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Original Article

Clinical efficacy of platelet-rich plasma combined with arthroscopic meniscal plasty on pain, function and physiologic indicators in elderly patients with knee meniscus injury: a retrospective observational study

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Abstract: Objective: To explore the clinical efficacy of platelet-rich plasma (PRP) combined with arthroscopic meniscal plasty on meniscus injury of the knee joint in the elderly. Methods: Fifty-six elderly patients with meniscus injuries were evaluated, including 28 patients who underwent arthroscopic meniscal repair and 28 patients who underwent arthroscopic meniscus repair combined with PRP injection. Primary outcomes included visual analogue scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Lysholm score, Lequesne index, Range of motion (ROM), and secondary outcomes included bone gla-protein (BGP), insulin-like growth factor-1 (IGF-1), and matrix metalloproteinase-1 (MMP-1). The primary and secondary measurement outcomes were assessed for each patient before and after the 12 weeks of treatment. Results: The VAS, WOMAC, Lysholm, Lequesne, and ROM were more improved in the PRP group compared to the control group (all $P < 0.05$). BGP, IGF-1, and MMP-1 were more reduced in the PRP group compared to the control group (all $P < 0.05$). Conclusion: The treatments of PRP combined with arthroscopic meniscal plasty can significantly improve the pain, function, and physiologicindicators in elderly patients.

Keywords: Platelet-rich plasma, knee joint, knee meniscus injury, arthroscopic meniscal plasty

Introduction

The meniscus is a vital component of the knee joint that performs several biological functions, including joint stabilization and stress absorption [1]. Meniscal injury is a frequently diagnosed problem that results in functional discomfort or degenerative changes to the knee joint, eventually leading to osteoarthritis and reducing the ability of the patient to carry out daily activities [2]. According to research, the prevalence of meniscal injuries in the knee joint in the elderly is increasing yearly, and the age is getting younger [3]. Therefore, the clinical focus is to heal the knee meniscal injury and improve knee functional recovery.

Surgical and conservative methods are typically considered after meniscal cartilage damage. Arthroscopic technology has advanced rapidly along with medical therapy, and it is now routinely used in the treatment of knee meniscal damage, and may aid in the recovery of knee range of motion and function [4]. However, even after arthroscopic surgery, a significant number of patients experience pain and dysfunction [5]. In addition, the regeneration and repair of articular cartilage are poor, hastening the progression of knee osteoarthritis [6, 7]. According to Medicare and Humana databases [8], 4.79%-9.47% of patients undergo revision arthroscopy or conversion to total knee arthroplasty (TKA) within a year after isolated meniscectomy.

Arthroscopy has several technical limitations and risks of recurrence that needs more research.

Platelet-rich plasma (PRP) has recently gained attention in the treatment of patients with knee osteoarthritis. Several studies have used PRP in a variety of settings, demonstrating its potential for cell proliferation through its receptor role [9, 10]. Intra-articular injections of PRP have been utilized to treat meniscal injuries of the knee joint, and it has been demonstrated to have a beneficial therapeutic effect [11]. Furthermore, intra-articular PRP injection has been shown to promote cartilage formation and prevent knee joint rupture [12]. PRP contains a high concentration of growth factors that promote tissue healing and repair, which is why clinical surgeons are interested in it [13]. In clinical practice, knee meniscus damage is considered to be healed in 12 weeks, allowing patients to resume normal activities [14]. Furthermore, the serum levels of BGP, IGF-I, and MMP-1 can be used as a sensitivity index to evaluate the severity of the disease [15]. Therefore, a 12-week follow-up study on the physiologic efficacy of PRP for the treatment of meniscal damage is required. This article introduces a completely new way to use PRP after arthroscopic surgery, which promotes meniscal regeneration and repair and can greatly improve the postoperative clinical efficacy. According to a literature review, such a study has not been done before. The purpose of this study was to evaluate the effect of arthroscopic surgery combined with PRP on the inflammatory factors in treatment of meniscus injury in elderly patients.

Materials and methods

Study design and patient inclusion

This study was approved by the ethics committee of the First Affiliated Hospital, Hengyang Medical School, University of South China (approval number: 2023U0220002) and adopted a retrospective cohort design. Through the electronic medical record system, 56 patients who underwent arthroscopic meniscus plasty in the First Affiliated Hospital, Hengyang Medical School, University of South China from January 2021 to March 2022 were selected according to the following.

