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Factors associated with adherence to treatment in children and adolescents with chronic rheumatic diseases

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Abstract

Objective: There are several factors that contribute to poor adherence to treatment in children and adolescents with chronic rheumatic diseases, worsening their quality of life and prognosis. Our aim was to assess the rates of adherence to treatment and to identify the socioeconomic and clinical factors associated.

Methods: The sample included 99 patients with juvenile idiopathic arthritis, systemic erythematosus lupus, dermatomyositis or juvenile scleroderma. All patients were followed at the outpatient pediatric rheumatology for a minimum period of 6 months. To assess adherence, a questionnaire was administered to the providers, which included three blocks: 1) demographic, clinical and laboratory data; 2) medication adherence; and 3) attending follow-up appointments, examinations and use of orthoses. A value lower than or equal to 80% of the prescribed was considered poor adherence.

Results: A total of 53% of patients showed good overall adherence, observed when the caregiver lived in a stable union marital status ($p = 0.006$); 20 patients (20.2%) presented poor medication adherence, related to the use of three or more medications daily ($p = 0.047$). The causes of poor adherence were forgetfulness, refusal, incorrect dose or lack of medication, personal problems, and financial difficulties.

Conclusions: We observed good overall treatment adherence in patients whose providers lived in stable union and poor adherence to medication in patients who used more than three types of medication daily. There was no association between the adherence rates and sex, age, time since diagnosis and disease activity.

J Pediatr (Rio J). 2012;88(6):483-8: Patient adherence, therapy, chronic disease, pediatrics, rheumatology.

Introduction

According to the World Health Organization, adherence to treatment can be defined as the degree of agreement between the patient's behavior - taking medication, following a diet or implementing lifestyle changes - and the recommendations from a health care provider.^{1,2} Regarding therapy, the term "good adherence" is used when there is regular use of more than 80% of medications and other prescribed treatment modalities.²⁻⁶

It is known that poor adherence to treatment contributes to increasing symptomatology and unnecessary hospitalizations, often causing irreversible damage.^{1,6-11} Poor adherence is characterized as intentional when the patient decides not to follow the guidelines because he is asymptomatic, he does not understand the need for treatment, or because the use of medications interferes with his quality of life. On the other hand, it may not be intentional

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when it happens due to forgetfulness of the patient/provider or by difficulty to accessing medications.^{2,12}

Studies assessing treatment adherence in chronic diseases report several factors related to poor adherence and different degrees of association between them,^{1,2,7,10,13} such as: financial difficulties, complexity of therapeutic, adverse events, unsatisfactory doctor/patient relationship, ignorance regarding pathophysiology of the disease and the mechanism of action of drugs and its benefits, lack of motivation by the family and other people, among others.

The interest in evaluating the adherence of children and adolescents with chronic diseases has increased in recent decades, and studies that evaluate adherence in rheumatic diseases, in most cases, include only patients with juvenile idiopathic arthritis (JIA).^{3,4,6,7,9,11-14} The rates of medication adherence in chronic rheumatic diseases in children range from 38 to 96%,^{2,4,6,7,11,13-15} and are lower in adolescents (50-55%).^{2,15} Regarding non-medication treatments, the adherence varies from 40 to 86% for exercises^{2,6,11,13,14} and about 50% for using orthoses.²

The identification of factors that lead to poor adherence among patients with rheumatic diseases contributes to the formulation of strategies to promote adherence, improving quality of life and long-term prognosis of patients. This systematic study assessed rates of adherence to medication and non-medication therapies, the causes of poor adherence and association with variables in children and adolescents with chronic rheumatic diseases.

Methods

Prospective study, which included 99 patients consecutively selected, aged between 2 and 18 years, with definitive diagnoses (according to international criteria) of JIA,^{16,17} systemic lupus erythematosus,¹⁸ juvenile dermatomyositis¹⁹ and scleroderma,²⁰ with follow-up of at least 6 months at our Pediatric Rheumatology Outpatient Clinic and using one or more drugs at the time of evaluation. To assess disease activity, clinical and laboratory parameters used in the daily clinical practice were considered.²¹⁻²⁴

A quantitative questionnaire was developed, divided in three blocks: 1) block referring to demographic data and information about the disease, obtained by review of medical records; 2) block on the adherence to medication therapy within the last 4 weeks; and 3) block referring to adherence to follow-up appointments and inter-consultation examinations (including physiotherapy), and use of orthosis in the last 12 weeks.

The adherence rates were calculated for the last two blocks of the questionnaire, through the ratio between the total performed by the patient and the total prescribed by

the health staff. The thresholds for assessing adherence were based on the literature²⁻⁶ and patients with adherence values lower than or equal to 80% were classified as patients with poor adherence. This margin of 20% was used to include patients normally adherent, but which have presented errors throughout the evaluation period.

