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Original Research Article

Patients' satisfaction with treatment using anti-rheumatic drugs, and their adherence to medication: A non-interventional, cross-sectional study among some Chinese outpatients

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Abstract

Purpose: *To determine satisfaction with treatment and adherence to medication amongst Chinese patients with rheumatoid arthritis.*
Methods: *This cross-sectional study enrolled 398 rheumatoid arthritis (RA) patients who filled out questionnaire during outpatient consultation. The Chinese version of the Treatment Satisfaction Questionnaire (C-TSQM-II) was used to evaluate treatment satisfaction, while the Chinese Compliance Questionnaire for Rheumatology (threshold ≤ 80) and the medication possession ratio (MPR) were used for the assessment of adherence to medication.*
Results: *In all medications, treatment satisfaction was higher in the mild subgroup and the moderate subgroup than in the severe subgroup ($p < 0.05$). Treatment satisfaction scores with respect to biological disease-modifying anti-rheumatic drugs (bDMARDs) were significantly lower in patients in the severe subgroup than in those in the moderate subgroup, with respect to convenience and global satisfaction ($p < 0.05$). Moreover, for bDMARDs therapies, treatment satisfaction was higher in the moderate subgroup than in the severe subgroup in all four areas examined ($p < 0.05$). The Chinese Compliance Questionnaire score showed that 156 patients (39 %) were adherent to medication, while 242 patients (61 %) were not. Results from MPR indicate that 310 patients (78 %) were adherent to medication, while 68 patients (22 %) were not. In the mild group, 96.5 % of patients were adherent to all medications, and 94.4 % were adherent to bDMARDs.*
Conclusion: *Patients were most likely unable to distinguish amongst disease progression, disease-induced damage, and other causes of pain or discomfort. Treatment satisfaction and medication adherence were higher in patients with mild rheumatoid arthritis.*

Keywords: *Compliance Questionnaire score, Rheumatoid arthritis, Treatment satisfaction, Treatment Satisfaction Questionnaire, Medication adherence, Treatment outcomes*

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune and inflammatory disease which manifests as painful, tender, and swollen joints. It may result in loss of function, poor quality of life, work disability, and severe socio-economic consequences [1]. It is considered a common

disease with a prevalence of 0.42 % [2]. To maintain quality of life, prevent structural injury, and normalize routine activities, RA patients need a treat-to-target (T2T) strategy [3,4]. Studies have shown that treatment of RA is at the rudimentary stage in China, and the T2T strategy has not been applied appreciably [5].

The current strategies support the diagnosis of the disease at an early stage and the commencement of effective therapy as soon as possible in order to achieve the desired goals. Treatment satisfaction plays a vital role in the assessment of a patient's overall health-related outcomes. However, since treatment satisfaction is influenced by various factors, it is not a well-known determinant of treatment efficacy in Chinese patients with RA [6]. Treatment satisfaction may vary as a function of disease severity, thereby leading to serious consequences. Therefore, a knowledge of patients' satisfaction concerning disease severity may help in achieving better treatment outcomes.

Treatment satisfaction in patients provides valuable insight into development of medication adherence. Poor patients' satisfaction leads to poor medication adherence which inevitably affects treatment outcomes in RA patients [7,8]. Medication adherence is defined as the degree to which the person's drug-taking behavior relates to the prescribed regimen of a health care provider [9]. Achieving these therapeutic goals requires adequate patient adherence and satisfaction with medications. No adequate studies have been carried out previously on the correlation between treatment satisfaction and medication adherence among Chinese patients with RA. Thus, there is insufficient data regarding treatment satisfaction and patient's adherence to medication, particularly among RA patients in China.

A better knowledge of the factors associated with patients' adherence to medication and treatment satisfaction is crucial for improving clinical care and treatment outcomes. The precise mechanism through which treatment satisfaction is correlated with adherence is unknown. Previous studies conducted among RA patients have associated treatment satisfaction with several factors that are identified as indicators of medication adherence.

