

ORIGINAL ARTICLE

Clinical study on betamethasone combined with platelet-rich plasma for frozen shoulder

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ABSTRACT

Objective: Under the support of visual ultrasound technology, this study investigates the efficacy of the combination of betamethasone and platelet-rich plasma (PRP) injections for the precise treatment of frozen shoulder. The findings aim to inform clinical practice.

Methods: A total of 84 patients with frozen shoulder who visited the outpatient department of a tertiary Class A hospital between January 2021 and June 2023 were selected. They were randomly assigned to receive either local betamethasone injection guided by visual ultrasound technology or combined betamethasone and PRP injection for precise treatment. The betamethasone local injection group comprised 42 patients, while the combined betamethasone and PRP injection group comprised 42 patients. The application of visual ultrasound technology identifies and marks the lesion site. Under ultrasound guidance, a posterior approach is used to puncture into the joint capsule space between the humeral head and glenoid labrum. Following successful puncture, drug injection therapy is administered. Shoulder joint pain levels and shoulder joint function were compared between the two groups at baseline, 6 weeks post-treatment, and 12 weeks post-treatment. Blood glucose levels were monitored at baseline, 1 day post-treatment, and 3 days post-treatment. Adverse reactions, including rash, abnormal liver function, gastrointestinal reactions, and dizziness/headache, were observed in this study.

Results: After 6 weeks and 12 weeks of treatment, the visual analogue scale (VAS) scores for shoulder pain severity and shoulder function were 3.62 ± 1.03 and 1.03 ± 0.25 , respectively, in the combined betamethasone and PRP injection group. In the betamethasone local injection group, these scores were 4.56 ± 1.31 and 1.54 ± 0.32 , respectively. Comparisons between the two groups yielded p values of .001 and $< .001$, indicating statistically significant differences. Constant-Murley Shoulder Function Score (CMS) results for the combined betamethasone and PRP injection group were 50.37 ± 6.23 and 80.72 ± 10.69 , respectively. For the betamethasone local injection group, the scores were 46.85 ± 6.11 and 73.54 ± 8.23 , respectively. Comparing the two groups, the p -values were .011 and $< .001$, respectively, indicating statistically significant differences. Comparison of blood glucose levels between the two groups: After 1 day and 3 days of treatment, fasting blood glucose levels in the combined betamethasone and PRP injection group were 5.67 ± 0.14 and 5.69 ± 0.13 mg/dL, respectively, while those in the betamethasone local injection group were 6.29 ± 0.35 and 6.35 ± 0.38 mg/dL, respectively. Compared between the two groups, the p -values were $< .001$ and $< .001$, respectively, indicating statistically significant differences. 2-hour postprandial blood glucose levels at 1 day and 3 days post-treatment were 6.85 ± 0.25 and 6.87 ± 0.28 mg/dL in the combined betamethasone and PRP injection group, and 8.34 ± 0.21 and 8.49 ± 0.34 mg/dL in the betamethasone local injection group. Comparisons between the two groups yielded p values of $< .001$ and $< .001$, respectively, indicating statistically significant differences. The incidence of adverse reactions in the combined betamethasone and PRP injection group was 11.90%, including 1 case of rash, 1 case of abnormal liver function, 2 cases of gastrointestinal reactions, and 1 case of dizziness and headache. The adverse reaction incidence rate in

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the betamethasone local injection group was 21.43%, including 2 cases of rash, 2 cases of abnormal liver function, 3 cases of gastrointestinal reactions, and 2 cases of dizziness and headache. Comparing the two groups, $p > .05$, indicating no statistically significant difference.

Conclusions: Compared with the betamethasone local injection group, the combined betamethasone and PRP injection group demonstrated lower VAS scores and higher CMS scores at 6 and 12 weeks post-treatment. Additionally, fasting blood glucose and 2-hour postprandial blood glucose levels were lower at 1 and 3 days post-treatment. There was no difference in the incidence of adverse reactions between the two groups. Ultrasound-guided injection of betamethasone combined with PRP demonstrates effective treatment for frozen shoulder and warrants further clinical application.

