Clinical Trial/Experimental Study

Medicine

OPEN

The combined application of pulsed electromagnetic fields and platelet-rich plasma in the treatment of early-stage knee osteoarthritis
A randomized clinical trial

Rong-da Xu, MM[a], Jia-hui Li, BM[a], He Zhang, MM[a], Hai-rui Liang, MM[a], Si-yu Duan, MM[a], Ming Sun, MM[a], Hang Wen, MM[a], Xue-ting Zhou, MM[a], Han-fei Liu, MM[a], Zhen-cun Cai, MD[a,b,*]

Abstract

Background: This study aims to evaluate the therapeutic efficacy of combined treatment with pulsed electromagnetic fields (PEMFs) and platelet-rich plasma (PRP) injection in improving pain and functional mobility among patients with early-stage knee osteoarthritis (KOA). We hypothesize that this combined therapy can yield superior treatment outcomes.

Methods: Based on the different treatment regimens, we divided 48 patients diagnosed with Kellgren-Lawrence grades I-III KOA into 3 groups: the PRP group, the PEMFs group, and the PRP + PEMFs group. Each subtype of KOA patients was randomly assigned to different treatment groups. In the PRP group, patients received intra-articular injections of leukocyte-rich platelet-rich plasma once a month for 3 consecutive months. In the PEMFs group, patients receive low-frequency PEMFs irradiation therapy with a frequency of 30 Hz and intensity of 1.5 mT, once daily, 5 times a week, for a consecutive treatment period of 12 weeks. In the PRP + PEMFs group, patients receive both of the aforementioned treatment protocol. The treatment effects on patients are evaluated at baseline and at weeks 4, 8, and 12 post-treatment. Assessment parameters include visual analog scale for pain, Western Ontario and McMaster Universities Osteoarthritis Index, Lequesne Index score, and knee joint range of motion.

Results: From the 4th to the 12th week of treatment, the visual analog scale scores, Western Ontario and McMaster Universities Osteoarthritis Index scores, and Lequesne index scores of patients in all 3 groups gradually decreased, while knee joint mobility gradually increased ($P < .05$). At weeks 4, 8, and 12 after treatment, the PRP combined with PEMFs group showed significantly better scores compared to the PRP group and the PEMFs group, with statistically significant differences ($P < .05$). A total of 7 patients experienced adverse reactions such as knee joint swelling, low-grade fever, and worsening knee joint pain after treatment, all of which disappeared within 1 week after treatment. The incidence of complications did not differ significantly among the 3 groups ($P = .67$).

Conclusion: PRP, PEMFs, and the combination of PRP and PEMFs therapy all effectively alleviate knee joint pain and improve joint function. However, compared to single treatment modalities, the combined therapy of PRP and PEMFs demonstrates more pronounced efficacy.

Abbreviations: K-L = Kellgren-Lawrence, KOA = knee osteoarthritis, LP-PRP = leucocyte-poor platelet-rich plasma, PEMFs = pulsed electromagnetic fields, PRP = platelet-rich plasma, VAS = visual analog scale, WOMAC = Western Ontario and McMaster Universities.

Keywords: knee osteoarthritis, platelet-rich plasma, pulsed electromagnetic fields

This research was supported by the Science and Technology Plan Project of Shenyang City (project no. 22-321-32-13), the Liaoning Provincial Department of Education Fund Project (project no. JYTMS20231396), and the Science and Technology Fund of the Education Department of Liaoning Province (project no. 2024).

Informed consent was obtained from the patients.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

All procedures adhere to the ethical standards of the institution and/or the national research committee. This study obtained approval from the Ethics Committee of Shenyang Medical College Affiliated Central Hospital (no. 20190020).

[a] Department of Orthopedics Surgery, Central Hospital Affiliated to Shenyang Medical College, Shenyang, China, [b] Key Laboratory of Human Ethnic Specificity and Phenomics of Critical Illness in Liaoning Province, Shenyang Medical College, Shenyang, China.

** Correspondence: Zhen-cun Cai, Department of Orthopedics Surgery, Central Hospital Affiliated to Shenyang Medical College, 5 Nanqi West Road, Shenyang, Liaoning 110024, China (e-mail: sychczc@163.com).*

How to cite this article: Xu R-d, Li J-h, Zhang H, Liang H-r, Duan S-y, Sun M, Wen H, Zhou X-t, Liu H-f, Cai Z-c. The combined application of pulsed electromagnetic fields and platelet-rich plasma in the treatment of early-stage knee osteoarthritis: A randomized clinical trial. Medicine 2024;103:35(e39369).

