Comparison of the therapeutic effect of microneedling with carbon dioxide laser in hypertrophic burn scars: a randomized clinical trial

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Background: Microneedling is recently used to treat skin scars mostly atrophic scars; however, there are limited data about its effectiveness on hypertrophic burn scars. Carbon dioxide (CO_2) laser is an effective method for the treatment of burn scars. Here, we aim to compare the efficacy of microneedling to CO_2 laser in the treatment of hypertrophic burn scars in a randomized clinical trial.

Methods: Patients with second and third-degree burn scars (n=60) were randomized to receive 3 sessions of microneedling (n=30) or CO_2 laser (n=30), 4-6 weeks apart. The outcomes, including physical characteristics of the scar scored by Vancouver Scar Scale (VSS) and patients' satisfaction with the treatment measured by Visual Analogue Scale (VAS), were investigated at baseline, at the end of the treatment period, and at the 3-month follow-up.

Results: The VSS score at the follow-up visit showed a significant reduction from 6.63±1.95 to 3.8±2.3 in the microneedling group and from 7.1+2.3 to 5.6±1.7 in the CO_2 laser group; while, the reduced VSS score was significantly higher in the microneedling group ($P<0.05$), especially in reducing the thickness ($P=0.001$) and pliability ($P=0.001$) scores. The patients' subjective assessments for acne improvement were significantly more satisfactory in the microneedling group ($P=0.025$).

Conclusion: Microneedling seems to be an effective method to improve hypertrophic burn scars. It also causes better scores in the physical characteristics of scar and the patients' satisfaction compared to the CO_2 laser at the 3-month follow-up.

Keywords: burn scar; CO_2 laser; microneedling; laser; minimal invasive technique

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INTRODUCTION

Burn injuries are common worldwide and implicated with serious medical challenges during the acute phase of treatment and thereafter. Approximately 77% of burn injuries develop pathological scarring of which 44% are hypertrophic scarring and 28% hypertrophic scarring with contractures [1]. Burn scars and contractures cause prolonged complications and debilitating functional disabilities for patients, and are esthetically unpleasing with consequent decrease in the quality of life, particularly when affecting exposed areas [2]. Hypertrophic burn scars are characterized by an excessive abnormal deposition of collagen in the dermis and subcutaneous layer of the skin [3,4]. Most of the current treatment options, including nonsurgical procedures, such as compression, intralesional corticosteroids, silicone gel, and fibrinolysis; or surgical procedures, such as skin grafting are far from being sufficient with a high recurrence rate [3].

Fractional lasers, including fractional ablative carbon dioxide (CO_2) laser, have been recently suggested as effective tools for the treatment of burn scars and have emerged as the effective arm of the treatment algorithm [5]. CO_2 laser ablation works by targeting water in the abnormal collagen of the skin and facilitating the remodeling response of healing. Consequently, it has been demonstrated to reduce scar thickness and pruritus and to improve scar pigmentation [5]. Microneedling is another new promising non-invasive method for scars and induction of percutaneous collagen [6,7].

At first, microneedling was proposed by Fernandes for skin rejuvenation [7], while it is now used to treat various skin alternations and skin scars, including thermal scars [8]. It has been found to promote the scar remolding by releasing the growth factors responsible for cell proliferation, increased synthesis and deposition of collagen - elastin complex, and transformation of collagen I to collagen III [6]. Microneedling is mostly used for facial atrophic scars of acne; however, there are limited data showing its efficacy on hypertrophic scars [8]. Considering the known positive effects of microneedling on the skin remolding process, this study aimed to examine its effectiveness on burn scars and compare it to CO_2 laser therapy through a prospective, randomized controlled study.

PARTICIPANTS AND METHODS

Participants and Study Design

The study was designed as a randomized; double blinded (assessor and analyst-blinded), controlled phase III clinical trial and conducted at Rasoul Akram Hospital, Department of Clinical Dermatology. Simple random sampling method The eligible patients were randomized 1:1 to receive microneedling (Amiea Med 2016, Germany, NEEDLE: 2mm) (n=30) or CO_2 laser therapy (n=30) (DEKA SmartXide 2016, Italy, (power: 15 stack:1 space:1000 dowling.time: 1000). A simple randomization was used to collect 60 patients, from 2017 to 2018, who fulfilled the following criteria: 1) aged between 15 and 55 years old; 2) second and third-degree burn scar. Exclusion criteria were: 1) any previous burn scar treatment; 2) any sign of local infection; 3) unwillingness of the patient to participate in the study. Computer-based random number generators were used to create a random allocation sequence to assign the treatment modality of each side. Randomization codes were secured until the end of the study. Blinded investigators to the randomization method and assigned treatments collected and analyzed the data. The patients did not know whether there is another treatment study group.

