

Original Article

Photodynamic therapy with bioresorbable polymers: a novel approach to hypertrophic scar management

Yiling Zhang*, Yichen Wang*, Qi Wang, Hui Lu, Hao Wang, Gang Zheng

Department of Dermatology, Xuzhou Central Hospital, Xuzhou 221009, Jiangsu, China. *Equal contributors and co-first authors.

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Abstract: Objective: To investigate the application of photodynamic therapy (PDT) combined with the bioabsorbable polymer poly (p-dioxanone) (PPDO) in the treatment of hypertrophic scars (HS). Methods: From April 2021 to April 2024, 120 HS patients were divided into two groups based on their treatment methods: 58 patients received PDT combined with triamcinolone acetonide (PDT+TAC group), and 62 patients received PDT combined with PPDO (PDT+PPDO group). Intergroup analyses compared clinical efficacy, Vancouver Scar Scale (VSS) scores, University of North Carolina (UNC) Scar Scale scores, pain (Visual Analogue Scale, VAS), pruritus (Four-Item Pruritus Questionnaire, FIIQ), and levels of transforming growth factor (TGF)- β 1, epidermal growth factor (EGF), and bone morphogenetic protein-7 (BMP-7). Adverse reactions and short-term recurrence were recorded, as well as psychological effect (Hospital Anxiety and Depression Scale, HADS), quality of life (Dermatology Life Quality Index, DLQI), and treatment satisfaction. Results: Clinical data showed that the overall efficacy of the PDT+PPDO group was superior to that of the PDT+TAC group. At 10 months post-treatment, compared to the PDT+TAC regimen, patients receiving PDT+PPDO treatment showed significantly lower scores on the VSS, UNC, VAS, FIIQ, HADS, and DLQI scales, suppressed TGF- β 1 and EGF expression, and enhanced BMP-7 expression (all $P > 0.05$). The short-term recurrence rate was significantly lower in the PDT+PPDO group, and patients had higher satisfaction with treatment outcomes (both $P > 0.05$). Conclusion: Evidence suggests that PDT+PPDO has clinical advantages for the treatment of HS.

Keywords: Photodynamic therapy, bioresorbable polymers, polydioxanone, hypertrophic scar, clinical study

Introduction

Hypertrophic scar (HS) is a pathologic scar caused by excessive wound healing, characterized by prominent scars at the edges of wounds [1]. HS usually stems from dermal damage caused by trauma, burns, surgical incisions, and insect bites. Its pathologic process involves persistent inflammation, excessive angiogenesis, and collagen accumulation in the reticular dermis [2, 3]. Affected individuals may experience clinical symptoms such as disfigurement, itching, and pain due to scarring, with an increased risk of developing scarring alopecia, rosacea, atopic dermatitis, and acne [4]. This not only seriously threatens the physical and mental health of patients but also negatively affects their quality of life [5]. Although there are many methods for treating HS, such as scar stretching, scar massage, intralesional injection, and pressure therapy, the efficacy is still

not ideal, and more effective countermeasures need to be explored [6]. Photodynamic therapy (PDT) is a phototherapy method with the advantages of high selectivity and favorable clinical safety [7]. It activates photosensitizers (such as 5-aminolevulinic acid [ALA]) through specific light sources to produce cytotoxic substances that inhibit abnormal cell proliferation, promote apoptosis, and regulate the skin's immune inflammatory response [8]. However, PDT has a poor permeability to HS tissues and fibroblasts, and a low quantum yield of cytotoxic reactive oxygen species (ROS), which limits its clinical efficacy [9]. On the other hand, triamcinolone acetonide (TAC), as a corticosteroid therapy for HS, has anti-inflammatory and immunosuppressive effects, reduces skin redness and exudation, inhibits excessive fibrous tissue proliferation, and helps reduce scar formation [10]. In the study by Zhuang et al. [11], TAC helped improve vascular distribution, flexibility, pig-

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mentation, and scar height in HS cases. Poly (p-dioxanone) (PPDO), as an absorbable polymer, has been widely used in the medical and cosmetic fields to improve skin quality [12]. It can promote local blood circulation and tissue metabolism through mechanical stimulation of scar tissue [13]. Furthermore, the trace amounts of carbon dioxide released during the degradation of PPDO threads stimulate fibroblasts to produce new collagen, thereby effectively repairing and remodeling scar tissue [14].

