Am J Transl Res 2023;15(2):1204-1214
www.ajtr.org /ISSN:1943-8141/AJTR0144841

Original Article

Comparisons of the effects of topical anti-scar drugs on post-surgical facial scar formation: a clinical investigation

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Received June 18, 2022; Accepted January 3, 2023; Epub February 15, 2023; Published February 28, 2023

Abstract: Objectives: Scarring is a common but intricate problem, and topical anti-scarring drugs are the most widely used treatment. However, the wide range of drugs available makes it difficult for doctors and patients to choose from because of the lack of clinical comparisons. Therefore, we conducted an observational study to compare the clinical efficacy of different topical anti-scarring drugs. Methods: Patients with post-suturing facial scars were enrolled in this study. The questionnaire was designed to record the basic characteristics of the patients. The Vancouver Scar Scale, SCAR scale, and measurements of scar width and thickness were used to evaluate scar quality. Patients who met the inclusion criteria were divided into four groups for comparison: the silicone preparation (SP), onion extract (OE), asiaticoside (AC) groups, and the untreated blank control (BC) group. The overall data were analyzed before they were confined to the zygomatic region. Results: A total of 127 eligible patients were enrolled in this study. The results of the total and zygomatic scars demonstrated that SP, OE, and AC groups resulted in narrower scars and lower scar scale scores. The SP group depicted higher melanin efficacy than the other two groups. The OE group had the best pliability, whereas the AC group had the thinnest scar. Conclusions: In this study, we acquired expertise with different topical anti-scar agents: SP significantly reduced melanin levels, OE mainly benefited scar pliability, and AC was better at reducing scar thickness. These differences may be more instructive for clinical applications.

Keywords: Topical anti-scarring drugs, silicone preparations, onion extracts, asiaticosides, clinical decision support

Introduction

Scars refer to general changes in skin tissue structure and morphology caused by various injuries. The incidence of scars can be as high as 40%-70%, especially in burn victims, postoperative patients, and people who undergo trauma [1]. Scars differ in appearance from the surrounding skin and can be flat, stretched, sunken, or raised, exhibiting a range of symptoms including inflammation, erythema, dryness, and itching [2]. Scars, especially hypertrophic scars and keloids, not only affect the aesthetic appearance and physiological function but can also cause anxiety and depression, influencing the quality of life of patients [3, 4].

Treatment of scars can be time-consuming, laborious, and costly. The global annual wound care products market is expected to reach $15-22 billion by 2024 [5]. Further, the problem of skin scarring adds to the burden of treatment [6], which in the United States alone will reach $35 billion annually by 2023 [7].

With the development of medical treatment, there are many available methods to prevent and improve scars, such as laser, radiotherapy, pressure, intratricial injection, surgical resection, gene, and epigenetic therapies [1, 8]. Most of these methods need to be performed by doctors and repeated many times to achieve good effects, which is not only time-consuming but

also prohibitive for many patients because of the high costs. However, topical drugs are easy to obtain, simple to use, and reasonably priced; therefore, they remain the preferred classic treatment for most patients with scars.

Despite the large array of topical anti-scar drugs, the most commonly used functional ingredients in clinical practice can be classified into three categories: silicone agents, onion extracts, and asiaticoside [9]. The anti-scarring mechanisms of these drugs have been well studied. Silicone preparations are synthetic polymers that are beneficial for creating a closed wound environment, reducing the loss of skin moisture, and increasing the hydration of the corneous layer, which not only benefits the stability of mast cells and inhibits the release of proinflammatory factors [3] but also helps to maintain the physiological balance of the epidermis and reduce the excessive secretion of proinflammatory cytokines by keratinocytes due to post-traumatic dehydration [10]. In addition, small molecules of silicone oil can penetrate the skin and inhibit the proliferation of fibroblasts [11], resulting in reduced collagen deposition. Onion extracts contain a series of phenolic compounds. Its derivatives, including quercetin, exhibit antioxidant, anti-inflammatory, and antibacterial effects. The possible mechanisms by which onion extract improves scarring may include: 1) stabilizing mast cells, inhibiting the release of histamine, thus reducing the local inflammatory response [12]; 2) inhibiting the proliferation of fibroblasts and upregulating the expression of MMP-1, which not only reduces collagen production but also promotes the degradation of extracellular matrix (ECM) [13, 14]; and 3) inhibiting the growth of bacteria and reducing the excessive inflammatory reaction of the body, which is conducive to wound healing and scar improvement [15]. Asiaticoside is a terpenoid compound extracted from *Centella asiatica* that reduces scar formation [16]. Possible mechanisms include: 1) inhibiting the TGF-β/Smad signaling pathway and reducing the expression of type I and III collagen [9, 17], 2) suppressing the growth differentiation factor-9 (GDF-9)/MAPK/Smad signaling pathway and inhibiting the excessive proliferation of fibroblasts [18], and 3) alleviating the inflammatory reaction and promoting scar maturation [19].

