

Correlation Study Between T Lymphocyte Subsets and Rheumatoid Arthritis

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Abstract: *Objective:* To study the effect of *Helicobacter pylori* infection on rheumatoid arthritis and T-lymphocyte subpopulations in patients with rheumatoid arthritis and to provide a new method for the treatment of rheumatoid arthritis by removing *Helicobacter pylori* from patients. *Methods:* 60 patients with rheumatoid arthritis admitted to the hospital from May 2022 to May 2023 were selected for the study, and all patients underwent a 13-carbon urea breath test to detect gastric *H. pylori* and the test results showed that 20 cases were negative and 40 cases were positive. The 40 positive patients were divided into the treatment group ($n = 20$) and non-treatment group ($n = 20$) by random number table method and the treatment group was given anti-*Helicobacter pylori* treatment, and the non-treatment group was given maintenance rheumatoid basic treatment, comparing the anti-cyclic citrulline peptide (CCP), DS28 score, peripheral blood T-lymphocyte subsets ($CD4^+$ T-lymphocytes, $CD8^+$ T-lymphocytes, $CD4^+/CD8^+$ ratio) before and after the treatment of patients by 13-carbon urea respiration test (pylori-negative group, 20 patients) and those who were positive for the treatment of *H. pylori* (pylori-positive group, 40 patients). Besides, the correlation of peripheral blood T-lymphocyte subsets and disease activity between treatment and non-treatment groups in the pylori-positive group was identified together with the correlation of DS28 scores, TNF- α levels, sedimentation and immunoglobulin, lymphocyte subsets in the pylori-positive treatment group and positive non-treatment group as well as the level of globulin, lymphocyte subsets, and peripheral blood lymphocytes before and after treatment. *Results:* Before treatment, CCP, DS28 score, $CD8^+$ T lymphocyte level of the pylori-negative group were lower than that of the positive group, and $CD4^+$ T lymphocyte and $CD4^+/CD8^+$ ratio were higher than that of the positive group ($P < 0.05$); after treatment, the indexes of the pylori-positive group improved, and there was no significant difference in the comparison of the indexes with those of the pylori-negative group ($P > 0.05$); the positive treatment group had a DS28 (3.19 ± 1.02) points, positive non-treatment group DS28 (5.36 ± 1.85) points, non-treatment group DS28 score and $CD4^+$ T lymphocytes, $CD4^+/CD8^+$ negative correlation with $CD8^+$ T lymphocytes showed a positive correlation ($P < 0.05$); before the treatment, pylori-positive treatment group and non-treatment group DS28 scores, TNF- α levels, peripheral blood T lymphocyte subpopulation levels were not significantly different ($P > 0.05$); after treatment, DS28 score, TNF- α level, $CD8^+$ T of the treatment group were lower than those of the non-treatment group, and $CD4^+$ T lymphocytes and $CD4^+/CD8^+$ ratio were higher than those of the non-treatment group ($P < 0.05$). *Conclusion:* *H. pylori* affects the level of T lymphocyte subsets in patients with rheumatoid arthritis, and there is a certain correlation between the two. Removal of *H. pylori* can improve the level of T lymphocyte subsets, which is important for the treatment of patients with rheumatoid arthritis.

Keywords: Peripheral blood T lymphocyte subsets; Rheumatoid arthritis; *Helicobacter pylori*; Intestinal flora dysbiosis

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1. Introduction

Rheumatoid arthritis is mainly characterized by morning stiffness, swelling and pain in the joints, and with the continuous progress of the disease, it can manifest as joint deformity, which seriously affects patients' daily activities ^[1]. Studies have shown that rheumatoid arthritis is affected by the intestinal flora of patients ^[2]. *Helicobacter pylori* causes biodiversity in the intestinal flora of patients, leading to intestinal flora disorders, which may affect the immune function of patients. The peripheral blood T lymphocyte subpopulation is an important immune cell. The onset of the patient may be accompanied by different immune abnormalities, rheumatoid arthritis pathogenesis, treatment process, immune cells are involved, and immune cell index changes can become a major indicator of the diagnosis of rheumatoid arthritis condition ^[3]. Most of the current research mainly focuses on the value of the improvement of peripheral blood T lymphocyte subpopulation on rheumatoid arthritis treatment and less attention is paid to the impact of rheumatoid arthritis intestinal flora on patients' immune cells. This paper focuses on the effect of intestinal flora dysbiosis on T lymphocyte subsets in rheumatoid arthritis patients.

