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The Effect of Intra-Articular Injection of PRP Combined with Sodium Hyaluronate and TCM Hot Compress Pack on Serum IL-1β and IL-6 in Patients with Knee Osteoarthritis

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Abstract: *Objective:* This study aims to investigate the impact of a combined intervention of intra-articular injections of platelet-rich plasma (PRP) and sodium hyaluronate, followed by traditional Chinese medicine (TCM) hot compress therapy, on serum levels of interleukin-1β (IL-1β) and interleukin-6 (IL-6) in patients with knee osteoarthritis (KOA). Additionally, it seeks to assess the clinical effectiveness and elucidate the potential mechanisms of this integrated treatment approach. *Methods:* A total of 86 KOA patients admitted to our hospital between August 2024 and July 2025 were randomly assigned to a study group and a control group, each with 43 patients. The control group was treated with intra-articular injection of PRP combined with sodium hyaluronate, while the study group received additional application of a TCM hot compress pack. Clinical efficacy, pain intensity (assessed using the numerical rating scale, NRS), joint function (evaluated using the WOMAC index), serum levels of IL-1β and IL-6, and quality of life (measured using the SF-36 scale) were compared between the two groups before and after the intervention. *Results:* The study group demonstrated a significantly greater total effective rate compared to the control group ($P < 0.05$). Following treatment, the study group exhibited markedly reduced NRS and WOMAC scores, along with lower serum levels of IL-1β and IL-6, all significantly superior to the control group ($P < 0.05$). Conversely, SF-36 scores in the study group were significantly elevated compared to the control group ($P < 0.05$). *Conclusion:* Intra-articular injection of PRP combined with sodium hyaluronate, supplemented by TCM hot compress pack, can effectively regulate serum IL-1β and IL-6 levels in KOA patients, alleviate pain, improve joint function and quality of life, and has good clinical application value.

Keywords: Knee osteoarthritis; Platelet-rich plasma; Sodium hyaluronate; Traditional Chinese medicine hot compress pack; Interleukin-1β; Interleukin-6

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1. Introduction

Knee osteoarthritis (KOA) is a prevalent chronic degenerative disease in orthopedics, characterized by cartilage degeneration and osteophyte formation, presenting with pain and limited mobility. The prevalence rate exceeds 30% among individuals over 60 years old, imposing a significant burden on society [1,2]. Clinical management primarily aims to alleviate symptoms, with intra-articular injection of platelet-rich plasma (PRP) combined with sodium hyaluronate being a common approach. PRP promotes cartilage repair, while sodium hyaluronate enhances joint lubrication; however, their efficacy in regulating inflammation is limited [3,4]. Traditional Chinese medicine (TCM) classifies KOA as "bone arthralgia," attributing its pathogenesis to liver and kidney deficiency and qi and blood stagnation. Hot compress with a TCM pack can promote blood circulation, remove blood stasis, warm the meridians, and relieve pain [5]. This study investigated the combined application of PRP + sodium hyaluronate with a TCM hot compress pack, exploring its effects on serum interleukin-1β (IL-1β) and interleukin-6 (IL-6) levels to provide a basis for optimizing treatment protocols.

2. Materials and methods

2.1. General information

Eighty-six patients diagnosed with KOA and admitted to our hospital between August 2024 and July 2025 were enrolled in the study. The inclusion criteria were as follows: (1) Meeting the diagnostic criteria for KOA as defined in the *Guidelines for the Diagnosis and Treatment of Osteoarthritis (2021 Edition)*; (2) Confirmation by knee joint X-ray or MRI of varying degrees of articular cartilage damage and osteophyte formation; (3) Age ranging from 45 to 75; (4) Knee pain NRS score of ≥ 4; (5) No intra-articular drug injections or external treatment with TCM in the past month; (6) Both patients and their family members have a clear understanding of the trial content and have signed informed consent forms. Exclusion criteria: (1) Knee joint deformities, suppurative inflammation, tuberculosis, malignant tumors, or other diseases caused by trauma; (2) A history of allergies to PRP, sodium hyaluronate, or TCM preparations; (3) Suffering from severe diseases of the hematopoietic system, cardiovascular system, liver, kidney, or other organs that render them unable to tolerate surgery.

Patients were randomly allocated into a control group (n = 43) and a study group (n = 43). The control group comprised 19 males and 24 females, with a mean age of 61.25 ± 5.32 years and a mean disease duration of 5.32 ± 1.89 years. Within this group, 20 patients were classified as K-L grade II and 23 as grade III. The study group included 20 males and 23 females, with a mean age of 60.89 ± 5.15 years and a mean disease duration of 5.45 ± 1.92 years. In this group, 21 patients were grade II and 22 were grade III. Baseline characteristics were comparable between the two groups ($P > 0.05$). The study protocol received approval from the relevant ethics committee.

2.2. Treatment methods

2.2.1. Control group

The control group received PRP combined with sodium hyaluronate injection: 8 mL of venous blood was drawn, centrifuged at 1500 r/min for 9 minutes to prepare 2 mL of PRP, which was then injected into the joint cavity through a lateral knee puncture; concurrently, 2 mL of sodium hyaluronate was also injected. The treatment was administered once every two weeks, for a total of two sessions, spanning a four-week period.

