ORIGINAL ARTICLE

EFFICACY AND SAFETY OF REGEN-SIL® IN POST-OPERATIVE SCARS MANAGEMENT

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Abstract

Scars are the result of skin healing process after incisions, burns, acne and other wounds resulting from sports or trauma. Scars have physical, cosmetic and emotional implications. We present a prospective, randomized, open clinical study, assessing the efficacy and safety of REGEN-SIL® siliconic gel, in therapeutic management of post-operative hypertrophic and keloid scars compared to the efficacy and safety of another silicone gel available on pharmaceutical market, both products being authorized as medical devices with the same therapeutic indications. One hundred patients undergoing incisions in the anterolateral cervical region for thyroid and parathyroid glands surgical approach were randomly assigned into two groups: REGEN-SIL® group (50 patients) and Silicone Gel group (50 patients). The application of silicone-based products started immediately after the sutures were removed. The scars evolution was assessed through Vancouver Scar Scale (VSS) at baseline, at one month and three months of treatment onset. Side effects that could occur following administration of both products have been monitored. In addition, patient and physician satisfaction were evaluated. Ninety-three patients completed the trial and all assessments of scars revealed significantly better improvement scaring process in REGEN-SIL® group than in Silicone Gel group after 3 months of treatment onset. No side effects were recorded in both groups. This study has demonstrated the superior efficacy of REGEN-SIL® in therapeutic management of post-operative hypertrophic and keloid scars, and also a greater appreciation from the side of patients and physicians *versus* the comparative product.

Rezumat

Cicatricile reprezintă rezultatul procesului de vindecare al pielii după incizii, arsuri, acnee şi alte răni rezultate din sport sau traume. Cicatricile au implicaţii fizice, cosmetice şi emoţionale. Prezentăm un studiu clinic prospectiv, randomizat, deschis, ce a evaluat eficacitatea şi siguranţa REGEN-SIL® gel siliconic, în managementul terapeutic al cicatricilor hipertrofice şi cheloide post-chirurgicale comparativ cu eficacitatea şi siguranţa unui alt gel siliconic existent pe piaţa farmaceutică, ambele produse fiind autorizate ca dispozitive medicale cu aceleaşi indicaţii terapeutice. O sută de pacienţi cărora li s-au practicat incizii în regiunea cervicală antero-laterală pentru abordul chirurgical al tiroidei şi al paratiroidelor au fost repartizaţi aleatoriu în două grupuri: grupul REGEN-SIL® (50 pacienţi) şi grupul Gel Siliconic (50 pacienţi). Administrarea produselor pe bază de silicon a început imediat după îndepărtarea firelor de sutură. Evoluţia cicatricilor a fost evaluată prin intermediul scalei *Vancouver Scar Scale* (VSS) la momentul includerii în studiu, la o lună şi la trei luni de la debutul tratamentului. Efectele adverse care ar fi putut să apară după administrarea ambelor produse au fost monitorizate. În plus, a fost evaluată satisfacţia pacienţilor şi a medicilor. Nouăzeci şi trei de pacienţi au finalizat studiul şi toate evaluările cicatricilor au pus în evidenţă o îmbunătăţire semnificativă a procesului de cicatrizare în grupul tratat cu REGEN-SIL® comparativ cu grupul tratat cu Gel Siliconic, după 3 luni de tratament. Nicio reacţie adversă nu a fost înregistrată în cazul ambelor grupuri. Acest studiu a demonstrat eficacitatea superioară a REGEN-SIL® în managementul terapeutic al cicatricilor hipertrofice şi cheloide post-chirurgicale şi o apreciere mai mare din punct de vedere al satisfacţiei medicilor şi a pacienţilor faţă de produsul cu care a fost comparat.

Keywords: silicones, scars, hypertrophic, keloid, post-operative, wounds

Introduction

Incisions, burns, acne, trauma and other wounds are associated with a natural healing process that lead to scar formation. This process is accompanied with physical, aesthetic, psychological and social consequences [19]. Itching [25, 26], stiffness, scar contractures, tenderness and pain are physical symptoms which manifest with the healing process. The visible scars often lead to significant cosmetic problems, psychological stress [2] and loss of self-esteem [23]. Keloid and hypertrophic scars impaired quality of life (QoL) in same extent as serious dermatologic conditions. Dermatology Life Quality Index (DLQI) is a validated dermatology specific QoL indicator. DLQI was quantified as being 7.79 for keloid and hypertrophic scars [3], 8.15 for vitiligo [9], 8.80 for severe atopic dermatitis [17] and psoriasis [15], 10.09 for scabies [12]. Visible scars have a greater impact on QoL, for example the DLQI for post-thyroidectomy scars was quantified as being 9.02 [6]. Silicones are the gold standard therapy in scar management, being enough supported by clinical trials that offer evidence-based recommendations [19]. Silicones are a non-invasive preventive and therapeutic measure. The main mechanism of action of silicon sheets or silicone gels is the hydrophobic occlusion and a consecutive underneath increase of hydration and decrease of trans-epidermal water loss (TEWL). TEWL cause a dehydration of dermal layers. Stimulation of keratinocytes in order to synthesize pro-fibrotic signals is a response of dehydration. Pro-fibrotic signals stimulate fibroblasts to produce excessive dermal collagen in order to obstruct the space which allows TEWL [21]. A reduction of angiogenesis and capillary perfusion is a beneficial consequence of hydration and occlusion which explains the efficacy of silicones in scar management. Additional mechanisms of action are: increasing of collagenase activity due to increasing of the skin surface temperature [20] and a realignment of collagen due to negatively charged static electric determined by friction between silicone gel and the skin surface [16].

