Positive affect as a predictor of adherence in patients with rheumatoid arthritis

Rodrigues JR[1], Faria DS[1], Neves JS[1], Silva J[1], Peixoto D[1], Alcino S[1], Afonso MC[1], Teixeira F[1], Afonso RM[2], Pereira H[3], Azevedo S[1], Costa JT[1]

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ABSTRACT

The study was conducted in order to investigate adherence in patients with rheumatoid arthritis (RA), correlating it with other variables such as affect and self-esteem. Seventy-eight patients with RA between 20 and 81 years of age were evaluated. Patients were assessed for Medical Outcomes Study (MOS) Measures of Patient Adherence, Rosenberg self-esteem scale and Short Portuguese version of the Positive and Negative Affect Schedule (PANAS). Pearson's correlation coefficient was used to assess the correlation between the therapeutic compliance and age, disease activity, disability, GPA, self-esteem, affect and inflammatory parameters. An independent T-test was used to evaluate differences in adherence within gender. The one-way analysis of variance (ANOVA) was used to determine associations between adherence and marital status, education level and employment status. A linear regression model was adjusted with stepwise data entry to determine predictors of therapeutic compliance.

Patients had a mean age of 57 years and disease duration of 12.8 years. We observed higher levels of adherence in patients with higher self-esteem ($r= 0.343$, $p<0.05$) and positive affect ($r= 0.345$, $p<0.01$). The adjusted linear regression model allowed the identification of positive affect as a RA patient's adherence predictor ($R = 0.347$, $p<0.05$).

In our study, high levels of self-reported adherence in RA patients were found. Positive affect seems to be an important determinant of therapeutic adherence in RA patients. These results suggest a relevant role of psychosocial aspects in therapeutic compliance and outcome, which should alert physicians to the need of an holistic approach of the patient.

Keywords: Patient Compliance; Rheumatoid Arthritis; Self-esteem; Treatment Compliance

1. Serviço de Reumatologia, Hospital Conde de Bertiandos, Ponte de Lima, Unidade Local de Saúde do Alto Minho
2. Center for Health Technology and Services (CINTESIS- FMUP), Universidade da Beira Interior (UBI)
3. Centro de Investigação em Ciências da Saúde (CICS-UBI), Universidade da Beira Interior (UBI)

INTRODUCTION

As defined by the World Health Organization, adherence is "the extent to which a person's behaviour - taking medication, following a diet and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider"[1]. Patient adherence to appropriately prescribed medications is essential for treatment efficacy and positive therapeutic outcomes[2]. It is estimated that approximately 50% of patients with chronic illnesses are non-adherent to their medication regimens[1]. Poor adherence is associated with treatment inefficacy, increased patient morbidity and mortality as well as increased healthcare costs[2-5]. In light of its prevalence and far-reaching consequences, it comes as no surprise that medication adherence is increasingly becoming recognized as a prominent challenge to clinicians, researchers and policymakers[2].

Medication adherence is affected by multiple determinants[6]. The development of interventions to enhance patient adherence to medication and maintain long-term persistence requires an understanding of the determinants of patient non-adherence to prescribed therapies. Understanding factors associated with maintaining one's medication regimen is important to patients, providers, and health plans[7]. External factors such as cost and access to the needed medication play a role in non-adherence[7]. The literature has reported some evidence of variation of adherence by age, race, co-morbidity status, and socioeconomic status[7-9]. Rolnick and colleagues found lower adherence in minorities, those with lower socioeconomic status, multiple

conditions, taking multiple drugs, and multiple dosing[7]. Patient's personality factors included forgetfulness, patient's coping behaviors, personality traits and quality of life[5].

Rheumatic diseases are a huge burden on the healthcare system worldwide.[5] Medication adherence is a crucial part in the management of rheumatic diseases, especially with many such patients requiring long-term treatment[5]. Adherence to medication in patients with rheumatoid arthritis (RA) is low, varying from 30 to 80%[10]. Medication nonadherence has negative consequences on RA pharmacological treatment, as disease-modifying antirheumatic drugs (DMARDs) reduce disease activity and radiological progression and improve long-term functional outcome in RA patients[10]. Thus, adherence to the prescribed drugs is important in the prognosis of the disease.

There is very little data on treatment compliance and its predictors in Portuguese RA patients. For this reason, and given the relevance of therapeutic compliance in RA, is fundamental to estimate its prevalence and possible determinants. The primary objective of this work was to investigate adherence in patients with RA, correlating it with affect and self-esteem. Other aims of this study were to identify an association between treatment compliance and socio-demographic aspects (gender, age, education level, marital and employment status) and clinical characteristics (disease activity, inflammatory parameters, disability status and global patient assessment).