Received: 22 November 2023 / Received in final form: 29 July 2024 / Accepted: 30 July 2024

http://dx.doi.org/10.1097/MD.0000000000039369

1. Introduction

Knee osteoarthritis (KOA) is a chronic degenerative joint disease caused by multiple factors, characterized by gradual softening and loss of joint cartilage, accompanied by subchondral bone sclerosis, synovitis, and osteophyte formation.[1,2] The eventual deformation of joint tissues is the primary cause of pain and functional disability, and sometimes surgical intervention may be necessary for intervention.[3] In the late stages of disease progression, joint replacement surgery is often necessary, and while it is an effective treatment option, it is not without complications.[4] Up to 30% of patients undergoing joint replacement surgery are dissatisfied with their postoperative daily activities, pain relief, and knee joint function. Therefore, it is crucial to identify alternative safe and effective treatment methods to joint replacement.[5,6] There are currently many conservative treatment options in clinical practice, such as oral and topical nonsteroidal anti-inflammatory drugs, intra-articular corticosteroid injections, and physical therapy.[7] Although these treatment modalities have their place in clinical practice, we still need to continuously develop new therapies or optimize existing ones.

In recent years, platelet-rich plasma (PRP) intra-articular injection therapy and pulsed electromagnetic fields (PEMFs) treatment, representing intra-articular therapy and physical therapy respectively, have been applied in clinical treatment of KOA. Studies have shown that both PRP and PEMFs have beneficial effects on the treatment of mild to moderate osteoarthritis patients.[8–11] PRP is plasma rich in platelets, in which the platelet content is enriched above normal levels through centrifugation and other processing methods, to obtain therapeutic blood components.[12] PRP contains abundant growth factors and cytokines, which are typically released by platelets after tissue injury, and may play a role in regulating tissue structural protection and regeneration processes.[8,13] PRP is considered to have the potential to promote tissue repair and regeneration due to its rich content of growth factors and other biologically active components. Therefore, it is widely used in medicine for treating various diseases or tissue injuries.

As a noninvasive physical method, PEMFs directly act on body tissues by generating specific frequencies and intensities of electromagnetic fields without the need for electrode implantation within the body. This microcurrent can be conducted through the body's tissues systemically or delivered to specific local tissues through targeted delivery methods.[14] It can be used for the treatment of diseases such as osteoarthritis, fracture repair, inflammation relief, and vascular regeneration.[15,16] The application of PEMFs is believed to stimulate intracellular metabolic activity, regulate cell functions, and promote cellular healing and regenerative abilities, which can play a positive role in the treatment process of these diseases.[17]

Although previous studies have demonstrated certain efficacy of treatments such as PRP or PEMFs for KOA, there are still some patients whose symptoms do not improve significantly after receiving treatment, suggesting that the current treatment protocols may have certain limitations. Therefore, optimizing treatment protocols has become a hot topic of research. Currently, there is a lack of related studies on the combined treatment of KOA with PRP and PEMFs in clinical practice. Therefore, this study proposes to use the combined treatment of PRP and PEMFs for early-stage KOA patients as an immediate treatment option to bridge the gap between conservative and surgical treatments. The initial hypothesis of this study is that patients will experience relief in knee osteoarthritis symptoms after the combined application of PRP and PEMFs. Additionally, we will explore the clinical efficacy of combined treatment in improving joint mobility function, aiming to optimize treatment protocols, enhance clinical therapeutic effects, and provide better treatment options for patients.