The questionnaires were administered to the primary provider by two evaluators who were not part of the regular patient care. The study was approved by the Research Ethics Committee of the institution, and the participants signed an informed consent form.

Descriptive analysis was performed to characterize the study population (means and standard deviation of age, age of onset, and disease duration of patients) To evaluate the risk factors related to treatment adherence, the Mann-Whitney test and the chi-square were used. Values of $p < 0.05$ were regarded as statistically significant.

Results

The 99 patients were assessed between June 2009 and August 2010. Among these, 53 (53.5%) presented good adherence to overall treatment (medication, follow-up appointments and exams). We did not observe significant differences between adherent and non-adherent participants, in relation to demographic and clinical data (Table 1).

Table 2 shows data on adherent and non-adherent patients regarding which provider responded the questionnaire, his level of education and marital status, family income and number of people at home. A higher frequency of adherence was observed in patients whose providers lived in a stable union marital status ($p = 0.006$). Regarding the remaining data, we did not observe any significant differences between adherent and non-adherent patients.

Regarding medication regimen, 79 patients (79.7%) presented good adherence. Table 3 presents the data of adherent and non-adherent patients to medication regimen, with respect to the way of acquisition of medications, who administers them, quantity, dosage, and route of administration. It could be observed that the use of higher daily intake of medications (over three different types) was associated with lower medication regimen adherence ($p = 0.047$).

Among patients with good medication adherence, 86.1% received medications free of charge, 17.8% by donation, 16.5% by distribution through the Brazilian public Unified Health System and 51.8% through both.

Causes of poor adherence to treatment were refusal ($n = 3$), suspension due to adverse effects ($n = 2$), forgetfulness ($n = 16$), wrong dose ($n = 2$) or lack of medication ($n = 5$). Medications with lower adhesion were:

Table 1 - Demographic and clinical data of adherent and non-adherent patients

Demographic and clinical data	Adherent patients (n = 53)	Non-adherent patients (n = 46)	p
Sex female/male	33/20	30/16	0.761*
Age at onset (mean in years \pm SD)	6.5 \pm 3.95	6.8 \pm 3.29	0.670†
Follow-up time (mean in years \pm SD)	6.4 \pm 3.52	6.2 \pm 3.46	0.744†
Age at moment of assessment (mean in years \pm SD)	12.9 \pm 3.08	13 \pm 3.74	0.611†
Age \leq 10 years	13	14	0.549*
Diagnosis			
Juvenile idiopathic arthritis	27	28	
Systemic lupus erythematosus	12	9	
Juvenile dermatomyositis	5	6	
Localized scleroderma	7	2	
Systemic scleroderma	1	0	
Overlap	1	1	
Active disease	27	22	0.757*

SD = standard deviation.

* Chi-square test.

† Mann-Whitney test.

Table 2 - Characteristics of the primary provider and socioeconomic status of adherent and non-adherent patients

Characteristics and socioeconomic status	Adherent (n = 53)	Non-adherent (n = 46)	p*
Mother respondent	32/53	29/46	0.932
Stable union	39/46	22/38	0.006†
Complete elementary school	26/52	29/45	0.152
Household income \leq 1 minimum wage	9/52	9/44	0.694
Families with more than 5 people	34/52	28/45	0.746

* Chi-square test.

† p < 0.05.

Table 3 - Way of acquisition and administration of medications in adherent and non-adherent patients

Acquisition and administration of medications	Adherent (n = 79)	Non-adherent (n = 20)	p*
Medication free of charge	68	18	0.643
Patient administers the medication	47	12	0.117
More than 3 medications per day	44	16	0.047†
Injectable medication	36	10	0.723
More than two doses per day	37	11	0.514

* Chi-square test.

† p < 0.05.

methotrexate ($n = 7$), hydroxychloroquine ($n = 3$) and azathioprine ($n = 2$).

Twenty patients (20.2%) presented low levels of attendance at follow-up appointments or inter-consultations, and the main causes were: transportation difficulties by financial problems ($n = 7$), mistake with the date scheduled ($n = 4$), personal problems ($n = 4$), not attending the appointment because they did not undergo the exams ($n = 3$), delayed or cancelled consultation ($n = 2$) and other ($n = 2$).

Ten out of 19 patients (52.6%) did not use prescribed orthosis, and the causes were refusal by the patient, ($n = 9$) and orthosis damage ($n = 1$).

Twelve patients (12.1%) did not undergo the exams due to personal problems ($n = 5$), forgetfulness ($n = 3$), technical problems in the laboratory ($n = 2$), refusal ($n = 1$), and transportation difficulties due to financial problems ($n = 1$).

Among 46 non-adherent patients, 19 (41.3%) had poor adherence to more than one type of intervention (medication appointments/inter-consultations, use of orthoses and undergoing exams).