Although there have been detailed reviews of these drugs, these studies have characterized their full functions, and comparisons of efficacy differences are still lacking. Moreover, the effectiveness of certain drugs lacks convincing clinical comparisons, which makes it difficult for doctors and patients to choose. Thus, we carried out a clinical retrospective study to investigate and compare the efficacy and adverse reactions of different anti-scar drugs to provide a reference for the clinical selection of topical anti-scar drugs.

Materials and methods

Study design

A single-center questionnaire-based retrospective study was performed to compare the effectiveness of topical anti-scar agents. Patients with facial scars derived from surgical suturing were recruited between January and December 2019 from the Department of Plastic Surgery at Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University. Operators and data analysts were strictly blinded during the experiment. Three investigators were responsible for the questionnaire survey, scar measurement, and photo shooting (DSC-W800, SONY Corp., Japan), two for data extraction and sorting, and three for data statistics and analysis. The study protocol was reviewed and approved by the Ethics Committee of Sir Run Run Shaw Hospital, Zhejiang University School of Medicine (No: 20211018-33). Written informed consent was obtained from all the patients.

Inclusion criteria and grouping

Patients included in the analysis had to meet the following criteria: 1) scars should result from surgical sutures rather than burns or other physical and chemical injuries; 2) received a single topical anti-scarring agent or without any treatment; 3) begin using the single drug within two weeks after stitch removal; 4) have been using anti-scarring agents for at least three months; 5) did not experience laser, pulse light, or other non-drug treatment; 6) no muscle damage; 7) no wound infection; and 8) no history of using other medications that may affect scar progression. Patients were divided into the following four groups according to the type of topical anti-scarring drug: silicone preparation (SP

group), onion extracts (OE group), asiaticoside (AC group), and the untreated blank control (BC group).

Questionnaire-based survey

Patients were required to fill out the pre-designed questionnaire, which mainly involved four parts: 1) identity information: name, gender, age, and contact information; 2) operation information: the specific date of the operation and the postoperative treatments for the scar; 3) use of topical anti-scar drugs: type/name of the drug, time of starting the drug use after surgery, duration of local drug use, adverse reactions and their severity such as mild, moderate, or severe itching, pain, and erythema; and 4) other drug use history that may affect the scar, including angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blocker (ARB), aspirin, paclitaxel, oxaloxone, pirfenidone, emodin and celecoxib, anti-allergy medications, and isobudine. Almost all types and trade names of topical anti-scar drugs were provided in the questionnaire: silicone preparations (e.g., Kelo-cote, Dermatix, Strataderm, Mepiform, and Mederma), onion extracts (e.g., ContractubexR), asiaticoside (e.g., LendinTM), corticosteroid ointment (e.g., Triamcinolone acetonide and desonide), immunomodulator (e.g., Tacrolimus and Imiquimod), traditional Chinese medical preparation (e.g., MEBO, Black cloth ointment); aloe extracts, vitamin (e.g., Vitamin E and Tretinoin), and anti-tumor drugs (e.g., Mitomycin C and Tamoxifen). The patients were only required to choose the drug they used. If the drug name was not found, they were required to write down the name of the drug, through which we could determine the type of anti-scar drug to which they belonged.

Scar measurements

Scar thickness was assessed using a nasal root height measuring instrument, and scar width was measured using an electronic vernier caliper.

Vancouver scar scale (VSS)

Scar conditions were quantified using the VSS by two independent physicians [20]. Four indicators, melanin (M), height (H), vascularity (V), and pliability (P), were used in this scale for the descriptive evaluation of the scar, and the scoring criteria were as follows: 1) M: 0 points, similar to the normal skin; 1 point, lighter color; 2 points, mixed color; 3 points, darker color; 2) H: 0 points, normal; 1 point, <1 mm; 2 points, 1-2 mm; 3 points, 2-4 mm; 4 points, >4 mm; 3) V: 0 points, similar to the normal skin; 1 point, the scar is slight pink; 2 points, reddish skin; 3 points, the skin color is purple; 4) P: 0 points, normal; 1 point, soft (the skin can deform with the least resistance); 2 points, pliant (able to deform under pressure); 3 points, hard (not deformable, moving like a block, pressure resistance); 4 points, bending (the tissue is like rope, and the scar will shrink when stretched); 5 points, contracture (permanent shortening of the scar resulting in disability and distortion). The total score on the scale is 15 points; the higher the score, the more serious the scar.

Scar cosmesis assessment and rating (SCAR) scale

The scars were scored using the SCAR scale with high-quality photographs [21]. The raters had no prior knowledge of the patient groups. The SCAR scale consists of six clinical and two patient items, namely: scar spread (0-4 points), erythema (0-3 points), dyspigmentation (0 or 1 point), track marks or suture marks (0 or 1 point), hypertrophy/atrophy (0-3 points), an overall impression (0 or 1 point), and scar itching (0 or 1 point) or pain (0 or 1 point) occurring 24 h before the survey. On a scale of 0 to 15, the higher the score, the worse is the scar.