2. Data and methods

2.1. General information

The study object was selected from 60 cases of rheumatoid arthritis patients admitted to our hospital during the time period from May 2022 to May 2023, of which 15 cases were male and 45 cases were female, with ages ranging from 35–78 years old, the average age (56.50 ± 18.33) years old, and the duration of the disease ranging from 6–36 months, the average duration of the disease (21.00 ± 7.00) months. All patients were tested for gastric *H. pylori* by a 13-carbon urea breath test, which showed 20 negative cases and 40 positive cases. There were 20 negative cases and 40 positive cases, including 11 males and 10 females in the negative group with a mean age of (55.56 ± 17.58) years old and 16 males and 16 females in the positive group with a mean age of (55.45 ± 17.75) years old. 40 positive patients were divided into the treatment group ($n = 20$) and the non-treatment group ($n = 20$) using the random number table method. There were 8 males and 7 females with mean age (55.36 ± 16.89) years old in the treatment group and 8 males and 9 females with mean age (55.36 ± 16.89) years old in the non-treatment group. There was no significant difference in the general information between the groups ($P > 0.05$), and they were comparable.

2.2. Inclusion and exclusion criteria

Inclusion criteria:

- (1) Patients have signed informed consent;
- (2) Meet the diagnostic criteria of rheumatoid arthritis ^[4];
- (3) Complete case data.

Exclusion criteria:

- (1) Major renal and respiratory diseases;
- (2) Chronic disease infections;
- (3) Poor compliance;
- (4) Severe gastrointestinal diseases.

2.3. Methods

All patients underwent a 13-carbon urea breath test to detect gastric *H. pylori* and were given methotrexate 10

mg/week and folic acid 10 mg/week as basic treatment. According to the negative and positive results of the 13-carbon urea respiratory test, the patients were divided into two groups, in which the positive patients were divided into the treatment group ($n = 20$) and the non-treatment group ($n = 20$) by using the random number table method. The non-treatment group was maintained in accordance with the routine rheumatoid basic treatment and was given prednisone acetate tablets (National Drug Code: H34021846, specification 5 mg \times 100 tablets, 3 times/d, 5 mg/time).

The treatment group was given amoxicillin capsule (State Drug Permit: H37021926) 1.0 g/bid, clarithromycin tablet (State Drug Permit: H20058305) 1.0 g/bid, pantoprazole (State Drug Permit: H20059019) 40 mg/bid, colloidal bismuth pectin capsule (State Drug Permit: H10920072) 2 capsules/bid orally, and if there is allergy to amoxicillin, then change to levofloxacin 100 mg/bid treatment for 2 weeks, stop the drug 1 month to review carbon-13.

2.4. Observation index

- (1) Comparison of carbon-13 urea respiratory test to detect gastric *H. pylori* negative patients and positive patients before and after treatment CCP, DS28 score, peripheral blood T lymphocyte subpopulations.
- (2) Correlation of peripheral blood T-lymphocyte subpopulations and disease activity between the treated and non-treated groups in the pylorus-positive group.
- (3) DS28 score, TNF- α level, blood sedimentation and immunoglobulin, lymphocyte subpopulations and peripheral blood lymphocyte levels in the pylori-positive and positive non-treatment groups.