2.2.2. Study group

The study group received additional treatment with a TCM hot compress pack: 100 g each of dodder seed, fried

mustard seed, perilla seed, and radish seed, along with 60 g of *Evodia rutaecarpa*, were heated in a constant temperature incubator to 65°C. The compress was applied to the affected area 24 hours after sodium hyaluronate injection, for 30 minutes each time, twice daily, five days a week, for a total of four weeks.

2.3. Observation indicators

2.3.1. Clinical efficacy

The efficacy was evaluated with reference to the "Guidelines for Clinical Research on New Traditional Chinese Medicines": markedly effective (NRS reduction ≥ 80%, symptoms disappeared), effective (NRS reduction 50–79%, symptoms alleviated), and ineffective (NRS reduction < 50%). The overall effective rate was calculated as (markedly effective + effective) / total number of cases × 100%.

2.3.2. Pain and joint function scores

Assessments were performed pre- and post-treatment. Pain was quantified via the Numerical Rating Scale (NRS, score range 0–10, where higher values denote more intense pain) [6], while joint function was assessed with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, score range 0–96, where higher scores reflect greater functional impairment).

2.3.3. Serum inflammatory cytokine level

Fasting blood samples (5 mL) were collected pre- and post-treatment. Following centrifugation at 3000 rpm for 15 minutes, serum concentrations of IL-1β and IL-6 were quantified using enzyme-linked immunosorbent assay (ELISA).

2.3.4. Quality of life score

The quality of life of patients was evaluated using the Short Form Health Survey (SF-36) both at baseline and following the completion of treatment [7]. Scores on this instrument span from 0 to 100, where elevated scores correspond to a more favorable quality of life.

2.4. Statistical methods

Statistical analysis was performed with SPSS software (version 26.0). Continuous variables, presented as mean ± standard deviation (SD), were compared using *t*-tests. Categorical variables, expressed as *n* (%), were analyzed with chi-square tests. A *P*-value of less than 0.05 was defined as statistically significant.

3. Results

3.1. Comparison of clinical efficacy between the two groups

The study group demonstrated a significantly higher overall response rate compared to the control group ($P < 0.05$), as detailed in **Table 1**.

Table 1. Comparison of clinical efficacy between the two groups [*n* (%)]

Group	Markedly effective	Effective	Ineffective	Total effective rate
Control group (*n* = 43)	15 (34.88)	17 (39.53)	11 (25.58)	32 (74.42)
Study group (*n* = 43)	24 (55.81)	16 (37.21)	3 (6.98)	40 (93.02)
χ^2-value				5.460
P-value				0.019

3.2. Comparison of NRS and WOMAC scores before and after treatment between the two groups

After the intervention, patients in the study group demonstrated significantly lower NRS and WOMAC scores compared to those in the control group ($P < 0.05$). Details are provided in **Table 2**.

Table 2. Comparison of NRS and WOMAC scores before and after treatment between the two groups (mean ± SD, points)

Group	NRS pain score		WOMAC index (points)	
	Before treatment	After treatment	Before treatment	After treatment
Control group (*n* = 43)	6.89 ± 1.02	3.62 ± 0.73	68.92 ± 7.56	45.89 ± 6.34
Study group (*n* = 43)	6.92 ± 1.05	2.15 ± 0.58	69.34 ± 7.62	32.67 ± 5.21
t-value	0.134	10.339	0.257	10.564
P-value	0.893	0.000	0.798	0.000

3.3. Comparison of serum IL-1β and IL-6 levels before and after treatment between the two groups

Following treatment, the study group exhibited a significant reduction in IL-1β and IL-6 levels compared to the control group ($P < 0.05$). Details are presented in **Table 3**.

Table 3. Comparison of serum IL-1β and IL-6 levels before and after treatment between the two groups (mean ± SD, pg/mL)

Group	IL-1β (pg/mL)		IL-6 (pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment
Control group (*n* = 43)	8.62 ± 1.35	5.31 ± 1.02	32.56 ± 4.28	21.45 ± 3.16
Study group (*n* = 43)	8.58 ± 1.41	3.25 ± 0.86	32.49 ± 4.35	14.28 ± 2.89
t-value	0.134	10.125	0.075	10.979
P-value	0.893	0.000	0.940	0.000

3.4. Comparison of quality of life scores before and after treatment between the two groups

After the intervention, the study group demonstrated significantly higher SF-36 scores compared to the control group ($P < 0.05$). For detailed results, refer to **Table 4**.