METHODS

It was an observational, cross-sectional and analytical study. Participants were consecutively recruited by their rheumatologist between November 2017 and January 2018. Inclusion criteria were defined as adult patients (≥18 years) with RA diagnosis, according to 2010 ACR/EULAR RA Criteria. Firstly, a written informed consent was obtained and then an anonymous questionnaire was filled by RA outpatients after observation at the rheumatology consultation. Patients answered the questionnaires without clinician's intervention and clinical data were collected afterwards and independently. Patient's data collection was done by at least two independent investigators and statistic was treated by independent investigators.

Sociodemographic (age, gender, marital status, years of schooling, employment status) and clinical data (disease duration, disability status, inflammatory parameters, disease activity, global patient assessment (GPA), treatment regimen and physical activity) were collected. Disability status was measured by the Health Assessment Questionnaire (HAQ) and disease activity was assessed by 28-joint Disease Activity Score with four variables (DAS28 4v). This score classifies disease activity as remission (≤ 2.6), low disease activity (> 2.6 to ≤ 3.2), moderate disease activity (> 3.2 to ≤ 5.1) and high disease activity (>5,1)[11].

Participants were then evaluated using the following instruments:

- *Medical Outcomes Study (MOS) Measures of Patient Adherence:* a measure containing five questions developed for assessing the adherence of patients. The general measure of adherence indicates a patient's tendency to adhere to medical recommendations. To score general adherence, we averaged together the responses to the five general adherence items after reversing the scoring of items 1 and 3. The total score is 30 points, with higher scores denoting higher adherence[12].
- *Rosenberg Self-esteem Scale:* a self-esteem assessment measure validated for the Portuguese language that contains ten questions designed to globally assess an individual's positive or negative attitude regarding himself/herself. The total score is 30 points, with higher scores denoting lower self-esteem[13].
- *The Short Portuguese version of the Positive and Negative Affect Schedule (PANAS)*: is a self-report questionnaire that consists of a 10 item scale to measure both positive and negative affect. Each item is rated on a Likert scale of 1 to 5. The total score is 50 points (reversing the scoring of items 1 and 3), with higher scores denoting higher positive affect[14].

All totally responded questionnaires by RA patients were included.

STATISTICAL ANALYSIS

Categorical variables are presented as frequencies and percentages, and continuous variables as means and standard deviations, or medians and interquartile ranges for variables with skewed distributions. Normal distribution of data was tested using the Shapiro-Wilk test or the asymmetry and kurtosis value analysis for psychometric variables (asymmetry and kurtosis 3 and 8 maximum values were acceptable, respectively). Pearson's correlation coefficient was used to assess

the correlation between the therapeutic compliance and age, disease activity, disability, GPA, self-esteem, affect and inflammatory parameters. The value of r 0.0-0.19 was accepted as very weak, 0.2-0.39 as weak, 0.4-0.59 as moderate, 0.6-0.79 as strong, and 0.80-1.0 as very strong[15]. An independent T-test was used to evaluate differences in adherence within gender. The one-way analysis of variance (ANOVA) was used to determine associations between adherence and marital status, education level and employment status. A linear regression model was adjusted with stepwise data entry to determine predictors of therapeutic compliance. All reported *p-values* were two-tailed, with a 0.05 significance level (α). Data analysis was carried out using SPSS software, version 23.

RESULTS

In total, 85 RA patients were initially invited to participate, of whom 7 were excluded as they didn't complete the questionnaire (4 patients) or refuse to participate (3 patients). The sociodemographic and clinical characteristics of RA patients are shown in Table I. In the overall sample, most patients were female (76.9%), married (74.4%) and retired (42.3%). The group had a mean age of 57.0 ±14.8 years and disease duration of 12.8±9.8 years. Most patients were categorized in remission (51.9%) and were under treatment with classical DMARDs (cDMARD's) (59.7%). Table II displays scores on the assessment measures for adherence, self-esteem and affect. Mean adherence was 25.8 ± 4.8, with 83% of patients obtaining a total score >15. Higher adherence levels correlated with lower disease activity (r= -0.269, $p<0.05$) and lower erythrocyte sedimentation rate (ESR) levels (r= -0.246, $p<0.01$). Patients with higher self-esteem and higher positive affect also had higher levels of therapeutic compliance (r= 0.343, $p<0.05$; r= 0.345, $p<0.01$, respectively). No significant differences were found between adherence and: gender, age, marital status, education level or employment status. There were no significant differences between adherence and different treatment modalities (cDMARD's *versus* biologic DMARDs) ($p=0.273$). Pearson correlation coefficients between MOS and the disease activity variables, GPA, self-esteem, affect and inflammatory parameters are displayed in Table III.