2.5. Statistical methods

SPSS 24.0 statistical software was used to analyze the data, and the expression of the measurement data was mean \pm standard deviation (SD), *T*-test was used, and *F*-test was used to compare the correlation between DS28 scores and peripheral blood T-lymphocyte subpopulations in the positive treatment group and the positive non-treatment group, and $P < 0.05$ was taken as the difference was statistically significant.

3. Results

3.1. Comparison of pylorus test negative patients with positive test indexes

After treatment, the indicators of the pylori-positive group all improved, and there was no significant difference between them and the indicators of the pylori-negative group ($P > 0.05$); see **Table 1** for details.

Table 1. Comparison of pylori-negative patients with positive test indexes between groups before and after treatment (mean \pm SD)

Group	CCP (RU/mL)		DS28 (points)		CD8 ⁺ T (%)		CD4 ⁺ T (%)		CD4 ⁺ /CD8 ⁺ (%)	
	Before	After	Before	After	Before	After	Before	After	Before	After
Negative group ($n = 20$)	5.55 \pm 1.85	4.25 \pm 1.63	5.01 \pm 2.01	5.00 \pm 1.89	20.36 \pm 7.02	19.25 \pm 7.88	25.63 \pm 8.66	26.22 \pm 8.66	1.45 \pm 0.66	1.49 \pm 0.60
Positive group ($n = 40$)	8.56 \pm 2.86	4.55 \pm 1.55	6.14 \pm 2.02	5.03 \pm 1.78	28.25 \pm 9.55	20.02 \pm 7.85	19.22 \pm 6.55	25.99 \pm 7.55	0.88 \pm 0.23	1.43 \pm 0.42
<i>t</i>	0.063	17.068	2.045	0.060	3.274	0.357	3.202	0.105	4.929	0.450
<i>P</i>	< 0.001	0.490	0.045	0.952	0.002	0.721	0.002	0.916	< 0.001	0.654

3.2. Correlation between peripheral blood T-lymphocyte subsets and disease activity

After treatment, DS28 (3.19 ± 1.02) score in the positive treatment group and DS28 (5.36 ± 1.85) score in the positive non-treatment group, the DS28 score in the non-treatment group was negatively correlated with CD4⁺ T lymphocytes and CD4⁺/CD8⁺, and positively correlated with CD8⁺ T lymphocytes ($P < 0.05$), as shown in Table 2.

Table 2. Correlation between peripheral blood T lymphocyte subsets and disease activity (mean \pm SD)

Item	Positive treatment group DS28 (3.19 ± 1.02) points		Positive non-treatment group DS28 (5.36 ± 1.85) points	
	F	p	F	p
CD4 ⁺ T	0.368	0.123	-0.421	< 0.001
CD4 ⁺ /CD8 ⁺	0.639	0.425	-0.754	< 0.001
CD8 ⁺ T	0.696	0.125	0.422	< 0.001

3.3. Comparison of clinical indexes between the pylori-positive treatment group and non-treatment group

After treatment, DS 28 score, TNF- α level and CD8⁺ T of the treatment group were lower than those of the non-treatment group, and CD4⁺ T lymphocytes and CD4⁺/CD8⁺ ratio were higher than those of the non-treatment group ($P < 0.05$), as shown in Table 3.

Table 3. Comparison of clinical indexes between *H. pylori* HP treatment group and non-treatment group before and after treatment (mean \pm SD)

Group	DS28 points		TNF- α (ng/mL)		CD8 ⁺ T (%)		CD4 ⁺ T (%)		CD4 ⁺ /CD8 ⁺ (%)	
	Before	After	Before	After	Before	After	Before	After	Before	After
Positive treatment group (n = 20)	6.20 \pm 3.02	3.19 \pm 1.02	3.33 \pm 1.22	1.33 \pm 0.74	32.36 \pm 10.23	19.59 \pm 6.58	19.88 \pm 7.55	26.55 \pm 8.52	0.82 \pm 0.24	1.45 \pm 0.52
Positive non-treatment group (n = 20)	6.22 \pm 3.12	5.36 \pm 1.85	3.34 \pm 1.21	2.89 \pm 0.98	32.34 \pm 10.22	26.39 \pm 8.25	19.36 \pm 7.66	20.66 \pm 6.85	0.81 \pm 0.23	1.10 \pm 0.36
t	0.020	4.593	0.026	5.681	0.006	2.881	0.216	2.446	0.134	2.474
P	0.983	< 0.001	0.979	< 0.001	0.995	0.007	0.833	0.019	0.893	0.018