Table 4. Comparison of quality of life scores before and after treatment between the two groups (mean ± SD, points)

Group	SF-36 score (points)	
	Before treatment	After treatment
Control group (n = 43)	52.34 ± 5.67	68.45 ± 5.89
Study group (n = 43)	52.67 ± 5.72	82.35 ± 6.12
t-value	0.269	10.731
P-value	0.789	0.000

4. Discussion

The core pathogenesis of KOA involves cartilage degradation mediated by inflammatory factors. IL-1β can activate matrix metalloproteinases (MMPs) to accelerate the degradation of cartilage matrix and inhibit the synthesis of proteoglycans by chondrocytes. As a key pro-inflammatory factor, IL-6 can amplify the inflammatory response and promote synovial hyperplasia and osteophyte formation. PRP contains platelets at a concentration 3 to 5 times higher than normal levels. Upon activation, it releases growth factors such as PDGF and TGF-β, which promote chondrocyte proliferation and repair while inhibiting synovial inflammation. Sodium hyaluronate supplements the viscoelasticity of joint synovial fluid, reducing friction and protecting cartilage [8]. TCM considers KOA to be a condition of "deficiency in the root and excess in the manifestation." In this study, the hot compress package demonstrates effects of warming and unblocking meridians, dispersing cold, and relieving pain: the warm-natured herbs *Evodia rutaecarpa* and *Perilla frutescens* seeds, combined with the thermal effect of the hot compress package, can dispel local cold, unblock meridians, and alleviate joint pain and stiffness caused by "cold coagulation and qi stagnation" and "meridian obstruction." Additionally, it has effects of promoting qi circulation and resolving phlegm, reducing swelling and dispersing nodules: stir-fried *Brassica alba* seeds and *Raphanus* seeds can regulate qi, resolve phlegm, eliminate food stagnation, and reduce bloating, aiding in the relief of swelling and effusion around the joints and alleviating local conditions of "phlegm-dampness and blood stasis obstruction." Cuscutae seeds nourish the liver and kidneys, strengthen tendons and bones, enhancing the repair capacity of tissues around the joints, making them suitable for joint discomfort associated with liver and kidney deficiency.

The findings of this study demonstrate a significantly higher overall treatment efficacy in the study group compared to the control group, indicating that the combined therapeutic regimen can markedly improve clinical outcomes. The analysis attributes this to the dual effects of warmth and pharmacology produced by the TCM hot compress pack in the study group: on one hand, it improves blood circulation around the patient's knee joint; on the other hand, it ensures the even distribution and full absorption and utilization of PRP and sodium hyaluronate in the knee joint cavity, further promoting repair of cartilage damage and exerting anti-inflammatory effects [9]. Additionally, after penetrating the skin and entering the body, the TCM herbs can directly inhibit the inflammatory response of the synovial tissue, achieving effects of promoting blood circulation to remove blood stasis, unblocking meridians, and relieving pain, thereby enhancing treatment efficacy.

In this investigation, the post-treatment NRS scores and WOMAC indices were markedly reduced in the study group compared to those in the control group. The analysis attributes this to the fact that the various growth factors released by PRP possess anti-inflammatory and regenerative properties, while hyaluronic acid can reduce

friction between joint surfaces. The hot compress therapy with TCM herbal packs can achieve the goals of dilating blood vessels and accelerating blood circulation through temperature stimulation, thereby relieving muscle fiber tension, blocking the transmission of pain signals, and exerting effects of promoting blood circulation, removing blood stasis, and relieving pain [10]. The improvement in joint function is closely related to cartilage repair, inflammation resolution, and pain relief. The combined treatment effectively improves symptoms such as knee stiffness and limited mobility through multifaceted regulation, thereby enhancing joint function.

After treatment, the serum concentrations of IL-1β and IL-6 in the study group were markedly reduced compared to those in the control group. This may be attributed to the high platelet content in PRP, which, when activated, secretes multiple growth factors including platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and insulin-like growth factor-1 (IGF-1). PDGF can promote chondrocyte proliferation and matrix synthesis, while TGF-β can inhibit synovial inflammation and reduce the secretion of inflammatory factors. The active ingredients in Angelicae Sinensis Radix and Chuanxiong Rhizoma can inhibit the expression of inflammatory factors IL-1β and IL-6, while olibanum and myrrh can inhibit prostaglandin synthesis and relieve pain. Combined with sodium hyaluronate, they can achieve a dual effect of "anti-inflammation + repair" and synergistically improve joint function.

The quality of life scores were significantly higher in the study group compared to the control group, reflecting an overall improvement in clinical outcomes. Since the daily activities of KOA patients are severely affected and restricted, and the long-term suffering from the disease also imposes a tremendous mental burden on them, the low quality of life in KOA patients is the result of multiple factors working together. Comprehensive treatment approaches can effectively reduce pain and improve the functional level of joints in KOA patients, thereby enabling rapid physiological recovery, enhancing social participation, and subsequently improving psychological well-being and quality of life.

5. Conclusion

In summary, the combined therapeutic approach involving intra-articular injections of PRP and sodium hyaluronate, together with the external application of TCM heat-retaining herbal packs, effectively lowers serum IL-1β and IL-6 levels in patients with KOA. This regimen not only relieves pain and improves joint mobility but also enhances patients' overall quality of life. The treatment demonstrates significant clinical effectiveness and a favorable safety profile, supporting its broader adoption in clinical practice.

Disclosure statement

The authors declare no conflict of interest.

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