The present study was aimed at assessing patients' treatment satisfaction in line with disease severity and medication adherence, as well as identification of factors that contribute to non-adherence to medication.

METHODS

Study design and population

This non-interventional cross-sectional study was conducted in The Second Affiliated Hospital of Nanchang University, Nanchang, China, from April 15, 2019 to January 1, 2022. The participants in this survey were diagnosed RA patients of Chinese origin who had been taking either DMARDs or medications other than DMARDs for more than 3 years.

Ethical approval and consent to participate

The research ethics committee of Nanchang University approved this study (approval no. GJJ210102 dated April 3, 2019). The study reporting adheres to the law of China and the V2008 Declarations of Helsinki [10]. Written informed consent was obtained from each patient who participated in this study after explaining the purpose of the study.

Inclusion criteria

Patients diagnosed with RA who had been taking either disease-modifying antirheumatic drugs (DMARDs) or medications other than DMARDs for more than 3 years, were included in the study.

Exclusion criteria

The excluded patients were those who were not willing to participate in the study, patients who were unable to either speak Chinese language or read Chinese literature, and pregnant women.

Demographic and disease characteristics

During routine rheumatologic medical follow-up, a meeting was arranged either with a nurse or a pharmacy student. Demographic characteristics such as age, sex, body mass index (BMI), duration of disease (RA), as well as assessment of low disease level and remission were obtained from the patients. Various criteria were used to measure the disease levels of patients through data on other disease-related characteristics from their medical files. Data regarding DMARDs and all other medications were obtained. Moreover, the participants were asked whether they had been taking the same treatment for the previous three months.

Classification of severity of RA disease

Joint tissue inflammation without swelling, pain and stiffness was considered mild RA, while joint

tissue inflammation with swelling and mild-to-moderate pain was considered a moderate RA. On the other hand, joint tissue inflammation with swelling, severe pain, and stiffness was considered a severe RA. These categorizations were based on institutional protocol for classifying severity of RA (unpublished).

Determination of treatment satisfaction

The self-reported Chinese Version of Treatment Satisfaction Questionnaire (C-TSQM-Ⅱ) was used to determine patients' satisfaction with RA treatment. It consisted of eleven questions in four areas: effectiveness of treatment, side effects, convenience of administration, and global satisfaction. The score in each domain ranged from 0 to 100, with 0 implying *extremely dissatisfied*, and 100 denoting *extremely satisfied* [6]. The treatment satisfaction of patients was assessed using the C-TSQM- Ⅱ for DMARDs as well as for all medications. The patients were subdivided into two groups i.e., patients receiving all medications and patients receiving biological disease-modifying antirheumatic drugs (bDMARDs). The two subgroups were analyzed with C-TSQM- Ⅱ based on the severity of RA (severe, moderate, and mild).

Determination of adherence to medication

The Chinese Compliance Questionnaire for Rheumatology was applied for the evaluation of medication adherence. It comprised 19 items set on a four-point response scale (4: fully agree, 3: agree, 2: not agree, 1: completely disagree) with Cronbach's α co-efficient of 0.87. A total score of 80 or less was considered as non-adherence [11].

Evaluation of medication possession ratio

The medication possession ratio (MPR) was calculated by dividing the number of supplied medications by the number of prescribed medications over 6 months. The number of bDMARDs dispensed during the period was obtained with the help of a pharmacist.

The results were first analyzed, and then translated into the English language. The Faculty of English language of the institute was involved in the translation process for both the questionnaires and the results.

Statistical analysis

Descriptive statistics were utilized to summarize all factors from surveys. Categorical variables are expressed as frequencies and percentages. Continuous variables are expressed as mean ± standard deviation (SD) or mean and interquartile range. The SPSS 26.0 (IBM Incorporation, Armonk, New York, United States) was used for statistical analysis. The Kolmogorov-Smirnov test was used to assess the normality of each parameter, while the Mann-Whitney *U*-test was used for statistical analysis of non-normal parameters. Differences were considered significant at *p*-values less than 0.05.