The present study assessed the efficacy and safety of REGEN-SIL® gel in therapeutic management of post-operative hypertrophic and keloid scars. REGEN-SIL® is a complex silicone-based product which contains 4 types of silicones: high and low molecular dimethicone, trimethylsiloxisilicate and dimethicone cross polymer. The balanced composition leads to a unique silicon product with excellent adhesive long lasting, wash off resistance that forms a highly hydrophobic barrier, but permeable for gases exchange. REGEN-SIL® was compared with another silicone-based product which contains siloxane, polydimethylsiloxane and alkyl methyl silicone. As siliconic products have diverse compositions, there is a high relevance to comparatively investigate the clinical efficacy of the different formulations. Few studies have evaluated the comparative efficacy of available products on the pharmaceutical market. Consequently, a prospective, comparative, randomized, open study has been conducted in order to assess the efficacy and safety of two products authorised as medical devices with the same therapeutic indications.

Materials and Methods

Study population

One hundred patients undergoing surgical incisions in the anterolateral cervical region for thyroid and parathyroid glands were evaluated for inclusion in study between June, 2015 and March, 2016. Participant inclusion criteria were as follows: patients with age between 18 and 75 years, regardless of sex, with sutured wounds after incisions from surgery for thyroid and parathyroid glands approach, patients with closed wounds without complications (infections), patients which signed the informed consent [7]. Exclusion criteria were as follows: patients that did not sign the informed consent, allergies to silicone, patients with open or infected wounds, patients who follow other treatments for therapeutic management of scar (topical corticosteroids, intralesional cortico-steroids, and/or 5-fluorouracil or other therapeutic options for scar management).

All patients were randomly assigned in one of the two arms of the study: REGEN-SIL® gel (Look Ahead, Iasi, Romania) or another silicone gel - Strataderm® (Stratpharma AG CH-4051, Basel, Switzerland) available on pharmaceutical market authorized for the same therapeutic indications. The arms were categorized as REGEN-SIL® group (50 patients) and Silicone Gel group (50 patients), respectively. Patients were instructed to use the product according to approved information: 1 application/day in a thin layer. If the area with scar was washed, the administration was repeated, in order to create a permanent contact of the product with the scar. The application of both silicone-based products started immediately after the sutures were removed.

Evaluation criteria and outcome measures

Efficacy assessment. At the initial point, the patients' scars were photographed and evaluated using the Vancouver Scar Scale (VSS) [13]: pigmentation, vascularity, height, pliability, pain, and itchiness being measured (Table I). The afore mentioned evaluation was performed by dermatologists; photos and evaluation through VSS being repeated after one month and three months of treatment. The scarring process depending on age was comparatively assessed taking into account the

VSS score for patients < 60 years and ≥ 60 years in both treatment groups.

Safety assessment. Side effects that could occur following administration of both products have been monitored.

Patient and physician satisfaction

The satisfaction level was evaluated according to a 5 point scale (1 – *weak*, 2 – *moderate*, 3 – *good*, 4 – *very good*, 5 – *excellent*) by both the patients and physicians, at one month and three months after treatment onset.

Statistical analysis

Descriptive statistics were used for demographic data. Z-test two samples for means was used to compare values between baseline and subsequent visits (intragroup analysis) and between treatment groups at subsequent visits (intergroup analysis). A p value less than 0.05 was considered statistically significant.

Approval and ethics statement

Both products are registered as medical devices and in this clinical study were used according to the information for users. The scientific research was thus conducted after a non-interventional design and no approval from national regulatory authority being requested.

This study was approved by the Ethics Committee of "Sfântul Spiridon" Emergency County Hospital, Iaşi, Romania. All patients were informed about the study details and signed the informed consent.

Table I

Vancouver Scar Scale (VSS) score [13]

Feature		Score
Pigmentation	Normal	0
	Hypopigmentation	1
	Mixed pigmentation	2
	Hyperpigmentation	3
Vascularity	Normal	0
	Pink	1
	Red	2
	Purple	3
Height	Normal	0
	< 2 mm	1
	2 - 5 mm	2
	> 5 mm	3
Pliability	Normal	0
	Supple (flexible with minimal resistance)	1
	Yielding (giving way to pressure)	2
	Firm (inflexible, not easily moved, resistant to manual pressure)	3
	Banding (rope-like tissue that blanches with extension of the scar)	4
	Contracture (permanent shortening of scar, producing deformity or distortion)	5
Pain	None	0
	Occasional	1
	Requires medication	2
Itchiness	None	0
	Occasional	1
	Requires medication	2

Results and Discussion

Baseline and clinical characteristics of the patients

This study enrolled one hundred patients, but only ninety-three patients finished the trial; the exclusion reasons from the study of the 7 patients are presented in Table II. All participants were female with a mean age of 50.4 years (total range 22 - 75 years, (Table III). All patients underwent incisions in the anterolateral cervical region for thyroid and parathyroid glands surgical approach (Table IV).

