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ORIGINAL RESEARCH

Predictors of medication nonadherence in patients with systemic lupus erythematosus in Sichuan: a cross-sectional study

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Purpose: The aim of this study was to determine the prevalence and predictors of medication nonadherence among patients with systemic lupus erythematosus (SLE) in Sichuan.

Patients and methods: A cross-sectional investigation was performed. Participants were recruited by consecutive sampling from the Rheumatic Clinic of a university hospital between June and September 2016. Patients' self-reported medication adherence was assessed by the eight-item Morisky Medication Adherence Scale. Additional surveys included patients' demographics, and clinical and treatment characteristics. Logistic regression analysis was used to identify the predictors of medication nonadherence.

Results: A total of 140 patients were included in analysis. The percentage of patients classified as nonadherent to medication was 75%. Low education, rural residency, childlessness, limited comprehension of medication instructions, side effects experienced, dissatisfaction with treatment and better physical health were associated with an increased risk of nonadherence.

Conclusion: This study demonstrated a high prevalence of medication nonadherence among SLE patients in Sichuan, and factors associated with the nonadherence are multifaceted. Interventions for these factors, such as appropriate adjustment of the service resources for patients with rheumatic disease in rural communities and improved communication between the health care providers and the patients, may contribute to improve the medication adherence of this cohort.

Keywords: systemic lupus erythematosus, medication management, adherence, predictors

Plain language summary

Systemic lupus erythematosus (SLE) is a common connective tissue disease with multiorgan involvement. It is associated with significant morbidity and mortality and has considerable adverse effects on the perception of health and daily activity of the patients. It is important to understand the prevalence and factors associated with medication nonadherence in these patients, as this is likely to contribute to develop targeted interventions to improve patients' adherence and their outcomes. However, prevalence and predictors of adherence problems in SLE patients, especially in those in developing countries such as China, have been inadequately studied. Therefore, Ms Xia's team preformed this study to investigate the prevalence and predictors of medication nonadherence in Chinese patients with SLE. This study included 140 patients from a university hospital between June and September 2016. The results show that there is a great prevalence of medication nonadherence among SLE patients in Sichuan, China. Low education, rural residency, childlessness, limited comprehension of medication instructions, side effects experienced, dissatisfaction with treatment and better physical health were associated with an increased risk of nonadherence. These findings suggest that adherence of patients with SLE may be improved by interventions for these predictors, such as appropriate adjustment of the service

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resources for patients with rheumatic disease in rural communities and improved communication between the health care providers and the patients, including the need for health care providers to identify and discuss any questions and concerns which the patient may have regarding their disease and its medications.

Introduction

Systemic lupus erythematosus (SLE) is a common connective tissue disease with multiorgan involvement. It occurs worldwide and disproportionally affects the people of African, Hispanic and Asia-Pacific origin.[1,2] In numerous studies, SLE has been shown to be associated with significant morbidity and mortality and has considerable adverse effects on the perception of health and daily activity of the patients.[3–5] Early diagnosis and treatment and, most importantly, patients' adherence to therapy recommendations are crucial for the improvement of patients' outcomes.[6,7] Conversely, inadequate adherence to drug therapy in SLE has been associated with a higher risk of flares, morbidity, hospitalizations and poor renal outcome.[8–10] Thus, it is important to understand the prevalence and factors associated with medication nonadherence in these patients, as this is likely to contribute to develop targeted interventions to improve patients' adherence and their outcomes.