RESULTS

Characteristics of patients

Three hundred and ninety-eight patients were enrolled and surveyed in this study. The demographic and clinical variables of the patients are depicted in Table 1. The mean age of the participants was 62.2 ± 14.2 years, and females comprised 72 % of the study population. The mean age of disease onset in patients was 54.1 ± 15.21 years, and mean disease duration was 9.1 ± 8.15 years. Moreover, 36.4 % of patients had low disease severity, while 64.3 % of the patients experienced remission. With respect to the different criteria used to determine the disease status, 65.8, 58.1, and 42.1 % belonged to Disease Activity Score-28 for RA based on the level of C-reactive protein (DAS28-CRP), physician's clinical judgment, and Computer Science and Artificial Intelligence (CSAI), respectively. Among subjects using conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), 72.1 % of the patients were on methotrexate, while 41.3 % were on medications other than methotrexate. On the other hand, 32.4 % of the patients were on bDMARDs, while 9 % of the patients were on targeted synthetic disease-modifying antirheumatic drugs (DMARDs). In addition, 26.4 % of patients using medications other than DMARDs were on corticosteroids, while 32.2 % of them were on non-steroidal anti-inflammatory drugs (NSAIDs).

Treatment satisfaction of patients as a function of disease severity

The C-TSQM-Ⅱ summary scores of RA patients following different self-assessments of severity are depicted in Table 2.

With respect to all medications, treatment satisfaction was higher in the mild subgroup than in the severe subgroup of RA patients in terms of effectiveness ($p = 0.0275$), side effects ($p < 0.0001$), convenience ($p = 0.0002$), and global satisfaction scores ($p < 0.0001$).

Table 1: Demographics and disease characteristics of RA patients

Characteristic		Values
Patients enrolled and surveyed		398
Gender	Female (%)	286 (72)
	Male (%)	112 (28)
Age (years)		62.2±14.21
Body mass index (kg/m^2)		22.7±4.14
Age at diagnosis (years)		54.1±15.21
Duration of RA (years)		9.1±8.15
Low disease level (%)		145 (36.4)
Remission (%)		253 (63.6)
Disease state criteria		
SDAI		148 (37.2)
CDAI		168 (42.2)
DAS28-CRP		262 (65.8)
DAS28-ESR		136 (34.2)
Boolean criteria		76 (19.1)
X-ray		127 (31.9)
Health Assessment Questionnaire		48 (12.0)
Quality of life (e.g., EQ-5D-5L)		17 (4.3)
Physicians' clinical judgment		231 (58.1)
Pt-GA VAS (mm)		129 (32.4)
Ph-GA VAS (mm)		145 (36.5)
Others		22 (5.6)
DMARD treatment		
csDMARD (MTX)		287 (72.1)
csDMARD (other than MTX)		164 (41.3)
tsDMARD (JAK inhibitor)		9 (2.3)
bDMARD		193 (48.4)
Medications other than DMARDs		
Corticosteroids		105 (26.4)
NSAIDs		128 (32.2)
Similar treatment for the past 3 months		355 (89.2)
Disease characteristics		
TJC28		1.1±1.3
SJC28		0.8±0.9
CRP (mg/dL)		0.7±0.92
ESR (mm/hour)		19.8±17.32
Ph-GA VAS, 0–100 mm		10.1±8.71
Pt-GA VAS, 0–100 mm		9.1±12.98
DAS28-CRP		2.1±0.42
DAS28-ESR		1.8±0.71
CDAI		3.3±2.17
SDAI		2.9±2.89

