The effectiveness of topical scar-reducing therapies administered for scarring due to burns and other causes: A retrospective pilot clinical research

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Date submitted:
Oct 019, 2017
Date accepted:
Aug 25, 2018
Online publication date:
December 15, 2018

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Keywords: Onion extract, scar, silicone, pressure garment, treatment.

ABSTRACT

Aims: Multiple modalities are used to treat scarring; however, data on the efficacy of the topical scar-reducing treatments most frequently used by patients is insufficient. This study aimed to retrospectively determine the effectiveness of topical scar-reducing treatments and patients' compliance.

Methods: The medical records of patients adimitted for the treatment of scarring were retrospectively evaluated. Patient satisfaction with the treatment was assessed via telephone interviews. Each patient also sent recent photographs of their scars. Pre- and post-treatment photographs were scored according to the Manchester Scar Scale, and in terms of vascularity and scar surface area (modified MSS).

Results: The study included 71 patients with a median scar age of 18 days at the time treatment was initiated. Mean duration of follow-up was 41 months. The prescribed treatments included onion extract, silicone gel or sheet, and a pressure garment. The patients reported that the treatments were effective, they were satisfied with the treatments, and the treatments were not excessively difficult to apply. MSS and ModMSS scores decreased significantly following treatment.

Conclusions: The prescribed topical scar-reducing treatments effectively improved the cosmetic appearance of the patients' scars and reduced scar-related symptoms. The effectiveness of the topical scar-reducing therapies increased as scar age decreased.

Introduction

The wound healing process consists of 3 phases: inflammation, proliferation, and tissue remodeling (1). This process repairs tissue integrity following any damage to the skin (1). Fibrous scar tissue is an imperfect structure, lacking skin appendages and normal epidermal and dermal architecture, that is formed as a result of the wound healing process to repair the tissue and prevent wound infection (1). Scars that occurred due to impaired wound healing and tissue remodeling can be variable in architecture; enlarged or contracted; depressed or elevated; atrophic or hypertrophic (1). Multiple treatment modalities are used to prevent the formation of abnormal scarring and improve the cosmetic appearance of scars by supporting the remodeling process. Topical onion extract (Contractubex® gel), silicone layer, silicone gel and pressure garments are among the most frequently used approaches. However, no long-term follow-up studies on the efficacy of topical scar-reducing treatment protocols, such as onion extract and silicone gel, have been published (1). These topical agents are readily available and can be used by patients following scarring without consulting a clinician (1).

There are several methods used by clinicians and patients for objective evaluation of scars (1,2). These scar scoring methods are also used to ensure that studies are comparable to each other and that the results can be standardized (2). The Manchester Scar Scale (MSS) scoring system is one such method (3). A verbal scale (VRAS) (score range: 0-10) is another method used to evaluate outcomes that was originally used to score pain (2). The present study aimed to retrospectively evaluate the efficacy of topical scar-reducing treatments based on telephone interviews with patients, and comparison of current and past scar photographs.

Methods

Patients that presented to the dermatology outpatient clinic with scarring during the period 2009-2016 were included in this retrospective study. Lesions that were initially photographed and treated with topical scar-reducing treatments were evaluated. Patient clinical characteristics were obtained from our medical records. Demographics, scar age, anatomic scar localization, approximate scar surface area (calculated from the initial photographs), whether or not the scar passed through

mobile skin areas, whether or not any surgical operation performed, whether or not the scar was located parallel to Langer's lines, the trauma that preceded scar formation, and if the trauma was a burn the degree of burn were recorded. Scar-related symptoms designated in patients' records, including pigmentation disorder, lymphedema, puffiness, depression, hardness, erythema/redness, infection, occupation of a large (>10 cm^2) surface area, irregularity of scar contours, chronic wound, pain, stinging, tingling, itching, xerosis, tightness, sweating imbalance, change in hair density, and limitation of motion, were also assessed.