Although several studies have explored the extent and risk factors of poor medication adherence among SLE patients, predictors of nonadherence among SLE patients are not well studied.[11,12] A systematic review demonstrated that the prevalence of medication nonadherence in SLE patients ranged from 3% to 76%, depending on the different assessment methods and the study population.[11] Patients being nonadherent to medication recommendations may be attributed to a number of causes, including age,[13] occurrence of adverse drug reactions,[14,15] having to take medicines more than once daily[16] and being a rural resident.[12,17] Moreover, marital status,[13,16] education level,[16,17] duration of the disease[13] and number of comorbidities[16] may predict treatment adherence in SLE patients, but some studies showed these factors were not risk factors for medication nonadherence of SLE patients.[18,19] Additionally, comprehension of medication instructions, treatment satisfaction and perceived physical health are often associated with nonadherence reported by other chronic disease groups.[20–23] However, the relationship between these factors and nonadherence in patients with SLE is unknown. Also, previous adherence studies on SLE were mainly carried out in developed countries.[11,12] To our knowledge, there is scant information about medication nonadherence of patients with SLE in developing countries such as China.

In view of this, the aims of the present study were: 1) to determine the prevalence of medication nonadherence of SLE patients in Sichuan, China and 2) to further explore its predictors.

Patients and methods

Study design and population

This study was a cross-sectional study. The primary investigators of this study (XX and HY) recruited participants in person by consecutive sampling from the Rheumatic Clinic of West China Hospital, Sichuan University between June and September 2016. To be included in the study, participants had to be ≥18 years; had to be diagnosed with SLE using the criteria of American College of Rheumatology of 1997;[24] should have been undergoing treatment with glucocorticoids, hydroxychloroquine and/or immunosuppressants at the time of enrollment, and should have adequate cognitive status as determined by communicating with the patients. Patients who could not speak/read in the Chinese language were excluded. Also, patients who were illiterate were excluded from the study.

Measures

All participants completed three paper questionnaires: sociodemographic, clinical and treatment characteristics survey; the Chinese version of the eight-item Morisky Medication Adherence Scale (MMAS-8) and the Chinese version of the Medical Outcomes Study 36-item Short Form (SF-36). Additionally, the investigators completed the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) based on the information provided by hospital records and the patients.

Sociodemographic, clinical and treatment characteristics survey

In this study, the sociodemographic, clinical and treatment characteristics survey included age, gender, residence, education level, marital status, fertility status, employment status, medical insurance, diagnosis duration of SLE, chronic comorbidity and type of SLE medicine. The questionnaire also addressed the following: satisfaction with treatment, frequency of dosing more than once daily, comprehension of medical instructions and presence of side effects. These indicators were measured by the following questions: Are you satisfied with the current treatment? Is your frequency of medication dosing more than once daily? Do you fully understand the medication instructions provided by your primary physician or nurse? Do you have any side effects such as concentric obesity, full moon face, nausea, vomiting and

so on"? For each question, the response options included "yes" and "no".

The Chinese version of the MMAS-8

The MMAS-8 Chinese scale was used to investigate medication adherence. The scale is a self-administered instrument with eight items, of which items 1–7 have two response options (yes/no) and item 8 is rated on a 5-point Likert scale. The total score ranges from 0 to 8.[25,42] A cutoff score of 6 is recommended to classify respondents as nonadherence (MMAS-8 $\leq$6) or adherence (MMAS-8 $>$6).[26] Previous studies have confirmed that the scale is simple and practical and has good reliability and validity.[27,43] The Cronbach's α coefficient of the scale in this study was 0.81.

The Chinese version of the Medical Outcomes Study SF-36

The SF-36 contains eight domains, which can be further summarized into two component scores: physical component summary (PCS) and mental component summary (MCS). After recoding, both the components can reach a maximum of 100. The SF-36 has been tested and recommended to be used in Chinese patients with SLE.[28] In this study, participants' physical and mental health was measured by the SF-36 PCS and the SF-36 MCS, respectively. Higher scores indicate better physical and mental health. The Cronbach's α coefficient of the scale in this study was 0.88.

The Systemic Lupus Erythematosus Disease Activity Index 2000

The SLEDAI-2K was used to measure the lupus disease activity within the past 30 days. It includes 24 clinical and laboratory variables that are weighted by the organ system. The total score of SLEDAI-2K ranges from 0 to 150, with higher score indicating higher disease activity.[29]

Statistical analysis

Descriptive statistics were used to summarize the characteristics of participants. Factors associated with medication nonadherence were explored using logistic regression analysis and are shown as odds ratios (ORs) with 95% CIs. All statistical analyses were performed using IBM SPSS version 21, and a P-value <0.05 was considered statistically significant.

