ORIGINAL RESEARCH

The Efficacy of Recombinant Human Type III Collagen in the Treatment of Atrophic Scars and Its Impact on p38 MAPK Signaling Pathway Proteins

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ABSTRACT

Objective • To investigate the effects of recombinant human type III collagen on atrophic scars and its impact on the p38 mitogen-activated protein kinase (p38MAPK) signaling pathway.

Methods • A total of 94 patients with atrophic scars admitted to our hospital from March 2020 to October 2022 were selected as subjects and evenly divided into a control group and an observation group. The control group (n = 47) received carbon dioxide fractional laser treatment, while the observation group (n = 47) was treated with recombinant human type III collagen dressings in addition to the laser treatment. Clinical efficacy, scar conditions, skin physiological parameters, serum levels of p38MAPK pathway-related proteins, and inflammatory markers were compared between the two groups.

Results • The overall effective rate in the observation group was 95.74%, significantly higher than 74.47% in the control group ($P < .05$). Before treatment, there was no significant difference in Vancouver Scar Scale (VSS) scores, stratum corneum hydration, and transepidermal water loss between the two groups ($P > .05$). After treatment, the VSS score in the observation group was significantly lower than in the control group ($P < .05$). Similarly, prior to treatment, there were no significant differences in serum levels of mitogen-activated protein kinase 1 (MEK1), mitogen-activated protein kinase 2 (MEK2), extracellular signal-regulated kinase 1 (ERK1), and extracellular signal-regulated kinase 2 (ERK2), interleukin-10 (IL-10) and tumor necrosis factor-alpha (TNF-α) between the two groups ($P > .05$). After treatment, levels of MEK1, MEK2, ERK1, ERK2, IL-10, and TNF-α in the observation group were significantly lower than those in the control group ($P < .05$).

Conclusion • Recombinant human type III collagen significantly improves the treatment of atrophic scars, effectively ameliorating scar conditions and skin physiology. It also regulates the p38MAPK signaling pathway and reduces inflammation. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Atrophic scars are a disfiguring skin condition, often occurring as a sequela to acne. They are characterized by noticeable depressions in the skin surface and can appear on the face, abdomen, or other areas. Particularly when located on the face, these scars significantly compromise aesthetic appearance, and can adversely affect social interactions and psychological well-being of the patients.[1] For atrophic scars, there has been a lack of highly effective treatments in the past. Surgical interventions are costly and painful, while traditional laser therapies carry significant risks.[2] Carbon dioxide fractional laser has recently gained widespread attention in the field of dermatological aesthetics and is increasingly being accepted by patients. It accelerates skin healing and stimulates collagen growth, thereby improving skin smoothness. However, postoperative issues such as hyperpigmentation and erythema still remain.[3] Related research suggests that the combined use of fractional laser and medication for the treatment of acne scars can both

enhance therapeutic efficacy and reduce adverse reactions post-laser treatment.[4]

Collagen is the primary constituent of dermal tissue in the skin, mainly consisting of types I and III. Type III collagen is the predominant type in the skin of infants and young children and is also a key component in the mechanism of scar-free wound healing in fetuses.[5] Recombinant human type III collagen is a large molecular substance produced using genetic engineering techniques. It has good tissue compatibility and water solubility, high safety profile, and can promote cell proliferation and migration. It also stimulates collagen regeneration and enhances the skin's reparative capacity.[6] The p38 mitogen-activated protein kinase (p38MAPK) pathway is a key conduit for the transduction of extracellular signals into the cell, participating in various pathological and physiological processes, including scar formation.[7]

To this end, the present study aims to assess the therapeutic efficacy of recombinant human type III collagen in improving scar conditions and skin physiology, as well as its ability to regulate the p38MAPK signaling pathway and reduce inflammation. We hypothesize that treatment with recombinant human type III collagen will result in a higher overall effective rate, lower Vancouver Scar Scale (VSS) scores, improved skin hydration, and reduced serum levels of p38MAPK pathway-related proteins and inflammatory markers compared to the control group receiving carbon dioxide fractional laser treatment alone.