2. Materials and methods

2.1. Participants

The study subjects were selected from patients diagnosed with knee osteoarthritis who were admitted to the department of orthopedics at Central Hospital Affiliated to Shenyang Medical College from September 2020 to September 2023.After admission, all patients undergo knee joint X-ray imaging (Netherlands, Philips digital radiography DR system), and classification of KOA is performed according to the Kellgren-Lawrence grading system.[18] The inclusion criteria are as follows: age ≥ 40 years old; Kellgren-Lawrence (K-L) grade I to III; knee joint pain ≥ 3 months; BMI < 30 kg/m^2; Platelet count ≥ 150,000/μL; acceptance of any treatment regimen according to the treatment plan; and patients voluntarily participate in the study and sign an informed consent form. The exclusion criteria are as follows: presence of bleeding disorders or undergoing anticoagulant therapy; history of or current diagnosis of cancer or tumors; previous knee surgery or planned knee joint surgery; intra-articular injection of corticosteroids or hyaluronic acid into the affected knee within the past 6 months; previous use of any autologous blood products or stem cell preparations; Kellgren-Lawrence grade IV, significant joint space narrowing, and marked deformity; rheumatoid arthritis or psoriatic arthritis; and plasma total cholesterol > 5.18 mmol/L or triglycerides > 1.7 mmol/L.

Based on the aforementioned inclusion and exclusion criteria, we ultimately enrolled 48 patients who met the inclusion criteria to participate in this study. KOA patients of different classifications were randomly assigned to treatment regimens. Patients were divided into 3 groups according to the different treatment modalities, with 16 cases in each group. Sixteen patients receiving PRP treatment were classified into the PRP group, 16 patients receiving PEMFs treatment were assigned to the PEMFs group, and the remaining 16 patients receiving PRP combined with PEMFs treatment were categorized into the PRP + PEMFs group. Data including patients' age, gender, BMI, K-L grade, etc., were recorded for the 3 groups. This study has been approved by the Medical Ethics Committee of Shenyang Medical College Affiliated Center Hospital (approval no.: 20190020). All patients provided verbal or written informed consent. This trial is registered in our hospital's clinical management system. (registry number: PR-XG005-02-OA-01).

2.2. Therapeutic methods

PRP group: The ACP preparation kit from the American company Arthrex was used. A 9-gauge blood drawing needle was attached to draw 15 mL of venous blood from the median cubital vein of the patient and placed in a Drucker Horizon 24 Flex centrifuge for centrifugation. This process was conducted to prepare leucocyte-poor platelet-rich plasma (LP-PRP), from which approximately 4 to 6 mL of LP-PRP was separated and extracted. During injection, the patient was placed in a supine position on the operating table with the knee flexed at 90°and the lower leg hanging naturally. Various bony landmarks around the knee joint were marked on the skin under ultrasound guidance, along with marks on both sides of the patellar ligament. The needle was inserted from the marked point towards the knee joint cavity, ensuring entry into the joint cavity. Bloodless fluid and inflammatory effusion were aspirated upon withdrawal. The prepared PRP was injected smoothly through the PRP injection tube once a month for a total of 3 consecutive injections.

PEMFs group: PEMFs treatment was administered using a pulsed electromagnetic therapy device. Two adjacent coils were placed respectively on the medial and lateral areas of the knee joint, with the gap between the coils positioned at the level of the joint line. The treatment frequency was set at 30 Hz with an intensity of 1.5 mT, administered once daily, 5 times per week, for approximately 20 minutes per session. Each treatment course consisted of 15 sessions, and 3 consecutive treatment courses were administered.

PRP + PEMFs group: PEMFs treatment occurred 1 week after PRP treatment. The treatment procedure in this group was the same as that in the PRP and PEMFs groups. In this study, all patients receiving PRP injections underwent routine blood tests, including complete blood cell count and coagulation function tests, as well as screening for infectious diseases, before injection.

2.3. Efficacy assessment criteria

Before and at weeks 4, 8, and 12 post-treatment, the therapeutic effect of patients was assessed using the visual analog scale (VAS) for pain, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Lequesne Index, and knee joint mobility.

2.4. Sample size estimation

Using the G.Power software program to calculate the sample size. Based on preliminary study results, sample analysis was conducted on the main outcomes of the study (WOMAC and Lequesne scores). Considering a significant decrease in the mean differences of WOMAC and Lequesne scores, the calculated sample size was 16 in each group to compare the mean differences in the 2 main study outcomes, with a significance level of 0.5 and a test power of 80%.

2.5. Statistical analysis

Analysis was conducted using SPSS 27.0 statistical software (Armonk, NY). Continuous data were expressed as mean ± standard deviation. Within-group comparisons before and after treatment were performed using repeated measures analysis of variance (ANOVA), with corrections applied using the Greenhouse-Geisser method. Further simple effects analysis was conducted when there was a statistically significant interaction. Bonferroni correction was applied for comparisons between different time points within each group. For comparisons among multiple groups for categorical variables, one-way ANOVA was used. Comparisons between groups for categorical data such as gender were performed using the chi-square test. The significance level (α) was set at 0.05 for all tests. A P value less than .05 was considered statistically significant in all analyses.