Inclusion criteria: (1) Patients of an age 65 to 75; (2) Patients with meniscal injury caused by long standing meniscus and cartilage wear or joint degradation; (3) Patients had arthroscopic repair with or without PRP after the failure of conservative treatment; (4) Patients with different degrees of knee pain, limited movement and other clinical symptoms; (5) Patients with complete case records.

Exclusion criteria: (1) Patients with congenital meniscus disease or developmental malformation; (2) Patients who also have osteoarthritis or neurovascular injury; (3) Patients with operative contraindications; (4) Patients with end-stage heart, brain or renal dysfunction; (5) Patients with blood system diseases; (6) Patients with diabetes, rheumatic diseases or severe cardiovascular and cerebrovascular diseases; (7) Patients with collateral ligament injury, intra-articular ligament injury or severe osteoarticular degeneration. The participants were recruited and divided into a PRP group and a control group, with 28 patients in each (**Table 1**). There were no significant differences in general data between the two groups ($P > 0.05$).

Data collection

Preoperative data of eligible patients, including age (years), sex (male/female), K-L grade (2/3), BMI (kg/m^2), hypertension, duration of disease, surgical time (min), drinking history, coagulation dysfunction, hypoalbuminemia, anesthesia time (min), coronary artery disease, and diabetes mellitus were collected from the patient records.

Treatment methods

Control group

Patients in the control group received arthroscopic meniscus plasty alone (**Figure 1**). (1) Patients were positioned supine. Following anesthesia, an incision was made in the outer upper part of the patella and the gap between the femoral lateral condyle, and 300 mL normal saline was injected into the suprapatellar capsule of the knee joint to make it dilate; (2) Arthroscope was placed, and the medial or lateral knee space was observed with the aid of the arthroscope to perceive the meniscus.

Table 1. Characteristics of patients

Group	PRP (n = 28)	CON (n = 28)	t/X^2	*p*
Age (years)	69.96 ± 4.02	69.50 ± 4.94	0.386	0.701
Sex (male/female)	14/14	13/15	0.071	0.789
K-L Grade (2/3)	16/12	15/13	0.072	0.788
Body Mass Index (kg/m^2)	26.91 ± 3.48	27.75 ± 3.08	-0.946	0.348
Hypertension	129 ± 5.03	128 ± 4.32	0.876	0.543
Duration of disease	20 ± 5.16	21 ± 6.38	0.443	0.676
Surgical time (min)	76 ± 5.21	75 ± 2.58	0.953	0.744
Drinking history	5/23	6/22	-0.843	0.727
Coagulation dysfunction	6/22	7/21	-0.753	0.567
Hypoalbuminemia	4/24	4/24	-0.357	0.434
Anesthesia time (min)	85 ± 5.35	83 ± 5.25	0.563	0.845
Coronary artery disease	4/24	5/23	-0.987	0.432
Diabetes mellitus	7/21	6/22	0.554	0.632

PRP, Platelet-rich plasma; CON, Control.

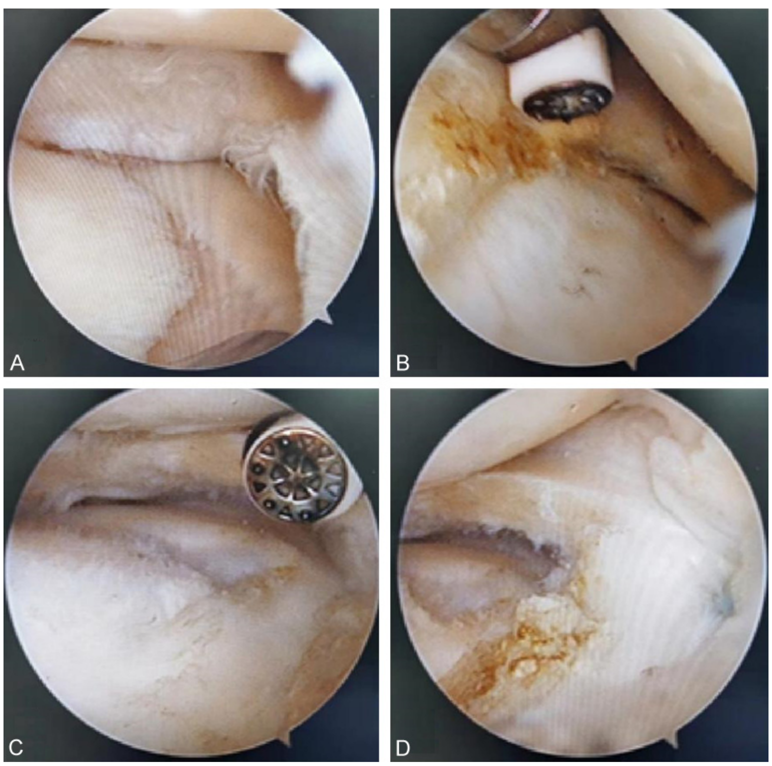

Figure 1. Arthroscopic image of the knee joint. A. Meniscal tear with complex and severe injury (K-L Grade 3). B and C. Arthroscopic image of intraoperative meniscus plasty. D. Arthroscopic image after partial meniscectomy.