SUBJECTS AND METHODS

Study Subjects

We selected 94 patients with atrophic scars treated at our hospital between March 2020 and October 2022 as study subjects. Basic information such as age, gender, duration of the condition, depth of scar indentation, location of the scar, and type of scar was collected for each patient. Based on the treatment methods, the patients were equally divided into a control group and an observation group, with 47 patients in each group. The control group received carbon dioxide fractional laser treatment, while the observation group was treated with recombinant human type III collagen dressings in addition to the laser treatment. This study was approved by the Medical Ethics Committee of our hospital, and informed consent was obtained from all participants.

Enrollment Criteria

Inclusion Criteria: (1) Age ≥ 18 years, no gender restrictions: This criterion aims to include adult patients of both genders who are eligible for the study. (2) Good treatment compliance, able to complete the entire treatment cycle: It is important to include patients who can adhere to the treatment protocol and complete the full course of treatment to obtain reliable and meaningful results. (3) No laser, antibiotic, or related treatments received in the 6 months prior to enrollment: This criterion aims to exclude patients who have received previous treatments that could potentially influence the outcomes of the study. By selecting patients who have not undergone recent treatments, the researchers can better assess the specific effects of the intervention being studied. (4) Strict sun protection post-treatment: Sun exposure can have an impact on scar healing and skin physiology. By including patients who are willing to adhere to strict sun protection measures, the researchers can minimize confounding factors and better evaluate the effects of the treatment. (5) Complete clinical data available: Having complete clinical data ensures that all necessary information is accessible for analysis and evaluation.

Exclusion Criteria: (1) Presence of other skin conditions such as eczema, skin infections, or skin tumors: Patients with other skin conditions may have factors that could influence the outcomes or complicate the interpretation of the study results. (2) Accompanied by significant organ dysfunction, coagulation abnormalities, mental or psychological disorders: These conditions may affect the overall health and well-being of the patients, potentially influencing their response to treatment and introducing confounding variables. (3) Damaged skin surrounding the scar: The presence of damaged skin surrounding the scar may interfere with the assessment of the specific effects of the treatment on the atrophic scar itself. (4) Allergic constitution, scar-prone or photosensitive constitution: Patients with these characteristics may have different sensitivities or reactions to the treatment, potentially affecting the outcomes. (5) Currently pregnant or breastfeeding: Pregnancy and breastfeeding introduce additional considerations and potential risks for both the mother and the child. Excluding these individuals helps ensure the safety of the participants and the accuracy of the study results.

Methods

Control Group. The control group underwent carbon dioxide (CO_2) fractional laser treatment. Prior to the procedure, the patients' faces were cleaned. Patients were then placed in a supine position and lidocaine ointment was applied to the affected area. This was followed by covering the area with plastic wrap for 40 minutes. The ointment was then wiped clean and the area was disinfected with 75% ethanol. The equipment used was a carbon dioxide laser treatment machine from Lumenis, USA, model: UltraPulse Encore. Initially, the machine was set to the ablation mode to smoothen the sharp edges of the scars, with a spot diameter of 2 mm and a pulse energy of 6.25 J/cm^2. Subsequently, the machine was switched to the fractional mode, and parameters were adjusted based on the severity of the scars and the skin condition. The spot diameter was set to 5 mm, the spot density was 5%, and the pulse energy ranged from 100 to 112 J/cm^2. Treatment was considered complete when the wound area showed a pinkish hue accompanied by minor bleeding and mild inflammatory edema. Treatment was administered three times, with a one-month interval between each session. Patients were instructed not to allow the treated area to come into contact with water for 5 days post-operation; not to peel off the scabs, allowing them to fall off naturally; to avoid consuming spicy and other irritating foods, as well as

abstaining from smoking and drinking; to avoid using cosmetics; and to take proper precautions against sun exposure to prevent sunburn on the treated area.

Observation Group. In addition to the treatment received by the control group, the observation group was treated with recombinant human Type III collagen dressings (produced by Shanxi Jinbo Biomedical Co., Ltd., approval number: Jin Medical Registration 20162640 010). After the procedure outlined above, the dressing was evenly applied to the affected area, left in place for 30 minutes per application, once per day. This treatment was continued for 10 days following the CO_2 fractional laser therapy.