Given the limited comparative analysis of the efficacy of PDT+PPDO versus PDT+TAC for treating HS patients, this study helps fill the relevant research gap and provides a new direction for the treatment of HS.

Materials and methods

General data

This retrospective study included 120 HS patients from April 2021 to April 2024. Patients were divided into two groups based on their treatment regimens: PDT+TAC group were treated with PDT plus TAC; 62 cases in PDT+PPDO group were treated with PDT+PPDO. This study was approved by the Ethics Committee of Xuzhou Central Hospital.

Participant selection

Inclusion criteria: Pathologically diagnosed hypertrophic scars [15]; age 18-50 years (peak period of collagen metabolism); scar located on the chest/shoulder back (high tension area); scar size: 2×5 cm to 5×10 cm; baseline Vancouver Scar Scale (VSS) score ≥ 8 (moderate to severe); body mass index (BMI): 18.5-24.9 kg/m²; hemoglobin ≥ 110 g/L, platelet count range: (100-300)×10⁹/L, alanine aminotransferase/aspartate aminotransferase (ALT/AST) $< 2 \times$ upper limit of normal (ULN), estimated glomerular filtration rate (eGFR) ≥ 60 ml/min; tolerance to treatment; complete clinical data.

Exclusion criteria: Allergy to PDT photosensitizers or contraindications to corticosteroids; current immunosuppressant therapy; history of keloids; active infection; suspected scar malignancy; previous scar chemotherapy; participation in other clinical trials within the past 1 month; pregnancy or lactation; autoimmune diseases or coagulation disorders; significant psychiatric or communication impairment.

Treatment methods

PDT+TAC group: The treatment regimen was initiated with PDT (20% ALA gel in light-stable packaging) on Day 1. Starting on Day 7, weekly concurrent PDT and TAC injections (40 mg/mL, Pfizer) were administered. TAC TA injections were continued at 50% reduced doses at weeks 9, 11, and 13. Bimonthly assessments were conducted during months 6 to 10. Supplemental PDT was initiated if the Vancouver Scar Scale (VSS) score reduction was $< 30\%$.

PDT+PPDO group: TAC injection was administered on Day 1. One week later (Day 7), a repeat TAC injection, PPDO threading (500 μ m, individually sterilized packaging), and PDT were performed. Weekly TAC injections and PDT sessions were continued thereafter. TAC injections at 50% reduced doses were administered at weeks 9, 11, and 13. Thread degradation was monitored by monthly ultrasound assessments from months 6 to 10.

PDT protocol: The affected area was treated with 20% ALA cream under 3 hours of occlusion, followed by irradiation with 635-nm red light (energy density: 80 J/cm²).

PPDO procedure: Using 5-0 PPDO threads, a crisscross mesh embedding was performed (spacing: 1×1 cm) [16], with threads inserted into the deep dermal layer down to the superficial subcutaneous fat layer (depth: approximately 2-3 mm). All procedures were performed by the same attending plastic surgeon with more than 5 years of experience in thread lifting, who had received specialized PPDO training prior to the study. The procedures mainly relied on anatomic landmarks and palpation, without the use of ultrasound guidance. **Figure 1** illustrates the changes observed in both groups before and after treatment.

Detection indicators

Clinical efficacy. Evaluation criteria: Clinical efficacy: Evaluation criteria: Significantly effective was defined as scar color close to normal skin, thickness < 1 mm, and no capillary congestion, pain or itching; effective as darker scar color, thickness 1-2 mm, and no obvious capillary congestion, pain or itching; ineffective as no significant improvement in scar morphology and obvious pain or itching. The treatment effi-

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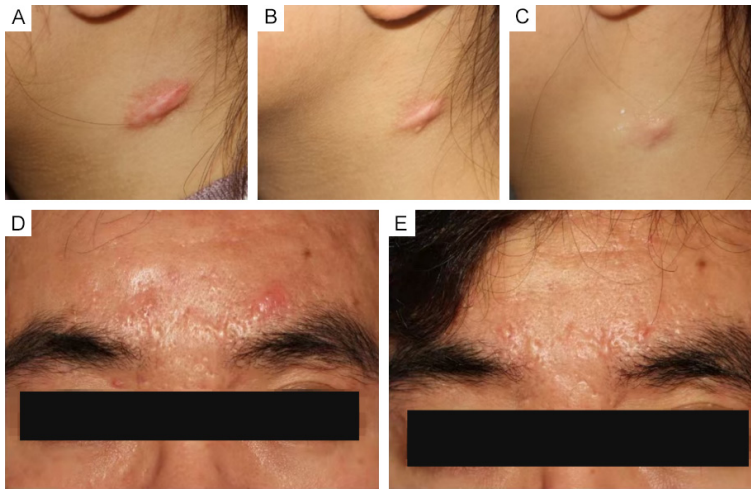


