ORIGINAL RESEARCH

Impact of Platelet-Rich Fibrin Combined with Silver Nanoparticle Dressing on Healing Time and Therapeutic Efficacy of Chronic Refractory Wounds

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ABSTRACT

Objective • This study aimed to investigate the clinical value of combining platelet-rich fibrin (PRF) with nano silver (AgNP) dressing in the treatment of chronic refractory wounds.

Methods • A total of 120 patients with chronic refractory wounds were selected from our hospital between January 2020 and January 2022. The patients were randomly divided into the control group and the study group, with 60 cases in each group. The control group received basic treatment combined with AgNP dressing, while the study group received PRF combined with AgNP dressing. A comparison was made between the two groups in terms of wound healing time, hS-CRP levels, VISUAL analogue scale (VAS) scores, procalcitonin (PCT) levels, clinical efficacy, and complications.

Results • Before treatment, there were no significant differences in hS-CRP, VAS, and PCT levels between the two groups ($P > .05$). However, after treatment, the study group showed significantly lower hS-CRP, VAS, and PCT levels compared to the control group ($P < .05$). The study group also exhibited a shorter wound healing time, a higher rate of excellent and good curative effect (95.00% vs 81.67%) compared to the control group ($\chi^2 = 5.175$, $P < .05$), and a lower incidence of wound complications (6.67% vs 21.67%) compared to the control group ($\chi^2 = 4.386$, $P < .05$).

Conclusions • The combination of PRF and AgNP dressing can effectively alleviate pain and local inflammation in patients with chronic refractory wounds, improve the wound healing rate, shorten the healing time, and reduce the risk of complications such as infection spread. (*Altern Ther Health Med.* 2023;29(6):264-267).

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INTRODUCTION

Chronic refractory wounds are characterized by chronicity, refractoriness, and high harm, which can negatively affect the patient's quality of life and prognosis.[1,2] Common types of chronic refractory wounds include chronic infectious wounds, chronic ulcers, burn wounds, and pressure ulcers.[3] These wounds are often characterized by ischemia and hypoxia, bacterial biofilm formation, secondary infection, and large wound defects, making them difficult to heal even with long-term treatment using conventional methods.[4]

Growth factor gel, negative pressure closed drainage, and hyperbaric oxygen therapy are currently the main clinical treatments for chronic hard-to-heal wounds. While these treatments can improve blood circulation, reduce the risk of infection, and accelerate wound healing, they still require lengthy treatment periods and may not result in quick healing. Frequent dressing changes and high treatment costs can also negatively impact the patient's physical and mental health.[1-4]

Recent studies have shown that synthetic silver nanoparticles (AgNP) dressing has a strong bactericidal effect and can promote the repair of damaged cells and wound healing.[5] Platelet-rich fibrin (PRF), a second-generation platelet concentrate, has also been widely used in various fields such as orthopedics, stomatology, and plastic surgery.[6] Therefore, exploring new treatment options, such as combining PRF with AgNP dressing, can be significant in shortening wound healing time, reducing complications, and improving patient outcomes.[5,6]

This study investigated the clinical value of PRF combined with AgNP dressing in the treatment of chronic refractory wounds.

Lin—PRF and AGNP Dressing for Chronic Refractory Wounds

PATIENTS AND METHODS

Study Design

This study employed a randomized controlled trial (RCT) design to investigate the clinical value of combining PRF with nano silver (AgNP) dressing in the treatment of chronic refractory wounds. A total of 120 patients with chronic refractory wounds were selected from our hospital between January 2020 and January 2022.

Patient Selection and Criteria

Patients with chronic refractory wounds were selected for this study and divided into a control group and a study group using a random number table method, with 60 cases in each group. The inclusion criteria were as follows: (1) Patients consistent with the diagnostic criteria of chronic refractory wounds[7]; (2) The duration of the non-healing wound was more than one month; (3) Age between 18 and 70 years; (4) Patients provided informed consent regarding the treatment procedure. The exclusion criteria were defined as follows: (1) Patients with concomitant blood infectious diseases; (2) Patients with an active infection in other anatomical sites; (3) Patients with mental or psychological disorders; (4) Patients with systemic lupus erythematosus; (5) Long-term use of corticosteroid drugs; (6) Patients with malnutrition, coagulation dysfunction, or moderate to severe anemia.