Key Words: Ultrasound visualization, Frozen shoulder, Betamethasone, Platelet-rich plasma injection technique

1. INTRODUCTION

Frozen shoulder, also known as adhesive capsulitis, is not entirely synonymous with shoulder peri-arthritis. It refers to a clinical condition characterized by shoulder joint pain, restricted shoulder joint mobility, and shoulder joint dysfunction, primarily caused by chronic inflammation and adhesions in soft tissues (including muscles, joint capsules, tendons, and bursae surrounding the shoulder joint) due to the combined effects of multiple factors. This condition adversely impacts patients' daily lives, making the diagnosis and treatment of frozen shoulder a subject of widespread clinical interest.^[1] For frozen shoulder, clinical practice advocates symptomatic support and medication. Betamethasone is a commonly used drug that suppresses inflammatory responses, effectively alleviating pain and improving shoulder joint function. However, the prolonged use of betamethasone may lead to adverse reactions with limited clinical efficacy.^[2] Platelet-rich plasma (PRP) is primarily derived from autologous whole blood. The plasma contains multiple growth factors that effectively suppress inflammatory mediators and promote shoulder joint mobility. It is now widely used in the treatment of frozen shoulder.^[3] However, there are currently few clinical studies reporting on the use of ultrasound-guided betamethasone combined with PRP injection therapy for frozen shoulder. In light of this, this study enrolled 84 patients with frozen shoulder to investigate the medical value of ultrasound-guided betamethasone with PRP injection therapy.

2. DATA AND METHODS

2.1 General information

A total of 84 patients with frozen shoulder were enrolled from the outpatient department of a tertiary Class A hospital between January 2021 and June 2023. They were divided into two groups based on treatment method: the combined betamethasone and PRP injection group ($n = 42$) and the betamethasone local injection group ($n = 42$). The combined betamethasone and PRP injection group comprised 18 males and 24 females; ages ranged from 41 to 72, with a mean

age of (56.48 ± 6.34); disease duration ranged from 1 to 11 months, with a mean duration of (5.74 ± 1.23) months. The betamethasone local injection group comprised 16 males and 26 females; ages ranged from 40 to 72, with a mean age of (56.73 ± 6.42); disease duration ranged from 1 to 10 months, with a mean duration of (5.83 ± 1.25) months. Comparison of data between the two groups revealed no statistically significant differences ($p > .05$).

Inclusion criteria for research objects were as follows:

- (1) Patients who were diagnosed with frozen shoulder based on MRI examination and clinical symptom analysis, meeting the diagnostic criteria for frozen shoulder outlined in the "Diagnosis and Treatment Guidelines for Scapulohumeral Peri-arthritis (Frozen Shoulder)";^[4]
- (2) Patients with varying degrees of shoulder joint pain and restricted shoulder joint mobility, with a shoulder pain score exceeding 4 points;
- (3) Patients with complete clinical data;
- (4) Patients with no history of allergy to the study medication;
- (5) Patients and their family members were informed of the proposed treatment plan and signed the informed consent.

Exclusion criteria were as follows:

- (1) Patients with shoulder joint pain caused by fractures, tuberculosis, tumors, etc.;
- (2) Patients who were diagnosed with secondary frozen shoulder;
- (3) Patients with a history of shoulder joint trauma or shoulder joint surgery;
- (4) Patients who used betamethasone or PRP therapy within 3 months prior to enrollment;
- (5) Patients with a history of diabetes, rheumatoid arthritis, tuberculosis, or cancer;
- (6) Patients with mental illness or cognitive impairment.