According to the injury type and location, the surgical method was confirmed under the microscope; (3) Blue forceps were used to bite the damaged edge, and a planer was used to repair the stump, and the meniscus was appropriately excised to remove joint lesions and free bodies. The joint cavity was examined at the end of the operation to avoid debris, and a cotton pad was used after compression dressing; (4) Following surgery, the knee joint was treated with ice and antibiotics.

PRP group

Patients in the PRP group received additional PRP: (1) The operative area was disinfected after anesthesia, and 25 mL of venous blood was collected and mixed with 3 ml of sodium citrate injection for anticoagulation; (2) PRP was prepared by two centrifugations. The blood was separated into serum, white membrane, and red blood cell layers during the first centrifugation, which was performed at a speed of 2,000 r/min for 10 minutes with a centrifugal radius of 15.5 cm; (3) The second centrifugation was performed for 10 minutes at a speed of 2,200 r/min, and it separated the platelet-deficient plasma layer and a PRP layer by absorbing red blood cells from the white blood cell layer obtained in the first centrifugation process; (4) 5 mL of PRP was extracted and injected into the injured joint cavity; (5) The knee joint was treated with ice and antibiotics after surgery.

<u>*Primary outcomes*</u>

Visual Analogue Scale (VAS): The VAS was used to evaluate the degree of pain sensation, with a score of 0 indicating no pain and 10 representing unbearable pain [16].

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): The WOMAC was used to evaluate pain, stiffness, and physical function, with lower scores indicating better physical condition [17].

Lysholm Scale: The Lysholm scale includes functional items such as claudication, support, locking, pain, instability, swelling, stair climbing, and squatting. The total score ranges from 0 to 100, with higher scores indicating better knee joint function [18].

Lequesne Index: The Lequesne index includes 10 items related to pain or discomfort, longest walking distance, and daily life dysfunction. It is used for patients with chronic knee osteoarthritis and takes approximately 3 to 5 minutes to measure [19].

Range of Motion (ROM): A plastic goniometer was used to measure the maximum motion of the knee joint [20].

These measures have been widely used in clinical practice and have been shown to have good reliability and validity in assessing joint pain, function, and quality of life in previous research, thus allowing for a comprehensive understanding of the effects of intervention. In addition, the measurement methods for these outcomes are relatively simple and easy to implement in practice, without imposing excessive burden on patients or researchers.

<u>*Secondary outcomes*</u>

Bone gla-protein (BGP), insulin-like growth factor-1 (IGF-1), and matrix metalloproteinase-1 (MMP-1) were measured for each patient before and after 12 weeks of treatment. After admission, before treatment, and 12 weeks after treatment, 3 ml of articular fluid was extracted from each subject and stored in an ultra-low temperature refrigerator at -80°C for subsequent detection. BGP, IGF-1, and MMP-1 levels were measured using an enzyme-linked immunosorbent assay (ELISA) [21] (lot no.: ab26; Wuhan Bau Bioengineering Co., LTD.).

Statistical analysis

SPSS 23.0 software (SPSS Inc., Chicago, IL, USA) was used. The measured data conforming to a normal distribution were expressed as mean (M) ± standard deviation (SD) and compared between groups using a t-test. The counted data were expressed in case (%), and compared using a Chi-square test. $P < 0.05$ was considered significant.

Results

Primary outcomes

The primary outcomes are shown in **Table 2**. The VAS, WOMAC, Lysholm score, Lequesne score, and ROM were improved significantly in both the PRP group and the control group (all $P < 0.05$); in addition, the improvements in the PRP group were greater (all $P < 0.05$).

Secondary outcomes

The secondary outcomes are shown in **Table 3**. The BGP, IGF-1, and MMP-1 were decreased significantly in both the PRP group and the control group ($P < 0.05$). In addition, the levels of BGP, IGF-1, and MMP-1 were significantly lower in the PRP group than in the control group after 12 weeks of treatment (all $P < 0.05$).