Patients with small scars (<5-10 cm2) that healed within 2 weeks of wounding were prescribed silicone gel at the clinical visit when the wounds were already healed, as silicone gel packs are smaller (10-15 gr) than onion extract gel and enough for 1-3 months treatment of a small scar. In patients with medium-sized scars (5-50 cm2) that healed within 2 weeks of wounding we prescribed onion extract gel at the clinical visit when the wounds were already healed as onion extract gel packs (100 gr) are bigger than silicone gel packs and sufficient for the entire treatment period of medium-sized scars. We recommended combination treatments consisted of pressure garment with a silicone sheet inside after healing in patients with large (>50 cm2) burn scars in appropriate anatomical locations that lasted longer than 2 to 3 weeks to heal following wounding and in some cases we combined this modality with onion extract gel especially in scars showing early signs of hypertrophy. In large scars located in areas inappropriate to use pressure garments, or in some medium sized scars amenable to use silicon sheets; the patients were prescribed silicon sheets to be used at least 20 hours a day. All of the patients were prescribed scar reducing treatments after completion of epithelization/wounds healed, when they applied at various time points post-injury.

Patients were contacted by telephone and administered survey questions about the duration of treatment, frequency of treatment application, treatment side effects, and final scar symptoms. In addition, patients were asked to evaluate the efficacy of the treatment, the level of difficulty in applying the treatment and the level of satisfaction with the treatment (patient outcome measures). Some of the patients agreed to come to the clinic and were evaluated and photographed by a doctor; other patients self-photographed the final state of their scar and e-mailed them to the researchers.

Initial and post-treatment scar photographs were scored by 2 independent clinicians (one-blinded) that were unaware of which treatment was given to each patient and the patients' survey question answers. Photographs were scored using the MSS photographic scoring method. MSS rates photographs of scars based on 5 criteria: general appearance, color (compared to surrounding skin), surface appearance, contour, and surface irregularity (3). MSS total scores range from 4 to 24 (3). As stated earlier, vascularity and scar surface area are additional important parameters for scoring photographs of scars (4). Vascularity was rated using the Vancouver Scar Scale (VSS), as normal (1 point), pink (2 points), red (3 points), and purple (4 points) (2). Scar surface area was rated according to the Patient and Observer Scar Assessment Scale (POSAS) for linear scars, as similar (1 point), expansion (2 points), contraction (3 points), and mixed (4 points) surface area (5). Sum of MSS score and scores for vascularity and scar surface area is termed as modified MSS (ModMSS) (Figure 1). Accordingly, MSS total score (4-24) and ModMSS total score (6-32) were calculated

MODIFIED MANCHESTER SCAR SCALE - PHOTOGRAPHY

General appearance of the scar – VAS

Excellent Poor

0 l----------l 10

Color (Relative to the surrounding normal skin)

1 Perfect □ hypopigmentation □

2 Slight mismatch □ hyperpigmentation □

3 Obvious mismatch □ mixed □

4 Gross mismatch □

Surface appearance

1 Matte □

2 Shiny □

Contour (Relative to the surrounding normal skin)

1 Flush with surrounding skin □

2 Slightly proud / intended □

3 Hypertrophic □

4 Keloid □

Surface distortion

1 None □

2 Mild □

3 Moderate □

4 Severe □

MSS score: .....

Vascularity (Relative to the surrounding normal skin)

1 Normal □

2 Pink □

3 Red □

4 Purple □

Scar surface area (Relative to the original wounding area)

1 Similar □

2 Expansion □

3 Contraction □

4 Mixed □

ModMSS score: .....

Figure 1. Modified MSS score sheet.

for each scar photograph. The study protocol was approved by the Local Ethics Committee (KU GOKAEK 2016/77). The study was conducted in accordance with the Declaration of Helsinki. Participants gave verbal informed consent to participate in the study during telephone survey.

Statistical analysis

Data were analyzed using SPSS Statistics for Windows v.22.0 (IBM Corp., Armonk, NY). Mean ± SD, median, range, frequency, percentage and ratio values were used for descriptive statistics. The normality of the distribution of the variables was determined via the Kolmogorov-Simirnov test. The Wilcoxon test was used to analyze dependent quantitative data. Spearman's correlation analysis was used for correlation analysis. The level of statistical significance was set as $p < 0.05$.

Results

The study included 71 patients (females: n = 40; males: n = 31) with a median age of 25 years (range: 2-77 years). Mean time from prescription of topical scar-reducing treatment to telephone interview was 41.0 ± 27.2 months (range: 1-82 months). Most of the patients' scars developed following burns and sur-

Table 1. Scar type, localization, and etiology.