Figure 1. Pre- and post-treatment changes in two patient groups. (A-C) A 25-year-old female presented with a 2-year-old scar following the excision of an intradermal nevus on the neck. After four sessions of photodynamic therapy (PDT)+TAC therapy, the scar showed progressive improvement from panel (A) to (C), with reduced erythema, elevation, and an overall appearance closer to normal skin. (D, E) A single application of combined PDT and poly (p-dioxanone) (PPDO) therapy was used to treat a 35-year-old male with longstanding (15 years) facial acne scars. (D) shows the condition before treatment, where there are obvious red inflammatory papules and uneven scar-like manifestations on the forehead skin. (E) shows the situation after treatment, where the red inflammatory symptoms have somewhat decreased, but there is still a certain degree of uneven skin texture.

cacy rate was the ratio of the sum of significantly effective cases plus effective cases to the total number of cases.

Scar condition: Scar condition was assessed using the Vancouver Scar Scale (VSS, 0-15 points) and the University of North Carolina (UNC) Scar Scale (0-12 points) before treatment and 10 months after treatment. The VSS scores scars on four aspects: skin color (0-3 points), thickness (0-4 points), vascular distribution (0-3 points), and flexibility (0-5 points), with a total score of 0-15 points. Higher scores indicated more severe scar conditions. The UNC scale was used to assess itching, pain, paresthesia, and flexibility at the affected area (0-3 points per item). Higher scores indicated greater scar severity.

Pain and itching: Scar pain was assessed using the Visual Analogue Scale (VAS). Patients rated their pain subjectively, with scores ranging from 0-10, indicating more severe pain. The Itching Assessment Scale (FIIQ) was used to assess itching severity in four areas: location of itching (1-5 points), intensity of itching (1-5 points), frequency of itching (1-5 points), and effect of itch-

ing on sleep (1-4 points), for a total score of 19 points. Higher scores indicated more severe itching.

Serological indicators: Fasting venous blood (5 mL) was collected from each patient at 8:00 a.m. before and after treatment. After centrifugation, the supernatant was stored at -8°C for analysis. Transforming growth factor (TGF)- $\beta 1$, epidermal growth factor (EGF), and bone morphogenetic protein-7 (BMP-7) were detected using enzyme-linked immunosorbent assay (ELISA). The intra-assay and inter-assay coefficients of variation (CV) for the ELISA kit were $<8\%$ and $<12\%$, respectively.

Adverse reactions: The number of cases of skin atrophy, pigmentation, folliculitis, and scar redness and swelling after treatment were observed

and recorded, and the overall incidence was calculated.

Short-term recurrence rate: A 6-month follow-up was conducted by telephone, follow-up visits, and review of pathology data to analyze the relapse rate during this period.

Mental status: The 14-item Hospital Anxiety and Depression Scale (HADS, 7 items each for anxiety and depression) was used to assess the patients' psychological status before and after treatment. Each item used a 4-point Likert scale (0-3 points), with a total score range of 0-42 points. Higher scores indicated more pronounced anxiety and depressive symptoms; a score ≥ 11 points confirmed the presence of related symptoms.

Quality of life: The Dermatology Life Quality Index (DLQI, 0-30 points) was used to assess the effect of HS on patients' diet and sleep; lower scores indicated poorer quality of life.