Statistical analysis

Quantitative data are presented as the mean ± standard deviation, and qualitative data are presented as numbers and percentages. In the analysis of patient characteristics, chi-square analysis was used for sex differences. Welch's ANOVA was used for age because the data violated the assumption of homogeneity of variance. The Kruskal-Wallis test, followed by Dunn's multiple comparisons test, was used to analyze the postoperative time, scar width, and data of the VSS and SCAR scales because they were not normally distributed. Statistical data analysis and image rendering were performed using GraphPad Prism (LaJolla, CA, USA; version 9.0 for Windows). $P<0.05$ was considered to be statistically significant ($^{*}P<0.05$, $^{**}P<0.01$).

Table 1. Characteristics of 127 patients with facial scars

Characteristics	BC n=12	SP n=71	OE n=28	AC n=16	*P*-value
Gender, n (%)					
Male	5 (41.67)	16 (22.54)	7 (25.00)	5 (31.25)	0.5[a]
Female	7 (58.33)	55 (77.46)	21 (75.00)	11 (68.75)	
Age, years, Mean ± SD	32.3±5.0	30.3±8.7	33.7±8.5	29.3±6.9	0.2[b]
Post-surgical months, Mean ± SD	6.50±0.90	7.41±1.74	6.46±0.84	6.13±0.34	<0.001[c,*]
Specific site of facial scar, n (%)					
Forehead	1 (8.33)	7 (9.86)	2 (7.14)	2 (12.50)	----
Orbital region	0 (0.00)	13 (18.31)	2 (7.14)	4 (25.00)	----
Nose	1 (8.33)	0 (0.00)	0 (0.00)	0 (0.00)	----
Cheek	2 (16.67)	6 (8.45)	0 (0.00)	0 (0.00)	----
Zygomatic region	4 (33.33)	14 (19.72)	9 (32.14)	7 (43.75)	----
Temporal	0 (0.00)	6 (8.45)	0 (0.00)	0 (0.00)	----
Mouth	0 (0.00)	5 (7.04)	8 (28.57)	1 (6.25)	----
Chin	4 (33.33)	20 (28.17)	7 (25.00)	2 (12.50)	----
Cause of injury, n (%)					
Trauma	4 (33.33)	35 (49.30)	13 (46.43)	10 (62.50)	----
Surgical excision	8 (66.67)	36 (50.70)	15 (53.57)	6 (37.50)	----
Side effects, n (%)					
papule	0 (0.00)	1 (1.41)	0 (0.00)	0 (0.00)	----
Erythema and itching	0 (0.00)	1 (1.41)	2 (7.14)	4 (25.00)	----

Note: a. chi-square test; b. Welch's test; c. Kruskal-Wallis test. The statistics and *P* values were obtained by the corresponding test method on the four groups of data. *P<0.01.

Results

Patient characteristics

A total of 140 cases were collected in this retrospective study. Twelve cases were excluded because of muscle injury. The remaining 128 patients involved 71 cases of silicone preparations, 28 cases of onion extracts, 16 cases of asiaticoside, 12 cases without treatment, and 1 case of *Aloe vera* gel. The same type of drugs with different trade names was grouped since the mechanism was relatively similar. The patient receiving *Aloe vera* gel was removed because it was insufficient for statistical analysis. Therefore, the patients were divided into the following four groups: silicone preparation (SP group, n=71), onion extracts (OE group, n=28), asiaticoside (AC group, n=16), and blank control (BC group, n=12). No significant differences were observed in age and sex among all groups, while there was a statistically significant difference in postsurgical scar duration. **Table 1** displays the overall distribution and characteristics of the 127 patients.

To exclude the influence of scar location, we divided the face into eight parts according to the direction of muscle movement: the forehead, orbit, nose, cheek, zygomatic, temporal, mouth, and chin. Only zygomatic scars were sufficiently isolated for statistical analysis (N≥4): 14 cases in the SP group, 9 cases in the OE group, 7 cases in the AC group, and 4 cases in the BC group. **Table 2** displays the characteristics of 34 patients with zygomatic scars. There were no significant differences in age, sex, or postsurgical scar duration among the four groups. The typical scar appearance in each group is displayed in **Figure 1**.

Side effects

Adverse effects occurring in all three types of topical anti-scar drugs are illustrated in **Table 1**. In the SP group, side effects were observed in 2/71 patients, including 1 with papules and 1 with pruritus and redness. In the OE group, skin itching and redness were observed in 2/28 patients. However, 4/16 patients in the AC group experienced itching and erythema.