RA: Rheumatoid arthritis, SDAI: Simple Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28-CRP: Disease Activity Score-28 for Rheumatoid Arthritis with the level of C-reactive protein; DAS28-ESR: Disease Activity Score-28 for Rheumatoid Arthritis with erythrocyte sedimentation rate; EQ-5D-5L: Euro quality of life scale-five dimension-five length; Pt-GA VAS: Patient-reported Global Anxiety-Visual Analog Scale; Ph-GA VAS: Physician-reported Global Anxiety-Visual Analog Scale; DMARDs: Disease-Modifying Antirheumatic Drugs; csDMARD (MTX): Conventional Synthetic Disease-Modifying Antirheumatic Drugs (methotrexate); tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs, JAK inhibitor: Janus kinase inhibitors; bDMARDs: biological Disease-Modifying Antirheumatic Drugs; NSAIDs: Non-steroidal anti-inflammatory drugs; TJC28: tender joint count based on 28-joint assessment; SJC28: Swollen Joint Count in 28 joints, CRP: C-Reactive Protein; ESR: Sed rate, or erythrocyte sedimentation rate

Moreover, treatment satisfaction for all medications was higher in the moderate subgroup than in the severe subgroup of RA patients with respect to effectiveness (p = 0.0142), side effects (p < 0.0001), convenience (p < 0.0001), and global satisfaction scores (p < 0.0001). In addition, comparison of treatment satisfaction with bDMARDs showed lower scores for convenience (p < 0.0001) and global satisfaction (p < 0.0001) in the severe subgroup patients than in those in the moderate subgroup. Treatment satisfaction with bDMARDs was higher in the moderate subgroup than in the severe subgroup of RA patients, with regard to effectiveness (p = 0.0101), side effects (p < 0.0001), convenience (p < 0.0001), and global satisfaction scores (p < 0.0001).

Assessment of medication adherence

Based on the Chinese Compliance Questionnaire for Rheumatology, a total of 156 (39 %) patients were adherent to medication, while 242 (61 %) patients were not adherent. Results of MPR calculation indicated that 310 patients (78 %) were adherent to medication, while 68 patients (22 %) were not adherent to medication. The Chinese Compliance Questionnaire for Rheumatology was also used to identify the factors that influenced non-adherence. The factors that were associated with non-adherence were female gender (p = 0.0412), age more than 60 years (p = 0.0392), economic burden (p = 0.0452), long disease duration (p = 0.0325), structural damage (p = 0.0411), co-morbidities (p = 0.0365), lack of family support (p = 0.0356), and poor medication knowledge (p = 0.0259). These data are presented in Table 3.

Assessment of medication adherence in the mild group showed that 96.5 % of patients were adherent to all medications and 94.4 % were adherent to bDMARDs.

DISCUSSION

In the current cross-sectional study, 398 patients with mean disease duration of 9 years participated by filling out the questionnaires. Seventy-two percent of patients on DMARDs were on methotrexate with or without other drugs, while 49 % used bDMARDs. Patient satisfaction with medication affects treatment outcomes. However, little is known about the status of patients' satisfaction with RA treatment in China.

Table 2: C-TSQM-II summary scores based on different self-assessments of severity by the enrolled and surveyed patients

Treatment	Severe	Moderate		Mild	
All medications (n)	**87**	**195**	**#*P*-value**	**116**	**#*P*-value**
Effectiveness	69 (5–91)	63 (5–92)	0.0142	75 (12–93)	0.0275
Side effects	51 (15–82)	63 (17–91)	<0.0001	71 (24–95)	<0.0001
Convenience	71 (21–88)	81 (23–93)	<0.0001	78 (27–89)	0.0002
Global satisfaction	57 (15–81)	66 (18–91)	<0.0001	77 (25–91)	<0.0001
bDMARDs (n)	**33**	**88**	**#*P*-value**	**72**	**#*P*-value**
Effectiveness	73 (45–91)	69 (33–92)	0.0943	81(55–93)	0.0101
Side effects	59 (37–82)	62 (51–82)	0.4303	82 (49–95)	<0.0001
Convenience	63 (47–78)	80 (48–93)	<0.0001	83 (74–89)	<0.0001
Global satisfaction	38 (26–63)	63 (27–91)	<0.0001	82 (62–91)	<0.0001