		n	%
Localization (n = 71)	Scalp	1	1.4
	Face	33	46.4
	Neck	5	7.0
	Chest	12	16.9
	Back	2	2.8
	Abdomen	4	5.6
	Arms	19	26.7
	Hands	8	11.3
	Legs	8	11.3
	Feet	1	1.4
Etiology (n = 71)	Burn	34	47.9
	Traumatic	15	21.1
	Surgery	18	25.4
	Infection	12	16.9
Burn levels (n = 35)	First	6	17.1
	Second	22	62.9
	Third	7	20.0
Scar type (n = 71)	Erythematous macular	38	53.5
	Atrophic macular	29	40.9
	Depressed	5	7.0
	Hypertrophic	11	15.5
	Keloid	5	7.0

(some scars may have >1 parameter present)

gery (Table 1). At the time the treatment was initiated, median scar age (after completion of epithelization/ wounds healed) was 18.0 days (range: 5-584 days). In total, 64.8% (n = 46) of the scars formed ≤1 month prior to presentation, versus >1 year for 9.9% (n=7). Median scar surface area was 10.0 cm2 (range: 0.5-500 cm^2). In 23 (32.4%) of the patients the scar passed through mobile skin areas and in 61 patients (85.9%) the scar was not parallel to Langer's lines. At treatment onset there were ≤3 scar symptoms in 41 (57.8%) of the patients. The most common scar symptom before treatment was erythema/ redness (n =63, 78.9%), pigmentation disorder (n=33, 26.8%), and tingling (n=23, 31.0%). The prescribed treatments included onion extract (n=27, 38.0%), silicone gel (n=19, 26.8%) or sheet (n=8, 11.3%), and combination treatments(n=9, 12.7%) (Figures 2-4). Patients used the treatments for a median duration of 90 days (range: 0-730 days). Only 8 (11.3%) patients experienced mild local side effects during the treatment.

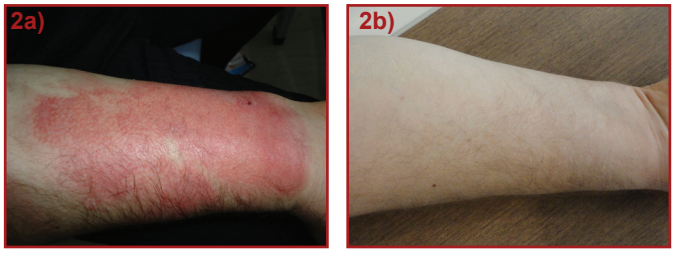

Figure 2. A 43-year-old male patient with a second-degree burn injury from hot water vapor on the volar side of the right forearm. Onion extract gel was prescribed when the scar was 16 day old. The patient applied topical onion extract gel with message 4 times daily for 3 months. His treatment efficacy score was 8 points, application difficulty score was 0 points, and satisfaction with treatment score 10 points. a. Pretreatment photograph at 16th day following epithelization. b. Photograph at 56 months post treatment.

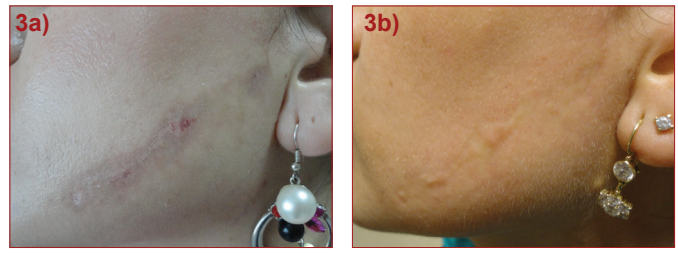

Figure 3. A 28-year-old female patient with a second-degree laser burn injury on the left cheek. Silicone gel was prescribed when the scar was 25 day old. She applied topical silicone gel twice daily for 11.5 months. Her treatment efficacy score was 7 points, application difficulty score was 1 point, and satisfaction with treatment score was 9 points. a. Pretreatment photograph at 25th day following epithelization. b. Photograph at 12 months post treatment.

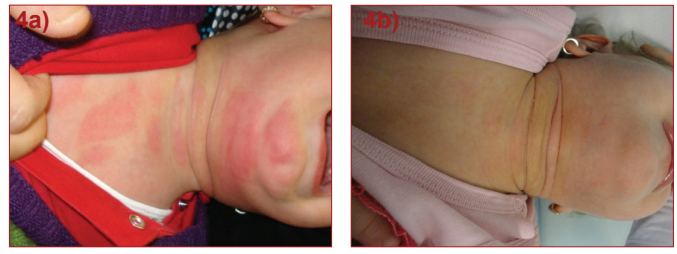

Figure 4. A 1.5-year-old female with a third-degree scald injury involving chin, anterior neck, and chest. Her parents were advised to apply a pressure garment layered inside a silicon sheet over night for at least 12 hour and topical onion extract gel 3 times daily. The treatment was administered for 3 months. Her parents' treatment efficacy score was 10 points, application difficulty score was 2 points, and satisfaction with the treatment score was 10 points 81 months post treatment. a. Pretreatment photograph at 30th day following epithelization. b. Photograph 3 months post treatment.