Table 2. Characteristics of 34 patients with zygomatic scar

Characteristics	BC n=4	SP n=14	OE n=9	AC n=7	*P* value
Gender, n (%)					
Male	1 (25.00)	5 (35.71)	2 (22.22)	1 (14.29)	0.74[a]
Female	3 (75.00)	9 (64.29)	7 (77.78)	6 (85.71)	
Age, years, Mean ± SD	32.50±6.76	32.50±9.61	34.89±11.66	29.86±9.84	0.85[b]
Post-surgical months, Mean ± SD	6.25±0.50	6.71±0.83	6.78±0.67	6.29±0.49	0.35[c]
Cause of injury, n (%)					
Trauma	1 (25.00)	8 (57.14)	6 (66.67)	4 (57.14)	----
Surgical excision	3 (75.00)	6 (42.86)	3 (33.33)	3 (42.86)	----

Note: a. chi-square test; b. Welch's test; c. Kruskal-Wallis test. The statistics and *P* values were obtained by the corresponding test method on the four groups of data.

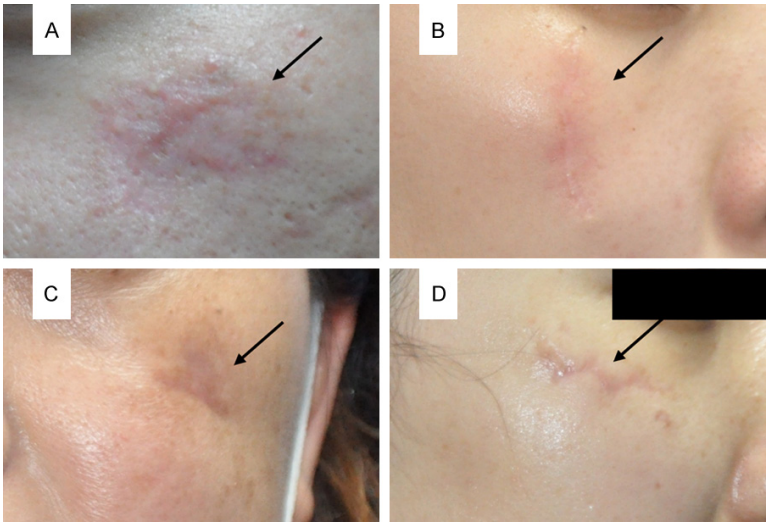

Figure 1. Representative scar appearance in each group. The four graphs respectively represent (A) blank control group, (B) silicone preparation group, (C) onion extract group and (D) asiaticoside group. The arrows pointed to the scar. The patient's eyes were cut out or covered from the photograph.

However, the symptoms were mild and resolved spontaneously.

Scar width

The overall facial scar width of the BC group was 2.59±1.71 mm, significantly wider than that of the SP group (1.30±0.77 mm), OE group (1.16±0.75 mm), and AC group (1.07±0.57 mm), while there was no statistical significance among the three experimental groups (**Figure 2A**).

For zygomatic scars, the scar widths of the four groups were: 3.02±2.18 mm for the BC group, 0.77±0.41 mm for the SP group, 1.22±0.51 mm for the OE group, and 1.03±0.42 mm for the AC group. The differences in zygomatic scar width among the four groups were consistent with the results of general facial scar width (**Figure 3A**).

Results of the VSS

When scars from all parts of the face were included in the analysis, the SP (0.86±0.66) and AC (0.69±0.60) groups demonstrated significantly lower melanin (M) scores than that of the BC group (1.58±0.99) (**Figure 2C**). The scar height (H) score of the AC group (0.87±0.72) was significantly lower than that of the BC group (1.75±0.87) (**Figure 2D**).

In terms of scar vascularity (V), the AC group (0.63±0.50) was significantly better than the OE (1.43±1.00) and BC (1.42±0.51) groups (**Figure 2E**). Further, the OE group (0.39±0.50) had the best pliability (P) over that of the BC (1.25±0.87), SP (0.97±0.76), and AC (1.38±1.26) groups (**Figure 2F**).

While for zygomatic scars, the SP group (0.71±0.73) demonstrated significantly lower melanin (M) score than that of the BC group (2.00±0.82) (**Figure 3C**). The AC group (0.71±0.76) depicted significantly lower scar height (H) than that of the BC group (2.50±0.58) (**Figure 3D**). However, the vascularity (V) score did not differ among the four groups (**Figure 3E**). Additionally, the zygomatic scars also

