

Original Research Article

A comparative study of the efficacy and safety of pure silica gel and chitosan quaternary ammonium salt silica gel in hypertrophic scar treatment

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Abstract

Purpose: To compare clinical efficacy of pure silica gel and chitosan quaternary ammonium salt silica gel (SQASC) in treatment of hypertrophic scars.

Methods: Eighty-four patients with hypertrophic scars, who were admitted to hospital, were randomly divided into study group and control group with 42 patients in each group. Study group was treated with SQASC while control group was treated with pure silica gel. Scar scores (Vancouver scar score, VSS), scar aesthetics (Patient and observer scar assessment scale, POSAS), symptom improvement and adverse reactions were compared between groups before and after treatment.

Results: Before treatment, there were no differences in VSS and POSAS scores for each aspect between groups. After treatment, VSS and POSAS scores for each aspect in study group were significantly lower than those in control group ($p < 0.05$). Congestion, itching, pain disappearance and thickness reduction occurred significantly earlier in study group than in control group ($p < 0.05$). Incidence of adverse reactions in study group was 4.76 %, which was significantly lower than 19.05% in control group ($p < 0.05$).

Conclusion: Compared with pure silica gel, SQASC effectively alleviates symptoms of hypertrophic scars and aesthetics with fewer adverse effects. In future studies, sample size will be increased and study duration will be extended appropriately.

Keywords: Pure silica gel (SQASC), Hypertrophic scar, Safety, Vancouver scar score, Scar assessment scale, Adverse reaction

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INTRODUCTION

Hypertrophic scars generally occur during healing of dermal skin injuries and manifest as redness and hardening of local skin tissues [1,2]. These scars may affect aesthetic appearance of patients and reduce their quality of life [3]. If clinical treatment of hypertrophic scars is not

timely, the condition may be aggravated. In severe cases, some limb functions can be affected resulting in disability [4].

Currently, relative clinical studies on hypertrophic scars have become a hotspot. However, no consensus has been reached on drugs and intervention solutions for prevention and

treatment of hypertrophic scars [5]. Some studies have indicated that clinical efficacy may be achieved by treating hypertrophic scars with silicone material products. Therefore, we compared clinical efficacy and safety of pure silica gel and silicone of quaternary ammonium salt of chitosan (SQASC) in treatment of hypertrophic scars.

METHODS

Patient data

Eighty-four patients with hypertrophic scars who were admitted to Lishui People's Hospital between January 2020 and December 2021 were included in this study. Patients were randomly divided into study and control groups with 42 patients in each group. Study group consisted of 23 males and 19 females aged 20 – 46 years, with mean age of 36.14 ± 3.15 years, mean disease course of 1.44 ± 0.50 years and mean body mass index (BMI) of 23.15 ± 1.02 kg/m². Control group comprised 24 males and 18 females, aged 21– 45 years, with mean age of 36.21 ± 3.04 years, mean disease course of 1.40 ± 0.50 years and mean BMI of 22.99 ± 1.31 kg/m².

There were no significant differences in clinical data between groups. All procedures performed in studies involving human participants were in accordance with standards of Ethics Committee of Lishui People's Hospital (approval no. LLW-FO-403) and with those of 1964 Helsinki Declaration and its later amendments for ethical research involving human subjects [6].

Inclusion criteria

Patients who met clinical diagnostic criteria related to hypertrophic scars (scars were higher than skin surface, duration of more than 6 months, congested capillaries were observed in scar tissue, scar surface was light or bright red, hard and may be accompanied by itching and pain) were included. Patients with more than two skin lesions, who received no form of treatment within one month before enrollment in the study and provided informed consent were also included.

Exclusion criteria

Patients with scars accompanied by cancer, with immune system disease, patients that had allergies to relevant drugs in this study and patients that had heart, liver, and/or kidney dysfunction were all excluded from this study.

Treatments

Patients in study group were treated with SQASC (Tianjin Joystar Science and Technology Co. Ltd; approval number/production license number: Jinjie CFDA 20192140102) while patients in control group were treated with pure silica gel (Hanson Medical, Inc. USA; approval number/production license number: CFDA 20162645091). Treatment was administered as follows: local lesions were completely rinsed and disinfected.

After drying skin surface, appropriate amounts of gel were applied to completely cover hypertrophic scar tissue (gel thickness was maintained between 0.5 and 1 mm). Thereafter, local skin was gently massaged so that gel effectively and fully contacted local skin tissue. Treatment was administered three times a day and drug efficacy was observed and compared after three months of continuous treatment.

Evaluation of parameters

Scar score (Vancouver scar score, VSS), scar aesthetics (Patient and observer scar assessment scale, POSAS), symptom improvement and adverse reactions were observed and compared between groups before and after treatment.