Treatment satisfaction: Ten months post-treatment, patients were asked to evaluate the surgical outcome using a questionnaire (options: "Very satisfied", "Satisfied", "Mostly satisfied",

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Table 1. Patient baseline data

Data	PDT+TAC group (n=58)	PDT+PPDO group (n=62)	χ^2/t	P
Gender			0.187	0.666
Male	35 (60.34)	35 (56.45)		
Female	23 (39.66)	27 (43.55)		
Age (years)	36.05±6.26	35.34±5.67	0.652	0.516
Body mass index (kg/m ²)	21.93±1.71	22.28±1.63	1.148	0.253
Scar location			0.937	0.816
Chest/abdomen	22 (37.93)	24 (38.71)		
Shoulder/back	13 (22.41)	15 (24.19)		
Head/face	13 (22.41)	16 (25.81)		
Neck	10 (17.24)	7 (11.29)		
Causes of scars			4.599	0.100
Operation	24 (41.38)	20 (32.26)		
Burns	25 (43.10)	22 (35.48)		
Other trauma	9 (15.52)	20 (32.26)		
Educational background			0.391	0.532
< Senior high school	36 (62.07)	35 (56.45)		
≥ Senior high school	22 (37.93)	27 (43.55)		

Note: PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TAC, triamcinolone acetoneide.

Table 2. Clinical treatment efficacy

Indicator	PDT+TAC group (n=58)	PDT+PPDO group (n=62)	χ^2	P
Excellence	29 (50.00)	41 (66.13)		
Effectiveness	16 (27.59)	16 (25.81)		
Ineffectiveness	13 (22.41)	5 (8.06)		
Overall efficacy	45 (77.59)	57 (91.94)	4.839	0.028

Note: PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TAC, triamcinolone acetoneide.

“Dissatisfied”). Overall satisfaction was the percentage of respondents who rated themselves “Very satisfied” or “Satisfied”.

Statistical analysis

Normality was tested using the Shapiro-Wilk method. Normally distributed continuous data were expressed as mean ± standard deviation; independent samples t-tests were used for between-group comparisons, and paired t-tests were used for within-group comparisons before and after treatment. Non-normally distributed continuous data were expressed as median (interquartile range) [M (Q1, Q3)]; Mann-Whitney U test was used for between-group differences. Categorical data were expressed as percentages; chi-square test was used for comparisons between two groups of categorical data. SPSS 26.0 software was used to analyze the

collected experimental data. P<0.05 was considered statistically significant.

Results

Patient baseline characteristics

As shown in **Table 1**, the baseline characteristics of the two patient cohorts were similar. No significant differences were observed between the groups in terms of sex, age, body mass index (BMI), scar location, cause of scars, or educational background (all P>0.05).

Clinical efficacy outcomes

Table 2 presents comparative data on treatment outcomes. The overall response rate of PDT combined with PPDO was superior to that of PDT combined with TAC therapy (P<0.05).

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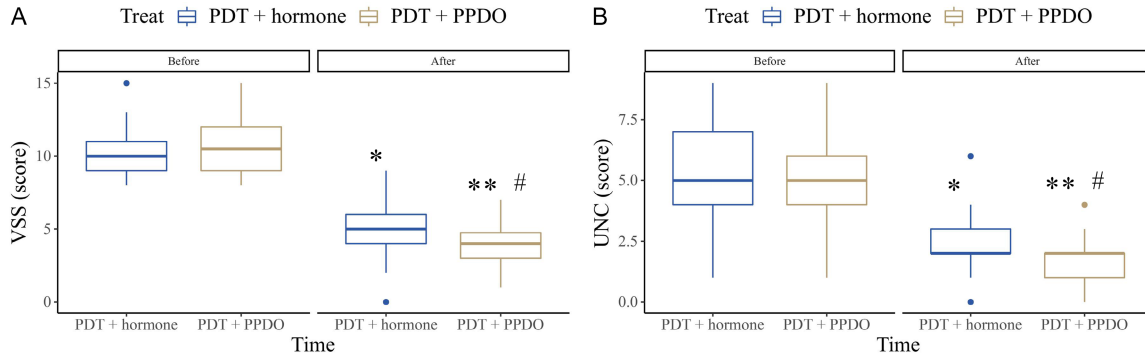


Figure 2. Scar assessment in the study groups pre- and post-therapy. A. VSS scores pre- and post-treatment. B. UNC scale scores pre- and post-treatment. Note: VSS, Vancouver Scar Rating Scale; UNC, University of North Carolina; PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TAC, triamcinolone acetonide. * $P<0.05$, ** $P<0.01$ vs. pre-treatment (within group); # $P<0.05$ vs. PDT+TAC group (same time point).