Ethics approval and informed consent

This study was approved by the West China Hospital Medical Ethics Committee (ID 20160041). The purpose, methods and procedure of the study were explained to the participants, and all of the participants had provided a written informed consent.

Results

Characteristics of participants

In total, 142 incident cases of SLE were recruited and included. However, 2 cases were omitted because of incomplete questionnaires, leaving 140 participants in the final analysis. The characteristics of the 140 participants are shown in Table 1. The mean age of participants was 36.9 years, but the majority of them were unemployed (82.1%). This may be attributed to the high level of disease activity of participants in our study. The mean SLEDAI-2K score was 10.1. Hair loss, rash, arthritis, low complement and proteinuria were the most frequent manifestations in the SLEDAI-2K. Additionally, a great majority of patients (82.9%) had comorbidity, and nephritis and hypertension were the most common. In this study, 65.7% of patients did not fully understand the instructions on medication provided by their primary physician or nurse and 64.3% of patients experienced side effects. The mean SF-36 PCS and SF-36 MCS scores was 49.6 and 47.3, respectively,

Table 1 Characteristics of participants

Variables	Mean (SD)	Minimum, maximum	Frequency (%)
Age, years	36.9 (13.9)	18, 72	
Gender, female			125 (89.3)
Residence, rural			55 (39.3)
Education level, $\leq$9 years			76 (45.0)
Single			40 (28.6)
Childlessness			41 (29.3)
Unemployed			115 (82.1)
Medical insurance, yes			92 (65.7)
Diagnosis duration, months	61.6 (75.7)	1, 363	
SLEDAI-2K	10.1 (4.4)	2, 24	
Comorbidity, yes			116 (82.9)
Type of SLE medicine			
GC			25 (17.9)
GC+HCQ			69 (49.3)
GC+ISD			24 (17.1)
GC+HCQ+ISD			22 (15.7)
Daily medication more than once, yes			84 (60.0)
Fully understanding medication instructions, no			92 (65.7)
Side effects experienced, yes			90 (64.3)
Satisfaction with treatment, yes			65 (46.4)
SF-36 PCS score	49.6 (12.1)	24.0, 79.8	
SF-36 MCS score	47.3 (13.7)	19.8, 74.7	

Abbreviations: GC, glucocorticoids; HCQ, hydroxychloroquine; ISD, immunosuppressive drug; SF-36, Short Form 36-item Health Survey; SF-36 MCS, mental component summary of SF-36; SF-36 PCS, physical component summary of SF-36; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