Variables were presented as mean and interquartile ranges. Mann-Whitney *U*-test was used for statistical analysis. #vs. value for the severe RA subgroup

Table 3: Factors contributed to non-adherence to medication among enrolled and surveyed patients

Patient characteristic	Odds ratio	CI (%)	*P*-value
Gender (*female *vs*. male)	1.1212	1.0122–1.5611	0.0412
Age (>60 years* *vs*. ≤ 60 years)	1.2312	1.0012–1.4211	0.0392
Economic burden (*presence *vs*. absence)	1.2354	1.0125–1.5241	0.0452
Disease duration in years (*longer *vs*. shorter)	1.3251	1.0011–1.5432	0.0325
DAS28-CRP (abnormal *vs*. normal)	0.9851	0.8211–1.4231	0.2351
DAS28-ESR (abnormal *vs*. normal)	0.9125	0.7524–1.5241	0.4512
Structural damages (*presence *vs*. absence)	1.2541	1.0011–1.6241	0.0411
Co-morbidities (*presence *vs*. absence)	1.3654	1.2458–1.6524	0.0365
Therapeutic care (satisfied *vs*. dissatisfied)	0.8561	0.7531–1.5421	0.2582
Tolerance to medication(s) (good *vs*. worse)	0.9521	0.8524–1.4258	0.3561
Medication knowledge (*poor *vs*. strong)	1.2569	1.1422–1.5248	0.0259
Family support (*lack *vs*. strong support)	1.2564	1.1256–1.6524	0.0356

Using Multivariate analysis, *p* value less than 0.05 and an odds ratio of more than 1 were considered significant. Data of patients with adherence (n = 156) were considered as the reference standard. *Significant parameter for no adherence. (DAS28-CRP: Disease Activity Score-28 for Rheumatoid Arthritis with the level of C-reactive protein, DAS28-ESR: Disease Activity Score-28 for Rheumatoid Arthritis with erythrocyte sedimentation rate)

Hence, this study was aimed at evaluating treatment satisfaction based on disease severity. The results revealed that patients in the severe subgroup were dissatisfied with bDMARDs and all medications when compared to those in the mild subgroup. This result is consistent with the finding in a subgroup study involving cross-sectional analysis which reported that prolonged disease duration along with economic burden led to dissatisfaction [12]. Therefore, the results of the present study support the current T2T strategy and indicate the need for early diagnosis and treatment of RA to prevent disease progression and improve quality of life. This concept is not largely endorsed in China. Although non-adherence may lead to low satisfaction, data regarding the relationship between treatment satisfaction and medication adherence is scanty [13]. Thus, this study also involved assessment of medication adherence in these patients.

Using the Chinese Compliance Questionnaire for Rheumatology and MPR, the populations of patients with medication adherence comprised 39 and 78 %, respectively. The results obtained for medication adherence in the current study are similar to those of a cross-sectional study in which different methods were used to assess treatment adherence [14]. The MPR was also calculated, and it gave a higher value than declarative adherence. Moreover, numerous studies have shown various socio-demographic factors and disease-related characteristics that influence low adherence. In the current study, poor medication knowledge, economic burden, lack of family support, presence of structural damages, and comorbidities were identified as the major factors that contribute to non-adherence [14]. Moreover, patients with older age and longer disease duration were found to have no adherence. This is in agreement with similar results in a 2-year prospective cohort study [15] and a cross-sectional descriptive study [16]. On the other hand, two cross-sectional studies [17,18] have shown that socio-demographic and disease characteristics have little or no influence on non-adherence. Sub-optimal therapeutic adherence in RA patients and socio-demographic and disease characteristics have effects on medication adherence. The current study found high

degrees of medication adherence and treatment satisfaction in the mild subgroup of RA patients. Usually, patients who are satisfied with treatment are more likely to show adherence to the medications, leading ultimately to greater treatment outcomes [19-21]. If patients have high treatment satisfaction, they will have high adherence to treatment regimens.