Treatment Procedure for the Control Group

The control group in this study received basic treatment combined with AgNP dressing. The treatment procedure involved several steps. Firstly, the wound was expanded until no suppuration, necrotic tissue, or swelling was present. Then, a 20 ml medical syringe was used to treat the exposed bone by rotating the needle to stimulate dense blood points, ensuring adequate blood supply to the area. The wound was washed with physiological saline and carefully removed dead skin. Subsequently, the wound was dried using sterile gauze. An externally applied recombinant bovine basic fibroblast growth factor (b-FGF) gel was administered, followed by applying AgNP antibacterial dressing. After a period of 5-7 days, the dressing was removed, and b-FGF gel was applied externally at a dose of 150U/m^2 of the wound area twice daily. The healing progress of the wound was observed, and treatment continued until complete wound healing was achieved.

Treatment Procedure for the Study Group

The study group received the PRF treatment, and the treatment protocol was followed by the control group. (1) Preparation of PRF; First, whole blood was collected, and 20 ml of the whole blood was extracted through the cubital vein with a sterile syringe. After the blood was collected, the whole blood was immediately centrifuged at 3000 r/min for 10 min, and then the centrifuged product was left standing for 4-5 min. After the blood sample was stabilized, a light-yellow gel in the middle layer was extracted with a 16G needle. (2) Treatment methods; The treatment methods for the study group were similar to those of the control group. After the conventional wound expansion treatment, the wound was cleaned with normal saline. Dead skin was carefully removed, and sterile gauze was used to dry the wound. The previously prepared PRF gel was evenly applied to cover the entire wound area. External AgNP antibacterial dressing was used to wrap the wound, and the dressing was removed after 5-7 days. During this period, the wound healing progress was closely monitored. If the wound did not heal, the aforementioned steps were repeated for continuous treatment until complete wound healing was achieved.

Observation Indicators and Comparison

The study compared various observation indicators between the two groups, including wound healing time, hypersensitive C-reactive protein (HS-CRP), and visual analogue score (VAS) of pain.[8]

Clinical Indicators. The VAS scores of both groups were compared on the 1st, 3rd, and 5th day of treatment. The VAS score, ranging from 0 to 10, reflects the intensity of pain experienced by the patients, with higher scores indicating greater pain sensation. Additionally, the wound healing time of both groups was compared.

Inflammation Indicators. Serum PCT and HS-CRP were compared between the two groups before and after treatment for 4 weeks. PCT was detected by the semi-quantitative colloidal gold immunocombination method, and HS-CRP was detected by the enzymatic method.[8] The reagents were purchased from Guosai Biotechnology Company.

Clinical Efficacy. After 3 weeks of treatment, the clinical efficacy and efficacy standards were compared between the two groups following the recommendations of Yu et al.[7] The efficacy standards were defined as (1) Excellent: the wound healed completely, the skin on the wound had no obvious pull, and the color was close to healthy skin; (2) Good: wound healing rate > 70%, no noticeable pulling of wound skin, natural appearance; (3) Poor: wound healing rate ≤70%, or there is evident strain and scar on the wound skin; Excellent rate = (excellent + good) a number of people/total number × 100%. (4) Wound complications: The occurrence of wound bleeding or exudation, infection diffusion, and scar hyperplasia were compared between the two groups to assess wound complications.

Statistical Analysis

The data analysis was conducted using Statistical Product and Service Solutions (SPSS) 22.0 (IBM, Armonk, NY, USA). The following variables were analyzed: age, course of disease, wound area, healing time, VAS, and PCT levels. The t test was employed to assess the significance of differences for these variables, with a $P < .05$ considered statistically significant. Additionally, the variables of gender, wound type, nursing satisfaction, and wound complications were analyzed using the chi-square test. A $P < .05$ was considered statistically significant for these variables.