Patients who did not use their treatment at all or used less than 15 days or used irregularly (less than 3 times weekly) are grouped into control group and other patients are grouped as treatment group. Control group is consisted of 8 patients (11.3%) and treatment group included 63 patients (88.7%).

The number of scar symptoms decreased significantly after treatment ($p<0.001$) and there were ≤3 scar symptoms in 63 (88.8%) of the patients. There were no symptoms related scarring in 25 (31.0%) of the patients after treatment, whereas the other patients had pigmentation disorder (n=24, 28.2%) and elevation of the scar (n=19, 23.9%). Patient reported outcomes evaluated with VRS including treatment efficacy, patient satisfaction and difficulty of application are shown in Table-2. There were significant differences in efficacy scores between treatment groups and control group additionally efficacy scores were significantly higher in silicone gel, onion extract gel, and combined treatments in comparison to silicone sheet, ($P<0.05$). Patient satisfaction scores were significantly higher in silicone gel, onion extract gel, and combined treatments in comparison to silicone sheet and control group ($p<0.05$). However, the patients reported that the silicone sheet and combined therapies were significantly more difficult to apply than the silicone gel and onion extract gel ($P<0.05$) (Table 2).

Based on evaluation of the pre- and post-treatment scar photographs, MSS and ModMSS scores were significantly lower post treatment in treatment groups but there was no significant difference in control and treatment group (Table 3).

Furthermore, the relationship between the patient reported outcomes in VRS and clinical characteristics of scar and treat-

Table 2. Patient rated efficacy, satisfaction and treatment application difficulty VRS scores for each group.

	Efficacy		Patient satisfaction		Treatment application difficulty	
	Median (range)	P	Median (range)	P	Median (range)	P
Total Treatment group	8.0 (0.0-10.0)	**0.001***	9.0 (3.6-10.0)	**0.004***	2.0 (0.0-10.0)	0.417*
Control	0.5 (0.0-10.0)**	**0.001**	2.3 (0.0-10.0)****	**0.004**	0.0 (0.0-10.0)	**<0.001**
Onion extract gel	9.0 (5.0-10.0)		10.0 (5.0-10.0)		2.0 (0.0-7.0)	
Silicone gel	8.0 (3.0-10.0)		10.0 (5.0-10.0)		0.0 (0.0-3.0)	
Silicon sheet	5.0 (0.8-10)***		6.0 (3.6-10.0)****		5.5 (2.0-10.0)*****	
Combined treatments	7.0 (0.0-10.0)		9.0 (5.0-10.0)		9 (1.0-10.0)*****	

(Kruskal-Wallis/Mann-Whitney U test)
*In comparison to control group.
**The control group was lower than the onion extract gel, silicone gel, silicone sheet, combination therapies ($p < 0.05$).
***The silicone sheet group was lower than the onion extract gel, silicone gel, combination treatments ($p < 0.05$).
****The control and silicone sheet groups were lower than onion extract gel, silicone gel and combination treatments ($p < 0.05$). The scores were not significantly different between the silicone sheet and control groups ($p > 0.05$).
*****Silicone sheet and combination treatment groups were significantly higher than the onion extract gel, silicone gel and the control groups ($p < 0.05$). The scores were not significantly different between the silicone sheet and combination therapies ($p > 0.05$).

ments were statistically evaluated (Table 4). This analysis revealed that, treatment efficacy is related with shorter scar age and treatment duration (p<0001) but not with scar surface area (p=0.109) probably due to different treatment regimes adopted to scar area. As expected higher treatment efficacy was correlated with fewer scar symptoms. There was a significant positive correlation (p<0.05) between the treatment application difficulty VRS score, and scar surface area. There was a significant negative correlation (p<0.05) between the patient treatment satisfaction VRS score, and scar age and the number of scar symptoms post treatment. There was a significant positive correlation between patient efficacy, satisfaction scores and treatment duration (Table 4). There wasn't a significant correlation (p>0.05) between the results of these three patient outcome measures, and patient age, the number of scar symptoms at presentation, or duration of treatment (data not shown).