3. Results

3.1. Baseline data

A total of 48 patients were included in this study. The PRP group consisted of 16 patients, including 5 males and 11 females, with a mean age of 55.25 ± 8.15 years. The PEMFs group comprised 16 patients, including 6 males and 10 females, with a mean age of 54.88 ± 6.46 years. The PRP + PEMFs group included 16 patients, including 2 males and 12 females, with a mean age of 55.63 ± 7.51 years. There were no statistically significant differences in gender (P = .75) or age (P = .96) among the 3 groups. According to the K-L grading, there were 12 patients with K-L grade I, 20 patients with K-L grade II, and 16 patients with K-L grade III. Patients with different stages of KOA were randomly assigned to treatment regimens. In the PRP group, 3 patients were K-L grade I, 7 patients were K-L grade II, and 6 patients were K-L grade III. In the PEMFs group, 5 patients were K-L grade I, 6 patients were K-L grade II, and 5 patients were K-L grade III. In the PRP + PEMFs group, 4 patients were K-L grade I, 7 patients were K-L grade II, and 5 patients were K-L grade III. There were no statistically significant differences in K-L grading among the 3 groups (P = .9). Refer to Table 1.

3.2. Results synthesis

Repeated measures analysis of variance was used to assess the effects of different interventions on knee joint function over time. Before treatment, there were no statistically significant differences in VAS scores, WOMAC scores, Lequesne index scores, and knee joint mobility among the 3 groups (P = .827, P = .814, P = .901, P = .955). After treatment at weeks 4, 8, and 12, VAS scores, WOMAC scores, Lequesne index scores, and knee joint mobility were significantly different compared to before treatment (P < .001). From week 4 to week 12 of treatment, VAS scores, WOMAC scores, and Lequesne index scores gradually decreased, while knee joint mobility gradually increased in all 3 groups (P < .001). At weeks 4, 8, and 12 after treatment, the PRP combined with ESWT group showed significantly better scores in all 3 measures compared to the PRP and PEMFs groups, with statistically significant differences observed (P < .05),as shown in Tables 2 to 5.

3.3. Adverse reactions

In this study, none of the 3 groups of patients experienced severe adverse reactions after treatment, and there were no withdrawals from the study due to treatment-related reasons. All adverse events were mild and transient. In the PRP group, 2 patients experienced mild swelling the day after injection, and another patient reported transient low-grade fever after treatment. In the PEMFs group, 1 patient experienced swelling 1 day after treatment, while 2 patients reported exacerbation of osteoarthritis pain. In the combined group, only 1 patient experienced mild swelling symptoms. In all cases, adverse reactions resolved within 1 week after treatment. There were no statistically significant differences in the incidence of complications among the 3 groups (P = .67).

4. Discussion

KOA is a chronic, degenerative joint disease characterized by abnormal joint tissue metabolism leading to anatomical and physiological changes.[3] In this study, PRP and PEMFs were

Table 1

Baseline data of 3 groups of patients.

Group	Sample size (n)	Age (yr)	Gender (n)		BMI (kg/m^2)	K-L grading (n)		
			Male	Female		I	II	III
PRP group	n = 16	55.25 ± 8.15	5	11	25.06 ± 2.52	3	7	6
PEMFs group	n = 16	54.88 ± 6.46	6	10	24.25 ± 3.19	5	6	5
PRP + PEMFs group	n = 16	55.63 ± 7.51	4	12	24.56 ± 3.22	4	7	5
Test value		0.04	0.58		0.3	1.04		
P value		.96	.75		.74	.9		

PEMFs = Pulsed electromagnetic fields, PRP = Platelet-rich plasma.

Table 2

VAS scores at different time points for 3 treatment groups (n = 16, $\bar{x} \pm s$).

