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Original Article

Clinical efficacy and safety of telitacicept combined with methotrexate in the treatment of rheumatoid arthritis

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Abstract: Objective: To investigate the clinical efficacy of telitacicept combined with methotrexate in treating rheumatoid arthritis (RA) and its effects on related indicators including inflammatory response, oxidative stress, and bone metabolism. Methods: Clinical data of 109 RA patients were retrospectively analyzed and divided into an observation group (n=59) and a control group (n=50). Disease activity scores, inflammatory response indicators, oxidative stress indicators, bone metabolism biomarkers, and imaging scores were compared before and after treatment. Results: After treatment, the observation group showed significantly lower disease activity scores and response indicators than the control group (all P<0.05), decreased malondialdehyde levels, increased superoxide dismutase and glutathione peroxidase levels (all P<0.05), and improved bone metabolism indicators such as procollagen type I N-terminal propeptide and matrix metalloproteinase-3. Some imaging scores indicated a short-term improvement trend. Conclusion: Telitacicept combined with methotrexate can effectively improve disease activity, inflammation, and oxidative stress in RA patients in the short term and exert positive effects on bone metabolism-indicators, but its long-term structural protective effect and underlying mechanism need further investigation.

Keywords: Rheumatoid arthritis, telitacicept, methotrexate, oxidative stress, bone metabolism, safety

Introduction

As a chronic, systemic autoimmune disease with high incidence, rheumatoid arthritis (RA) is characterized by abnormal synovial hyperplasia and inflammatory cell infiltration, which leads to cartilage erosion and bone destruction [1]. RA patients mainly present with morning stiffness, joint tenderness, dysfunction and restricted mobility. Without effective control, the condition may progress to joint deformity and functional loss, making RA a major cause of disability and labor loss [2]. At present, the therapeutic goal for RA is to achieve symptom remission or low disease activity by controlling inflammatory responses, maximize joint function and structural protection, and improve long-term prognosis [3]. Methotrexate is the first-line agent, exerting anti-inflammatory, immunosuppressive and analgesic effects to alleviate clinical symptoms [4]. However, clinical practice has shown that some RA patients exhibit an inadequate response, poor efficacy or intolerance to methotrexate monotherapy, resulting in persistent disease activity, progressive joint damage and considerable room for efficacy improvement [5, 6]. Consequently, the exploration of effective and safe combination therapies based on methotrexate has become a research hotspot.

In recent years, with in-depth research on RA, the role of B cells in antigen presentation, antibody production and cytokine network activation has attracted wide attention, and targeting B-cell pathways has emerged as a key therapeutic strategy [7]. Telitacicept is the world's first bispecific fusion protein drug targeting B-lymphocyte stimulator (BLyS) and a proliferation-inducing ligand (APRIL). It inhibits B-cell differentiation and maturation, reduces pathogenic autoantibody production and attenuates immune responses [8]. Its remarkable efficacy in systemic lupus erythematosus and other autoimmune diseases provides a theoretical basis for RA treatment. Theoretically, combin-

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ing the targeted B-cell-modulating effects of telitacicept with the broad anti-inflammatory and immunoregulatory properties of methotrexate may produce synergistic outcomes. Thus, this study investigated the clinical efficacy, safety and multi-dimensional impacts (inflammation, oxidative stress, bone metabolism) of telitacicept combined with methotrexate in RA patients, aiming to provide evidence for its clinical application.

Materials and methods

Patient selection

This retrospective study retrieved clinical data of 109 rheumatoid arthritis (RA) patients diagnosed in the Department of Rheumatology and Immunology of Hubei Provincial Hospital of Integrated Chinese and Western Medicine between January 2022 and December 2023. Patients were divided into two groups by treatment regimen: the control group (n=50) received methotrexate monotherapy, and the observation group (n=59) received telitacicept combined with methotrexate.

Inclusion criteria: Conforming to RA diagnostic criteria [9]; complete baseline data and laboratory results; joint function grade I-III; active disease stage; disease duration ≥6 months.