Randomization and Blinding

Interventions and Outcome Measures

The patients received 3 sessions of microneedling or CO_2 laser, 4 to 6 weeks apart. The primary endpoint was quantifying scar appearance in response to the treatment. In this regard, two blinded dermatologists evaluated the standardized digital photographs of scars using Vancouver Scar Scale (VSS). Sullivan first described VSS in 1990 scoring the scars from 0 to 13 in accordance with four characteristics of vascularity (zero: normal, one: pink, two: red, three: purple), height/thickness (zero: flat, one: < 2mm, two: 2-5mm, three: > 5mm, pliability) pigmentation (zero: normal, one: hypopigmentation, two: hyperpigmentation), and pliability (zero: normal, one: supple, two: yielding, three: firm, four: ropes, five: contracture) (9).

The secondary outcome was the patients' satisfaction with the treatment, which was scored by a 100-mm VAS. On this scale, the patients were asked to place a vertical mark on a horizontal 100-mm line to represent their satisfaction with the treatment in which 0 indicates no satisfaction and 100 indicate extreme satisfaction. The measurement in millimeters was converted to the same number of points, ranging from 0 to 100. A score of <30 was considered weak; 30-70 moderate; and >70 good satisfaction. The data were measured and collected in predesigned sheets at time zero (before the intervention), at the end of the treatment, at the follow-up visit, 3 months after the end of the treatment.

Statistical Methods

The quantitative results were expressed as mean ± standard deviation (SD). The qualitative data were presented as percentage. Normally distributed data were analyzed by parametric tests, otherwise analyzed by nonparametric ones using the SPSS software version 24 (Chicago, Illinois, United States), and parametric and non-parametric tests. Repeated t-test and one-way Analysis of Variance (ANOVA) were used to compare the mean of quantitative variables based on qualitative variables over time. For the qualitative variables, chi-square test was used. A P-value < 0.05 was significant.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and the Medical Research Involving Human Subjects Act. The Ethics Committee of Tehran University of Medical Sciences approved the research protocol. The written informed consent was obtained from all the participants.

The ethical code of this trial was IR.IUMS.FMD.REC.1395.9411166003 and the IRCT number was IRCT20140624018210N6.

RESULTS

In total, 30 microneedling treated patients were compared to 30 cases in the CO_2 laser treated group. The scars were mostly located on arm, forearm and trunk. Table 1 presents the patients' demographic data, which are comparable among the study groups.

Assessment of the patients' photographs showed a global improvement in total VSS score in both treated groups over time (P<0.05). The final VSS score at the follow-up visit showed a significant reduction from 6.63±1.95 to 3.8±2.3 (P=0.001) in the microneedling group and from 7.1+2.3 to 5.6±1.7 (P=0.001) in the CO_2 laser group. The reduced VSS score was significantly more in the microneedling group compared to the CO_2 laser group (P<0.05). The analysis of the variables of VSS showed that microneedling method was superior to CO_2 in reducing the thickness (P=0.001) and pliability (P=0.001) scores within the visits. Although the vascularity and pigmentation scores showed a significant reduction over time in total population, there was no significant difference between the treatment groups as shown in Table 2.

The patients' satisfaction at the final visit, 3 months after the end of the treatment, was significantly more with the microneedling therapy than with CO_2 laser ablation (P=0.025). Fifteen (50%) of the patients in the microneedling group scored

Table 1. The patients' demographic characteristics

Characteristics	Microneedling group N=30	CO_2 laser group N=30	*P*-value
Mean±SD age, y (range)	32±5y	37±4y	
Male/female, n (%)	9(30%)/21(70%)	9(30%)/21(70%)	

*Y: year; *n: number

Table 2. Response to treatments

	Total N=60			Microneedling group N=30			CO_2 laser group N=30		
	1st visit	2nd visit	Follow-up visit	1st visit	2nd visit	Follow-up visit	1st visit	2nd visit	Follow-up visit
VSS score; Mean±SD									
Vascularity (0-3)	1±0.8	0.87±0.5	0.72±0.5	1.1±0.8	0.89±0.5	0.57±0.5	0.9±0.7	0.85±0.5	0.88±0.5
Height/thickness (0-3)	1.4±0.8	1.15±0.6	1±0.68	1.3±0.7	1.1±0.7	1±0.68	1.5±0.8	1.3±0.6	1±0.68
Pigmentation (0-2)	1.9±0.58	1.7±0.57	1.7±0.63	2±0.6	1.75±0.5	1.71±0.6	1.9±0.5	1.65±0.63	1.69±0.68
Pliability (0-5)	2.1±0.7	1.7±0.7	1.3±0.9	2±0.8	1.6±0.8	1±0.98	2.1±0.7	1.8±0.7	1.7±0.7
Total	6.86±2.1	5.6±1.9	4.7±2.2	6.63±1.9	5.2±1.8	3.8±2.3	7±2.3	6±2	5.6±1.7
Patients' satisfaction, VAS; n (%)									
Weak (<30%)	15 (25%)			4 (13.3%)			11 (36.7%)		
Moderate (30-70%)	26 (43.3%)			11 (36.7%)			15 (50%)		
Good (>70%)	19 (31.7%)			15 (50%)			4 (13.3%)		

*n: number; VSS, Vancouver Scar Scale; SD, standard deviation; VAS, Visual Analogue Scale their satisfaction as good, while only 4 (13.3%) of the patients treated with CO_2 laser expressed good satisfaction with scar improvement as indicated in Table 2.