Discussion

Meniscal injury is common and limits various biological functions such as femur concussion, lubrication, and joint stabilization, and seriously affects patients' work and life [22]. Therefore, the key to knee meniscal injury is to preserve the normal tissue and repair the damaged part as much as possible to restore the function of the knee joint [23].

The main finding of this study is that PRP combined with arthroscopic meniscal plasty treatment improved the clinical efficacy of elderly patients more effectively than arthroscopy alone.

Arthroscopic meniscus plasty is regarded as one of the most effective treatments for knee meniscal injury [24]. Although symptoms such

Table 2. Primary outcomes before and after treatment

Variable		PRP (n = 28)	CON (n = 28)	*t*	*p*
Visual Analog Scale (mm)	Pre	6.89 ± 0.45	6.87 ± 0.67	0.104	0.918
	Post	1.05 ± 0.16	2.38 ± 0.28	-21.181	0.000*
	t	65.544	36.241		
	p	0.000†	0.000†		
Western Ontario and McMaster Universities Osteoarthritis Index (score)	Pre	77.18 ± 3.62	76.76 ± 3.51	0.438	0.663
	Post	52.46 ± 4.11	62.91 ± 3.14	-10.682	0.000*
	t	21.5	13.459		
	p	0.000†	0.000†		
Lysholm (score)	Pre	50.33 ± 3.43	50.17 ± 3.32	0.187	0.852
	Post	82.31 ± 5.31	79.10 ± 5.24	2.275	0.027*
	t	-26.325	-28.426		
	p	0.000†	0.000†		
Lequesne (score)	Pre	16.09 ± 1.29	16.35 ± 1.50	0.677	0.502
	Post	12.26 ± 1.18	13.64 ± 1.31	-4.128	0.000*
	t	11.098	7.904		
	p	0.000†	0.000†		
Range of Motion (°)	Pre	90.79 ± 6.68	91.85 ± 5.73	0.638	0.526
	Post	118.55 ± 7.87	109.81 ± 5.51	4.815	0.000*
	t	-12.185	-13.684		
	p	0.000†	0.000†		

Independent t-test: *$P < 0.05$. Paired t-test: †$P < 0.05$. PRP, Platelet-rich plasma; CON, Control.

Table 3. Secondary outcomes before and after treatment

Variable		PRP (n = 28)	CON (n = 28)	*t*	*p*
Bone Gla Protein (ng/ml)	Pre	17.61 ± 1.33	17.38 ± 1.56	0.59	0.588
	Post	9.99 ± 1.75	12.83 ±1.23	-7.028	0.000*
	t	17.147	11.354		
	p	0.000†	0.000†		
Insulin-like Growth Factor 1 (ng/ml)	Pre	15.54 ± 1.34	15.59 ± 1.41	0.155	0.877
	Post	10.09 ± 1.31	11.31 ± 1.27	-3.706	0.000*
	t	12.36	13.37		
	p	0.000†	0.000†		
Metalloproteinase 1 (ng/ml)	Pre	16.10 ± 1.40	16.58 ± 1.55	-1.205	0.234
	Post	9.63 ± 1.14	10.78 ± 1.54	-3.172	0.002*
	t	17.378	17.303		
	p	0.000†	0.000†		

Independent t-test: *$P < 0.05$. Paired t-test: †$P < 0.05$. PRP, Platelet-rich plasma ; CON, Control.