Exclusion criteria: Use of glucocorticoids or disease-modifying anti-rheumatic drugs within 1 month prior to enrollment; hypersensitivity to study drugs; complicated by joint deformity, fracture or other joint diseases; other autoimmune diseases; pregnancy or lactation; coagulation disorders, severe organ dysfunction, or malignant tumors.

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Hubei Provincial Hospital of Integrated Chinese and Western Medicine. Informed consent was waived by the committee due to its retrospective nature involving only analysis of existing clinical data.

Treatment protocols

The control group received methotrexate monotherapy (Shanghai Shangyao Xinyi Pharmaceutical Co., Ltd., National Medicine Approval No. H31020644): 10 mg orally once weekly. Besides, folic acid supplementation was administered concomitantly at a frequency of once weekly, on days separate from methotrexate dosing, in order to mitigate methotrexate-related adverse reactions.

The observation group received telitacicept combined with methotrexate (RemeGen Co., Ltd., Yantai; National Medicine Approval No. S20210008): 160 mg subcutaneously once weekly, on the basis of methotrexate. Both groups received treatment for a unified course of 3 months.

Outcome measures

Primary outcomes: (1) Clinical efficacy [10]. Marked efficacy: Joint tenderness, morning stiffness and restricted mobility were significantly relieved or basically disappeared, with Disease Activity Score 28 (DAS28) <2.6. Effective: Symptoms were moderately relieved, with DAS28 ranging from 2.6 to 5.1. Ineffective: Symptoms were unchanged or aggravated, with DAS28 >5.1. Total effective rate = marked efficacy rate + effective rate. (2) Bone erosion: All patients underwent hand (including wrist) X-ray and wrist magnetic resonance imaging (MRI) before and 3 months after treatment. The Sharp/van der Heijde scoring system was used to assess bone erosion and joint space narrowing on X-rays. The Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) was applied to evaluate bone erosion, synovitis and bone marrow edema on MRI images.

Secondary outcomes: (1) Clinical manifestations. The number of tender and swollen joints, and duration of morning stiffness were recorded before and after treatment. (2) Pain intensity and disease activity. Visual Analogue Scale (VAS) and DAS28 were used for evaluation. VAS scores ranged from 0 to 10, with higher scores indicating more severe pain. DAS28 was calculated based on the count of tender and swollen joints among 28 specific joints. (3) Inflammatory response. Fasting venous blood samples (5 mL) were collected before and 3 months after treatment, centrifuged at 3,000 r/min for 15 min. The serum was separated and stored at -80°C. Immunoturbidimetry was used to detect rheumatoid factor (RF, Shenzhen Genrui Biotechnology Co., Ltd., YDLC-15315) levels. Chemiluminescent immunoassay was employed to measure anti-cyclic citrullinated peptide antibody (anti-CCP, Shanghai Yaji Biological Co., Ltd., CL06768) levels. Westergren method

Table 1. Comparison of general data

Clinical data	Control group (n=50)	Observation group (n=59)	$\chi^2/t/Z$	*P*
Gender (Male/Female)	22/28	25/34	0.029	0.864
Joint function (Grade I/Grade II/Grade III	9/25/16	12/30/17	0.412	0.680
Disease course ($\bar{x}\pm s$, years)	5.43±1.57	4.70±1.82	0.821	0.413
Number of involved joints ($\bar{x}\pm s$, units)	4.36±1.40	4.56±1.26	0.785	0.434
Body mass index ($\bar{x}\pm s$, kg/m^2)	23.52±3.17	23.74±2.90	0.378	0.706