Table II

Exclusion reasons of patients from initial lot

Exclusion reasons	Number of patients		
	REGEN-SIL® group	Silicone Gel group	Total
Dropping out for personal reasons	2	3	5
Using of both products	1	-	1
Development of post-operative ecchymosis in surgical incision area, independently from topical application of product	1	-	1
Total excluded patients	4	3	7
Patients that completed the study	46	47	93

Table III

Demographic characteristics of both groups

Demographic characteristics	REGEN-SIL® group (n = 46)	Silicone Gel group (n = 47)	Total
Age			
mean ± SD, years	53.6 ± 11.6	47 ± 11	50.4 ± 11.7
[min, max], years	[25 - 75]	[22 - 70]	[22 - 75]
Sex			
F/M, n	46/0	47/0	93/0

F – female, M – male, max – maximum, min – minimum, n – number of patients, SD – standard deviation

Table IV

Surgical interventions

Surgical interventions	REGEN-SIL® group (n = 46)	Silicone Gel group (n = 47)	Total
Benign total thyroidectomy	42	44	86
Malignant total thyroidectomy	1	2	3
Benign right thyroid lobectomy	-	1	1
Benign left thyroid lobectomy	1	-	1
Malignant total thyroidectomy and selective neck dissection (central and 3rd sectors)	1	-	1
Benign total thyroidectomy, subtotal parathyroidectomy	1	-	1
Total	46	47	93

The practiced surgical technique was the horizontal incision in anterolateral cervical region, with 7 cm length, at 2 cm cranial to the sternal manubrium and closure. Suture was carried out with heavy resorbable vicryl 30 for median raphe of infrahyoid muscles (strap muscles), heavy absorbable suture for subcutaneous, fast absorbable suture 30 for separate suture intradermal, Steri-strip of 5 mm on the whole length of the wound. After sutures were removed, no significant differences were observed between groups regarding VSS scores at baseline (Table V).

Table V

Vancouver Scar Scale (VSS) scores at baseline

Score		Baseline mean ± SD	Intergroup statistical significance (p, α = 0.05)
Pigmentation	REGEN-SIL® group (n = 46)	1.89 ± 0.31	NS (p = 0.779)
	Silicone Gel group (n = 47)	1.87 ± 0.34	
Vascularity	REGEN-SIL® group (n = 46)	2.48 ± 0.50	NS (p = 0.475)
	Silicone Gel group (n = 47)	2.40 ± 0.50	
Height	REGEN-SIL® group (n = 46)	2.28 ± 0.45	NS (p = 0.247)
	Silicone Gel group (n = 47)	2.17 ± 0.48	
Pliability	REGEN-SIL® group (n = 46)	2.04 ± 0.36	NS (p = 0.602)
	Silicone Gel group (n = 47)	2.08 ± 0.41	
Pain	REGEN-SIL® group (n = 46)	0.93 ± 0.25	NS (p = 0.299)
	Silicone Gel group (n = 47)	0.98 ± 0.15	
Itchiness	REGEN-SIL® group (n = 46)	0.87 ± 0.34	NS (p = 0.130)
	Silicone Gel group (n = 47)	0.96 ± 0.20	
Total VSS	REGEN-SIL® group (n = 46)	10.5 ± 2.23	-
	Silicone Gel group (n = 47)	10.47 ± 2.07	

n – number of patients, NS – not statistically significant, SD – standard deviation

Efficacy assessment

Changes from baseline at 1 month after treatment onset

Intragroup analysis. At 1 month after treatment onset, a decrease of vascularity (-24.59%, $p < 0.001$), height (-11.40%, $p < 0.001$) and itchiness (-19.54%, $p = 0.041$) score was recorded for REGEN-SIL® group compared to baseline. These differences reached statistical significance. No significant differences were observed for pigmentation, pliability and pain compared with baseline in REGEN-SIL® group (Table VI). Total VSS score decreased by 11.61% in REGEN-SIL® group, compared with baseline, after 1 month from treatment onset.

Intergroup analysis. Pigmentation, height, pliability and pain score differed insignificantly between groups. Vascularity and itchiness scores turned out to decrease significantly in REGEN-SIL® group compared to Silicone Gel group: -8.33% ($p = 0.008$) and -19.54%

(p = 0.036), respectively after 1 month. The difference in terms of total VSS score was also in favour of REGEN-SIL® treatment (-4.52% compared with Silicone Gel group), after 1 month from treatment onset (Table VI).

Table VI

The values recorded for clinical parameters evaluated at 1 month after treatment onset

Score		Baseline	After 1 month (1st follow-up)				
			INTRAGROUP			INTERGROUP	
		mean ± SD	mean ± SD	% compared to initial	Statistical significance (p, α = 0.05)	% intergroup difference	Statistical significance (p, α = 0.05)
Pigmentation	REGEN-SIL® group (n = 46)	1.89 ± 0.31	1.78 ± 0.42	-5.82%	NS	-1.65%	NS (p = 0.76)
	Silicone Gel group (n = 47)	1.87 ± 0.34	1.81 ± 0.40	-3.20%	NS		
Vascularity	REGEN-SIL® group (n = 46)	2.48 ± 0.50	1.87 ± 0.34	-24.59%	S, p < 0.001	-8.33%	S, p = 0.008
	Silicone Gel group (n = 47)	2.40 ± 0.50	2.04 ± 0.29	-15%	S, p < 0.001		
Height	REGEN-SIL® group (n = 46)	2.28 ± 0.45	2.02 ± 0.15	-11.40%	S, p < 0.001	-4.82%	NS (p = 0.15)
	Silicone Gel group (n = 47)	2.17 ± 0.48	2.11 ± 0.37	-2.76%	NS		
Pliability	REGEN-SIL® group (n = 46)	2.04 ± 0.36	2.02 ± 0.15	-0.98%	NS	+1.98%	NS (p = 0.44)
	Silicone Gel group (n = 47)	2.08 ± 0.41	1.98 ± 0.15	-5.10%	NS		
Pain	REGEN-SIL® group (n = 46)	0.93 ± 0.25	0.89 ± 0.31	-4.30%	NS	-2.19%	NS (p = 0.62)
	Silicone Gel group (n = 47)	0.98 ± 0.15	0.91 ± 0.29	-7.14%	NS		
Itchiness	REGEN-SIL® group (n = 46)	0.87 ± 0.34	0.70 ± 0.46	-19.54%	S, p = 0.041	-19.54%	S, p = 0.036
	Silicone Gel group (n = 47)	0.96 ± 0.20	0.87 ± 0.34	-9.37%	NS		
Total VSS	REGEN-SIL® group (n = 46)	10.50 ± 2.23	9.28 ± 1.83	-11.61%	-	-4.52%	-
	Silicone Gel group (n = 47)	10.47 ± 2.07	9.72 ± 1.83	-7.07%			

n – number of patients, NS – not statistically significant, S – statistically significant, SD – standard deviation