MSS and ModMSS score changes after treatments did not reveal any correlation with clinical variables including patient age, scar age, scar surface area, number of scar symptoms at presentation, number of scar symptoms post treatment, or duration of treatment (data not shown). However, MSS and Mod MSS changes with treatments were strongly correlated with VRAS parameters as expected (Table 5).

Discussion

Current treatment guidelines on the treatment of scarring focus on pathological scarring, particularly on the prevention and treatment of keloid and hypertrophic scars (6-8); however, studies on the maturation and reduction of normal scarring are few in number (1,9-16). Topical treatments such as onion extract gel and silicone gel are often used by individuals without first consulting a physician to improve the cosmetic appearance of newly formed scars (1). In general, individuals only present to a physician when scarring exacerbates or when there is scar elevation, such as hypertrophic scarring or keloid formation (1).

Current treatment guidelines recommend onion extract gel, silicone gel and sheet, and pressure garments for the prevention of the development of and for early treatment of proliferative scars (6-8). Onion extract gel was also reported to improve scar morphology and reduce the severity and extent of scar symptoms (7). It is thought that onion extract gel's mechanism of action on scars are antioxidant/antiproliferative effects, induction of matrix metalloproteinase 1, regulation of extracellular matrix remodeling, and reduction of fibroblast proliferation (1). Topical silicone gel has been widely used for scar reduction since the 1980s (17). It is thought that silicone gel and sheet do not act directly on scar tissue, but rather by covering the skin surface, which hydrates and moisturizes the skin, and improves the general condition of the scar (1). An in vitro study reported that keratinocytes regulate fibroblast behavior via occlusion and the resulting hydration effect of silicone, which suppresses fibroblast proliferation, and collagen and glycosaminoglycan

Table 3. Photographic scar scores, and the number of scar related symptoms before and after treatment.

		Pre-Treatment		Post-treatment		P*
		Median	Mean ± SD	Median	Mean ± SD	
MSS	Treatment	11.9	12.3 ± 3.4	7.4	8.5 ± 4.3	**<0.001**
	Control	10.0	9.9 ± 1.2	10.7	10.7 ± 1.6	0.249
	P**	0.095		0.139		
ModMSS	Treatment	16.0	16.3 ± 4.3	9.5	11.2 ± 5.0	**<0.001**
	Control	13.0	13.4 ± 2.1	14.6	14.1 ± 2.4	0.753
	P**	0.106		0.130		
Scar symptom count	Treatment	3.0	3.8 ± 2.2	1.0	1.4 ± 1.6	**<0.001**
	Control	2.6	2.1 ± 1.4	2.0	2.1 ± 1.5	0.705
	P**	0.054		0.144		

*Wilcoxon test, **Mann-Whitney U test

Table 4. The relationship between patient outcome measures and clinical variables.

		Treatment efficacy	Treatment application difficulty	Patient Satisfaction
Scar age	r	–0.422	0.131	–0.370
	P	**<0.001**	0.278	**0.001**
Scar surface area (cm^2)	r	–0.192	0.295	–0.159
	P	0.109	**0.012**	0.186
Post-treatment number of scar symptoms	r	–0.702	0.197	–0.616
	P	**<0.001**	0.100	**<0.001**
Treatment Duration	r	0.380	0.154	0.353
	P	**0.001**	0.201	**0.003**

(Spearman's correlation)

Table 5. The relationship between patient outcome measures and pre- to post-treatment change in photographic scar evaluation scores.

		MSS change	ModMSS change
Treatment efficacy	r	0.650	0.501
	P	**0.007**	**0.007**
Treatment application difficulty	r	–0.523	–0.403
	P	**0.032**	**0.027**
Patient Satisfaction	r	0.501	0.502
	P	**0.008**	**0.007**

(Spearman's correlation)

synthesis (18).

Pressure garments exert their anti-scarring effects via the constant pressure applied, which restricts capillary perfusion, preventing oxygen and nutrients from reaching hyperproliferative scar tissue, and also triggers apoptosis (7-19); however, pressure garments are difficult to use and cannot be used everywhere on the body (6). Current treatment guidelines recommend that pressure garments be used prophylactically following wound recovery when spontaneous healing is delayed >2 to 3 weeks and in cases of widespread scarring as we do (8).

