5)		8 (100)	
	Firm	37 (80.4)		49 (77.8)	
	Contracture	0		2 (50)	
	Rope	3 (100)		0	
Height (mm)	Flat	—	0.007	—	< 0.001
	< 2	27 (96.4)		16 (100)	
	2–5	30 (85.7)		28 (93.3)	
	> 5	10 (50)		16 (43.2)	
History of treatment	Yes	7 (87.5)	0.7	12 (60)	0.1
	No	60 (80)		48 (76.2)	

IPL = intense pulsed light.

intradermal injection, cryosurgery, corticosteroid intradermal injection) have been used to treat these scars [1,13,21,23].

Intralesional corticosteroid injection is the first therapeutic step among physicians. Increasing vasoconstriction in scars, corticosteroids inhibit inflammation and mitosis, decrease scar volume significantly, soften it, reduce its height, and reduce symptoms such as itching and pain [1,13,21,23].

Intralesional corticosteroid injection used along with both methods in the present research is one of the main methods in the treatment of keloid and hypertrophic scars, and can be used alone or in combination with other methods. Corticosteroid softens colloids but is not able to narrow the scar or remove it completely. Intralesional corticosteroid injection decreases fibroblast proliferation, collagen synthesis, and glycosaminoglycan, and inhibits the production of inflammatory mediators [1,13,21,23].

According to electronic search conducted in this study as well as the authors' knowledge, lack of access to similar studies was one of the limitations of this research; thus, we could not compare the results of this study in terms of some variables. Another limitation of this study was the lack of investigation in terms of duration of scars in response to treatment. Nonsimilarity of some demographic characteristics and basic clinical status in both methods and the small sample size in

terms of various layers of studied variables were further limitations of the present study. Therefore, necessary conditions have not been provided that would allow us to comment on the results of this research definitely and appropriately.

This study has shown that making use of a combination of intralesional corticosteroid injection and IPL or cryotherapy is effective and desirable in the treatment of keloid and hypertrophic scars and has no significant complications. Moreover, according to the results of this research, it can be stated that therapeutic method is selected based on patient age, causes of scar, scar area, scar clinical status (vascularity, pigmentation, pliability and height), patient's opinion, and patient's economic conditions.

Author contribution

M.M. contributed to the analysis, interpretation of data, and writing of this manuscript, A.R. and S.S. contributed to the acquisition of data, the design of manuscript, the final approval of the version to be published, and the drafting of the manuscript. This research was supported by grant number 1497 from Mazandaran University of Medical Sciences of Iran.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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