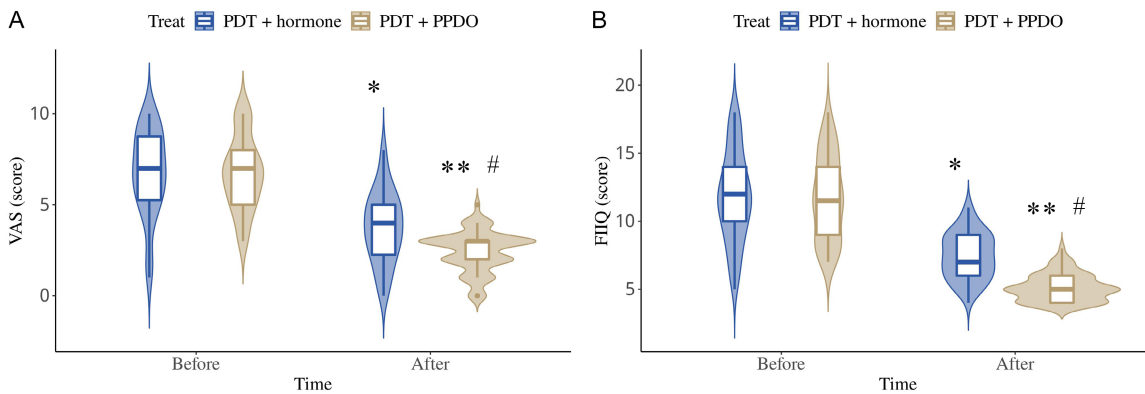


Figure 3. Pre- and post-treatment pain and itching assessments. A. Comparative analysis of VAS scores pre- and post-treatment. B. FIIQ scores obtained pre- and post-treatment for each cohort. Note: VAS, Visual Analog Scale; FIIQ, Four-Item Itch Questionnaire; PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TAC, triamcinolone acetonide. * $P<0.05$, ** $P<0.01$ vs. pre-treatment values within groups; # $P<0.05$ vs. PDT+TAC group at matched time points.

Scar assessment before and after treatment

Figure 2 shows the scar condition before and after treatment scar status assessed by VSS and UNC scales. Baseline scores showed no difference between the groups ($P>0.05$). After treatment, scores decreased significantly in both cohorts ($P<0.05$), with a greater decrease in the PDT+PPDO group ($P<0.05$).

Changes in pain and itching intensity

Figure 3 displays the assessment results of pain and pruritus before and after treatment using VAS and FIIQ. Although there was no difference in baseline scores between the groups ($P>0.05$), both regimens resulted in significant clinical improvement ($P<0.05$). In contrast, the group receiving PDT+PPDO treatment had lower VAS and FIIQ scores after treatment ($P<0.05$).

Serum biomarker measurements

As shown in **Figure 4**, serum biomarker levels measured by ELISA at baseline were comparable between the two groups (all $P>0.05$). After treatment, TGF- β 1 and EGF were significantly downregulated in both groups, while BMP-7 was significantly upregulated (all $P<0.05$). Notably, the PDT+PPDO group showed a more significant regulatory effect on these three biomarkers compared to the PDT+TAC group ($P<0.05$).

Adverse reaction incidence and short-term recurrence

The inter-group safety and short-term recurrence outcomes (**Table 3**) revealed a comparable overall incidence of adverse reactions (dermatophagia, pigmentation, folliculitis, scar red-

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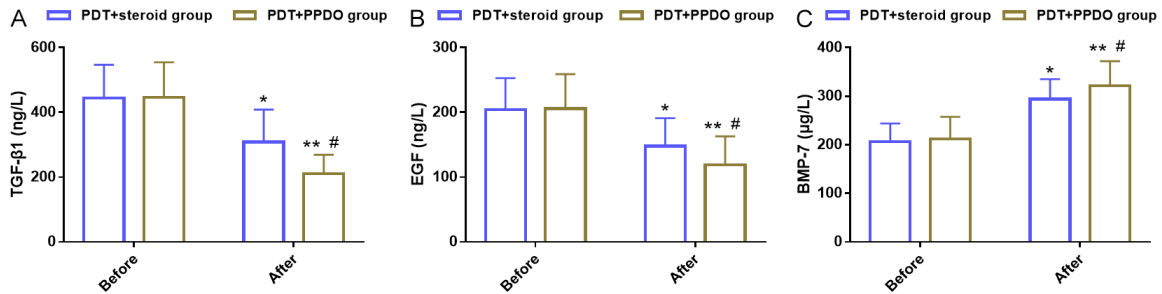


Figure 4. Serum markers before and after treatment. A. TGF-β1 levels in the two groups before and after treatment. B. EGF levels in the two groups before and after treatment. C. BMP-7 levels in the two groups before and after treatment. Note: PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TGF-β1, transforming growth factor-β1; EGF, epidermal growth factor; BMP-7, bone morphogenetic protein-7; TAC, triamcinolone acetonide. *P<0.05, **P<0.01 (intra-group comparison vs. pre-treatment measurement); #P<0.05, compared to the PDT+TAC group at the same time point.