Since positive affect showed a significant correlation with adherence, a linear regression model was created to determine whether or not affect was a predictor of

TABLE I. SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF AR PATIENTS

Socio-demographic characteristics	n (%)
Gender	
Female	60 (76.9%)
Male	18 (23.1%)
Age mean ± SD (in years)	57.0 ± 14,86
Marital Status	
Single	7 (9.0%)
Divorced	4 (5.1%)
Married	58 (74.4%)
Widow	9 (11.5%)
Education Level	
Illiteracy	2 (2.7%)
Primary school	45 (60.0%)
High school	28 (37.3%)
Employment status	
Unemployed	13 (16.7%)
Medical Leave	5 (6.4%)
Employed	20 (25.6%)
Retired	33 (42.3%)
Student	3 (3.8%)
Other	4 (5.1%)
Regular physical activity	
Yes	18 (24.3%)
No	56 (75.7%)
Clinical characteristics	
Treatment regimen	n (%)
cDMARDs	46 (59.7%)
bDMARDs	30 (39.0%)
Glucocorticoid	1 (1.3%)
Disease Activity (DAS28 4v score)	n (%)
Remission (≤ 2.6)	40 (51.9%)
Low disease activity (> 2.6 to ≤ 3.2)	19 (24.7%)
Moderate disease activity (> 3.2 to ≤ 5.1)	12 (15.6%)
High disease activity (>5,1)	6 (7.8%)
Disability (HAQ)	
Low disability (0 to ≤ 1)	45 (58.4%)
Moderate disability (> 1 to ≤ 2)	27 (35.1%)
High disability (> 2 to 3)	5 (64%)
Inflammatory parameters	
High ESR (mm/h)	52 (66,7%)
High CRP (mg/dL)	43 (55,1%)

cDMARDs – Classic Disease-modifying Antirheumatic Drugs, bDMARDs - Biologic Disease-modifying Antirheumatic Drugs; HAQ - Health Assessment Questionnaire; ESR - Erythrocyte Sedimentation Rate; CRP - C-Reactive Protein

TABLE II. SCORES ON THE ASSESSMENT MEASURES FOR RA PATIENTS

	Mean ± SD	Minimum	Maximum
MOS	25.8±4,8	13	30
ROSENBERG	30.5±5,7	17	40
PANAS	3.5±0,7	1.9	5

MOS - Medical Outcomes Study (Measures of Patient Adherence); Rosenberg -Rosenberg Self-esteem Scale; PANAS - Short Portuguese version of the Positive and Negative Affect Schedule

TABLE III. PEARSON CORRELATION COEFFICIENTS BETWEEN MEDICAL OUTCOMES STUDY (MOS) MEASURES OF PATIENT ADHERENCE AND OTHER VARIABLES

		p-value
Disease Activity	-0.269	<0,05
HAQ	-0.210	0,09
GPA	-0.211	0,08
Self-esteem	0.343	<0,05
Positive Affect	0.345	<0,01
Negative Affect	0.073	0,56
ESR	-0.246	<0,01
CRP	-0.120	0,75

HAQ - Health Assessment Questionnaire; GPA – Global Patient Assessment; ESR - Erythrocyte Sedimentation Rate; CRP - C-Reactive Protein

therapeutic compliance in RA patients. Although a significant correlation between negative affect and adherence was not found (p=0.56), authors considered it relevant so it was also included in the model.

The adjusted linear regression model allowed the identification of positive affect as RA patient's adherence predictor. This model explains 35% of variation in adherence (R = 0.347) with the positive affect being the most predominant variable.

DISCUSSION

Treatment adherence has not been widely examined for chronic inflammatory rheumatic conditions[16]. However, the current literature suggests that nonadherence is an important problem[16,17], and for this matter, RA has been the most studied rheumatic condition[16]. In our study, we found high levels of self-reported adherence in RA patients. Similarly, Taal and colleagues interviewed 71 patients of whom 66 (93%) had no difficulty adhering to medications[18]. Owen and coworkers interviewed 178 patients of whom 113 (63%) claimed that they did not alter the dose of their medication from the prescriber's indications[19]. Park *et al.* used electronic devices to measure openings of pill bottles over a one-month period in 121 patients[20]. In this sample, 38% had presumably perfect adherence based on openings of pill bottles. Among a cohort of 26 RA patients adherence was reported as 96% based on self-report, 77% based on pill counts and 58% based on a laboratory assay measuring a metabolite of D-penicillamine, over a 4 week period[21]. Thus, patient interviews or self-administered questionnaires may, on the other hand, overestimate adherence and lead to misinterpretation of treatment outcomes.