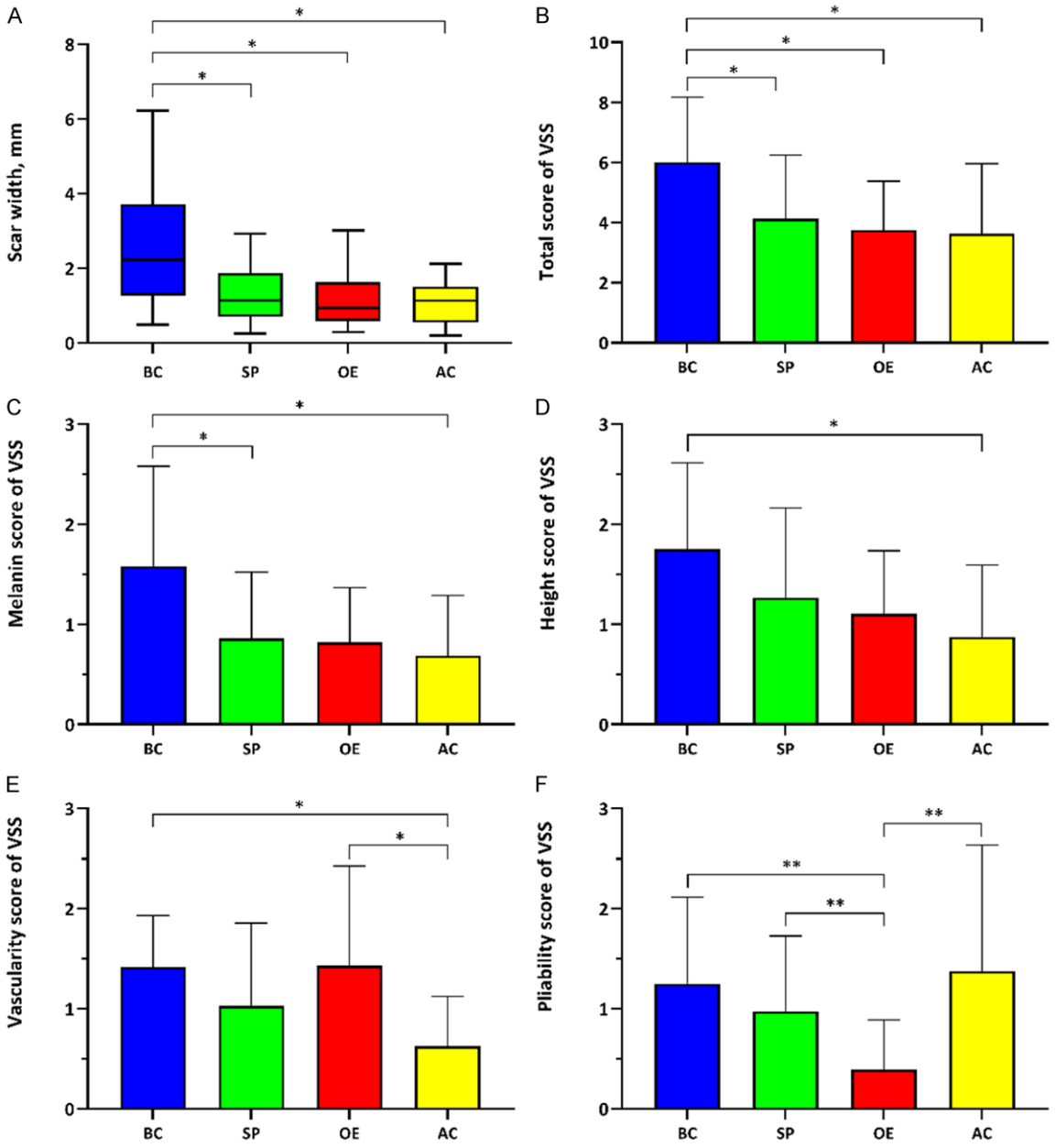

Figure 2. Overall facial scar assessment results. (A) The scar width, (B) VSS total score, (C) Melanin score, (D) Scar height score, (E) Vascularity score, (F) Pliability score. BC = blank control group; SP = silicone preparation group; OE = onion extract group; AC = asiaticoside group. Scar width was expressed as mean with maximum and minimum, and VSS scores were expressed as mean with standard deviation. Kruskal-Wallis H test followed by Dunn's multiple comparisons test, $^{*}P<0.05$, $^{**}P<0.01$.

depicted significantly lower pliability scores in the OE group (0.22±0.44) than in the BC group (1.75±0.96), without statistical differences among the three experimental groups (**Figure 3F**).