Table 2 Factors associated with medication nonadherence in patients with SLE

Variables	Univariate analysis OR (95% CI; *P*-value)	Multivariate analysis OR (95% CI; *P*-value)
Age, years	1.02 (0.99–1.05; *P*=0.234)	1.02 (0.97–1.07; *P*=0.399)
Female	1.10 (0.33–3.71; *P*=0.875)	0.64 (0.07–5.70; *P*=0.693)
Rural	**2.74 (1.14–6.58; *P*=0.025)**	**2.90 (1.09–7.75; *P*=0.034)**
Education level, ≤9 years	**3.06 (1.31–7.15; *P*=0.010)**	**3.11 (1.20–8.09; *P*=0.020)**
Single	2.32 (0.88–6.10; *P*=0.090)	1.02 (0.19–5.49; *P*=0.982)
Childlessness	**3.13 (1.12–8.76; *P*=0.030)**	**3.21 (1.03–10.05; *P*=0.045)**
Unemployed	0.52 (0.16–1.62; *P*=0.258)	0.24 (0.05–1.31; *P*=0.100)
Medical insurance, yes	**0.39 (0.16–0.98; *P*=0.044)**	0.52 (0.13–2.04; *P*=0.348)
Diagnosis duration, months	**1.01 (1.00–1.02; *P*=0.034)**	1.01 (0.99–1.02; *P*=0.233)
SLEDAI-2K	0.93 (0.86–1.01; *P*=0.101)	1.03 (0.88–1.20; *P*=0.719)
Comorbidity, yes	2.08 (0.82–5.29; *P*=0.125)	2.24 (0.49–10.24; *P*=0.299)
Type of SLE medicine		
GC (ref.)		
GC+HCQ	0.97 (0.33–2.81; *P*=0.949)	0.41 (0.07–2.32; *P*=0.310)
GC+ISD	0.77 (0.22–2.74; *P*=0.683)	0.20 (0.03–1.66; *P*=0.137)
GC+HCQ+ISD	1.07 (0.28–4.16; *P*=0.918)	0.40 (0.04–3.60; *P*=0.412)
Daily medication more than once, yes	**2.18 (1.00–4.74; *P*=0.049)**	2.51 (0.67–9.39; *P*=0.171)
Full understanding medication instructions, no	**4.33 (1.94–9.70; *P*<0.001)**	**3.95 (1.56–9.98; *P*=0.004)**
Side effects experienced, yes	**2.84 (1.29–6.22; *P*=0.009)**	**2.42 (1.11–5.28; *P*=0.027)**
Satisfaction with treatment, yes	**0.29 (0.13–0.66; *P*=0.003)**	**0.29 (0.09–0.93; *P*=0.037)**
SF-36 PCS score	**1.04 (1.01–1.08; *P*=0.020)**	**1.12 (1.03–1.22; *P*=0.007)**
SF-36 MCS score	1.00 (0.98–1.03; *P*=0.813)	0.95 (0.89–1.01; *P*=0.110)

Note: The bold value indicates statistical significance at the 0.05 level.

Abbreviations: GC, glucocorticoids; HCQ, hydroxychloroquine; ISD, immunosuppressive drug; OR, odds ratio; SF-36, Short Form 36-item Health Survey; SF-36 MCS, mental component summary of SF-36; SF-36 PCS, physical component summary of SF-36; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

indicating poor physical health and mental health of this cohort.

The proportion of patients not adhering to medication and predictors thereof

In keeping with an MMAS-8 ≤6, 105 (75%) cases in the sample of patients did not adhere to SLE treatment. In the multiple logistic regression analysis, as shown in Table 2, the risk for medication nonadherence to SLE treatment was significantly higher for those with a low level of education, rural residency, childlessness, limited comprehension of medication instructions, side effects experienced, dissatisfaction with treatment and better physical health.

Discussion

In our study, we investigated the prevalence of medication nonadherence among Chinese SLE patients using a self-report questionnaire MMAS-8 and explored its predictors. According to the cutoff criteria of MMAS-8 for medication nonadherence, we found that 75% of the participants were categorized as nonadherent.

A recent systematic review of medication adherence among SLE patients has shown that over half of the patients are nonadherent to medication,[12] results that are similar to our finding. It suggests that, as elsewhere, nonadherence is common in patients with SLE in Sichuan, China. Considering the negative impacts of medication nonadherence on patients' outcome, health care utilization and cost,[8–10] studies aimed at developing strategies to promote adherence among these patients are needed.

In terms of predictors of medication nonadherence, our study revealed that the risk of medication nonadherence was higher for those who live in rural region, which agrees with the finding of Abdul-Sattar and Abou El Magd.[17] One of the possible reasons may be the fact that rural communities usually lack rheumatologic services, and poor availability of health care increases the risk of nonadherence.[30] It suggests to policymakers that appropriate adjustment of the service resources for patients with rheumatic disease in rural communities may contribute to improve the adherence of SLE patients. Another possible reason for the higher risk of nonadherence in rural patients is their low level of education. Nonadherence in our study was associated with lower level of education, which is consistent with an adherence study conducted in USA by Garcia-Gonzalez et al.[31] These results may be attributed to the fact that patients with lower level of