Changes from baseline at 3 months after treatment onset

Intragroup analysis. At 3 months after treatment onset, a significant decrease for all parameters of VSS score was recorded compared to baseline in REGEN-SIL® group: pigmentation (-71.46%, p < 0.001), vascularity (-70.16%, p < 0.001), height (-70.61%, p < 0.001), pliability (-62.74%, p < 0.001) pain (-41.93%, p < 0.001), itchiness (-29.88%, p = 0.003). Total VSS score decreased by 63.23% compared with baseline in REGEN-SIL® group (Table VII).

Intergroup analysis. With the exception of the itchiness score, as shown in Table VII, significant differences were recorded between groups at 3 months after treatment onset. Administration of REGEN-SIL® proved a significant decrease in VSS for REGEN-SIL® group compared with Silicone Gel group in pigmentation (-31.65%, p = 0.01), vascularity (-27.45%, p = 0.001), height (-28.72%, p = 0.003), pliability (-24%, p < 0.001), pain (-33.33%, p = 0.005). The difference in terms of total VSS score was maintained after 3 months in favour of REGEN-SIL® treatment (-26.7% compared to total VSS in Silicone Gel group, after 3 months).

Overall, significant reduction of VSS score were observed with the use of REGEN-SIL®. Evolution of VSS scores are also represented in Figure 1.

Table VII

The values recorded for clinical parameters evaluated at 3 months after treatment onset

Score		Baseline	After 3 months (2nd follow-up)				
			INTRAGROUP			INTERGROUP	
		mean ± SD	mean ± SD	% compared to initial	Statistical significance (p, α = 0.05)	% intergroup difference	Statistical significance (p, α = 0.05)
Pigmentation	REGEN-SIL® group (n = 46)	1.89 ± 0.31	0.54 ± 0.50	-71.46%	S, p < 0.001	-31.65%	S, p = 0.01
	Silicone Gel group (n = 47)	1.87 ± 0.34	0.79 ± 0.41	-57.75%	S, p < 0.001		
Vascularity	REGEN-SIL® group (n = 46)	2.48 ± 0.50	0.74 ± 0.44	-70.16%	S, p < 0.001	-27.45%	S, p = 0.001
	Silicone Gel group (n = 47)	2.40 ± 0.50	1.02 ± 0.39	-57.50%	S, p < 0.001		
Height	REGEN-SIL® group (n = 46)	2.28 ± 0.45	0.67 ± 0.47	-70.61%	S, p < 0.001	-28.72%	S, p = 0.003
	Silicone Gel group (n = 47)	2.17 ± 0.48	0.94 ± 0.38	-56.68%	S, p < 0.001		
Pliability	REGEN-SIL® group (n = 46)	2.04 ± 0.36	0.76 ± 0.43	-62.74%	S, p < 0.001	-24%	S, p < 0.001
	Silicone Gel group (n = 47)	2.08 ± 0.41	1.00 ± 0.36	-51.92%	S, p < 0.001		
Pain	REGEN-SIL® group (n = 46)	0.93 ± 0.25	0.54 ± 0.50	-41.93%	S, p < 0.001	-33.33%	S, p = 0.005
	Silicone Gel group (n = 47)	0.98 ± 0.15	0.81 ± 0.40	-17.34%	S, p = 0.006		
Itchiness	REGEN-SIL® group (n = 46)	0.87 ± 0.34	0.61 ± 0.49	-29.88%	S, p = 0.003	-15.27%	NS, p = 0.24
	Silicone Gel group (n = 47)	0.96 ± 0.20	0.72 ± 0.45	-25%	S, p = 0.001		
Total VSS	REGEN-SIL® group (n = 46)	10.50 ± 2.23	3.86 ± 2.85	-63.23%	-	-26.70%	
	Silicone Gel group (n = 47)	10.47 ± 2.07	5.28 ± 2.40	-49.57%			

n – number of patients, NS – not statistically significant, S – statistically significant, SD – standard deviation

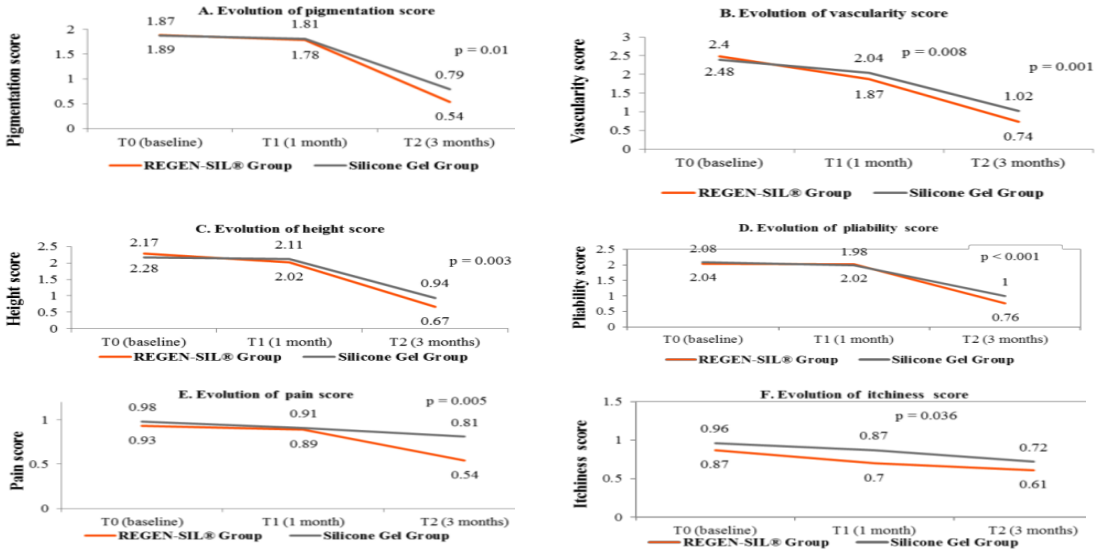

Figure 1.