Vancouver scar score (VSS) was used to evaluate scar status before and after treatment. VSS contains four dimensions: color, vascularity, thickness, and softness. Scores for dimension ranged from 0 to 3, 0 to 4, 0 to 3 and 0 to 5, respectively. Lower scores indicate milder symptoms.

Patient and observer scar assessment scale (POSAS) was utilized to evaluate scar aesthetics. Patient scar evaluation includes six dimensions with total possible scores of 6 - 60 points. Observer scar evaluation include five dimensions with total possible scores of 5 - 50 points. Higher scores indicated worse scar appearance.

Symptom improvement comprised measurement of time until capillary congestion disappearance, itching disappearance, pain disappearance and thickness reduction.

Statistical analysis

The SPSS 22.0 software was employed for all statistical analyses. Measurement and enumeration data are expressed as mean \pm standard deviation (SD) and cases (%),

respectively. T-test and χ^2 test were applied for analysis. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Vancouver scar score (VSS)

Before treatment, there were no significant differences in VSS dimensions between groups. Following treatment, all VSS dimensions in study group were statistically lower than those in control group ($p < 0.05$; Table 1).

POSAS scores

Before treatment, there were no significant differences in POSAS dimension scores between groups. Following treatment, all POSAS dimension scores in study group were statistically significantly lower than those in control group ($p < 0.05$; Table 2).

Symptom improvement over time

Time until congestion, itching, pain disappearance and thickness reduction were significantly shorter in study group than in control group ($p < 0.05$; Table 3).

Adverse reactions

Incidence of adverse reactions in study group was only 4.76%, which was significantly lower than 19.05% in control group ($p < 0.05$; Table 4).

DISCUSSION

Clinical studies indicated that hypertrophic scars are skin fibrotic disease and are caused by excessive deposition of collagen-based extracellular matrix [7]. In patients with hypertrophic scars, skin lesions expand during disease progression [8,9]. Skin lesion area may exceed original extent of injury, which can lead to destruction of patient's skin aesthetics. Additionally, local skin tissue around hypertrophic scar may experience adverse reactions such as itching and pain. For some hypertrophic scars that occur in joints, severe conditions may trigger limited activities in patients. These scars not only affect patient's normal activities but also result in adverse psychological states [10,11].

Although a consensus on pathogenesis of hypertrophic scars has not been established, a substantial proportion of clinical views suggest that hypertrophic scars typically occur three months after injury [12]. Following skin injury, hypertrophic scars may arise due to an

imbalance between collagen synthesis and degradation. The process of local connective tissue hyalinization and skin collagen synthesis and deposition can also influence hypertrophic scar formation. Fibroblasts accumulate during normal healing of damaged skin tissues to form fibrous tissues. In the process of hypertrophic scar formation, the fibrous tissues show ectopic changes and excessive secretion of extracellular matrix leads to a large accumulation of type I collagen and disorganization. In addition, the formation of hypertrophic scars may also be heritable [13]. As indicated by preceding clinical studies and current medical theory, it is generally believed that no specific therapy is available for treatment of hypertrophic scars [14]. Thus, novel options for clinical prevention and treatment of hypertrophic scars should be developed. There are many therapeutic measures used to improve symptoms in clinical practice, including drug therapy, surgical treatment and laser therapy. However, these treatment regimens often result in relapse, especially in the latter two methods. These clinical practices are often combined with other treatment methods, such as silicone gel, to prevent hypertrophic scars. Studies have shown that silicone gel when applied postoperatively to hypertrophic scars may reduce local platelet-derived growth factor (PDGF) levels, but its overall clinical efficacy is unsatisfactory [15]. In the hospital, based on clinical experience, SQASC has resulted in good outcomes in the treatment of hypertrophic scars.

In this study, VSS and POSAS scores of patients treated with SQASC were significantly lower ($p < 0.05$) than scores for group that received treatment with pure silica gel. Additionally, time for capillary congestion, itching, and pain disappearance and thickness reduction times were significantly reduced in study group compared to control group. Furthermore, incidence of adverse reactions in study group was 4.76 %, which was significantly lower than 19.05 % in control group ($p < 0.05$). Therefore, SQASC has a significant comparative advantage over pure silica gel in treatment of hypertrophic scars, which is consistent with previous reports [16,17]. After an in-depth investigation, it was discovered that comparative advantage of SQASC mainly resulted from chitosan quaternary ammonium salt and silicone components in its component materials. Chitosan quaternary ammonium salt functions to inhibit hypertrophic scars by regulating various related factors. First, chitosan quaternary ammonium salt can regulate ratio of type I to type III collagen in fibroblasts to effectively decompose collagen cells.