Observation Indicators

Clinical Efficacy: A reduction in scar area of more than 60%, with skin color at the affected area approaching that of normal skin and a flattened appearance, is considered significantly effective; a reduction in scar area of 30-60%, with some improvement in skin color and indentation at the affected area, is considered effective; a reduction in scar area of less than 30%, with no improvement in skin color and indentation at the affected area, is considered ineffective.[8] Significantly effective and effective are counted as overall effective.

Scar Condition: The Vancouver Scar Scale (VSS) was used to assess the scar condition before and after treatment in both groups. The assessment includes four components: color (0-3 points), pliability (0-5 points), vascularity (0-3 points), and thickness (0-4 points), with a total score ranging from 0 to 15. A lower score indicates a milder scar condition.[9]

Skin Physiological Parameters: Before and after treatment, patients had a clean facial surface and were kept in a constant temperature and humidity environment for 30 minutes. The skin's stratum corneum moisture content at the affected area was measured using a skin moisture analyzer (Germany CK Company, model: CM825), and the transepidermal water loss at the affected area was measured using a skin moisture loss analyzer (Germany CK Company, model: TM300).

p38MAPK Pathway Proteins and Inflammatory Factor Levels: Before and after treatment, 3 mL of fasting venous blood was drawn from the patients, centrifuged (speed: 3000 r/min, time: 10 min, radius: 15 cm) to obtain serum. The levels of p38MAPK pathway-related proteins [Mitogen-activated protein kinase 1 (MEK1), Mitogen-activated protein kinase 2 (MEK2), Extracellular signal-regulated kinase 1 (ERK1), Extracellular signal-regulated kinase 2 (ERK2)], and inflammatory factors [Interleukin-10 (IL-10) and Tumor Necrosis Factor-alpha (TNF-α)] were detected using an enzyme-linked immunosorbent assay (ELISA) with a Bio-RAD enzyme-linked immunosorbent assay system (Bio-RAD, USA, model: Bio-RAD550).

Statistical Methods

Graphing software GraphPad Prism 8 was used for data visualization, and data processing and analysis were conducted using SPSS 22.0. Measurement data that conformed to a normal distribution were expressed as (mean ± standard deviation) using mathematical formula. Comparisons between the groups were performed using the *t* test. Count data were presented as 'n (%)' and comparisons between the group were conducted using the χ^2 test. $P < .05$ indicates a statistically significant difference.

RESULTS

Comparison of Baseline Data

In the control group, there were 47 patients, including 14 males and 33 females, with an average age of 32.77 ± 6.54 years, an average scar duration of 3.52 ± 1.26 years, and an average scar depth of 0.53 ± 0.12 mm. The scar locations were as follows: 41 cases on the cheeks, 4 cases on the forehead, and 2 cases on the temples. The scar types included 26 cases of boxcar, 14 cases of rolling, and 7 cases of icepick. In the observation group, there were 47 patients, including 18 males and 29 females, with an average age of 34.29 ± 7.12 years, an average scar duration of 3.81 ± 1.38 years, and an average scar depth of 0.56 ± 0.14 mm. The scar locations were as follows: 37 cases on the cheeks, 7 cases on the forehead, and 3 cases on the temples. The scar types included 23 cases of boxcar, 15 cases of rolling, and 9 cases of icepick. There were no significant differences in baseline characteristics between the two groups ($P > .05$). Please refer to Table 1 for details.

Comparison of Clinical Efficacy

The overall efficacy rate in the observation group was 95.74%, significantly higher than that in the control group, which was 74.47% ($P < .05$). Please refer to Table 2 for details.