Group	Before treatment	4 weeks treatment	8 weeks treatment	12 weeks treatment	*F* value	*P* value
PRP group	8.31 ± 1.01[bc]	7.19 ± 0.91[ac]	6.13 ± 0.89[ab]	5.38 ± 0.81[abc]	79.859	<.001
PEMFs group	8.25 ± 0.78[bc]	6.94 ± 0.77[ac]	5.88 ± 0.72[ab]	5.06 ± 0.68[abc]	94.412	<.001
PRP + PEMFs group	8.44 ± 0.81[bc]	5.13 ± 0.96[ac]	3.44 ± 0.73[ab]	2.75 ± 0.58[abc]	323.114	<.001
F value	0.191	25.97	57.847	68.256		
P value	.83	<.001	<.001	<.001		

F time = 611.481, *P* time < .001; *F* group = 32.333, *P* group < .001; *F* time*group = 37.127, *P* time*group < 0.001. “a” indicates a significant difference compared to before treatment (*P* < .05); “b” indicates a significant difference compared to 4 weeks of treatment (*P* < .05); “c” indicates a significant difference compared to 8 weeks of treatment (*P* < .05). All pairwise comparisons have undergone Bonferroni correction.
PEMFs = pulsed electromagnetic fields, PRP = platelet-rich plasma.

Table 3

WOMAC scores at different time points for 3 treatment groups (n = 16, $\bar{x} \pm s$).

Group	Before treatment	4 weeks treatment	8 weeks treatment	12 weeks treatment	*F* value	*P* value
PRP group	35.88 ± 3.7[bc]	32.56 ± 3.41[ac]	28.19 ± 3.71[ab]	18.62 ± 2.19[abc]	397.086	<.001
PEMFs group	35.06 ± 4.54[bc]	32.69 ± 4.33[ac]	28.94 ± 4.37[ab]	20.88 ± 3.28[abc]	280.783	<.001
PRP + PEMFs group	35.94 ± 4.6[bc]	31.38 ± 2.78[ac]	23.5 ± 2.31[ab]	14.56 ± 2.07[abc]	629.107	<.001
F value	0.206	14.529	10.904	24.777		
P value	.81	<.001	<.001	<.001		

F time = 1666.233, *P* time < .001; *F* group = 3.678, *P* group = 0.03; *F* time*group = 28.963, *P* time*group < 0.001. “a” indicates a significant difference compared to before treatment (*P* < .05); “b” indicates a significant difference compared to 4 weeks of treatment (*P* < .05); “c” indicates a significant difference compared to 8 weeks of treatment (*P* < .05). All pairwise comparisons have undergone Bonferroni correction.
PEMFs = pulsed electromagnetic fields, PRP = platelet-rich plasma.

Table 4

Lequesne index scores at different time points for 3 treatment groups (n = 16, $\bar{x} \pm s$).

Group	Before treatment	4 weeks treatment	8 weeks treatment	12 weeks treatment	*F* value	*P* value
PRP group	10.53 ± 4.03[bc]	9.59 ± 4.10[ac]	8.53 ± 4.21[ab]	7.38 ± 4.04[abc]	18.805	<.001
PEMFs group	10.47 ± 3.66[bc]	9.28 ± 3.57[ac]	8.25 ± 3.46[ab]	7.09 ± 3.47[abc]	22.487	<.001
PRP + PEMFs group	9.97 ± 3.72[bc]	7.59 ± 3.19[ac]	5.34 ± 2.29[ab]	3.63 ± 0.81[abc]	104.693	<.001
F value	0.105	2.817	4.274	7.219		
P value	.9	.01	.02	.002		

F time = 122.218, *P* time < .001; *F* group = 12.336, *P* group < .001; *F* time*group = 13.922, *P* time*group < .001. “a” indicates a significant difference compared to before treatment (*P* < .05); “b” indicates a significant difference compared to 4 weeks of treatment (*P* < .05); “c” indicates a significant difference compared to 8 weeks of treatment (*P* < .05). All pairwise comparisons have undergone Bonferroni correction.
PEMFs = pulsed electromagnetic fields, PRP = platelet-rich plasma.

Table 5

Knee joint mobility at different time points for 3 treatment groups (n = 16, $\bar{x} \pm s$).