The scores of the four clinical items mentioned above were added to obtain the total VSS score. The results demonstrated that the total score of the BC group (6.00±2.17) was significantly higher than that of the SP (4.13±2.12), OE (3.75±1.62), and AC (3.63±2.33) groups, without statistical difference in the total score among the experimental groups (**Figure 2B**). The zygomatic scar showed consistent results: the BC group (7.50±2.38) was significantly

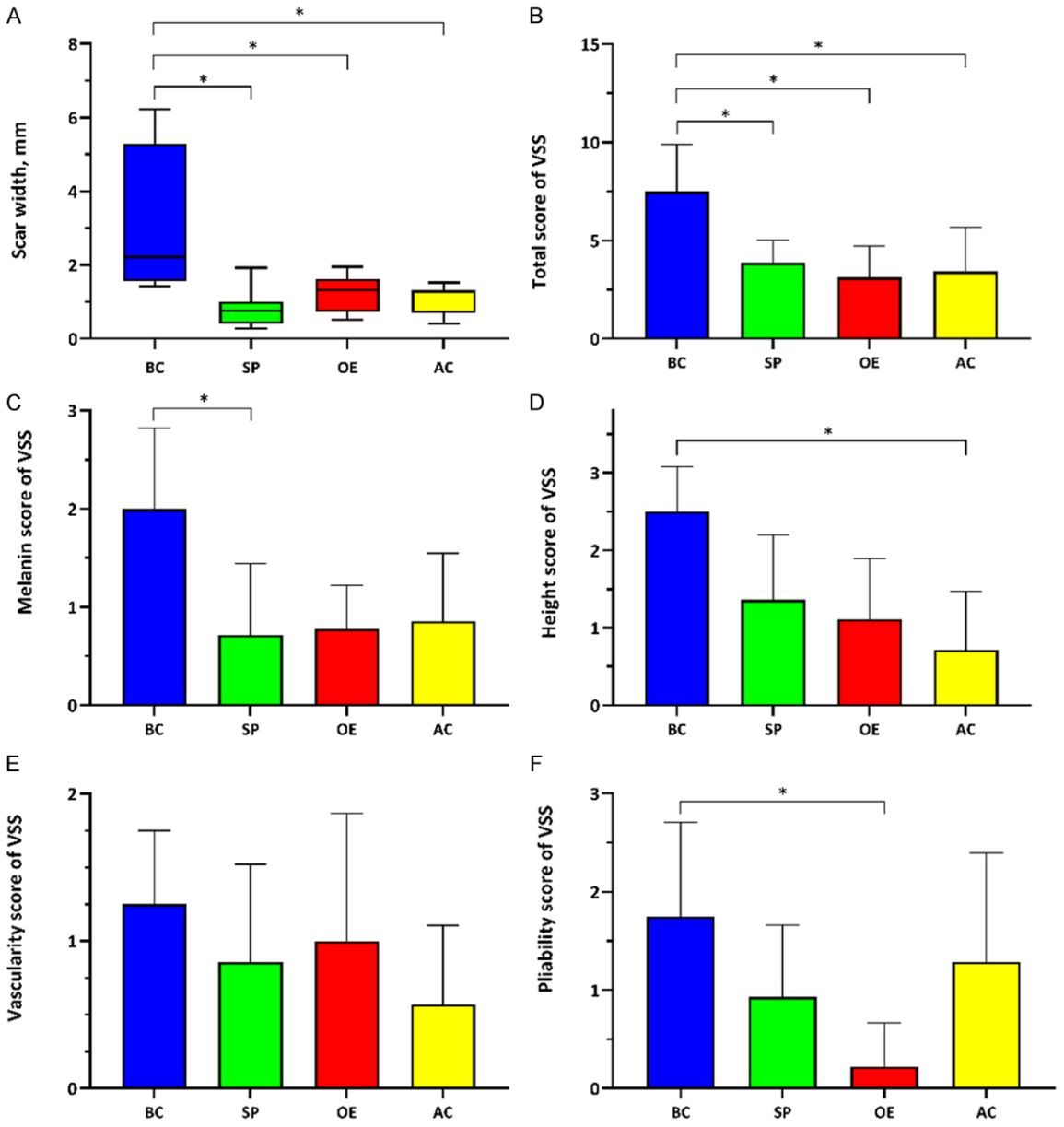

Figure 3. Zygomatic scar assessment results. (A) The scar width, (B) VSS total score, (C) Melanin score, (D) Scar height score, (E) Vascularity score, (F) Pliability score. BC = blank control group; SP = silicone preparation group; OE = onion extract group; AC = asiaticoside group. Scar width was expressed as mean with maximum and minimum, and VSS scores were expressed as mean with standard deviation. Kruskal-Wallis H test followed by Dunn's multiple comparisons test, *P<0.05.

higher than that of the SP (3.86±1.17), OE (3.11±1.62), and AC (3.43±2.23) groups (**Figure 3B**).