was used for erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP, Wuhan Yicheng Biotechnology Co., Ltd., KTE6004-1) levels. Enzyme-linked immunosorbent assay (ELISA) kits were applied to detect interleukin-6 (IL-6, Chuzhou Shinuoda Biotechnology Co., Ltd., SND-H1925) and tumor necrosis factor-α (TNF-α, Wuhan Feien Biote Co., Ltd., EH0302) levels. (4) Liver function indicators. Serum samples were tested on an automatic biochemistry analyzer to detect alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin (TBil) levels before and after treatment. (5) Renal function indicators. Serum creatinine (Scr) and blood urea nitrogen (BUN) levels were detected by automatic biochemistry analyzer, and estimated glomerular filtration rate (eGFR) level was calculated. (6) Oxidative stress indicators. Serum samples were analyzed by colorimetric methods. Malondialdehyde (MDA) level was measured by thiobarbituric acid method; superoxide dismutase (SOD) activity was detected by WST-1 method; glutathione peroxidase (GSH-Px) activity was measured by NADPH-coupled assay. (7) Bone metabolism indicators. Serum procollagen type I N-terminal propeptide (PINP) level was determined by electrochemiluminescence. Matrix metalloproteinase-3 (MMP-3) level was quantified by ELISA before and 3 months after treatment. (8) Adverse reactions. Loss of appetite, diarrhea, skin rash and other adverse events were recorded and compared between the two groups.

Statistical analysis

Data analysis was performed using SPSS 25.0 software. Shapiro-Wilk test was used for continuous data first. Normally distributed data were presented as mean ± standard deviation and analyzed by paired t-test (intra-group comparison) or independent samples t-test (inter-group comparison). Non-normally distributed data were presented as medians (interquartile range) and analyzed by nonparametric tests. Categorical data were expressed as number and percentage, and compared by chi-square test or Fisher's exact test. For continuous variables showing mild skewness on normality testing, parametric tests were still used if the sample size was relatively large and the distribution was essentially symmetric, yet caution is warranted when interpreting the results. All tests were two-tailed, with P<0.05 considered significant.

Results

Comparison of baseline clinical data

No significant differences were observed in gender, joint function grade, age, disease duration, or number of involved joints between the two groups (all P>0.05), indicating good comparability. See **Table 1**.

Comparison of clinical efficacy

The total effective rates of the observation group and control group were 93.22% and 78.00%, respectively, with the observation group showing a significantly higher rate (all P<0.05). See **Table 2**.

Comparison of bone erosion

Before treatment, no significant differences existed in Sharp/van der Heijde scores and RAMRIS scores between the two groups (both P>0.05). After treatment, both scores decreased in both groups, and the observation group was lower than the control group (both P< 0.05). See **Table 3**.

Comparison of clinical manifestations, pain intensity, and disease activity

Before treatment, no significant differences were found in tender/swollen joint counts, morning stiffness duration, VAS scores, or

Table 2. Comparison of clinical efficacy between the two groups [n (%)]

Group	Significant effect	Effective	Invalid	Total effective
Control group (n=50)	19 (38.00)	20 (40.00)	11 (22.00)	39 (78.00)
Observation group (n=59)	33 (55.93)	22 (37.29)	4 (6.78)	55 (93.22)
χ^2				5.283
P				0.022

Table 3. Comparison of bone erosion between the two groups ($\overline{x}\pm s$, points)

Indicator		Control group (n=50)	Observation group (n=59)	*t*	*P*
Sharp/van der Heijde score	Before treatment	9.12±1.33	9.23±1.20	0.454	0.651
	After treatment	8.24±0.80*	7.90±0.63*	2.481	0.015
RAMRIS	Before treatment	6.44±1.40	6.71±1.27	1.055	0.294
	After treatment	5.42±0.70*	4.93±0.60*	3.936	<0.001

Note: Compared to before treatment in this group, *P<0.05. RAMRIS, Rheumatoid Arthritis Magnetic Resonance Imaging Score.

Table 4. Comparison of clinical manifestations, pain degree and disease activity between the two groups ($\overline{x}\pm s$)

Indicator		Control group (n=50)	Observation group (n=59)	*t*	*P*
Count of tender and swollen joints (units)	Before treatment	8.80±1.65	8.91±1.40	0.377	0.707
	After treatment	4.12±1.20*	2.55±0.87*	7.897	<0.001
Duration of morning stiffness (min)	Before treatment	105.3±28.6	109.7±31.4	0.759	0.449
	After treatment	42.8±18.9*	63.5±22.7*	5.117	<0.001
VAS score (points)	Before treatment	6.16±1.10	6.25±1.03	0.441	0.660
	After treatment	3.22±0.56*	1.94±0.50*	12.604	<0.001
DAS28 (points)	Before treatment	4.91±1.10	4.95±1.04	0.195	0.846
	After treatment	3.26±0.76*	2.55±0.60*	5.448	<0.001

Note: Compared to before treatment in this group, *P<0.05. VAS, Visual Analogue Scale; DAS28, Disease Activity Score 28.