Table 1. Comparison of General Data Between The Two Groups

Group	n	Age (Years)	Incurable Course of Wound (Days)	Wound Area (cm)²	Gender Male	Gender Maidenly	Wound Type Chronic Infection	Wound Type Chronic Ulcer	Wound Type Other Types
Study Group	60	30.35 ± 4.15	46.41 ± 5.12	22.35 ± 4.15	37(61.67)	23(38.33)	26(43.33)	20(33.33)	14(23.33)
Control Group	60	29.89 ± 3.89	46.68 ± 4.80	22.17 ± 4.02	35(58.33)	25(41.67)	27(45.00)	21(35.00)	12(20.00)
t/χ^2		0.626	0.298	0.241	0.139		0.197		
P value		.532	.766	.810	.709		.906		

RESULTS

Comparison of General Data between the Two Groups

Table 1 displays the comparison of general data between the two groups. There were no significant differences observed in terms of age ($t=0.626$), course of wound healing ($t=0.298$), wound area ($t=0.241$), gender ($\chi^2=0.139$), and wound type ($\chi^2=0.197$) ($P>.05$).

Comparison of Clinical Indicators between the Two Groups

Table 2 presents the comparison of clinical indicators between the two groups. There were no significant differences in VAS between the two groups on day 1 of treatment ($t=0.841$) ($P>.05$). However, on the 3rd day ($t=6.225$) and the 5th day ($t=10.304$) of treatment, the study group exhibited lower VAS scores compared to the control group ($P<.05$). Additionally, the study group demonstrated a shorter wound healing time ($t=8.091$) compared to the control group.

comparison of Inflammatory Indicators between the Two Groups

Table 3 presents the comparison of inflammatory indicators between the two groups. Prior to treatment, there were no significant differences in HS-CRP ($t=1.304$) and PCT ($t=0.519$) between the two groups ($P>.05$). However, after 2 weeks of treatment, the study group exhibited lower levels of HS-CRP ($t=5.606$) and PCT ($t=5.077$) compared to the control group ($P<.05$).

Comparison of Clinical Efficacy between the Two Groups

Table 4 presents the comparison of clinical efficacy between the study group and the control group. The excellent and good rate in the study group (95.00%) was higher than that in the control group (81.67%) ($\chi^2=5.175$, $P<.05$).

Comparison of Wound Complications between the Two Groups

Table 5 displays the comparison of wound complications between the study group and the control group. The incidence of wound complications in the study group (6.67%) was lower than that in the control group (21.67%) ($\chi^2=4.386$, $P<.05$).

DISCUSSION

Chronic refractory wounds require the implementation of diverse treatment regimens tailored to individual patient needs. These regimens may encompass interventions such as advanced dressings, negative pressure wound therapy, bioengineered skin substitutes, and surgical interventions.[7-9]

Table 2. Comparison Of Clinical Indicators Between The Two Groups ($\bar{x} \pm s$)

Group	n	VAS(points) 1 d	VAS(points) 3 d	VAS(points) 5 d	Wound healing time (D)
Study Group	60	5.47 ± 0.55	4.59 ± 0.93	2.63 ± 0.52	28.75 ± 3.38
Control Group	60	5.56 ± 0.62	3.42 ± 1.12	3.79 ± 0.70	34.26 ± 4.05
χ^2		0.841	6.225	10.304	8.091
P value		.402	<.001	<.001	<.001

Table 3. Comparison of Inflammatory Indicators Between the Two Groups ($\bar{x} \pm s$)

Group	n	Hs-crp (mg/L) Pre-treatment	Hs-crp (mg/L) After 2 weeks of treatment	PCT(ng/ml) Pre-treatment	PCT(ng/ml) After 2 weeks of treatment
Study Group	60	4.57 ± 0.40	3.46 ± 0.43	0.85 ± 0.19	0.33 ± 0.07
Control Group	60	4.45 ± 0.59	3.82 ± 0.25	0.83 ± 0.23	0.41 ± 0.10
t		1.304	5.606	0.519	5.077
P value		0.195	<.001	.605	<.001

Abbreviations: Hs-CRP, hypersensitive C-reactive protein; PCT, procalcitonin.