Evolution of VSS scores (statistically significant at p < 0.05 within intergroup)

In order to assess the efficacy differences between REGEN-SIL® and Silicone Gel, the percentage of patients with clinical normalized parameters (0 score), after 3 months of treatment were represented (Figure 2).

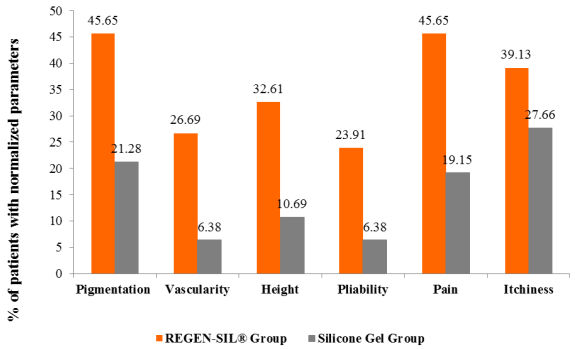

Figure 2.
Normalization of clinical parameters after 3 months of treatment

Age depending scarring assessment

Intragroup analysis. No significant statistical difference was registered between patients younger than 60 years and patients older than 60 years, after 1 month and 3 months, for patients treated with REGEN-SIL® or patients treated with Silicone Gel (except for pliability score with statistically significant difference in Silicone Gel group, after 1 month) (Table VIII).

Patients younger than 60 years - Intergroup analysis. Vascularity turned out to decrease significantly in REGEN-SIL® group compared to Silicone Gel group in patients younger than 60 years after 1 month treatment onset. With the exception of the pigmentation and itchiness score, as shown in Table IX and Figure 3, significant differences were recorded between groups, in patients younger than 60 years, at 3 months after treatment onset. The administration of REGEN-SIL® proved a significant decrease in VSS compared with Silicone Gel group: vascularity (-25%, $p = 0.01$), height (-32.63%, $p < 0.01$), pliability (-16.84%, $p < 0.01$), pain (-31.33%, $p = 0.01$) (Table IX). The difference in terms of total VSS score was maintained after 3 months in favour of REGEN-SIL® treatment (-26.49% compared to total VSS in Silicone Gel group) for patients younger than 60 years.

Patients older than 60 years - Intergroup analysis. The itchiness score turned out to decrease significantly in REGEN-SIL® group compared to Silicone Gel group in patients older than 60 years, after 1 month treatment onset. With the exception of the vascularity and pliability score, as shown in Table IX and Figure 4, insignificant differences were recorded between groups, in patients older than 60 years, at 3 months after treatment onset.

Table VIII
The values recorded for clinical parameters depending on age – intragroup analysis

		Pigmentation	Vascularity	Height	Pliability	Pain	Itchiness	Total VSS score
REGEN-SIL® group								
After 1 month								
Intragroup	< 60 years, mean ± SD	1.82 ± 0.39	1.82 ± 0.39	2.04 ± 0.19	2.04 ± 0.19	0.93 ± 0.26	0.71 ± 0.46	9.36 ± 2.80
	≥ 60 years, mean ± SD	1.72 ± 0.46	1.94 ± 0.24	2.00 ± 0.00	2.00 ± 0.00	0.83 ± 0.38	0.67 ± 0.49	9.16 ± 1.57
	% intragroup difference	5.81%	-6.19%	2.00%	2.00%	12.05%	5.97%	+2.18%
	Statistical significance (p, α = 0.05)	NS (p = 0.45)	NS (p = 0.37)	NS (p = 0.42)	NS (p = 0.42)	NS (p = 0.36)	NS (p = 0.74)	-
After 3 months								
Intragroup	< 60 years, mean ± SD	0.50 ± 0.51	0.75 ± 0.44	0.64 ± 0.49	0.79 ± 0.42	0.57 ± 0.50	0.54 ± 0.51	3.79 ± 2.89
	≥ 60 years, mean ± SD	0.61 ± 0.50	0.72 ± 0.46	0.72 ± 0.46	0.72 ± 0.46	0.50 ± 0.51	0.72 ± 0.46	3.99 ± 2.85
	% intragroup difference	18.03%	-4.17%	11.11%	-9.72%	-14.00%	25.00%	+ 5.27%
	Statistical significance (p, α = 0.05)	NS (p = 0.47)	NS (p = 0.78)	NS (p = 0.58)	NS (p = 0.63)	NS (p = 0.64)	NS (p = 0.25)	-
Silicone Gel group								
After 1 month								
Intragroup	< 60 years, mean ± SD	1.83 ± 0.38	2.03 ± 0.28	2.10 ± 0.38	2.29 ± 0.49	0.90 ± 0.30	0.85 ± 0.36	10.0 ± 2.19
	≥ 60 years, mean ± SD	1.71 ± 0.49	2.14 ± 0.38	2.14 ± 0.38	2.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	9.99 ±1.25
	% intragroup difference	7.65%	-5.14%	-1.87%	-14.50%	-10.00%	-15.00%	+0.1%
	Statistical significance (p, α = 0.05)	NS (p = 0.57)	NS (p = 0.43)	NS (p = 0.78)	S (p < 0.01)	NS (p = 0.10)	NS (p = 0.01)	-
After 3 months								
Intragroup	< 60 years, mean ± SD	0.68 ± 0.47	1.00±0.39	0.95±0.39	0.95 ± 0.32	0.83 ± 0.38	0.75 ± 0.44	5.16 ± 2.39
	≥ 60 years, mean ± SD	0.86 ± 0.38	1.14±0.38	0.86±0.38	1.29 ± 0.49	0.71 ± 0.49	0.57 ± 0.53	5.43 ± 2.65
	% intragroup difference	-20.93%	-12.28%	10.47%	-26.36%	16.90%	31.58%	+ 5.23%
	Statistical significance (p, α = 0.05)	NS (p = 0.35)	NS (p = 0.35)	NS (p = 0.55)	NS (p = 0.08)	NS (p = 0.61)	NS (p = 0.41)	-