DAS28 scores between the two groups (all P>0.05). After treatment, both groups exhibited reduced tender/swollen joint counts and shortened morning stiffness duration, with decreased VAS and DAS28 scores (all P<0.05). See **Table 4**.

Comparison of inflammatory response indicators

No inter-group differences were noted in the levels of inflammatory factors (RF, CRP, anti-CCP, ESR, IL-6, and TNF-α) before treatment (all P>0.05). After treatment, all inflammatory indicators decreased in both groups, with the observation group showing significantly lower levels (all P<0.05). This indicated that the combination therapy suppressed inflammatory responses and prevented disease progression. See **Table 5**.

Comparison of liver function indicators

No significant differences in liver function indicators were observed between the two groups before and after treatment (all P>0.05), suggesting that adding telitacicept had no obvious effect on liver function. See **Table 6**.

Comparison of renal function indicators

There were no significant differences in renal function indices between the two groups before and after treatment (all P>0.05), indicating that the addition of telitacicept did not exert a notable effect on renal function. See **Table 7**.

Comparison of oxidative stress indicators

Before treatment, MDA, SOD, and GSH-Px levels showed no significant differences between

Table 5. Comparison of inflammatory response indicators between the two groups ($\bar{x}\pm s$)

Indicator		Control group (n=50)	Observation group (n=59)	*t*	*P*
RF (U/L)	Before treatment	172.32±32.10	177.78±25.55	0.989	0.325
	After treatment	62.20±13.05*	35.72±10.66*	11.660	<0.001
CRP (mg/L)	Before treatment	11.42±3.15	11.93±2.66	0.917	0.361
	After treatment	7.11±2.03*	5.05±1.63*	5.875	<0.001
Anti-CCP (RU/mL)	Before treatment	87.12±13.15	90.12±12.62	1.213	0.228
	After treatment	52.30±8.77*	39.02±7.14*	8.714	<0.001
ESR (mm/h)	Before treatment	47.82±12.10	50.03±11.13	0.993	0.323
	After treatment	30.34±8.77*	23.21±8.10*	4.409	<0.001
IL-6 (pg/mL)	Before treatment	104.22±22.77	108.33±19.20	1.023	0.309
	After treatment	70.32±8.40*	56.33±9.55*	8.050	<0.001
TNF-α (pg/mL)	Before treatment	12.22±3.10	12.67±2.20	0.883	0.379
	After treatment	7.12±2.42*	3.20±1.20*	10.960	<0.001

Note: Compared to before treatment in this group, *P<0.05. RF, rheumatoid factor; CRP, C-reactive protein; anti-CCP, anti-cyclic citrullinated peptide antibody; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α.

Table 6. Comparison of liver function indicators between the two groups ($\bar{x}\pm s$)

Indicator		Control group (n=50)	Observation group (n=59)	*t*	*P*
ALT (U/L)	Before treatment	39.11±6.30	40.22±4.12	1.104	0.272
	After treatment	38.30±5.77	39.12±4.30	0.849	0.398
AST (U/L)	Before treatment	29.20±4.55	28.72±4.20	0.572	0.568
	After treatment	28.55±5.11	28.03±4.78	0.548	0.585
ALP (U/L)	Before treatment	78.10±12.33	79.52±10.77	0.642	0.522
	After treatment	79.42±10.63	80.10±10.33	0.338	0.736
TBil (μmol/L)	Before treatment	8.94±2.10	9.04±1.77	0.270	0.788
	After treatment	9.04±1.76	9.07±1.40	0.099	0.921

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; TBil, total bilirubin.