Discussion

The present study, whose main characteristic was the systematization of data collection through a specific questionnaire, assessed the rates of adherence to drug and non-drug treatments in patients with chronic rheumatic diseases, the causes of poor adherence, and possible associations with variables. We observed good adherence to overall treatment in patients whose providers lived in stable union and poor adherence to therapy in those who used more than three different medications daily. On the other hand, disease activity, which is determinant for a poor prognosis, was not associated with adherence.

In the present study, the rate of adherence to medication was of 79.7%, and use of orthosis was of 52.6%, consistent with the literature.^{2,4,6,7,11,13,14}

We may interpret the stable union of patients' providers as a facilitating factor for greater family cohesion. The relation between good familiar cohesion and better adherence rates is a fact already observed in previous studies.^{2,7,9,15} In these cases, it is estimated that there is more familiar support, facilitating the adherence of patients. Although findings suggest a relationship between familiar cohesion and good adherence, a good familiar cohesion not always reflects in a better quality of life related to health in children and healthy adolescents.²⁵

Studies on adherence in patients with JIA reported higher adherence rates among patients whose families have a higher socioeconomic level,^{4,6,7} a fact that was not observed in our sample. Such finding may be explained by the fact

that most of our patients (86.8%) have low income, which did not allow a good differentiation between social classes. However, all our patients have free access to medications, either through donations or by government programs of access to expensive medication. Recently, we developed a specific questionnaire to identify factors associated with poor adherence, the Adherence Questionnaire in Pediatric Rheumatology [Questionário de Adesão em Reumatologia Pediátrica (QARP)], which assessed the socioeconomic parameters, relation with staff and health system, health conditions, treatment and provider/patient relationship. Our preliminary results show that the QARP identified higher correlation between poor adherence and socioeconomic parameter and can be a useful tool for early detection of patients at risk of poor adherence to treatment.²⁶

The complexity of the regimen is a factor that can interfere with treatment adherence rates.^{5,7,9,10} In the present study, the daily use of more than three different drugs was an indicator of poor adherence. This finding, which confirms a hypothesis made in developing the study design, is worrisome because children with chronic rheumatic diseases make use of various drugs and associations, with higher risk for poor adherence to medication, which could worsen their prognosis and quality of life.

Unintentional poor adherence behaviors, such as forgetfulness and the lack of use by unavailability of drugs, were prevalent and also reported in other studies.^{2,3,6,7} To characterize the types of poor adherence is useful for formulating specific strategies for each type, such as the creation of measures to recall schedules of medications in cases of unintentional poor adherence, and the promotion of education and awareness of providers and patients in intentional cases.²

There was a lower adherence rate to immunosuppressive drugs and disease modifiers. A study in patients with JIA in Boston and in Rio de Janeiro also demonstrated poor adherence to methotrexate.⁶ Thus, it is important to investigate the adherence of patients in case of poor response to the drug treatment, once the failure may not be the medication, thereby avoiding unnecessary changes in therapy.

The flaws in follow-up appointments and inter-consultations were also reported in other studies,^{7,9} and the most common causes were difficulties with transportation and with scheduling appointments, similarly to our findings. It needs a careful assessment by the social worker, so that these problems are predicted and the transportation is guaranteed. Furthermore, the healthcare team should facilitate the scheduling of appointments with the multi-professional team, as well as the collection of exams and procedures performance. The highest adherence rates found in our study may be related to factors intrinsic to our service, which includes multidisciplinary support and supply of drugs free of charge to most patients (86.1% of patients

with good medication adherence received medications for free, as stated in the results).

Another factor that may have contributed to achieving higher rates of adherence was the method used to assess it. It is recognized that the use of interviews and self-report questionnaires may overestimate the adherence rates.^{2,6,8,9,14} Other methods of adherence assessment should be applied to better accuracy of results.^{8,10} In a study for the assessment of adherence to antibiotic prophylaxis in patients with sickle cell anemia, authors stated that adherence should be assessed by several methods, due to its complexity.²⁷

Among the limitations of the study, we point that the small number of patients included may have hampered its discriminatory power, especially in the association of adherence with data such as disease activity and education level of the provider. The fact that there is no significant number of patients with higher income may also have hindered the assessment of adherence rates and socioeconomic factors. Similarly, the inclusion of patients with different rheumatic diseases that require different approaches and treatment plans, may have hampered the evaluation of the relationship between adherence rates and clinical factors. Additionally, we used only one method (interview) to assess adherence rates.

Healthcare professionals should be alert to factors related to poor adherence, such as lack of family cohesion and therapy with more than three different medications daily. The creation of strategies to promote good adherence and the continuous monitoring of patients with chronic rheumatic diseases in childhood and adolescence with risk factors for developing poor adherence are important to achieving the best response to medication and non-medication treatments.

The real impact of treatment adherence in children and adolescents with chronic rheumatic diseases is still unknown, and further studies are needed with larger number of patients, to assess causes of poor adherence and its consequences in the long-term prognosis of these patients.

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