Based on patient demographics and disease characteristics, all patients either had low disease levels or were in remission. However, there were disagreements between physician-assessed disease severity and self-assessed disease severity. This discrepancy most likely indicates that the disease severity was either underestimated by the physicians or (more likely) that RA-independent factors (e.g., pain from osteoarthritis or other causes) affected the self-assessed disease severity. It is most likely that the patients were not able to distinguish amongst disease severity, damage caused by disease, and other causes of pain or discomfort. However, these independent factors most likely affected treatment satisfaction and medication adherence.

Limitations of the study

Although the study highlighted several findings, it has certain limitations. For example, a possible overestimation of adherence with self-reported adherence by patients might have resulted in recall biases. Furthermore, adherence is a process that may change over time due to patient's beliefs. Therefore, a longitudinal study is needed, since a cross-sectional study is unable to measure changes over time. Future research is required to recognize the true mechanisms by which treatment satisfaction is correlated with adherence to anti-rheumatic medications. In survey-based studies, the degree of response of a specified, sampled population should be over 65 %, or there should be robust measures to ensure that non-response bias is minimal. However, there was no information on the sampling frame, sampling procedures, sample size determination, and response rate, and there was no discussion on the representativeness of the samples and any potential for sampling bias. Moreover, a fuller analysis of the data should be considered e.g., only a comparison of different subgroups using descriptive statistics was done, but these differences were not tested between subgroups. Moreover, it would have been helpful to use a logistic regression model to identify which characteristics are associated with low adherence. The number of patients on csDMARD monotherapy, bDMARD monotherapy, combination therapy of csDMARD and bDMARD, or tsDMARD must be reported and compared. In addition, the number of patients on glucocorticoids monotherapy or in combination with DMARDs must be reported. Although the relationship between patient satisfaction and adherence is an important issue, the analysis is descriptive. In this study, the relationship between satisfaction and adherence was not necessarily clear. In addition, the definition of the severity of RA disease based on "joint tissue inflammation without swelling, pain, and stiffness" is not widely accepted because it is very subjective.

CONCLUSION

The findings of this study show that treatment satisfaction and medication adherence are higher in the mild subgroup than in severe subgroup, suggesting a possible association between both. The findings also indicate that patients with rheumatoid arthritis show a reduction in compliance with prescribed medication is associated with older age, disease duration, socioeconomic status, presence of comorbidities, reduced mobility, lack of family support, and lack of knowledge about the prescribed medications. Improvement in treatment satisfaction enhances medication adherence. The study further highlights the suboptimal therapeutic adherence in RA patients and the need to improve it by identifying the modifiable factors associated with patients' satisfaction and treatment adherence.

DECLARATIONS

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Ethical approval

This study was approved by the Ethics Committee of Nanchang University (approval no. GJJ210102).

Availability of data and materials

The datasets used and/or analyzed during the

current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors have read and approved the manuscript for publication. Huying Zhang was the project administrator and contributed to supervision, visualization, resources, and the literature review of the study. Yurong Gu contributed to resources, funding, and literature review of the study, and drafted, and edited the manuscript for intellectual content. Lu Chen contributed to the resources, methodology, conceptualization, literature review, and software of the study. Jinwei Zhu contributed to the literature review, investigation, methodology, resources, and data curation of the study. Chao Luo contributed to the literature review, data curation, formal analysis, methodology, and resources of the study. Weijun Zhou contributed to the literature review, formal analysis, methodology, resources, and supervision of the study. All authors agree to be accountable for all aspects of work with regard to integrity and accuracy.

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