Comparison of Scar Condition

As shown in Figure 1, the color VSS score in the control group before and after treatment was 2.14 ± 0.32 and 0.83 ± 0.24 respectively; the softness VSS score was 2.26 ± 0.46 and 0.75 ± 0.23 respectively; the vascular distribution VSS score

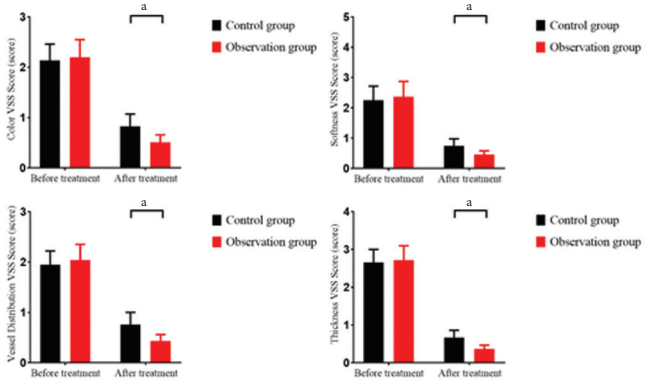
Table 1. Baseline Data

Data	Control Group (n = 47)	Observation Group (n = 47)	t/χ^2	*P* value
Gender			0.758	.384
Male	14	18		
Female	33	29		
Average Age (years)	32.77 ± 6.54	34.29 ± 7.12	1.078	.284
Average Duration of Illness (years)	3.52 ± 1.26	3.81 ± 1.38	1.064	.290
Average Scar Depth (mm)	0.53 ± 0.12	0.56 ± 0.14	1.115	.268
Scar Locations			1.223	.542
Cheeks	41	37		
Forehead	4	7		
Temples	2	3		
Scar Types			0.438	.791
Boxcar	26	23		
Rolling	14	15		
Icepick	7	9		

Table 2. Comparison of Clinical Efficacy

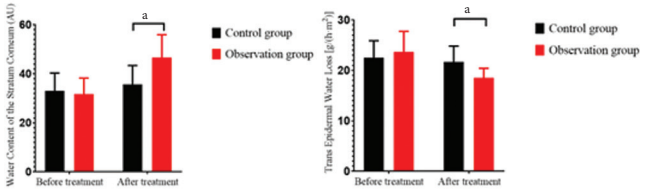
Group	Number of Cases	Significant Improvement	Effective	Ineffective	Overall Efficacy Rate (%)
Control Group	47	21	14	12	74.47%
Observation Group	47	30	15	2	95.74%
χ^2	-	-	-	-	8.393
P value	-	-	-	-	.004

Figure 1. Comparison of Scar Condition



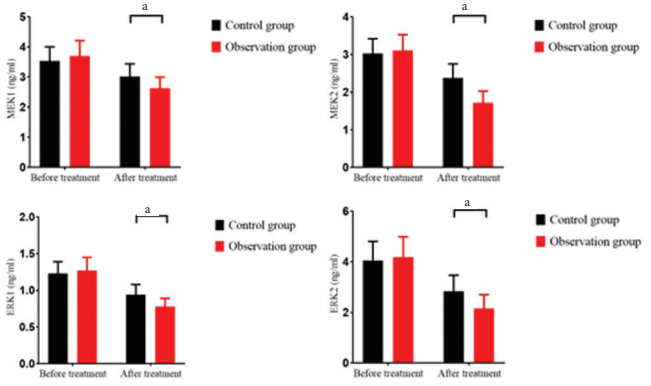
[a]indicates a comparison with $P < .05$

Figure 2. Comparison of Skin Physiological Parameters



[a]indicates a comparison with $P < .05$

Figure 3. p38MAPK Pathway Protein Levels



[a]indicates a comparison with $P < .05$

was 1.95 ± 0.27 and 0.76 ± 0.24 respectively; and, the thickness VSS score was 2.66 ± 0.34 and 0.67 ± 0.19 respectively. In the observation group, the color VSS score before and after treatment was 2.20 ± 0.35 and 0.51 ± 0.15 respectively; the softness VSS score was 2.37 ± 0.50 and 0.46 ± 0.12 respectively; the vascular distribution VSS score was 2.04 ± 0.31 and 0.43 ± 0.13 respectively; and, the thickness VSS score was 2.72 ± 0.38 and 0.37 ± 0.10 respectively. Before treatment, there was no significant difference in VSS scores between the two groups ($P > .05$); after treatment, the VSS scores in the observation group were significantly lower than those in the control group ($P < .05$).