Table 7. Comparison of renal function indicators between the two groups ($\bar{x}\pm s$)

Indicator		Control group (n=50)	Observation group (n=59)	*t*	*P*
Scr (mg/dL)	Before treatment	0.80±0.16	0.82±0.13	0.720	0.473
	After treatment	0.82±0.17	0.84±0.20	0.557	0.579
BUN (mmol/L)	Before treatment	5.12±1.33	5.24±1.20	0.495	0.622
	After treatment	5.18±1.17	5.27±1.15	0.404	0.687
eGFR (mL/min/1.73 m^2)	Before treatment	104.52±12.10	105.72±11.40	0.532	0.596
	After treatment	102.46±10.77	102.42±13.64	0.017	0.987

Scr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate.

the two groups (all P>0.05). After treatment, MDA levels decreased while SOD and GSH-Px levels increased in both groups; the observation group had lower MDA levels and higher SOD and GSH-Px levels (all P<0.05). These results showed that the combination therapy inhibited oxidative stress and alleviated clinical symptoms. See **Table 8**.

Comparison of bone metabolism indicators

PINP and MMP-3 levels showed no significant inter-group differences before treatment (both P>0.05). After treatment, PINP levels increased and MMP-3 levels decreased in both groups (both P<0.05). The observation group had higher PINP levels and lower MMP-3 levels (both

Table 8. Comparison of oxidative stress indicators between the two groups ($\bar{x}\pm s$)

Indicator		Control group (n=50)	Observation group (n=59)	*t*	*P*
MDA (μmol/L)	Before treatment	5.82±1.33	5.88±1.20	0.248	0.805
	After treatment	4.11±1.20*	3.40±1.17*	3.120	0.002
SOD (U/mL)	Before treatment	62.10±12.32	61.11±10.20	0.459	0.647
	After treatment	72.36±13.55*	79.12±12.10*	2.751	0.007
GSH-Px (U/L)	Before treatment	65.34±10.10	65.12±12.46	0.100	0.921
	After treatment	72.33±9.11*	78.12±10.12*	3.115	0.002

Note: Compared to before treatment in this group, *P<0.05. MDA, malondialdehyde; SOD, superoxide dismutase; GSH-Px, glutathione peroxidase.

Table 9. Comparison of bone metabolism indicators between the two groups ($\bar{x}\pm s$)

Indicator		Control group (n=50)	Observation group (n=59)	*t*	*P*
PINP (μg/L)	Before treatment	21.07±3.20	20.72±2.94	0.595	0.553
	After treatment	25.10±4.55*	28.66±4.12*	4.285	<0.001
MMP-3 (ng/mL)	Before treatment	98.32±13.20	96.73±12.10	0.656	0.513
	After treatment	82.10±9.52*	57.32±8.55*	14.312	<0.001

Note: Compared to before treatment in this group, *P<0.05. PINP, procollagen type I N-terminal propeptide; MMP-3, matrix metalloproteinase-3.

Table 10. Comparison of adverse reactions occurring during treatment between the two groups of patients

Group	Anorexia (cases)	Diarrhea (cases)	Rash (cases)	Total number of adverse reactions (cases)	Adverse reaction rate (%)
Control group (n=50)	1	1	0	2	4.00
Observation group (n=59)	2	1	1	4	6.78
χ^2					0.177
P	-	-	-	-	0.674

P<0.05). The results indicated that the combination therapy significantly improved bone metabolism and promoted recovery. See **Table 9**.

Comparison of adverse reactions

During treatment, 1 case of anorexia and 1 case of diarrhea occurred in the control group, with an adverse reaction rate of 4.00%. 2 cases of anorexia, 1 case of diarrhea and 1 case of rash occurred in the observation group, with an adverse reaction rate of 6.78%. No significant difference was noted in the adverse reaction rate between the two groups (P>0.05). See **Table 10**.