Group	Before treatment	4 weeks treatment	8 weeks treatment	12 weeks treatment	*F* value	*P* value
PRP group	98.44 ± 5.69[bc]	100.06 ± 5.58[ac]	101.94 ± 4.77[ab]	103.88 ± 4.66[abc]	40.948	<.001
PEMFs group	98.75 ± 5.92[bc]	99.75 ± 5.92[ac]	101.87 ± 5.67[ab]	103.00 ± 5.50[abc]	33.783	<.001
PRP + PEMFs group	99.06 ± 5.84[bc]	101.69 ± 5.64[ac]	103.81 ± 5.74[ab]	105.63 ± 5.56[abc]	68.777	<.001
F value	0.046	10.172	14.741	23.392		
P value	.97	<.001	<.001	<.001		

F time = 230.605, *P* time < .001; *F* group = 17.626, *P* group < .001; *F* time*group = 3.531, *P* time*group = .01 < .05. “a” indicates a significant difference compared to before treatment (*P* < .05); “b” indicates a significant difference compared to 4 weeks of treatment (*P* < .05); “c” indicates a significant difference compared to 8 weeks of treatment (*P* < .05). All pairwise comparisons have undergone Bonferroni correction.
PEMFs = pulsed electromagnetic fields, PRP = platelet-rich plasma.

combined for the treatment of KOA patients. According to our research findings, during the 12-week treatment period, the scores of VAS, WOMAC, and Lequesne assessments in all 3 groups showed a significant decrease, while knee joint mobility improved. These differences were statistically significant compared to the baseline levels before treatment (*P* < .001). This indicates that all 3 treatment methods are feasible for patients with KOA, providing valuable reference for related clinical practices.

Platelet-rich plasma is mainly divided into leukocyte-rich platelet-rich plasma and LP-PRP. They have similar concentrations of platelets and growth factors, but there are differences in the concentrations of white blood cells and pro-inflammatory cytokines. Excessive white blood cells in leukocyte-rich PRP may induce inflammation regeneration by secreting inflammatory cytokines, thereby exacerbating the inflammatory response at the site of action.[19,20] Therefore, LP-PRP was chosen for the treatment of KOA patients in this study. In the PEMFs group, 2 patients experienced worsening knee joint pain after treatment, whereas no exacerbation of knee joint pain due to inflammatory reactions was observed in the other 2 groups. However, this difference was not statistically significant ($P > .05$). In this study, both the PRP group and the combined group were able to effectively alleviate pain symptoms in KOA patients, confirming the feasibility of PRP treatment in KOA patients. Riewruja et al[21] reported improvements in VAS and WOMAC pain and function scores in KOA patients receiving intra-articular PRP injection therapy. Intra-articular PRP injection significantly reduced pain and improved physical function. However, significant differences in patient platelet counts and variations in PRP preparation methods may result in notable differences in platelet concentration, quantity, and concentrations of released biologically active growth factors after centrifugation.[22,23] This could also be why some researchers believe that PRP has no significant benefits in improving knee joint pain or slowing disease progression in KOA patients.[24]

In this study, the PEMFs group also played a certain positive role in improving pain and knee joint mobility in KOA patients. Compared to the PRP group, there were no significant differences in treatment outcomes. Although PEMFs are not considered the optimal choice for treating KOA, they did indeed have beneficial effects in this study. Bagnato et al[25] found that patients treated with a wearable pulsed electromagnetic field therapy device experienced a decrease in analgesic intake and significant reductions in VAS pain scores and WOMAC pain scores compared to patients receiving a placebo, 1 month after treatment. However, other studies have indicated that no significant beneficial effects on pain and physical function were observed after 6 weeks of PEMFs treatment.[26]This outcome may be attributed to differences in treatment devices and parameters, as well as variations in treatment frequency and duration, further limiting the potential for comparing efficacy. In addition, fewer patients received PEMFs treatment in this study; therefore, the generalizability of the results needs to be confirmed in larger-scale clinical trials.

Our study results confirm that the combined treatment of PRP and PEMFs significantly improves the relief of knee joint pain and restoration of function compared to their individual applications. At each time point after treatment, the VAS scores, WOMAC scores, and Lequesne index scores in the PRP + PEMFs group were lower than those in the PRP and PEMFs groups, while knee joint mobility was higher than in the PRP and PEMFs groups. These differences were statistically significant ($P < .05$), indicating that the combined application has superior efficacy compared to individual treatments. The potential mechanism of the combined treatment may involve the joint suppression of inflammatory factor expression and the synergistic promotion of growth factor secretion through the activation of signaling pathways. From the 4th week to the 12th week of treatment, the VAS scores, WOMAC scores, and Lequesne index scores gradually decreased, while knee joint mobility gradually increased in all 3 groups ($P < .001$), indicating that the combined treatment significantly improved overall knee joint function in the long-term efficacy. Furthermore, there were no significant differences among the 3 groups in the overall incidence of complications ($P = .67$). All patients did not experience any serious adverse reactions after treatment, and all adverse reactions resolved within 1 week after treatment. Although we observed significant improvement in efficacy through the combined treatment of KOA patients with PRP and PEMFs, considering the individual differences among patients and the heterogeneity of treatment regimens, it is still possible that some patients may not experience relief from pain symptoms or improvement in physical function. Therefore, further treatment may be necessary to meet the needs of patients.