Table 3. Incidence of adverse events and post-treatment short-term recurrence

Indicator	PDT+TAC group (n=58)	PDT+PPDO group (n=62)	χ ²	P
Dermatophia	2 (3.45)	1 (1.61)		
Pigmentation	3 (5.17)	2 (3.23)		
Folliculitis	2 (3.45)	2 (3.23)		
Scar redness/swelling	4 (6.90)	3 (4.84)		
Total adverse reactions	11 (18.97)	8 (12.90)	0.826	0.363
Recurrence	12 (20.69)	3 (4.84)	-	0.012

Note: PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TAC, triamcinolone acetonide.

Table 4. Mental status pre- and post-therapy

Indicator	PDT+TAC group (n=58)	PDT+PPDO group (n=62)	Z	P
Anxiety (points)				
Before	12.00 (9.75, 13.00)	12.00 (8.00, 13.00)	-0.442	0.659
After	7.00 (6.00, 9.00)*	7.00 (6.00, 7.00)**	-2.184	0.029
Depression (points)				
Before	11.00 (9.00, 12.00)	11.00 (9.00, 12.00)	-0.165	0.869
After	7.00 (6.00, 8.00)*	6.00 (5.00, 7.00)**	-3.295	0.001

Note: PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TAC, triamcinolone acetonide. *P<0.05, **P<0.01 (intra-group comparison vs. pre-treatment measurement).

ness/swelling) (all P>0.05). However, the PDT+PPDO regimen had a lower short-term (within six months) recurrence rate (P<0.05).

Mental health assessment The HADS assessment of mental status, as shown in **Table 4**, indicated no significant difference in anxiety or depression between groups at baseline (P>0.05). After treatment, all scores in both cohorts showed significant decreases, with the PDT+PPDO group consistently showing better results (P<0.05).

Quality of life assessment: Based on the DLQI assessments (**Table 5**), the quality of life scores

were similar between the two groups at baseline (P>0.05). After treatment, scores in each group decreased significantly, with the final score in the PDT+PPDO group being significantly lower than that of the other group (P<0.05).

Patient satisfaction: **Table 6** summarizes the treatment satisfaction of the two groups. The overall satisfaction rate of the PDT+PPDO group (83.87%) was better than that of the PDT+TAC group (67.24%) (P<0.05).

Discussion

This study evaluated the clinical efficacy of PDT combined with PPDO and PDT combined with

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Table 5. Quality of life pre- and post-treatment

Indicator	PDT+TAC group (n=58)	PDT+PPDO group (n=62)	Z	P
DLQI (points)				
Before	10.00 (8.00, 11.25)	9.00 (8.00, 11.25)	-0.763	0.445
After	5.00 (4.00, 6.00)*	3.00 (2.75, 4.00)**	-6.643	<0.001

Note: PDT, photodynamic therapy; PPDO, poly (p-dioxanone); DLQI, Dermatology Life Quality Index; TAC, triamcinolone acetone. *P<0.05, **P<0.01 (intra-group comparison vs. pre-treatment measurement).

Table 6. Treatment satisfaction assessment

Indicator	PDT+TAC group (n=58)	PDT+PPDO group (n=62)	χ^2	P
Very satisfied	20 (34.48)	30 (48.39)		
Satisfied	19 (32.76)	22 (35.48)		
Basically satisfied	9 (15.52)	5 (8.06)		
Dissatisfied	10 (17.24)	5 (8.06)		
Total satisfaction	39 (67.24)	52 (83.87)	4.522	0.034

Note: PDT, photodynamic therapy; PPDO, poly (p-dioxanone); TAC, triamcinolone acetone.