Results of the SCAR scale

All facial scars were analyzed together (**Table 3**), and zygomatic scars were further analyzed separately (**Table 4**). Every drug could promote scar spread, hypertrophy/atrophy, and the total score range. Erythema, dyspigmentation, scar itching, and pain were not significantly different between the topical and untreated BC groups. Track or suture marks seemed to be alleviated in the SP and AC groups in overall facial scar analysis, whereas the analysis of the zygomatic scar did not depict differences. The overall impression score in the SP group was lower than that of the BC group for both overall and zygomatic scars, while the OE and AC groups

Table 3. The SCAR Scale results for overall facial scar

	BC	SP	OE	AC	*P*-value
Clinician Items					
Scar spread	2.5 (2~3)	1 (0~1.5)	1 (0~1.25)	1 (0~2)	<0.001*
Erythema	1 (0.75~1.25)	0 (0~1)	1 (0~1)	0 (0~1)	0.04*
Dyspigmentation (includes hyperpigmentation and hypopigmentation)	0.5 (0~1)	0 (0~1)	1 (0~1)	1 (0~1)	0.80
Track marks or suture marks	1 (0~1)	0 (0~0)	0 (0~0.25)	0 (0~0)	0.03*
Hypertrophy/Atrophy	2 (1~2)	0 (0~1)	0 (0~1)	0 (0~0.25)	0.01*
Overall impression	1 (1~1)	0 (0~1)	1 (0~1)	1 (0~1)	0.009*
Patient items					
Have you been bothered by any itch from the scar in the past 24 h?	0 (0~0)	0 (0~0)	0 (0~0)	0 (0~0)	1
Have you been bothered by any pain from the scar in the past 24 h?	0 (0~0)	0 (0~0)	0 (0~0)	0 (0~0)	1
Total score range	7 (6.75~8.25)	2 (1~4)	3.5 (2~5)	2 (1~4.25)	<0.001*

Values are the median (interquartile range). Scar spread: SP vs BC, adjusted P=0.0001; OE vs BC, adjusted P=0.0039; AC vs BC, adjusted P=0.0225. Erythema: SP vs BC, adjusted P=0.1588; OE vs BC, adjusted P=1; AC vs BC, adjusted P=0.0655. Track marks or suture marks: SP vs BC, adjusted P= 0.0342; OE vs BC, adjusted P= 0.1505; AC vs BC, adjusted P=0.0323. Hypertrophy/Atrophy: SP vs BC, adjusted P=0.0143; OE vs BC, adjusted P=0.0459; AC vs BC, adjusted P=0.0101. Overall impression: SP vs BC, adjusted P=0.0051; OE vs BC, adjusted P=0.1663; AC vs BC, adjusted P=0.0742. Total score range: SP vs BC, adjusted P=0.0003; OE vs BC, adjusted P=0.0253; AC vs BC, adjusted P=0.0071. *Statistically significant difference, Kruskal-Wallis H test (P<0.05).

Table 4. The SCAR Scale results for zygomatic scars

	BC	SP	OE	AC	*P*-value
Clinician Items					
Scar spread	2 (2~2)	0 (0~1)	0 (0~1)	0 (0~0.5)	0.008*
Erythema	1 (0.75~1)	0 (0~0)	0 (0~1)	0 (0~1)	0.26
Dyspigmentation (includes hyperpigmentation and hypopigmentation)	0.5 (0~1)	0 (0~0.75)	0 (0~1)	0 (0~1)	0.81
Track marks or suture marks	0.5 (0~1)	0 (0~0)	0 (0~0)	0 (0~0.5)	0.71
Hypertrophy/Atrophy	2 (1.75~2)	0 (0~0.75)	0 (0~1)	0 (0~0)	0.002*
Overall impression	1 (1~1)	0 (0~0)	0 (0~0)	0 (0~0)	0.006*
Patient items					
Have you been bothered by any itch from the scar in the past 24 h?	0 (0~0)	0 (0~0)	0 (0~0)	0 (0~0)	1
Have you been bothered by any pain from the scar in the past 24 h?	0 (0~0)	0 (0~0)	0 (0~0)	0 (0~0)	1
Total score range	6.5 (6~7)	2 (1~2)	2 (1~3)	1 (1~2)	<0.01*

Values are the median (interquartile range). Scar spread: SP vs BC, adjusted P=0.0084; OE vs BC, adjusted P=0.0178; AC vs BC, adjusted P=0.0135. Hypertrophy/Atrophy: SP vs BC, adjusted P=0.0064; OE vs BC, adjusted P=0.02; AC vs BC, adjusted P=0.0008. Overall impression: SP vs BC, adjusted P=0.0044; OE vs BC, adjusted P=0.0231; AC vs BC, adjusted P=0.0136. Total score range: SP vs BC, adjusted P=0.0099; OE vs BC, adjusted P=0.0485; AC vs BC, adjusted P=0.0198. *Statistically significant difference, Kruskal-Wallis H test (P<0.05).

demonstrated advantages only for zygomatic scars.

Discussion

Scarring results from skin tissue injury that damages the dermis [22]. Abnormal wound healing often leads to pathological scars, such as hypertrophic scars and keloids, which not only affect aesthetics but also lead to local deformities and dysfunction, affecting the physical and mental health of patients [23]. Although numerous non-topical methods exist to prevent and improve scars, topical preparations are still the most preferred method for doctors and patients because of their easy availability, simple use, and reasonable price [1]. Although there have been detailed reviews of topical anti-scar drugs [9], there is still a lack of evidence for comparing their actual effects. Thus, we carried out this questionnaire-based retrospective study to compare the effects of various drugs. Three types of commonly used topical anti-scar drugs were included, namely silicone preparations, onion extracts, and asiaticoside ointments.