4. Discussion

Rheumatoid arthritis is an immune disease related to T-lymphocytes, and the cause of its development is complex, but it is related to genetics and environment^[5]. Patients with decreased immune function and inflammatory factors lead to cartilage damage and patients may develop joint deformity, which seriously affects their normal life^[6]. Studies have shown that T-lymphocyte dysfunction is associated with the development of rheumatoid arthritis, and monitoring T-lymphocyte levels can help in the early diagnosis of the disease^[7]. Currently, some studies have suggested that the presence of *Helicobacter pylori* is associated with some rheumatoid arthritis patients^[8]. There are fewer studies investigating the correlation between rheumatoid arthritis with *H. pylori* patients and T-lymphocyte dysfunction and analyzing the correlation between rheumatoid arthritis with *H. pylori* patients and T-lymphocyte dysfunction can help to evaluate the impact of *H. pylori* clearance on the therapeutic efficacy of rheumatoid treatment.

The results of this study showed that before treatment, the levels of CCP, DS28 score and CD8⁺ T in the

pylori-negative group were lower than those in the positive group, and the CD4⁺ T and CD4⁺/CD8⁺ ratios were higher than those in the positive group ($P < 0.05$). It is suggested that the presence of *H. pylori* in patients with rheumatoid arthritis has a certain impact on immune function. DS28 (3.19 ± 1.02) in the positive treatment group and DS28 (5.36 ± 1.85) in the positive non-treatment group, the DS28 score in the treatment group was positively correlated with the peripheral blood T lymphocyte subpopulation, and the DS28 score in the non-treatment group was negatively correlated with CD4⁺ T, CD4⁺/CD8⁺, and negatively correlated with CD8⁺ T ($P < 0.05$). It is suggested that there is a correlation between *H. pylori* and lymphocyte level changes in rheumatoid arthritis. *Helicobacter pylori* in rheumatoid arthritis patients cause elevated levels of immune complexes. *H. pylori* is a spiral-shaped bacterium that survives within the epithelium of the gastric mucosa and produces a large number of toxins, causing damage to the gastric mucosa of patients and disruption of the integrity of the intestinal mucosa, which results in the displacement of lymphoid organs and abnormal levels of lymphocytes [9]. After treatment, the DS28 score, TNF- α level, and CD8⁺ T of the treatment group were lower than those of the non-treatment group, and the CD4⁺ T lymphocytes and CD4⁺/CD8⁺ ratio were higher than those of the non-treatment group ($P < 0.05$). It is suggested that the removal of *H. pylori* from rheumatoid arthritis patients helps to improve the level of T lymphocyte subsets in patients. Wang Z *et al.* (2023) showed that peripheral blood lymphocytes showed a negative correlation with D-lactic acid levels and a positive correlation with immunoglobulins [10]. Rheumatoid arthritis patients have *Helicobacter pylori* will affect the patient's immune regulation function, stimulate the lymphocytes to cause immune function damage and reduce the T-lymphocyte immunoregulatory function is reduced, so the *H. pylori* in rheumatoid arthritis patients can effectively regulate the patient's immune function, which is of great value in the treatment of rheumatoid arthritis.

5. Conclusion

In summary, rheumatoid arthritis-like *H. pylori* will affect the level of T lymphocyte subpopulations, with a certain relevance, the removal of *H. pylori* and the correction of intestinal flora can improve the level of T lymphocyte subpopulations, which is important for the treatment of rheumatoid arthritis patients.

Disclosure statement

The author declares no conflict of interest.

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