In summary, this study demonstrates that all 3 treatment regimens significantly improve pain levels and joint function in early KOA patients. However, the combined use of PRP and PEMFs achieved better results in alleviating pain and improving function, thus serving as a reasonable choice for treating early KOA patients. This study provides more references for the clinical treatment of early KOA, but the feasibility of the combined treatment approach still needs further exploration. However, the study also has some limitations. Firstly, the sample only included individuals with K-L grades I to III, and it is unclear whether it is effective for patients with K-L grade IV. Secondly, the sample size was small, and larger-scale studies are needed in the future to verify the effectiveness of PRP and PEMFs combined application in treating KOA. Finally, there was a lack of radiological evaluation, and more detailed clinical assessments will be needed through long-term follow-up.

5. Conclusion

PRP, PEMFs, and the combination of PRP and PEMFs treatments have all demonstrated positive effects on early KOA, effectively alleviating knee joint pain and improving joint function. However, compared to single treatment modalities, the combined treatment of PRP and PEMFs shows more significant effects.

Acknowledgments

We wish to thank all patients and medical staff for their co-operation.

Author contributions

Conceptualization: Rong-da Xu, Jia-hui Li.
Data curation: Rong-da Xu.
Formal analysis: He Zhang, Hai-rui Liang, Si-yu Duan, Ming Sun, Hang Wen, Xue-ting Zhou, Han-fei Liu.
Funding acquisition: Zhen-cun Cai.
Investigation: Jia-hui Li, He Zhang, Hai-rui Liang, Si-yu Duan, Ming Sun, Hang Wen, Xue-ting Zhou, Han-fei Liu.
Methodology: Rong-da Xu, Zhen-cun Cai.
Project administration: Rong-da Xu, He Zhang, Si-yu Duan, Ming Sun, Hang Wen, Xue-ting Zhou, Han-fei Liu.
Resources: Zhen-cun Cai.
Software: Rong-da Xu, Jia-hui Li.
Supervision: Rong-da Xu, Zhen-cun Cai.
Validation: Rong-da Xu.
Writing – original draft: Rong-da Xu, Jia-hui Li.
Writing – review & editing: Rong-da Xu, Zhen-cun Cai.

References

[1] Charlesworth J, Fitzpatrick J, Perera NKP, Orchard J. Osteoarthritis – a systematic review of long-term safety implications for osteoarthritis of the knee. BMC Musculoskelet Disord. 2019;20:151.
[2] Jang S, Lee K, Ju JH. Recent updates of diagnosis, pathophysiology, and treatment on osteoarthritis of the knee. Int J Mol Sci . 2021;22:2619.
[3] Primorac D, Molnar V, Rod E, et al. Knee osteoarthritis: a review of pathogenesis and state-of-the-art non-operative therapeutic considerations. Genes (Basel). 2020;11:854.
[4] Rodríguez-Merchán EC. Intraarticular injections of mesenchymal stem cells in knee osteoarthritis: a review of their current molecular mechanisms of action and their efficacy. Int J Mol Sci. 2022;23:14953.
[5] Rodríguez-Merchán EC. Intra-articular platelet-rich plasma injections in knee osteoarthritis: a review of their current molecular mechanisms of action and their degree of efficacy. Int J Mol Sci . 2022;23:1301.
[6] Shohat N, Heller S, Sudya D, et al. Mild radiographic osteoarthritis is associated with increased pain and dissatisfaction following total knee arthroplasty when compared with severe osteoarthritis: a systematic review and meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2022;30:965–81.
[7] Gobbi A, Lad D, Petrera M, Karnatzikos G. symptomatic early osteoarthritis of the knee treated with pulsed electromagnetic fields: two-year follow-up. Cartilage. 2014;5:78–85.