as pain and functional limitation can be successfully treated by meniscal arthroscopic surgery, it can easily damage cartilage tissue during treatment, reducing the effectiveness of surgical treatment [25]. Clinical therapy would become more difficult if the cartilage tissue injury worsened because this could lead to articular cartilage degeneration [26]. Biological studies have shown that the dispersion force disappears after meniscectomy, and direct contact occurs between the femoral malleolus and tibial plateau [27, 28]. The surface stress will gradually increase, which can lead to degeneration of the knee joint [29]. Studies have confirmed that the probability of degenerative changes in the affected knee after partial meniscectomy is four to six times that of the healthy side of the knee joint [30]. Therefore, preserving the meniscus as much as possible has become a mainstream concept and surgical principle of meniscus treatment. Arthroscopic meniscus suturing can effectively reconstruct the specific anatomic structure and shape of the meniscus, and finally, restore the function of the meniscus. An arthroscopic suture is more helpful to alleviate damage to articular cartilage and can delay the process of secondary osteoarthritis of the knee joint to some extent [31]. According to the literature, the formation of synovial tissue and meniscus originates from mesenchymal cells together. They have a similar blood supply and have certain repair abilities. If the synovial tissue flap is inserted into the white area of the meniscus during repair of the tear, chondroid recovery is obvious, which proves its effectiveness [32]. Apart from specific excision and repair, tissue engineering repair technology has recently emerged as a treatment method. Specifically, tissue engineering repair technology is used to repair the meniscus structure that includes three main parts, namely seed cells, biologic factors, and meniscus scaffold. The biologic factors can fully induce seed cells to differentiate into related chondrocytes. These include fibrocyte growth factor, transforming growth factor, insulin-like growth factor, and platelet-derived growth factor [33]. PRP is a blood product created by centrifuging a patient's own blood, with a platelet concentration 3-8 times that of whole blood platelets [34], and it can release a significant number of endogenous growth factors, making it a valuable source of growth factors [35]. PRP has been shown in animal experiments to significantly increase meniscus cell activity, and it contains fibrin, which acts as a scaffold for meniscus healing [36]. Furthermore, PRP plays an important role in facilitating tissue repair and regeneration after injury [37]. In this study, PRP gel was used to suture the meniscus injury site and the PRP gel was used independently after arthroscopic meniscus plasty. PRP can reduce pain and inflammation by accelerating tissue repair through various growth factors [38, 39]. Scientific studies have confirmed that PRP plays an important role in promoting articular cartilage healing and bone tissue regeneration [40]. According to relevant scientific conclusions, its specific mechanism of action is as follows: PRP can be fully mixed with thrombin, calcium chloride or matrix normal saline to form a gel, in which platelet particles contained in PRP can release a variety of growth factors that play a role [41]. Platelet activation occurs 10 minutes after the end of the clotting process, and its pre-synthesized growth factors can be secreted within one hour. After the initial mass release of growth factors, platelets begin to synthesize and secrete additional factors, such as inflammatory cytokines. In addition, platelets are easily activated during agglutination, and relevant particles are fully fused and mixed with platelets by effectively adding histone and enzyme side chain components to make them active. At the same time, growth factors can effectively bind to the outer surface of cell membranes through transmembrane receptors to induce the division and differentiation of mesenchymal stem cells and endothelial cells, and finally promote the regeneration and healing of bone tissue [42]. The growth factors secreted by PRP have been proven to have good biologic function, and are conducive to recovery. The use of PRP improved WOMAC, Lysholm, Lequesne, and ROM in this study. Moreover, the patient's knee range of motion and knee function scores were improved. The VAS score of patients treated with arthroscopic meniscoplasty combined with PRP was lower than that of patients treated with arthroscopic meniscoplasty alone. This suggests that combined therapy can effectively relieve the symptoms of joint pain and promote recovery of knee function. The results of this study show that PRP combined therapy has significantly greater therapeutic effect on knee joint pain and function than arthroscopy alone.

BGP is a regulating hormone that is secreted by osteoblasts and osteoclasts and functions as a physiologic signal of bone conversion [43]. Serum osteocalcin levels increased significantly when bone turnover increased; otherwise, they decreased [44]. IGF-1 can stimulate the growth of preosteoblasts, which then mature into osteoblasts, allowing bone mass to remain balanced. The expression of IGF-1 is closely related to growth hormone [45]. Furthermore, IGF-I has anti-inflammatory and anti-aging properties that may protect the endothelium [46]. MMP-1 is a member of the MMP family that can pass through the degradation barrier. Articular cartilage fibers are lost as a result of collagen and proteoglycan degradation, resulting in cartilage damage [47]. BGP, IGF-1, and

MMP levels were significantly lower in the PRP group than the control groups in this study. This might be because activated platelets in PRP can produce a variety of growth factors and inflammatory regulators to maintain the metabolic balance of articular cartilage. These findings suggest that PRP combined with arthroscopic meniscal plasty may regulate BGP, IGF-1, and MMP-1 levels, protect chondrocytes, and promote cartilage regeneration in elderly patients. However, the sample size in this study is small, and the follow-up period is short. In the future, conducting studies with large sample size and a long follow-up period may improve the reliability.

Conclusion

PRP combined with arthroscopic meniscal plasty is more effective than arthroscopic meniscal plasty alone for improving not only pain but also clinical efficacy. This approach can be recommended for clinical use because it can improve patients' symptoms in a short period and has some clinical value for patients with mild meniscus lesions or who are delaying knee replacement.

Disclosure of conflict of interest

None.

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