The above findings are clinically significant. The VSS is a widely used tool for scar assessment, considering various scar characteristics such as pigmentation, vascularity, pliability, and height. The significant reduction in VSS scores in the observation group indicates that the treatment with recombinant human type III collagen, in addition to carbon dioxide fractional laser treatment, effectively improves the overall appearance and quality of atrophic scars. This suggests that the intervention can lead to a visible reduction in scar height, redness, and other scar-related features, resulting in a more aesthetically pleasing outcome.

Comparison of Skin Physiological Parameters

As shown in Figure 2, in the control group, the corneal layer moisture content before and after treatment was 33.08 ± 7.23 AU and 35.72 ± 7.66 AU respectively, and transepidermal water loss was 22.52 ± 3.37 g/(h.m^2) and 21.68 ± 3.12 g/(h.m^2) respectively. In the observation group, the corneal layer moisture content before and after treatment was 31.74 ± 6.51 AU and 46.63 ± 9.28 AU respectively, and transepidermal water loss was 23.69 ± 4.05 g/(h.m^2) and 18.54 ± 1.89 g/(h.m^2) respectively. Before treatment, there were no significant differences in corneal layer moisture content and transepidermal water loss between the two groups ($P > .05$). After treatment, the observation group showed significantly lower transepidermal water loss and significantly higher corneal layer moisture content compared to the control group ($P < .05$)

The above findings are clinically significant. Stratum corneum hydration reflects the water content within the outermost layer of the skin, while transepidermal water loss represents the loss of water through the skin barrier. The observed improvements in these skin physiological parameters in the observation group indicate that treatment with recombinant human type III collagen contributes to enhanced skin hydration and improved barrier function. This suggests that the intervention helps to optimize the skin's moisture content, leading to better skin health, elasticity, and texture. The reduction in transepidermal water loss indicates a more efficient skin barrier, potentially reducing dryness, tightness, and discomfort associated with atrophic scars.

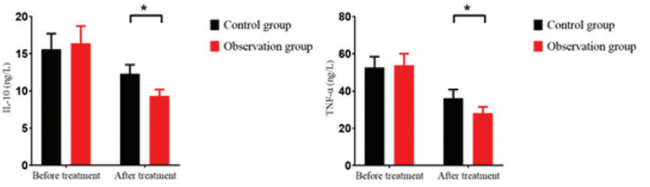
p38MAPK Pathway Protein Levels

As shown in Figure 3, in the control group, the levels of MEK1 before and after treatment were 3.54 ± 0.47 and 3.02 ± 0.42 respectively, MEK2 levels were 3.03 ± 0.39 and 3.11 ± 0.42 respectively, ERK1 levels were 1.23 ± 0.16 and 0.94 ± 0.14 respectively, and ERK2 levels were 4.05 ± 0.76 and 2.84 ± 0.63 respectively. In the observation group, the levels of MEK1 before and after treatment were 3.70 ± 0.51 and 2.63 ± 0.37 respectively, MEK2 levels were 3.11 ± 0.42 and 1.72 ± 0.31 respectively, ERK1 levels were 1.27 ± 0.18 and 0.78 ± 0.11 respectively, and ERK2 levels were 4.19 ± 0.80 and 2.16 ± 0.54 respectively. Before treatment, there were no significant differences in MEK1, MEK2, ERK1, and ERK2 levels between the two groups ($P > .05$); after treatment, the levels of MEK1, MEK2, ERK1, and ERK2 in the observation group were significantly lower than those in the control group ($P < .05$).

The above findings are clinically significant. The p38MAPK signaling pathway plays a crucial role in scar formation and wound healing. The observed downregulation

of MEK1, MEK2, ERK1, and ERK2 levels in the observation group suggests that treatment with recombinant human type III collagen may modulate this pathway, leading to a decrease in scar-related signaling. This modulation helps to achieve reduction in scar formation and promotion of scar remodeling. By targeting the p38MAPK pathway, the intervention may contribute to improved scar outcomes, such as reduced scar height, improved scar pliability, and a more normalized scar appearance.