n – number of patients, NS – not statistically significant, S – statistically significant, SD – standard deviation

Table IX

The values recorded for clinical parameters depending on age – intergroup analysis

		Pigmentation	Vascularity	Height	Pliability	Pain	Itchiness	Total VSS score
< 60 years								
After 1 month								
Intragroup	REGEN-SIL® group, mean ± SD	1.82 ± 0.39	1.82 ± 0.39	2.04 ± 0.19	2.04 ± 0.19	0.93 ± 0.26	0.71 ± 0.46	9.36 ± 2.80
	Silicone Gel group, mean ± SD	1.83 ± 0.38	2.03 ± 0.28	2.10 ± 0.38	2.29 ± 0.49	0.90 ± 0.30	0.85 ± 0.36	10.0 ± 2.19
	% intergroup difference	- 0.55%	- 10.34%	-2.86%	+10.91%	+ 3.23%	-16.47%	+ 6.83%
	Statistical significance (p, α = 0.05)	NS (p = 0.97)	S (p = 0.02)	NS (p = 0.36)	NS (p = 0.19)	NS (p = 0.68)	NS (p = 0.19)	-
After 3 months								
Intragroup	REGEN-SIL® group, mean ± SD	0.50 ± 0.51	0.75 ± 0.44	0.64 ± 0.49	0.79 ± 0.42	0.57 ± 0.50	0.54 ± 0.51	3.79 ± 2.89
	Silicone Gel group, mean ± SD	0.68 ± 0.47	1.00 ± 0.39	0.95 ± 0.39	0.95 ± 0.32	0.83 ± 0.38	0.75 ± 0.44	5.15 ± 2.39
	% intergroup difference	-26.47%	-25%	-32.63%	-16.84%	-31.33%	-28%	-26.49%
	Statistical significance (p, α = 0.05)	NS (p = 0.1)	S (p = 0.01)	S (p < 0.01)	S (p < 0.01)	S (p = 0.01)	NS (p = 0.07)	-
≥ 60 years								
After 1 month								
Intragroup	REGEN-SIL® group, mean ± SD	1.72 ± 0.46	1.94 ± 0.24	2.00 ± 0.00	2.00 ± 0.00	0.83 ± 0.38	0.67 ± 0.49	9.16 ± 1.57
	Silicone Gel group, mean ± SD	1.71 ± 0.49	2.14 ± 0.38	2.14 ± 0.38	2.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	9.99 ±1.25
	% intergroup difference	+ 0.58%	-9.35%	-6.54%	-	-17%	-33%	- 8.30%
	Statistical significance (p, α = 0.05)	NS (p = 0.97)	NS (p = 0.19)	NS (p = 0.31)	NS	NS (p = 0.07)	S (p < 0.01)	-
After 3 months								
Intragroup	REGEN-SIL® group, mean ± SD	0.61 ± 0.50	0.72 ± 0.46	0.72 ± 0.46	0.72 ± 0.46	0.50 ± 0.51	0.72 ± 0.46	4.00 ± 2.85
	Silicone Gel group, mean ± SD	0.86 ± 0.38	1.14 ± 0.38	0.86 ± 0.38	1.29 ± 0.49	0.71±0.49	0.57 ± 0.53	5.43 ± 2.65
	% intergroup difference	-29.07%	-36.84%	-16.28%	-44.19%	-29.58%	-20.83%	-26.31%
	Statistical significance (p, α = 0.05)	NS (p = 0.18)	S (p = 0.02)	NS (p = 0.53)	S (p = 0.01)	NS (p = 0.33)	NS (p = 0.51)	-

n – number of patients, NS – not statistically significant, S – statistically significant, SD – standard deviation

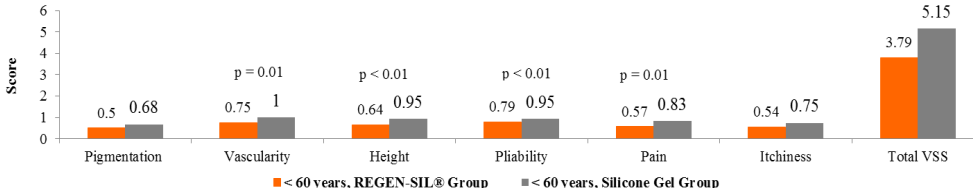

Figure 3.