Table 4. Comparison of Nursing Satisfaction Between The Two Groups [n (%)]

Group	n	Diff	Good	Superiorities	Nursing Satisfaction Rate
Study Group	60	3 (5.00)	20 (33.33)	37 (61.67)	57 (95.00)
Control Group	60	11 (18.33)	24 (40.00)	25 (41.67)	49 (81.67)
χ^2					5.175
P value					.023

Table 5. Comparison of Wound Complications Between the Two Groups [n (%)]

Group	n	Spread of Infection	Ooze Blood or Fluid	Scar Hyperplasia	Total Complication Rate
Study Group	60	1 (1.67)	2 (3.33)	1 (1.67)	4 (6.67)
Control Group	60	4 (6.67)	6 (10.00)	3 (5.00)	13 (21.67)
χ^2					4.386
P value					.036

In this study, patients with chronic refractory wounds were treated with different regimens. The findings revealed that patients in the study group who received PRF combined with AgNP dressing had a significantly shorter wound healing time of 28.75 days compared to patients in the control group who received conventional treatment, which took 34.26 days. These results indicate that PRF combined with AgNP dressing can accelerate the healing process of chronic refractory wounds.

Furthermore, the study demonstrated that the incidence of HS-CRP, VAS, PCT, and wound complications in the study group was lower than in the control group after treatment. It suggests that PRF combined with AgNP dressing can effectively control local infections, reduce inflammatory responses, alleviate pain, and minimize the risk of wound complications during treatment for patients with chronic refractory wounds. The findings of this study align with previous research. Oe et al[9] demonstrated the antimicrobial properties of AgNP incorporated into hydrogels, which supports our use of AgNP dressing to control local infections in chronic refractory wounds. Additionally, the study by Bozkurt and Uslu[10] on platelet-rich fibrin application in wound healing further strengthens our results, as PRF combined with AgNP dressing in our study contributed to faster wound healing and reduced complications.

The potential mechanisms underlying the observed differences between the two groups can be attributed to the broad bactericidal spectrum of AgNP dressing. Clinical studies have demonstrated its effectiveness in combating various pathogenic bacteria, including *Staphylococcus Aureus* and *Escherichia Coli*, leading to the containment of chronic and refractory wound infections and facilitating tissue repair and healing.[10] Furthermore, AgNP functions as a natural antibacterial material, offering enhanced safety and reliability compared to traditional antibacterial dressings. Its prolonged and stable antibacterial effect ensures minimal toxic reactions and reduces the risk of drug resistance.[8] PRF, as a biomaterial with a dense fibrin network, exhibits the ability to continuously release numerous growth factors involved in tissue repair and angiogenesis, including vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF). This release of growth factors facilitates stem cell proliferation, migration, differentiation, and angiogenesis, ultimately accelerating the regeneration and repair of both hard and soft tissues in wounds, leading to a shortened healing time.[9]

Study Limitations

A few limitations of this study are acknowledged. Firstly, the lack of a control group receiving a placebo or alternative treatment makes it difficult to compare the effectiveness of PRF combined with AgNP dressing directly. Secondly, the study primarily focused on short-term outcomes, such as pain relief and wound healing rate, without considering long-term follow-up or patient-reported outcomes. Lastly, the study did not address potential patient characteristics or wound etiology variations, which could impact treatment outcomes. These limitations highlight the need for future research to address these gaps and provide a more comprehensive understanding of the treatment's efficacy and applicability.

CONCLUSION

In conclusion, the combination of PRF and AgNP dressing demonstrates significant efficacy in the treatment of chronic refractory wounds. This treatment approach effectively alleviates patients' pain and local inflammation, enhances wound healing rates, shortens healing time, and reduces the risk of infection spread and complications. These findings highlight the clinical value and potential for the widespread application of PRF combined with AgNP dressing in the management of chronic refractory wounds.

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