Figure 4. Inflammatory Factor Levels



[a]indicates a comparison with $P < .05$

Inflammatory Factor Levels

As shown in Figure 4, the levels of IL-10 in the control group before and after treatment were 15.62 ± 2.09 ng/L and 12.34 ± 1.20 ng/L respectively, and the levels of TNF-α were 52.71 ± 5.82 ng/L and 36.23±4.54 ng/L respectively. In the observation group, the levels of IL-10 before and after treatment were 16.41 ± 2.34 ng/L and 9.36 ± 0.84 ng/L respectively, and the levels of TNF-α were 53.86 ± 6.25 ng/L and 28.15 ± 3.38 ng/L. Before treatment, there were no significant differences in the levels of IL-10 and TNF-α between the two groups ($P > .05$). After treatment, the levels of IL-10 and TNF-α in the observation group were significantly lower than those in the control group ($P < .05$)

DISCUSSION

Depressed scars are a common clinical condition that imposes a significant physiological and psychological burden on patients. Depressed scars often result from defects in the skin, subcutaneous tissue, or deep tissues caused by wound healing. Their occurrence may be associated with conditions such as acne, smallpox, herpes, chickenpox, and others. In recent years, with the increasing demand for aesthetics, clinical treatment faces new challenges.[10] Carbon dioxide fractional laser is a commonly used method for treating depressed scars. It offers advantages such as minimally invasive, rapid effectiveness, minimal adverse reactions, and short recovery time. It operates by using a photothermal effect to ablate depressed scars, followed by thermal peeling and coagulation to induce the formation of a three-dimensional columnar micro-treatment zone at the lesion site. In this micro-treatment zone, small pores are formed between small pores and normal tissues after the trauma, leading to thermal bridging. This initiates the skin's wound repair mechanism. After going through the stages of inflammation, proliferation, and remodeling, it achieves skin regeneration at the lesion site and reconstruction of the dermal framework structure, promoting scar healing and improving skin smoothness.[11] Moreover, previous studies have indicated that carbon dioxide fractional laser, as an ablative fractional laser, can vaporize scar tissue and stimulate the remodeling and regeneration of collagen fibers, achieving a peak reduction in scars. However, its standalone application yields limited efficacy in some patients.[12]

Collagen is a large structural protein composed of three peptide chains with a triple helical structure, exhibiting a flexible bend of 164.88 degrees.[13] In infancy and early childhood, Type III collagen accounts for 80% of the collagen in the skin, while Type I collagen comprises 20%. When the skin is injured, fibroblasts from bone marrow stem cells can synthesize Type III collagen, which promotes wound healing and reduces scar formation.[14] As individuals grow and develop, Type III collagen gradually decreases while Type I collagen increases. In adulthood, Type III collagen accounts for 20% of the collagen in the skin, while Type I collagen comprises 80%. This results in reduced skin elasticity, diminished healing capacity, and a greater susceptibility to scar formation. In the field of biomedicine, Type III collagen primarily functions to improve skin barrier function and facilitate skin repair following damage.[15] Recombinant human Type III collagen, a synthetically engineered protein with human collagen characteristics, plays a crucial role in the treatment of atrophic scars. It provides an optimal moist environment, promoting autolytic debridement of wound tissue and facilitating the removal of necrotic tissue and exudates, thus reducing fluid accumulation. Additionally, it offers a slightly acidic, low-oxygen environment, inhibiting bacterial growth.[16] Some researchers have suggested that after treatment with carbon dioxide fractional laser, the application of topical medications within the micro-treatment area can penetrate the stratum corneum. This helps maintain a moist environment in the micro-treatment area, promotes epithelialization, enhances skin hydrophilicity, increases skin moisture content, improves skin barrier function, and reduces the risk of skin infections.[17]