2.2 Methods

The combined betamethasone and PRP injection group received ultrasound-guided betamethasone + PRP injection therapy, while the betamethasone local injection group received ultrasound-guided betamethasone therapy. The detailed methods are as follows:

- (1) Instrument Parameters: Treatment is performed by using the Philips advanced intelligent color Doppler ultrasound diagnostic system (Model: HD15) provided by Shanghai Jumu Medical Equipment Co., Ltd. The ultrasound probe frequency is set to (5-12) MHz.
- (2) PRP Preparation Method: In a sterile environment, opened the PRP device. Using a pre-filled syringe containing 5 mL of anticoagulant, 20 mL of venous blood were drawn. The syringe was gently shaken to ensure thorough mixing of the venous blood with the anticoagulant. The 20 mL of venous blood were injected into the PRP device through its blood inlet port. The sample was centrifuged for 5 minutes at 2,500 rpm. After separating the serum, the bottom layer of red blood cells was retained in the red blood cell compartment. The PRP device was inverted and centrifuged again for 5 minutes at 3,500 rpm. After analyzing the serum, the bottom layer of red blood cells was transferred into the PRP chamber. 4 mL of PRP were withdrawn from the chamber for subsequent use.
- (3) Procedures: the patient was instructed to assume a lateral recumbent or seated position, ensuring the affected shoulder joint was fully exposed within the clinician's field of view. Perform the routine skin disinfection was performed for draping over the affected shoulder area. Coupling agent was applied to the ultrasound probe with a sterile endoscopic sleeve covering. The probe was positioned around the shoulder joint, examining it in a top-to-bottom, inner-to-outer sequence. Surrounding vascular and neural structures were observed to identify and mark the lesion site. Subsequently, under ultrasound guidance, a 22G needle was advanced via the posterior approach, ensuring the needle progresses from posterolateral to anteromedial into the joint capsule space between the humeral head and glenoid labrum. Following successful puncture, patients in the study group received two injections: the first involved injecting 2 mL of compound betamethasone injection (manufacturer: Chongqing Huapont Pharmaceutical Co., Ltd.; National Drug Approval Number H20093412; specification: 1 mL:0.5 mg) into the joint cavity by using a syringe. The second injection involved injecting 2 mL of PRP into the

joint cavity by using a syringe, with a 15-day interval between injections. The control group received two injections of 2 mL of compound betamethasone injection into the joint cavity under ultrasound guidance, with a 15-day interval. After the injection, the injection site was covered with a sterile dressing. The patient was instructed to move the shoulder joint to promote even distribution of the medication. The patient was advised to perform shoulder joint exercises throughout the treatment period.

2.3 Indicator observation

- (1) Shoulder joint functional rehabilitation outcomes: Before treatment, 6 weeks after the second treatment, and 12 weeks after the second treatment.
 - A. Shoulder joint pain intensity: Assessment criteria was based on the visual analogue scale (VAS), with a total score of 10 points. Higher scores indicate more severe pain.
 - B. Shoulder Joint Function: The evaluation standard was based on Constant-Murley Shoulder Function Score Scale (CMS), with a total score of 100 points. A higher score indicates better recovery of shoulder joint function.
- (2) Blood glucose measurements: On an empty stomach and 2 hours after meals, 2 mL of fasting blood and 2 mL of 2-hour postprandial blood (venous) were drawn before treatment, 1 day after the second treatment, and 3 days after treatment. The blood samples were centrifuged and separated. An automated biochemical analyzer (manufacturer: Jiangxi Tekang Technology Co., Ltd.; model: TC6090) was used to measure the patients' fasting blood glucose and 2-hour postprandial blood glucose levels.
- (3) Adverse reactions: including rash, abnormal liver function, gastrointestinal reactions, and dizziness or headache.

2.4 Statistical methods

SPSS 25.0 statistical software was applied to statistical analysis, and the normally distributed measurement data were represented by mean \pm standard deviation ($\bar{x} \pm s$), with *t*-test used; categorical data were expressed as frequency (*n*) and percentage (%), and analyzed by using chi-square (χ^2) tests. *p* value < .05 was considered statistically significant.

3. RESULTS

3.1 Comparison of shoulder pain severity and shoulder function between the two groups

At 6 weeks and 12 weeks post-treatment, the combined betamethasone and PRP injection group demonstrated lower

VAS scores and higher CMS scores in comparison to the betamethasone injection group alone ($p < .05$) (see Tables 1 and 2).