Discussion

In recent years, the incidence of RA has been on the rise in China, with a higher predilection for females and an age-dependent increase [11]. Although methotrexate is unanimously recommended as a first-line disease-modifying antirheumatic drug (DMARD) in domestic and international guidelines, monotherapy achieves clinical remission in only approximately 30% of patients, leaving a large number of patients facing progressive radiographic damage and functional disability [12, 13]. Despite the expanding application of biologics and targeted synthetic DMARDs along with the growing popularity of treat-to-target strategies, their use is limited by high costs and poor accessibility in primary healthcare settings [14]. Thus, exploring safe, effective, and cost-efficient novel combination regimens has become a current research hotspot.

Telitacicept is a recombinant human BLyS/APRIL bispecific fusion protein. It simultaneously inhibits B-cell differentiation and autoantibody production, interferes with T-cell co-

stimulatory signals, suppresses B-cell-mediated humoral immune responses, and thereby reduces the generation of pathogenic autoantibodies [15]. In contrast, methotrexate reduces purine synthesis by inhibiting dihydrofolate reductase and downregulates the release of multiple proinflammatory cytokines, including IL-6 and TNF-α [16].

The results of this study demonstrated that compared to the control group, the observation group achieved superior improvements after treatment, with a higher total effective rate and lower levels of multiple clinical indicators (tender/swollen joint counts, morning stiffness duration, VAS, and DAS28 scores). These findings indicate that telitacicept combined with methotrexate has distinct advantages over methotrexate monotherapy in pain relief and functional improvement. This may be attributed to the complementary mechanisms of the two drugs, which synergistically inhibit immune-inflammatory responses through multiple pathways, leading to more significant improvements in clinical symptoms and functions.

Persistent synovitis and subsequent tissue destruction represent the core pathological processes of RA. Positive RF and anti-CCP antibodies at baseline indicate excessive B-cell activation; elevated CRP and ESR levels reflect acute-phase inflammatory burden; and proinflammatory cytokines such as IL-6 and TNF-α drive synovial hyperplasia and cartilage destruction [17]. The results of this study showed that the observation group had lower levels of all inflammatory indicators after treatment than the control group, suggesting that the combination regimen exerts a more potent effect in alleviating inflammatory responses in RA patients. The underlying mechanism may be that telitacicept reduces the source of inflammation-driving autoantibodies by B-cell targeting and indirectly modulates T-cell activation, while methotrexate effectively inhibits proliferating immune cells and cytokine storms. The combination blocks the inflammatory cascade through multiple links, namely autoantibody production, cytokine storms and acute-phase protein synthesis, which constitutes the key reason for the superior efficacy of the observation group. Beyond inflammatory responses, oxidative stress induced by excessive reactive oxygen species (ROS) production in the setting of chronic inflammation is another crucial factor promoting RA pathogenesis. The imbalance between oxidation and antioxidation exacerbates tissue damage and further activates synovial fibroblasts [18, 19]. The results of this study revealed that the observation group had lower MDA levels and higher SOD and GSH-Px levels compared to the control group after treatment, indicating that the combination therapy has certain advantages over methotrexate monotherapy in mitigating oxidative stress in RA patients. Previous studies have suggested that telitacicept may indirectly reduce ROS generation by inhibiting upstream immune activation in inflammatory responses, while methotrexate may regulate oxidative stress through its effects on cellular metabolic processes [20]. However, these pathways were not directly examined in this study, and their specific molecular mechanisms remain to be further elucidated.

Imbalanced bone metabolism and joint structural damage are the core contributors to RA-related disability [21, 22]. Regarding bone metabolism, serum PINP is a key marker of bone formation, and its reduced levels indicate insufficient osteogenic activity; elevated MMP-3 reflects accelerated cartilage matrix degradation. The results of this study showed that PINP and MMP-3 levels were improved in the combination therapy group compared to the control group, suggesting that bone metabolism-related indicators may undergo certain changes in the short term. Nevertheless, it should be noted that PINP and MMP-3 are indirect markers of bone metabolism that primarily reflect bone formation and matrix degradation processes, and their alterations are insufficient to comprehensively represent bone turnover status. Given that PINP is associated with bone formation and MMP-3 participates in matrix decomposition, this finding implies that the regimen may exert a more balanced and positive role in promoting bone remodeling and inhibiting osteoclastogenesis. The underlying mechanism may be that telitacicept suppresses osteoclast differentiation and function by inhibiting B cells and the expression of related osteoclastogenic cytokines, while methotrexate downregulates MMP transcription. Together, they promote the rebalance of osteoblastogenesis and osteoclastogenesis, facilitating bone matrix repair [23]. In terms of imaging, an annual increment of ≤0.5 in the Sharp/van der Heijde score is regarded as the gold