Most of our patients were under treatment with DMARDs. Harley, Frytak and Tandon[22] found that among 1668 patients receiving methotrexate and followed for one year, 64% achieved at least 80% adherence. Regarding biologic DMARDs (bDMARDs), adherence in 853 etanercept users and 141 infliximab users was assessed over one-year period based on pharmacy dispensing with adherence ≥80% occurring in 68% and 81% of users, respectively[22]. One explanation for these results is based on the route and frequency of administration among the three therapies. Previous studies have shown that patients who administer therapy subcutaneously frequently miss injections[23,24] and patients with RA and diabetes miss injections because of anxiety[23,25], and are reluctant to administer injections to themselves[23]. It was also demonstrated that patients with RA who switch from self-administered subcutaneous injection to intravenous infusion prefer the latter[26]. Wendling *et al.* reported nonadherence in only 1 of 41 infliximab users over a mean follow-up period of 15.3 months[27]. We found no differences between adherence and different treatments (cDMARDs vs bDMARDs).

Despite the evidence of variation of adherence by age, race, co-morbidity status, and socioeconomic status[7-9], no significant differences have been found between adherence and other sociodemographic data, such as gender, age, marital status, education level or employment status in this study. Rolnick and colleagues found lower adherence in minorities, those with lower socioeconomic status, multiple conditions, taking multiple drugs, and multiple dosing[7].

In RA, low disease activity or remission is an achie-

vable goal with cDMARDs and/or bDMARDs. A study developed for the assessment of medication persistence in RA patients treated with DMARDs verified that after 6 months of follow-up, patients with early RA who were adherent with DMARDs had lower disease activity scores (DAS28 4v score) and had less disability, with more frequent and earlier sustained remission than non-adherent patients[28]. Similarly, in our study, although the correlations were weak, we found lower disease activity and lower ESR levels in patients with higher adherence, but we didn't find any correlation between adherence and disability. Several other studies have also reported that severity of function impairment or disability did not affect medication adherence[29-32]. It's also known that adherence is recognized to require sustained behavioral change, influenced by both environmental and psychological factors[33]. We demonstrated that psychological factors, namely affect, may influence adherence. In the present study, RA patients with higher self-esteem and higher positive affect presented higher levels of therapeutic compliance. In our model, affect explains 35% of the adherence variation, with positive affect being the most predominant variable. This indicates that, even if affect seems to play an important role in adherence, many other factors are also implicated and should be sought and characterized. The authors highlight that negative affect remained non-statistically significant after the multivariate analysis, which reinforces the weight of positive affect in therapeutic compliance. Thus, a strategy aiming the creation of a positive attitude towards adherence could be much more effective than solely avoiding *less positive* conceptions around treatment. Also, patient's engagement with compliance could be more modifiable by a positive reinforcement during medical appointment than by punishment for non-adherence.

Our investigation also verified that influence on adherence remains qualitatively similar across therapy types (cDMARDs vs bDMARDs). Non-adherence may, therefore, be more linked to individual patient beliefs and well-being than to the actual disease or type and efficacy of treatment. An individual's illness perception, such as beliefs about disease consequences or perceived personal control, influence coping, including self-management strategies in response to the perception of a health threat[34].

This study has some potential limitations. Firstly, accurately defining and measuring adherence is difficult. Also, our sample is quite small and would be advisable to collect data from larger samples. In this study, only self-administered questionnaires regarding adherence were applied, and this can be regarded as a limitation because self-administered questionnaires can overestimate real adherence. We tried to mitigate this aspect by assuring the patient that data collection would be done by at least two independent investigators and statistic would be treated by independent investigators, but we realize this to be a limitation of this type of studies.

CONCLUSIONS

Medication adherence is affected by multiple determinants. The development of interventions to enhance patient adherence to medication and maintain long-term persistence requires an understanding of the determinants of patient non-adherence to prescribed therapies. Clinicians should routinely evaluate adherence issues during clinic visits, especially, but not only, in patients that are not responding as expected to medication.

As mentioned, self-administered questionnaires may overestimate adherence. More research is needed to investigate how to assess, predict and improve adherence. The prevalence and types of non-adherence and risk factors for non-adherence should be explored in more diverse populations.

CORRESPONDENCE TO
Joana Ramos Rodrigues
Serviço de Reumatologia, Hospital Conde de Bertiandos,
Ponte de Lima
E-mail: joanarodrigues_90@hotmail.com

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