TAC in the treatment of HS. We initially observed that the PDT+PPDO combination therapy achieved better therapeutic effects. In addition, patients who received PDT+PPDO treatment showed more significant improvement in scar conditions compared to patients who received PDT-TAC treatment. Wei et al. [17] pointed out that PDT combined with intralesional injection of TAC and 5-fluorouracil was effective in treating acne-related HS, which can flatten, shrink, and soften scars. PPDO promotes natural skin regeneration by stimulating collagen production, reducing scar formation, and accelerating skin repair [18]. Gupta et al. [19] found that PPDO performed better than Poly-geline 910 in improving scar repair, effectively reducing scar spread and enhancing scar quality. In addition, PPDO can be used as a prophylactic internal support matrix for silicone gel breast fixation, which helps prevent undesirable scar formation [20]. In the treatment of HS, PDT+PPDO is significantly more effective in relieving pain and itching than PDT combined with TAC. Kim et al. [21] reported that PPDO can be used for acupuncture to treat patients with nonspecific chronic neck pain, and can effectively relieve neck pain. PPDO is used as a non-surgical treatment for knee osteoarthritis, and can relieve persistent pain in patients within 30 weeks, demonstrating definite clinical value for long-term pain management [22]. In this study, we also observed that after PDT+PPDO intervention, the levels of TGF- β 1 and EGF in patients with HS were significantly down-

regulated, while the BMP-7 level was significantly upregulated, suggesting that the above indicators may play a mediating role in the process of scar improvement. TGF- β 1 is known to be involved in the pathogenesis of HS, especially in the early stages of the disease, and has a positive effect on scar repair by targeting TGF- β 1 in keratinocytes [23]. EGF and TGF- β 1 are both cytokines released from fibrin clots and damaged tissues, which are mainly used to recruit neutrophils to the wound. Although they help wound healing, overexpression can lead to scar formation and proliferation [24]. BMP-7 is a member of the TGF- β 1 superfamily and helps to reduce β 1-related fibrosis in various tissues and inhibit β 1-induced differentiation of rat dermal cells into fibroblast-like cells [25, 26]. Guo et al. [27] reported that BMP-7 can inhibit excessive scar formation by activating BMP-7/Mothers against Decapentaplegic Homolog (Smad) 1/5/8 axis, showing potential in the treatment of HS. On the other hand, in the treatment of HS, PDT+PPDO is as safe as PDT combined with TAC and can effectively prevent short-term (within six months) recurrence. PPDO is convenient to use, has strong applicability and good biocompatibility, and can be naturally biodegraded, ensuring its high safety and low irritation risk [18]. We found that under PDT+PPDO intervention, patients with HS experienced better relief of anxiety and depression, and their quality of life was significantly improved. Finally, PDT+PPDO markedly improved patients' satisfaction with the treatment.

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This study has some limitations: First, there was a lack of basic research to verify the specific mechanism of PDT+PPDO therapy in the treatment of HS, and further research is needed to gain a deeper understanding of the mechanism of action of this therapy. Second, there was a lack of cost-benefit analysis, and supplementary research may help promote the clinical application of PDT+PPDO therapy. Third, this study evaluated the overall effectiveness and safety of the two intervention regimens under the clinical pathway, rather than a completely symmetrical intervention comparison, which may introduce bias; this factor needs to be further controlled through prospective studies, stratified design, or adjustment of injection time. Fourth, this study did not conduct subgroup analysis of scars from different causes or locations. Given that the pathophysiologic characteristics of different subtypes may affect treatment response, future studies should conduct stratified studies based on specific scar types to clarify differences in efficacy. Fifth, the follow-up period was relatively short (only 6 months), and it is necessary to extend the follow-up period (at least 12-18 months) to comprehensively assess the recurrence rate in patients with HS treated with PDT+PPDO. Finally, the combined PDT and PPDO therapy has not yet been attempted to treat chronic wound fibrosis (such as diabetic foot). Future studies should supplement relevant validations to expand the application value of this therapy.

In conclusion, the combined PDT and PPDO therapy is effective in treating patients with HS, effectively repairing scars, relieving pain and itching, and actively regulating abnormal serum marker levels (TGF- β 1, EGF, BMP-7), while ensuring a certain level of safety. Furthermore, this therapy can reduce the short-term recurrence risk, alleviate patients' negative emotions, and improve their quality of life and treatment satisfaction.

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Disclosure of conflict of interest

None.

Address correspondence to: Gang Zheng, Department of Dermatology, Xuzhou Central Hospital, Xuzhou 221009, Jiangsu, China. Tel: +86-0516-96120; E-mail: gz11zg@163.com

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