standard for successful structural protection; the RAMRIS can sensitively detect synovitis, bone marrow edema and early erosion within 12 weeks. The results of this study showed that the observation group had lower Sharp/van der Heijde and RAMRIS scores than the control group after treatment, suggesting that inflammation-related imaging manifestations may be improved in the short term. It should be noted that although the MRI RAMRIS score decreased significantly from baseline after treatment, suggesting some short-term improvement in synovitis and inflammation-related imaging findings, there is currently no universally accepted threshold for short-term RAMRIS score changes that can be directly equated with "clinically significant structural protection". Previous studies have often used an annual increase of ≤0.5 in the Sharp/van der Heijde score or long-term stability of the RAMRIS score as a reference standard for structural protection [24, 25]. However, the follow-up period in this study was only 3 months, and the observed decrease in RAMRIS score was more likely to reflect an improvement in inflammatory activity rather than a clear reversal of structural bone erosion. Therefore, the interpretation of imaging results in this study mainly emphasizes the "short-term improvement trend", and its long-term structural protective significance still needs to be verified through longer-term follow-up. Regarding safety, this study demonstrated no significant differences in liver or renal function indices between the two groups before and after treatment, with comparable adverse reaction rates. These findings indicate that the combination of telitacicept and methotrexate has favorable safety and tolerability profiles, without significantly increasing the risk of liver or renal function impairment.

This study has certain limitations. First, it is based on retrospective data with a relatively limited sample size and a single-center cohort, coupled with a short follow-up duration. These factors may have compromised the robustness and generalizability of the study results. Although baseline clinical and laboratory data were collected, the study design and sample size precluded further analysis of the potential value of baseline factors such as anti-CCP levels, B-cell subset characteristics or specific genetic backgrounds in predicting the benefits of combination therapy. Given the high cost of targeted biologics like telitacicept, identifying the optimal beneficiary population is crucial for optimizing clinical decision-making and resource allocation.

Second, the imaging follow-up duration was relatively short, with X-ray and MRI assessments performed only 3 months after treatment initiation, which was insufficient to comprehensively reflect long-term changes in structural joint damage. The related conclusions still need to be verified by longer follow-up periods and more systematic imaging evaluations. In addition, this study did not measure core regulators of bone turnover such as the receptor activator of nuclear factor-κB ligand (RANKL)/osteoprotegerin (OPG) axis or more sensitive bone resorption markers, nor did it validate changes in bone metabolism through bone histology or more advanced imaging techniques. Therefore, the conclusions regarding improvements in bone metabolism should be interpreted with caution. Future studies should focus on well-designed prospective, multicenter, large-sample and long-term follow-up trials, combined with pharmacoeconomic analyses, to further validate the results of this study and enhance its clinical application value. It should be noted that X-ray structural damage is usually difficult to reverse in a short period of time. The score changes observed within 3 months in this study may have been related to score errors and changes in imaging manifestations after inflammation control. The structural protective significance still needs to be verified through long-term follow-up. It should be noted that X-ray structural damage is usually difficult to reverse in the short term. The changes in scores within 3 months in this study may be related to scoring errors and changes in imaging manifestations after inflammation control. Its structural protective significance still needs to be verified by long-term follow-up.

In conclusion, tasimipide combined with methotrexate can significantly improve the joint symptoms of RA patients in the short term, reduce disease activity, and inhibit inflammatory responses and oxidative stress. It also has a positive effect on bone metabolism-related indicators, but its long-term effect on joint structure protection still needs to be confirmed by further studies.

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Disclosure of conflict of interest

None.

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