3.2 Evaluation of the blood glucose levels in the two groups

After the second treatment on Day 1 and Day 3, the combined betamethasone and PRP injection group exhibited lower fasting blood glucose and 2-hour postprandial blood glucose levels in comparison to the betamethasone local injection group ($p < .05$) (see Tables 3 and 4).

3.3 Evaluation of adverse reactions in the two groups

The combined betamethasone and PRP injection group reported 1 case of rash, 1 case of abnormal liver function, 2 cases of gastrointestinal reactions, and 1 case of dizziness and headache; the betamethasone local injection group reported 2 cases of rash, 2 cases of abnormal liver function, 3 cases of gastrointestinal reactions, and 2 cases of dizziness and headache. The adverse reaction incidence rate of 11.90% in the combined betamethasone and PRP injection group was lower than that of 21.43% in the betamethasone local injection group ($\chi^2 = 1.371$, $p = .242$), with no statistically significant difference ($p > .05$).

Table 1. Comparison of VAS scores between the combined betamethasone and PRP injection group and the betamethasone local injection group ($\bar{x} \pm s$, scores)

Group	n	Before treatment	6 weeks after treatment	12 weeks after treatment
Combined betamethasone and PRP injection group	42	7.85±1.34	3.62±1.03	1.03±0.25
Betamethasone local injection group	42	7.63±1.29	4.56±1.31	1.54±0.32
<i>t</i>		0.767	3.656	8.139
<i>p</i>		.446	.001	< .001

Table 2. Comparison of CMS scores between the combined betamethasone and PRP injection group and the betamethasone local injection group ($\bar{x} \pm s$, scores)

Group	n	Before treatment	6 weeks after treatment	12 weeks after treatment
Combined betamethasone and PRP injection group	42	33.59±4.16	50.37±6.23	80.72±10.69
Betamethasone local injection group	42	33.72±4.18	46.85±6.11	73.54±8.23
<i>t</i>		0.143	2.614	3.449
<i>p</i>		.887	.011	.001

Table 3. Comparison of fasting blood glucose levels between the combined betamethasone and PRP injection group and the betamethasone local injection group ($\bar{x} \pm s$, mmol/L)

Group	n	Before treatment	1 day after treatment	3 days after treatment
Combined betamethasone and PRP injection group	42	5.63±0.11	5.67±0.14	5.69±0.13
Betamethasone local injection group	42	5.64±0.12	6.29±0.35	6.35±0.38
<i>t</i>		0.398	10.659	10.650
<i>p</i>		.692	< .001	< .001

Table 4. Comparison of 2-hour postprandial blood glucose levels between the combined betamethasone and PRP injection group and the betamethasone local injection group ($\bar{x} \pm s$, mmol/L)

Group	n	Before treatment	1 day after treatment	3 days after treatment
Combined betamethasone and PRP injection group	42	6.82±0.23	6.85±0.25	6.87±0.28
Betamethasone local injection group	42	6.83±0.24	8.34±0.21	8.49±0.34
<i>t</i>		0.195	29.576	28.836
<i>p</i>		.8462	< .001	< .001

4. DISCUSSION

The shoulder joint is a vital component of the human body and the joint with the greatest range of motion. It plays a crucial role in facilitating upper limb mobility. The quality of shoulder joint function directly impacts individual daily activities and the overall quality of life. Frozen shoulder is a common clinical disorder of the shoulder joint system, characterized primarily by shoulder pain and progressive limitation of both active and passive range of motion. The exact pathogenesis of frozen shoulder remains under investigation, but it is believed that chronic inflammation and fibrosis of the joint capsule and surrounding ligamentous tissues constitute the primary pathological changes.^[5] Following the onset of frozen shoulder, patients often experience worsening spontaneous shoulder pain and restricted joint mobility. Without timely intervention, this condition may progress to joint stiffness, degeneration, or disability. In severe cases, it can lead to osteoporosis. Therefore, it is essential to perform a timely clinical treatment for frozen shoulder.