VSS score difference between REGEN-SIL® and Silicone Gel group – patients < 60 years at 3 months after treatment onset (statistically significant at p < 0.05 within intergroup)

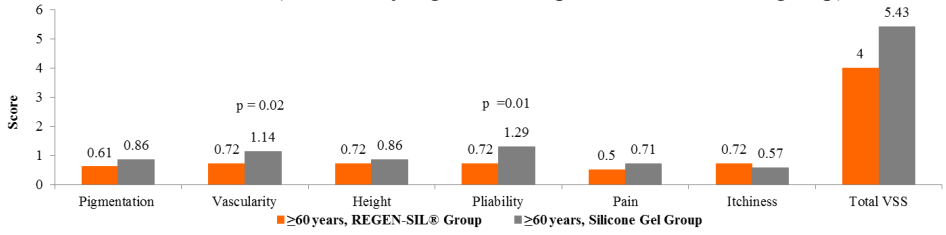

Figure 4.

VSS score difference between REGEN-SIL® and Silicone Gel group – patients ≥ 60 years at 3 months after treatment onset (statistically significant at p < 0.05 within intergroup)

Administration of REGEN-SIL® proved a significant decrease in VSS compared with Silicone Gel group: vascularity (-36.84%, p = 0.02), pliability (-44.19%, p = 0.01) (Table IX). The difference in terms of total VSS score was maintained after 3 months in favour of REGEN-SIL® treatment (-26.31% compared to total VSS in Silicone Gel group, after 3 months) in patients older than 60 years.

Safety assessment

No side effects were recorded and compliance was optimal in both groups.

Patient and physician satisfaction

There was no significant difference between groups regarding satisfaction of patients after 1 month, but significant differences were recorded after 3 months. The cosmetic results of treatment were appreciated as *very good* and *excellent* by 95.65% of patients treated with REGEN-SIL® *versus* 82.98% treated with Silicone Gel, after 3 months. A remarkable difference was recorded after 3 months for overall satisfaction: 97.83% of patients assessed the overall satisfaction of REGEN-SIL® treatment as being *very good* and

excellent compared to only 82.98% of patients treated with Silicone Gel (Table X, Figure 5).

Table X

Patient satisfaction

Patient satisfaction	After 1 month (1st follow-up)					After 3 months (2nd follow-up)				
	mean ± SD	Intergroup Statistical significance (p, α = 0.05)	% patients			mean ± SD	Intergroup Statistical significance (p, α = 0.05)	% patients		
			Good	Very good	Excellent			Good	Very good	Excellent
Cosmetic results										
REGEN-SIL® group (n = 46)	4.48 ± 0.51	NS, p = 0.260	-	52.17	47.83	4.48 ± 0.51	S, p = 0.045	4.35	13.04	82.61
Silicone Gel group (n = 47)	4.36 ± 0.61		6.38	51.06	42.55	4.51 ± 0.78		17.02	14.89	68.09
Overall satisfaction										
REGEN-SIL® group (n = 46)	4.50 ± 0.51	NS, p = 0.040	0.00	50.00	50.00	4.87 ± 0.40	S, p = 0.001	2.17	8.70	89.13
Silicone Gel group (n = 47)	4.26 ± 0.64		10.64	53.19	36.17	4.47 ± 0.78		17.02	19.15	63.83

n – number of patients, NS – not statistically significant, S – statistically significant, SD – standard deviation

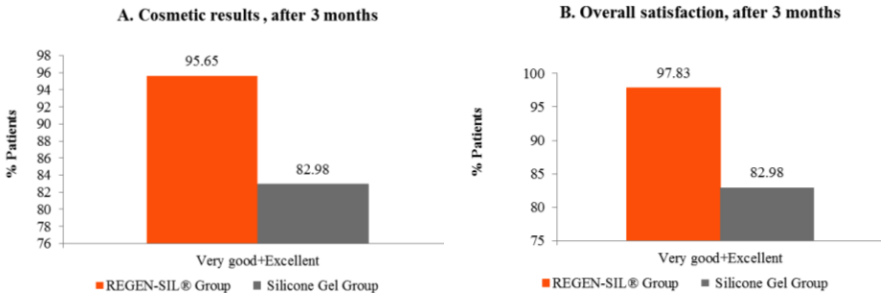

Figure 5.
Patient satisfaction

An important difference regarding physicians satisfaction was recorded after 3 months of treatment: physicians have appreciated the overall satisfaction as being *very good* and *excellent* for 95.66% patients treated with REGEN-SIL® compared to only 74.47% patients treated with Silicone Gel (Table XI, Figure 6).

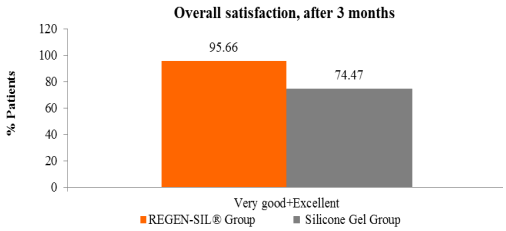

Figure 6.
Physician satisfaction

Table XI

Physician satisfaction

Physician satisfaction	After 1 month (1st follow-up)					After 3 months (2nd follow-up)				
	mean ± SD	Intergroup Statistical significance (p, α = 0.05)	% patients			mean ± SD	Intergroup Statistical significance (p, α = 0.05)	% patients		
			Good	Very good	Excellent			Good	Very good	Excellent
Cosmetic results										
REGEN-SIL® Group (n = 46)	4.63 ± 0.61	NS (p = 0.145)	6.52	23.91	69.57	4.76 ± 0.48	NS (0.882)	2.17	19.57	78.26
Silicone Gel Group (n = 47)	4.43 ± 0.74		14.89	27.66	57.45	4.75 ± 0.57		6.38	80.85	12.77
Overall satisfaction										
REGEN-SIL® Group (n = 46)	4.76 ± 0.43	S, p = 0.003	-	23.91	76.09	4.72 ± 0.54	S (p < 0.001)	4.35	19.57	76.09
Silicone Gel Group (n = 47)	4.38 ± 0.77		25.53	29.79	44.68	4.19 ± 0.82		25.53	29.79	44.68

n – number of patients, NS – not statistically significant, S – statistically significant, SD – standard deviation

Undoubtedly, silicone-based products are effective in scar management. The efficacy and safety of their administration are supported by numerous studies [1, 8, 24], and they become the gold standard for scar management [21]. Numerous silicone-based products are available on pharmaceutical market, but clinicians should select products, considering their sustained efficacy and safety.