Table 1: Comparison of VSS dimensions between groups (mean \pm SD, n = 42)

Group	Color (Point)		Thickness (Point)		Softness (Point)		Vascularity (Point)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group	2.19 \pm 0.40	0.81 \pm 0.40	2.77 \pm 0.43	0.81 \pm 0.40	3.95 \pm 0.31	0.93 \pm 0.34	2.45 \pm 0.50	1.50 \pm 0.50
Control group	2.21 \pm 0.42	1.14 \pm 0.42	2.79 \pm 0.42	1.12 \pm 0.40	3.98 \pm 0.27	1.26 \pm 0.40	2.50 \pm 0.50	2.07 \pm 0.50
t-value	0.2235	3.6873	0.2156	3.5515	0.4729	4.0738	0.4583	5.2241
P-value	0.8237	0.0004	0.8298	0.0006	0.6375	0.0001	0.6480	0.0000

Table 2: Comparison of POSAS scores between groups (mean \pm SD, n = 42)

Group	Patient score (Point)		Observer score (Point)		Total score (Point)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group	12.33 \pm 2.32	6.00 \pm 0.58	8.95 \pm 0.73	4.95 \pm 0.38	21.29 \pm 2.36	10.95 \pm 0.66
Control group	12.40 \pm 2.38	7.95 \pm 0.66	8.98 \pm 0.68	6.52 \pm 0.59	21.38 \pm 2.52	14.48 \pm 0.80
t value	0.1365	14.383	0.1949	14.4984	0.1689	22.0584
p-value	0.8918	0.0000	0.8460	0.0000	0.8663	0.0000

Table 3: Comparison of symptom improvement times between groups (mean \pm SD, n = 42)

Group	Congestion disappearance (day)	Itching disappearance (day)	Pain disappearance (day)	Thickness reduction (day)
Study group	11.33 \pm 1.51	11.33 \pm 1.44	15.36 \pm 1.41	21.33 \pm 2.16
Control group	13.26 \pm 1.31	14.95 \pm 1.51	19.98 \pm 1.85	26.64 \pm 2.41
t value	6.2569	11.2436	12.8719	10.6333
P-value	0.0000	0.0000	0.0000	0.0000

Table 4: Comparison of adverse reactions between both groups (n = 42, %)

Group	Erythema	Allergic reaction	Pigment change	Adverse reactions
Study group	1 (2.38)	0 (0.00)	1 (2.38)	2 (4.76)
Control group	3 (7.14)	2 (4.76)	3 (7.14)	8 (19.05)
χ^2 value		-		4.0865
P-value		-		0.0432

Additionally, it promotes repair of blood circulatory system at injured tissues to increase local oxygen content and repress "hypoxia response" [18,19]. Secondly, chitosan quaternary ammonium salt regulates tissue cells to become epithelialized for promotion of wound healing. Thirdly, chitosan quaternary ammonium salt regulates immune response in skin tissue lesions to suppress bacterial reproduction and effectively prevent infection.

The mechanism of action of silicone components on hypertrophic scars is different from that of SQASC [20,21]. Firstly, silicone dressings seal and hydrate skin lesions. Therefore, water can accumulate to transfer from the local skin lesions to the stratum corneum, which can inhibit proliferation of fibroblasts and collagen deposition, resulting in improved clinical efficacy. Furthermore, hydration increases electric ion that induces remodeling of collagen deposition process [22]. Secondly, under hydrating conditions, oxygen permeability at lesions is enhanced, hypoxia responses are inhibited and proliferative process of local blood vessels and related tissues is hindered. Local skin temperature increases under silicone dressing coverage, which enhances collagenase activity and promotes hydrolysis to inhibit scar generation. Therefore, the two active ingredients in SQASC may function synergistically to repair scars during clinical treatment. Compared with pure silica gel, use of SQASC in treatment of hypertrophic scars effectively improve scar symptoms and aesthetics with fewer adverse effects.

Limitations of this study

Number of selected cases were relatively small and source was relatively single. Study duration was short and it was a single-center study. To overcome this challenge, study will be conducted in multi-center hospitals to strengthen conclusions and enrich value of study.

CONCLUSION

Compared with pure silica gel, SQASC effectively improves symptoms of hypertrophic scar and aesthetics with better safety. In future studies, sample size will be increased and study duration will be extended appropriately.

DECLARATIONS

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None provided.

Ethical approval

Approval for this study was obtained from the Ethics Committee of Lishui People's Hospital in China (approval no. LLW-FO-403).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by authors named in this article and all liabilities pertaining to claims relating to content of this article will be borne by authors. Shenglin Wu and Yuan Jiang designed and performed study, supervised data collection, analyzed data, interpreted data, prepared manuscript for publication and reviewed draft of manuscript. The manuscript was read and approved by all authors for publication.

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