At present, due to the lack of a clear understanding of the etiology of frozen shoulder in clinical practice, no unified, standardized and effective diagnostic and treatment guidelines have been established. Therefore, clinical management primarily focuses on symptomatic support and medication to rapidly alleviate shoulder pain and restore shoulder joint mobility. Glucocorticoid medications (betamethasone) are commonly used in clinical treatment for frozen shoulder. They promote the elimination of inflammatory substances and block the transmission of pain signals in the affected area, thereby achieving the therapeutic goals of alleviating pain and restoring shoulder joint function. However, the treatment course for frozen shoulder is relatively long. Prolonged betamethasone injections may lead to adverse reactions such as liver function abnormalities, skin rashes, gastrointestinal reactions, and dizziness/headaches. This often reduces patient compliance with treatment, thereby affecting therapeutic outcomes.^[6] With the advancement of biotechnology, various novel biomaterials have been developed for clinical use and are increasingly applied to the treatment of frozen shoulder, yielding favorable outcomes. PRP is a platelet-rich aggregate primarily obtained by centrifuging autologous whole blood to concentrate platelets, thereby increasing the concentration of platelets, white blood cells, and fibrin in plasma. Concurrently, PRP contains multiple growth factors that suppress the activity and release of inflammatory cytokines, promote cell proliferation and differentiation, and facilitate tissue repair. It is now widely applied in the field of orthopedics.^[7] With advancements in ultrasound technology, it has gradually become an auxiliary tool in disease treatment, enabling precise interventional procedures through ultrasound guidance. The

study found that the pain scores in the combined betamethasone and PRP injection group were lower than those in the betamethasone local injection group, with no difference in the incidence of adverse reactions between the two groups. The analysis of the reasons is as follows: Betamethasone belongs to the category of corticosteroids, possessing potent anti-inflammatory properties that can rapidly alleviate shoulder joint pain symptoms; PRP contains protease-activated receptor 4 peptide, which exhibits anti-injury effects and exerts analgesic action; Betamethasone and PRP possess distinct mechanisms of action. Their combined application produces a synergistic effect, enhancing analgesia and thereby reducing shoulder joint pain severity. Furthermore, utilizing ultrasound visualization for the injection of Betamethasone and PRP enables direct targeting of the affected site, precise drug dosing and consequently minimizes adverse reactions while improving the safety of drug therapy.^[8] The study found that the combined betamethasone and PRP injection group demonstrated superior shoulder joint function in comparison to the betamethasone local injection group, consistent with the findings of Dong Xinhua et al.^[9] The analysis of its mechanism is as follows: PRP primarily originates from autologous venous blood, being an extract of autologous venous blood. When platelets are activated, they release dense granules, alpha granules, and other substances. These substances contain multiple cytokines essential for tissue repair, which can halt the chronic inflammatory and fibrotic processes in the joint capsule and surrounding ligamentous tissues, thereby improving shoulder joint function.^[10] Betamethasone, as a glucocorticoid medication, is used in the treatment of frozen shoulder to reduce local inflammation and alleviate shoulder joint pain. However, long-term use of betamethasone can affect the body's metabolism and induce adverse reactions such as abnormal blood glucose fluctuations. These fluctuations can trigger oxidative stress reactions, damage blood vessels, increase the risk of infection, and simultaneously impair nerves, activating pain mechanisms that exacerbate shoulder joint pain.^[11,12] The study found that blood glucose levels increased in the groups receiving 1-day and 3-day topical betamethasone injections, while no significant changes were observed in the combined betamethasone and PRP injection group. This demonstrates that the combination therapy of betamethasone and PRP injections can reduce abnormal blood glucose fluctuations and prevent adverse events.

5. CONCLUSIONS

The ultrasound-guided betamethasone + PRP injection technique demonstrates favorable therapeutic outcomes for frozen shoulder. It effectively alleviates shoulder pain, im-

proves shoulder function, and helps control blood glucose fluctuations, while exhibiting minimal adverse reactions. This approach is worth an increased clinical promotion.

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AUTHORS CONTRIBUTIONS

Daxing Guo contributed to the study argumentation and manuscript drafting; Ping li contributed to the guidance of the manuscript drafting and technical operation.

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The authors declare no conflicts of interest.

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The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

DATA SHARING STATEMENT

No additional data are available.

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