education often have less knowledge of medication and poor comprehension of consequences of nonadherence.[32] Thus, improving the medication knowledge of patients, especially of patients with low education, may help to improve the adherence in patients with SLE. Side effect experienced is another factor associated with nonadherence in this study, which concurs with previous studies.[11,12] Oliveira-Santos et al[15] have shown that 13.8% of SLE patients stopped taking their medicine because it made them feel worse. These results reflect that the patient does not know how to properly cope with the discomfort caused by taking medicines, and to alleviate the discomfort, medication is discontinued. Therefore, improving the coping skills for self-management of treatment, side effects perhaps can reduce medication nonadherence in SLE patients. This view has been confirmed in other chronic conditions.[33]

Additionally, the observed association between nonadherence and comprehension of medication instructions, treatment satisfaction and perceived physical health in this study agrees with some studies conducted in other chronic diseases.[20–23] First, limited comprehension of medication instructions significantly increased the risk of nonadherence in patients with SLE. In our study, 65.7% of the patients reported limited comprehension of medication instructions, which may reflect poor doctor–patient communication. Previous qualitative data have shown that poor communication is an important barrier to adherence in SLE patients.[34] Therefore, improved communication between the health care provider and the patient is needed, and it may be beneficial to improve the adherence of this cohort. Second, we found that nonadherence was more common among participants who were not satisfied with treatment. Previous studies performed in other chronic diseases have linked treatment satisfaction to patients' attitudes or beliefs toward taking medications, which is recognized to be a precursor to medication adherence.[35] So, it can be speculated that interventions aimed at improving patients' attitudes or beliefs toward taking medications may improve patients' treatment satisfaction and also can improve their adherence. Third, those who perceived better physical health in our study were more likely to be nonadherent, which is in accordance with a previous study that reported 7.72% of the patients stop taking medicine when they feel better.[15]

Although two studies have shown that being single is the predictor of nonadherence in SLE patients,[16,36] our study did not find the correlation between marital status and adherence. However, we found that nonadherence is more common in those who are childless. This may be explained by the impact of fertility concerns on adherence in patients with SLE. For many SLE patients, the illness coincides with their childbearing years, and they may fear of a negative effect of medication on fertility/fetus. According to a survey by Xu et al,[37] 79% of SLE patients believe that they should stop taking glucocorticoids when they are planning to have children. The fact is, however, that the adherence to glucocorticoids before, during and after pregnancy is important for the safety of the mother and the infant.[38] Health care workers should enhance fertility guidance in this group to correct their misperception in this area, which may also improve their medication adherence.

There are several possible limitations to our study. First, due to limited time and financial constraints, the study was conducted at a single center, which may have resulted in overestimation or underestimation of the prevalence of medication nonadherence of SLE patients in Sichuan, China. This is mitigated by the fact that the chosen center was a large tertiary referral hospital serving patients from a wide cross section of Sichuan. Second, we selected a self-report questionnaire as a tool for measuring adherence. Though the validity of the self-report adherence tool has been questioned in earlier studies,[39] in more recent reports, it has been found to compare favorably with the electronic monitoring devices.[40,41] Third, our study is a cross-sectional study which allows only for correlation, not causation. Fourth, more details on patients were not collected, which may have had an impact on adherence. These limitations should be addressed in future related studies.

Conclusion

Our study demonstrates that there is a great prevalence of medication nonadherence among SLE patients in Sichuan, China. Given the negative consequences of nonadherence, patients should be assessed for early identification and intervention. What is more, our study reveals that patients would be at increased risk for nonadherence if they have low education, live in a rural region, are childless, have limited comprehension of medication instructions, have experienced side effects, are not satisfied with the treatment, and have better physical health. These findings suggest that patients' adherence may be improved by interventions for these factors, such as appropriate adjustment of the service resources for patients with rheumatic disease in rural communities and improved communication between the health care providers and the patients, including the need for health care providers to identify and discuss any questions and concerns which the patient may have regarding their disease and its medications.

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Disclosure

The authors report no conflicts of interest in this work.

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