Ho et al. (14) reported that onion extract gel decreased the rate of scar formation following laser tattoo removal. Draelos et al. (12,15) shave-excised seborrheic keratosis lesions of the chest and evaluated effects of onion extract gel application after wound healing. They reported that the scars treated with onion extract gel had better color, texture, and general appearance, and were softer than those that weren't treated with onion extract gel. A split scar study on cesarean scars showed that onion extract gel applied in early postoperative period (starting at postoperative 7 days) effectively reduces scar height and the severity of scar symptoms (11). Another split-scar cesarean scar study based on the POSAS score noted that early postoperative (starting at postoperative 5-10 days) use of onion extract gel reduces the severity of scarring, stiffness, and scar irregularity (16); however, neither this study nor the one previously mentioned (11) observed a significant difference in the general appearance of the scar or POSAS scores between two sides.

Topical silicone gel is effective for preventing hypertrophic scar and keloid development in postoperative wounds (20). Kim et al. (9) reported that topical silicone gel and silicone sheet were similarly effective for preventing post-surgery scar formation. Interestingly, immediate postoperative wound dressing with silicone sheet instead of waiting for completion of epithelization resulted in cosmetically more pleasing postoperative scars (13). A retrospective study by Parry et al. (10) on early (first 1-3 months) treatment with silicone gel and pressure garment therapies in pediatric patients with facial skin grafting wounds showed that the scar maturation rate increased and scar scale scores, especially vascularity and pigmentation subscores, significantly decreased as compared to later initiation of treatments as we do. In the present study the scar-reducing effectiveness of all these therapies were evaluated and all were noted to be effective, although various treatment protocols were administered in accordance with scar surface area, scar topography, scar age, and preceding wound healing time. We detected significant change in MSS and ModMSS scores with the treatment, but not for the control group. However patient rated efficacy scores were significantly higher in onion extract gel, silicon gel, silicon sheet and combination treatments more than those of control group. Silicon sheet got significantly lower efficacy rating than other treatment groups. Additionally patient satisfaction scores were significantly higher in onion extract gel, silicon gel and combination treatment groups than those of silicon sheet and control groups. Patients rated difficulty of application significantly more in silicon sheet and combination treatment groups than in others.

The present study has some limitations, including a small patient population, retrospective design, being not randomized and inclusion of multiple scar etiologies, types, and durations. Since the scar size determines the treatment; the decreased treatment efficacy and the decrease in patient satisfaction observed in patients with medium and large scars treated with silicon sheet alone arise the questions of whether these are the results of treatment compliance in these patients or impaired fitness of the selected treatment agent or the wideness of the scar area. This subject comprises one of the most important limitations of this study. In our study, pre- and post-treatment photographs of scars of patients were compared and the treatments were shown to be effective in in-group pre- and post-treatment comparisons, but the effect of spontaneous scar maturation on these results could not be assessed clearly as pre-treatment scores of control group tended to be insignificantly lower. Additionally the small number of control group made interpretation of the results slightly difficult. As such, additional larger scale prospective studies on topical scar-reducing treatment of similar types of scars with similar etiologies are needed.

Most of the present study's patients reported that the topical scar-reducing treatments were effective and easy to apply, and that they were satisfied with the treatments. Additionally, a significant decrease in the number of scar symptoms and a significant decrease in post-treatment scar scale scores were observed following the prescribed topical scar-reducing treatments. Moreover, treatment efficacy and patient satisfaction increased as scar age decreased. Another important finding is that as scar surface area increased the application of each treatment became more difficult, as patients with the largest scars were prescribed more complex to apply treatments, such as silicon sheet and combination treatments. Furthermore, as

the level of difficulty of treatment application increased treatment efficacy and patient satisfaction decreased. The observed decrease in the number of scar symptoms post-treatment was positively correlated with treatment efficacy and patient satisfaction, and negatively correlated with the level of application difficulty. Pre- to post-treatment change in scar scale scores was positively correlated with treatment efficacy and patient satisfaction, and negatively correlated with application difficulty.

In conclusion, the present retrospective pilot study shows that the prescribed topical scar-reducing treatments effectively improve the cosmetic appearance of scars and reduce the number of scar-related symptoms, and that the effectiveness increases as scar age decreases.

Acknowledgements:

The authors thank Scott Barry Evans for his assistance in native English speaker language editing. This study did not receive any public, commercial, or not-for- profit sector funding.

Author contributions Study Design: HMA, BA; data collection: BA, AT; data analysis: BA, EÇ; literature research: BA; writing: HMA, BA; final approval: HMA, BA, AT, EÇ

Conflicy of Interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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