This study demonstrated that the total effective rate in the control group treated with carbon dioxide fractional laser alone was only 74.47%, while the observation group, which received carbon dioxide fractional laser in combination with recombinant human type III collagen protein, achieved a total effective rate of 95.74%. Thus, the total effective rate in the observation group was substantially higher than that in the control group. VSS is an important tool for assessing scar conditions, covering aspects such as color, softness, vascular distribution, and thickness. It offers advantages such as comprehensive content and ease of operation. A larger difference in VSS scores before and after treatment indicates a better treatment outcome.[8] In this study, the VSS scores of patients in the observation group were significantly lower than those in the control group. These results suggest that adjunctive treatment with recombinant human type III collagen can better improve the scar condition in patients and enhance treatment efficacy. Compared to single laser therapy, the advantage of adjunctive treatment with

recombinant human type III collagen lies in its weakly acidic characteristics close to the skin's pH value, strong moisture-retaining ability, and hydrophilicity. Additionally, the gel formulation exhibits good adhesion, enabling it to adhere strongly to the wound, forming a protective barrier on the skin. This encourages epithelial cell attachment and growth. Therefore, recombinant human type III collagen can provide a mildly acidic, moist, and strongly adhering environment for wound healing.

Depressed scars are a manifestation of damaged skin barrier function. Transepidermal water loss (TEWL) measurement assesses the water loss from the skin to the external environment and serves as a crucial indicator of skin barrier function. Additionally, the stratum corneum hydration level is another parameter reflecting skin barrier function. Under normal circumstances, it helps maintain skin elasticity and softness, and plays a role in the activity of certain enzymes during the process of stratum corneum cell maturation and shedding.[18] The results of this study indicate that post-treatment, the observation group exhibited significantly better TEWL and stratum corneum hydration levels compared to the control group, suggesting that the topical application of recombinant human type III collagen can improve the physiological state of the patients' skin. This may be attributed to recombinant human type III collagen being a water-soluble protein, with a structure closely resembling the stratum corneum of the skin. It can rapidly penetrate the skin, forming a network structure by binding with the water present in the stratum corneum, thereby retaining moisture.

The p38MAPK signaling pathway plays a crucial role in the development of various skin disorders, including acne, diabetic foot ulcers, psoriasis, and more. When the body is exposed to external stimuli such as inflammatory factors, physiological stress, or thermal injury, extracellular signals change leading to the activation of the p38MAPK signaling pathway. This, in turn, regulates relevant genes, affecting cell differentiation, proliferation, and apoptosis.[19] The p38MAPK signaling pathway plays a key role in wound healing and repair, and its inhibition or overactivation can both impact wound healing or lead to scar formation.[20] ERK1, ERK2, MEK1, and MEK2 are important members of the MAPK family. MEK1 and MEK2 serve as activators of ERK1 and ERK2, participating in the regulation of cell growth and differentiation.[21] Additionally, the p38MAPK signaling pathway is a crucial inflammation-related pathway, and its activation can further promote the transcription and synthesis of inflammatory factors.[22] IL-10 and TNF-α are two important inflammatory factors that can influence local blood flow, activate mitogen-activated protein kinases, degrade collagen fibers, synthesize matrix metalloproteinases, and ultimately lead to scar formation.[20,23] In this study, the serum levels of MEK1, MEK2, ERK1, ERK2, IL-10, and TNF-α in the observation group were significantly lower than those in the control group after treatment, indicating that recombinant human type III collagen can inhibit the activation of the p38MAPK signaling pathway and reduce inflammatory reactions. This may be an important mechanism of action for the treatment of atrophic scars using this method. The reason for this may lie in the ability of recombinant human type III collagen to stimulate the skin to initiate the repair process uniformly. Cells, when stimulated, can influence the p38MAPK signaling pathway through intermediate steps, thereby inhibiting the phosphorylation of the MAPK family, promoting the reduction of levels of ERK1, ERK2, MEK1, and MEK2 in the p38MAPK signaling pathway, thus inhibiting p38MAPK signaling pathway activation and reducing inflammation.