Patients with facial postoperative scars were chosen as the research subjects for the following reasons: facial skin is often exposed and easily injured, and facial scars are often the most worrying for patients because they influence aesthetics. The treatment is highly active, and more cases can be collected. Furthermore, because facial scars are easy to see, there are few privacy concerns. Moreover, including scars after suturing can make the data more consistent and comparable. This study first analyzed

the relationship between the type of local anti-scarring drug and scar quality in all facial scar data. We further focused on zygomatic scars because after subdividing the scar position, only zygomatic scars in the four groups met the required sample size for analysis.

Our results are generally consistent with those of previous studies that confirmed the effectiveness of the three classes of drugs in scar improvement [24-26]. The difference is that we looked for possible differences in the actual effects of these three drug types considering that scars are not uniform and the qualities are determined by the scar color, thickness, pliability, and symptoms of itching or pain. Therefore, the focus of scar treatment may differ between patients. Given that different classes of anti-scar drugs have different mechanisms of action, we suspected that their strengths might be different. Acquiring their respective specialties is expected to help doctors choose more appropriate medications based on the most prominent scar characteristics.

The four items defined by the VSS provided some information about possible differences in the efficacy of each class of drugs: silicone preparations could significantly improve scar melanin, onion extracts showed excellent performance in improving scar pliability, and the asiaticoside had a comprehensive effect on the melanin, height, and vascularity of facial scars, especially in reducing scar thickness.

The results of the SCAR scale also supported that the use of any drug could improve the overall scar quality, especially scar spread and hypertrophy/atrophy. Unlike the VSS results, the SCAR scale did not indicate any differences in dyspigmentation. This may be because the dyspigmentation defined by the SCAR scale included hyperpigmentation and hypopigmentation, while melanin involved in VSS only considered hyperpigmentation. No differences in erythema were observed among the groups, which was consistent with the VSS results. The SP and AC groups seemed to be beneficial in reducing track or suture marks, but the referability of this index may be relatively poor because it is closely related to the suture method. Invisible marks can be attributed to intradermal sutures. However, there was a shortcoming in our SCAR scale analysis because we assessed SCAR scale from high-quality photos without knowledge of itching or pain in the past 24 h, leading to missing data for these two items, which might have affected the results to a certain extent. However, combined with the information on adverse drug reactions in the questionnaire, we found no itching or pain in either group when the analysis was limited to the zygomatic site.

In addition to the anti-scarring effect, drug safety is an important reference for clinical selection. To this end, our results suggested a higher incidence of adverse reactions of asiaticoside (25.00%) than that of silicone preparations (2.82%) and onion extracts (7.14%). However, asiaticoside has been reported to exert anti-sensitization effects [27, 28]. The reason could be irritation caused by other components contained in the asiaticoside drugs or bias caused by the small sample size. However, these symptoms were mild and could be resolved.

It is worth mentioning that our previous study found that ACEI and ARB antihypertensive drugs may inhibit scarring [29-32]. Therefore, we specifically set questions in the questionnaire to investigate whether the patients had taken any of these drugs to rule out the potential influence on scar formation.

However, our study still had some limitations. The sample size of this survey was small, which can produce sampling errors, and there may be recall bias regarding the duration of drug use and complications. Moreover, objective measurements of scars such as color meters, moisture meters, and other more advanced and systematic measuring instruments have not been performed [33, 34]. Despite these limitations, our study does provide insights into the practical effects of various anti-scar drugs and a possible research avenue for solving treatment problems. For more convincing results, larger sample size and scientifically designed randomized clinical trials are expected.

In conclusion, silicone preparations, onion extracts, and asiaticoside could effectively reduce scar width and improve the overall appearance of postsurgical scars, each of which has merits and limitations. Silicone preparations can effectively reduce the melanin of scars. Onion extracts are beneficial in improving scar pliabil-

ity. While asiaticoside displays a more enhanced influence on scar thickness. Therefore, to obtain a better anti-scar effect, it may be necessary to consider a combination of these drugs, and our results may provide a certain reference for treatment.

Acknowledgements

This work was supported by grants from National Natural Science Foundation of China (No. 82172206 and 81671918), Zhejiang Provincial Medical and Healthy Science Foundation of China (No. 2019KY754 and 2019KY757), Zhejiang Provincial Science and Technology Project of China (No. LGF22H-150002), and General Program of Education Department of Zhejiang Province (No. [2021]7). They did not play a role in the preparation of data or the manuscript.

Disclosure of conflict of interest

None.

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