DISCUSSION

Our results indicate that 3-session treatment with both microneedling and CO_2 laser significantly improved the burn scars, while microneedling was more effective in the normal processing of the scars, especially in reducing their the thickness/height and pliability. Moreover, the patients' satisfaction with improvement of the scars was significantly more in the group treated with microneedling than in those treated with CO_2 laser.

Although, application of unfractional CO_2 laser had serious limitations in the burn population due to its high rate of side effects [11], fractional laser delivery has been recently suggested as a promising method for the treatment of hypertrophic scar [12]. A reduction in post-burn itch and nail deformity is also seen in patients treated with fractional CO_2 laser [5,13]. However, there are few reports of failure of CO_2 laser in keloid improvement [14] or even hypertrophic scar formation following CO_2 laser therapy [15]. CO_2 laser has a wavelength of 10,600 nm targeting water of abnormal collagen below the surface of the skin to produce heat, leading to ablation of the tissue. Consequently, it induces the repair and re-epithelialization of the intact surrounding skin [5]. The mechanisms of CO_2 laser action likely involve collagen and molecular profile alterations such as changes in expression of matrix metalloproteinase (MMP), transforming growth factor beta (TGF-β), and vascular endothelial growth factor (VEGF) [16-18]. Treatment with fractional ablative CO_2 laser in 1-6 sessions has been demonstrated to change the scar collagen subtype profile resembling that of normal skin [19]. A cohort study of 452 fractional ablative CO_2 laser treatments for post burn hypertrophic scar showed that this method effectively reduced the scar thickness and improved the pigmentation [5]. Our findings also represent the significant VSS improvement in accordance with vascularity, pliability, thickness and pigmentation of burn scars treated with CO_2 laser compared to pre-treatment session. The mean decrease of VSS score was 1.5 points after 3 therapy sessions. Recently, N Li et al. reported a decrease of approximately 6 points of VSS following the 4- 8 sessions of ultra-pulsed fractional CO_2 laser [20]. Additionally, J Poetschke et al. found that a single course of fractional CO_2-laser decreased the total VSS score to approximately 4.6 points 6 months after treatment of burn scars. All the categories also showed a more significant decrease in scoring compared to our findings of the 3-month follow-up visit [2]. As the most notable development occurs 1 to 3 months postoperatively, the scores continuously decrease in 6 months, postoperatively; it seems that their scores in the third month are closer to those of ours. Results may also vary due to differences in laser systems, device settings, and treatment frequencies.

Laser treatments work based on ablation and destruction of superficial skin layers requiring a long time for healing with provoking an acute inflammatory response and a high risk of infection. However, the less intense inflammatory response inducing following microneedling and sparing the superficial skin layer, activates different mechanisms to facilitate the repair [6]. The proliferation phase starts immediately after completing microneedling and re-epithelialization after 24 hours. Thus, microneedling is considered a safe, simple, and quick method without needing post-interventional monitoring [21]. The needles also breakdown the old hardened scar layer and allow it to normal skin remolding and revascularization [8]. Microneedling causes degradation of excessive fibrotic tissue and collagen type I, the scar collagen, by activation of MMPs and TGF-β3, and promotes the formation of collagen type III, the physiological collagen [6,22]. Furthermore, microneedling with 1-3 mm needles causes deposition of new collagen from a depth of 0.6 mm toward the basal membrane [6]. Safonov et al. reported that microneedling was effective in improvement of keloids [23]. Additionally, the post-burn permanent or lasting erythema is found to respond well to microneedling [6,24]. KH Busch et al. have recently suggested the microneedling as an effective method for the treatment of mature hypertrophic burn scars, through increase of skin moisture and reduction of transepidermal water loss [21]. Our results also showed the superiority of microneedling to CO_2 laser ablation in the treatment of second and 3rd-degree burn scars and the patients' satisfaction with the treatment results.

There were some limitations in this study.

First, since degradation and visible improvement of hypertrophic burn scars takes many months, more studies with a longer follow-up period to assess effect of microneedling and CO_2 laser on the treatment of scars are required. Furthermore, previous studies indicated that the optimal therapeutic effect of CO_2 laser took about 6 months to be established. Second, our study had no treatment side effects.

CONCLUSION

Microneedling seems to be a promising method for the treatment of hypertrophic scars. Interestingly, our results indicate that it is superior to CO_2 laser therapy regarding scar improvement and patients' satisfaction up to three months after treatment.

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