This study aimed to assess both efficacy and safety of REGEN-SIL® in therapeutic management of post-operative scars and to compare the efficacy and safety of REGEN-SIL® *versus* another silicone gel available on Romanian market. Both products are authorized as medical devices with the same therapeutic indication. The baseline evaluation of surgical scars revealed no statistically significant differences in VSS score. All parameters of VSS, with exception of itchiness score were recorded as being significantly lower in REGEN-SIL® group compared with Silicone Gel group, after 3 months of treatment. Total VSS score decreased by 63.23% in REGEN-SIL® group, compared with baseline. The total VSS score decreased more in REGEN-SIL® than in Silicone Gel group, the difference between groups being 26% after 3 months of treatment.

The recorded results are similar to those presented by other clinical trials. Medhi B *et al*., [16] evaluated the efficacy of silicone gel (Kelo-cote®, Wockhardt Limited, Mumbai, India) for prevention of post-operative hypertrophic and keloid scars. The recorded decreases for VSS in present study were in similar trend to those presented by Medhi B *et al.,* (16). Kim SM *et al*., [13] compared the efficacy of silicone gel (Kelo-Cote™, SejongMedix, Seoul, Korea) *versus* silicone sheets (Scarclinic™-Thin, Hans Biomed, Seoul, Korea) in preventing of the post-surgical scars and no significant differences were recorded between silicone gel and silicone sheets. Scar evolution was similar to that recorded in the current study [13]. The younger patients were most targeted in our comparative evaluation, because it is commonly recognized that a temporal delay in wound healing, but not in quality of healing, occurs in elderly comparing to young patients [10]. The slow metabolism rate and less tensile strength determine the low chance to develop hypertrophic and keloid scars in elderly [14]. Younger patients displayed a prolonged high turnover state and a retarded rate of maturation compared with patients older than 55 years that displayed an accelerated maturation [4]. This observation is attributed to skin physiology related on age: the young skin has more elastic fibres which lead to a greater tension and the rate of collagen synthesis is greater in young people [22]. More delayed wound healing with a better quality of scarring process in patients older than 60 years was remarked in our investigated group, also. An increasing trend of VSS scores were recorded for patients younger than 60 years compared to patients older than 60 years, after 1 month of treatment onset, but without statistical significance in both groups. Treatment with both silicone-based products equilibrated the difference between age groups, and a decreasing of VSS scores was remarked for patients younger than 60 years compared to those recorded for patients older than 60 years, at 3 months after treatment onset. The comparative assessment of scarring process depending on age revealed that REGEN-SIL® is more efficient than the comparative product in post-operative scar management both in young and elderly patients. Total VSS score decreased more in REGEN-SIL® group than in Silicone Gel group. The differences between groups were 26.49% at patients younger than 60 years and 26.31% at patients older than 60 years, respectively in favour of REGEN-SIL®, at 3 months after treatment onset.

No side effects were recorded in both groups, which support optimal tolerability of silicone-based products.

This study has the limitation to assess the efficacy and safety only after 3 months of treatment and no other follow-up was stipulated in clinical trial protocol after 3 months. No other observations were carried out for scar progression. Another limitation is assessment of scarring process between the two sexes, because the assessed lot included only female, taking into account the high prevalence of thyroid and parathyroid pathology in female. As in many previous clinical studies reported, the efficacy of silicone-based products is demonstrated on all types of scars: burn scars [18], post laser exfoliation erythema, hypertrophic and keloid scars [5]. Further studies are necessary in order to investigate if REGEN-SIL® provides more efficacy than other topical silicone-based products on scarring of wounds situated in different anatomical sites. Skin of shoulders, neck, presternum, knees and ankles are more susceptible to high tension thus developing hypertrophic scars whereas keloid scars are developed with predilection on anterior chest, earlobes, upper arms and cheeks.

Conclusions

The actual research was focused to assess the comparative efficacy and safety of REGEN-SIL® *versus* another silicone gel available on pharmaceutical market, in therapeutic management of post-operative scars. This research is justified by structural variety of silicones, but also by the quantitative ratios between silicones that individualizes silicone-based topical products. It is, under our knowledge, the first study that compared the efficacy and safety of two silicone-based gels, the results of actual study being in interest of

therapeutic decision for health care professionals [11]. The current study determined that REGEN-SIL® is more efficient than the comparative product in therapeutic management of post-operative scar. The difference between the two products in terms of efficacy is explained by the complex formula of REGEN-SIL® that contains 4 types of silicones: high and low molecular dimethicone, trimethylsiloxisilicate and dimethicone crosspolymer. High and low molecular dimethicone form a protective, fine and hydrophobic barrier on the skin and leaves a silky and un-sticky sensation, trimethylsiloxisilicate creates rapidly a persistent and protective hydrophobic film and dimethicone crosspolymer creates a gel structure.

In conclusion, there are numerous available silicone-based products used for management of scars, but the first choice of the clinicians should be based on both efficacy and safety of the product. The results of this study indicate that REGEN-SIL®, a complex silicone gel is both efficient and safe in therapeutic management of post-operative hypertrophic and keloid scars, being more efficient than the comparative product and more appreciated by patients and physicians.

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