[8] Moretti L, Maccagnano G, Coviello M, et al. Platelet rich plasma injections for knee osteoarthritis treatment: a prospective clinical study. J Clin Med. 2022;11:2640.
[9] Tong J, Chen Z, Sun G, et al. The efficacy of pulsed electromagnetic fields on pain, stiffness, and physical function in osteoarthritis: a systematic review and meta-analysis. Pain Res Manag. 2022;2022:9939891.
[10] Iannitti T, Fistetto G, Esposito A, Rottigni V, Palmieri B. Pulsed electromagnetic field therapy for management of osteoarthritis-related pain, stiffness and physical function: clinical experience in the elderly. Clin Interv Aging. 2013;8:1289–93.
[11] Shen L, Yuan T, Chen S, Xie X, Zhang C. The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials. J Orthop Surg Res. 2017;12:16.
[12] Le ADK, Enweze L, Debaun MR, Dragoo JL. Current clinical recommendations for use of platelet-rich plasma. Curr Rev Musculoskelet Med. 2018;11:624–34.
[13] Gobbi A, Dallo I, D'Ambrosi R. Autologous microfragmented adipose tissue and leukocyte-poor platelet-rich plasma combined with hyaluronic acid show comparable clinical outcomes for symptomatic early knee osteoarthritis over a two-year follow-up period: a prospective randomized clinical trial. Eur J Orthop Surg Traumatol. 2023;33:1895–904.
[14] Vadalà M, Morales-Medina JC, Vallelunga A, Palmieri B, Laurino C, Iannitti T. Mechanisms and therapeutic effectiveness of pulsed electromagnetic field therapy in oncology. Cancer Med. 2016;5:3128–39.
[15] Caliogna L, Medetti M, Bina V, et al. Pulsed electromagnetic fields in bone healing: molecular pathways and clinical applications. Int J Mol Sci. 2021;22:7403.
[16] Dolkart O, Kazum E, Rosenthal Y, et al. Effects of focused continuous pulsed electromagnetic field therapy on early tendon-to-bone healing. Bone Joint Res. 2021;10:298–306.
[17] D'Ambrosi R, Ursino C, Setti S, Scelsi M, Ursino N. Pulsed electromagnetic fields improve pain management and clinical outcomes after medial unicompartmental knee arthroplasty: a prospective randomised controlled trial. J ISAKOS. 2022;7:105–12.
[18] Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16:494–502.
[19] Yin W, Qi X, Zhang Y, et al. Advantages of pure platelet-rich plasma compared with leukocyte- and platelet-rich plasma in promoting repair of bone defects. J Transl Med. 2016;14:73.
[20] Gupta A, Jeyaraman M, Potty AG. Leukocyte-rich vs. leukocyte-poor platelet-rich plasma for the treatment of knee osteoarthritis. Biomedicines. 2023;11:141.
[21] Riewruja K, Phakham S, Sompolpong P, et al. Cytokine profiling and intra-articular injection of autologous platelet-rich plasma in knee osteoarthritis. Int J Mol Sci. 2022;23:890.
[22] Parrish WR, Roides B, Hwang J, Mafilios M, Story B, Bhattacharyya S. Normal platelet function in platelet concentrates requires non-platelet cells: a comparative in vitro evaluation of leucocyte-rich (type 1a) and leucocyte-poor (type 3b) platelet concentrates. BMJ Open Sport Exerc Med. 2016;2:e000071.
[23] Bansal H, Leon J, Pont JL, et al. Platelet-rich plasma (PRP) in osteoarthritis (OA) knee: Correct dose critical for long term clinical efficacy. Sci Rep. 2021;11:3971.
[24] Bennell KL, Paterson KL, Metcalf BR, et al. Effect of intra-articular platelet-rich plasma vs placebo injection on pain and medial Tibial Cartilage volume in patients with knee osteoarthritis: the RESTORE randomized clinical trial. JAMA. 2021;326:2021–30.
[25] Bagnato GL, Miceli G, Marino N, Sciortino D, Bagnato GF. Pulsed electromagnetic fields in knee osteoarthritis: a double blind, placebo-controlled, randomized clinical trial. Rheumatology (Oxford). 2016;55:755–62.
[26] Mccarthy CJ, Callaghan MJ, Oldham JA. Pulsed electromagnetic energy treatment offers no clinical benefit in reducing the pain of knee osteoarthritis: a systematic review. BMC Musculoskelet Disord. 2006;7:51.