The observed improvements in scar condition, skin physiological parameters, and the p38MAPK pathway have significant clinical implications for patients with atrophic scars in real-world scenarios. (1) Improved Scar Condition: The study demonstrates that treatment with recombinant human type III collagen significantly improves scar condition compared to carbon dioxide fractional laser treatment alone. This means that patients can expect a reduction in the noticeable depressions on the skin surface caused by atrophic scars. Improved scar condition can have a positive impact on aesthetic appearance, which is particularly important for scars located on the face. By enhancing the physical appearance of scars, the intervention can potentially improve patients' confidence, self-esteem, and overall psychological well-being. (2) Enhanced Skin Physiology: The study shows that treatment with recombinant human type III collagen leads to improved skin physiological parameters, including increased stratum corneum hydration and reduced transepidermal water loss. These improvements indicate better skin barrier function and hydration, which are essential for maintaining skin health. By enhancing skin hydration and barrier function, the intervention may help improve overall skin quality, elasticity, and texture. This can contribute to healthier-looking skin and may alleviate discomfort associated with dryness and skin tightness often experienced by individuals with atrophic scars. (3) Regulation of the p38MAPK Pathway: The study reveals that treatment with recombinant human type III collagen regulates the p38MAPK signaling pathway, which plays a crucial role in scar formation and wound healing. By modulating this pathway, the intervention has the potential to influence the underlying mechanisms of scar development and promote scar remodeling. The downregulation of mitogen-activated protein kinase proteins (MEK1, MEK2, ERK1, and ERK2) indicates a possible attenuation of scar-related signaling pathways. This modulation may contribute to the reduction of scar formation and the promotion of scar-free wound healing. (4) Reduction of Inflammation: The findings demonstrate that treatment with recombinant human type III collagen leads to lower levels of inflammatory markers, such as IL-10 and TNF-α. Atrophic scars are often associated with chronic inflammation, which can impede the healing process and contribute to scar formation. By reducing inflammation, the intervention may facilitate a more favorable

healing environment, potentially leading to improved scar outcomes and a reduction in scar-related symptoms such as redness, itching, and discomfort.

Limitations: (1) Sample Size: The study might have a relatively small sample size, which could limit the generalizability of the results. Conducting larger-scale studies with a more diverse population would provide a more robust understanding of the effects of recombinant human type III collagen on atrophic scars. (2) Duration of Follow-up: The duration of follow-up in the study might be limited, which could affect the assessment of long-term outcomes. Longer follow-up periods would allow for a more comprehensive evaluation of the sustained effects of the intervention on scar improvement and skin physiology. (3) Single-Center Study: Since the study was conducted at a single center, there might be limitations in terms of the diversity of patients and potential variations in treatment protocols. Conducting multi-center studies involving different geographical locations and diverse patient populations would provide more comprehensive insights into the effectiveness of the intervention and enhance the generalizability of the results.

Future Directions: (1) Mechanistic Studies: Further investigation into the underlying mechanisms of action of recombinant human type III collagen on scar remodeling and the p38MAPK signaling pathway would deepen our understanding of the intervention's therapeutic potential. This could involve *in vitro* studies, animal models, or molecular analysis to elucidate the specific molecular processes involved. (2) Long-term Follow-up: Long-term studies with extended follow-up periods are needed to assess the durability and stability of the observed improvements in scar condition, skin physiology, and p38MAPK pathway regulation. This would provide insights into the long-lasting effects of the intervention and its impact on scar recurrence. (3) Patient-reported Outcomes: Future research could incorporate patient-reported outcome measures, such as quality of life assessments and patient satisfaction surveys, to evaluate the impact of the intervention on the psychosocial well-being of individuals with atrophic scars. This would provide a more holistic understanding of the intervention's effects beyond objective scar assessment. (4) Combination Therapies: Investigating the potential synergistic effects of recombinant human type III collagen with other treatment modalities, such as laser therapies or topical agents, could lead to the development of more comprehensive and effective treatment approaches for atrophic scars.

CONCLUSION

The treatment of atrophic scars with recombinant human type III collagen can effectively improve the condition of scars and the physiological state of the skin. It regulates the levels of proteins in the p38MAPK signaling pathway and inflammatory factors, thereby enhancing the therapeutic effect. It can be considered as an effective adjunctive method for the treatment of atrophic scars. However, the exact mechanism of action when treating atrophic scars with recombinant human type III collagen still requires further in-depth and large-scale clinical research.

AUTHOR DISCLOSURE STATEMENT

The authors declare that they have no competing interests.

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