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Major Article

Patient compliance with antimicrobial drugs: A Chinese survey

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Background: Antimicrobial therapy is among the mainstream treatment modalities employed in clinical settings. Antimicrobial sensitivity of the pathogen and patient compliance are key determinants of the efficacy of antimicrobial therapy.
Objective: In this study, we sought to investigate the factors that affect patient compliance to antimicrobial therapy in a Chinese teaching hospital to enhance patient compliance and to prevent abuse and misuse of antibiotics by patients.
Methods: A questionnaire survey was conducted among patients willing to answer all the questions who were prescribed antimicrobial drugs orally, and for whom at least half of the duration of therapy was not under the supervision of a doctor or nurse. Data analyses were performed using Kruskal-Wallis test and multivariate logistic regression.
Results: A total of 720 patients participated in the survey; of these, 714 patients provided complete data and were included in the analysis. Up to 86.97% of patients showed noncompliance to antimicrobial therapy (total compliance score < 8), whereas 13.03% of patients showed good compliance (total compliance score = 8). On multivariate analyses, understanding of the treatment was an important factor associated with compliance.
Conclusions: A range of factors were associated with compliance to antimicrobial therapy, including understanding of the treatment, gender, age, home address, education level, and family income.

Antimicrobial therapy is among the greatest medical advances of all times. Antimicrobial drugs refer to chemicals that kill or inhibit the growth of microorganisms; these include antibiotics, semiantibiotics, and synthetic drugs. Clinical application of antimicrobial drugs has reduced morbidity from infectious diseases and saved countless lives.[1-3]

Incorrect use and abuse of antibiotic agents are key drivers of the spread of antimicrobial drug resistance. Antimicrobial drug resistance is a key concern while instituting therapy for bacterial infections.[4-7] Based on the involved molecular mechanisms, resistance to antimicrobial drugs can be divided into intrinsic resistance and acquired resistance. Besides, the cultural perceptions, needs of patients, misdiagnosis, financial interests, competence of medical personnel, and aggressive drug marketing are known to affect the development of drug resistance.[8-13] Despite several interventions to promote rational use of antimicrobial drugs, rapid spread of bacterial resistance and poor patient compliance continue to be a global challenge.[8-13] China is among the most severely influenced countries with respect to inappropriate use of antibiotics; the number of infections caused by drug-resistant pathogens account for about 30% of all patients.[14-17] Clinically isolated strains of *Escherichia coli* resistant to ciprofloxacin are a major concern in China.[15,17] Therefore, concerted efforts to enhance patient compliance and to prevent abuse and misuse of antibiotics by patients are required.

In this study, we investigated the factors that affect patient compliance to antimicrobial therapy in a Chinese teaching hospital setting. The objective was to understand the factors that affect patient compliance and to identify the reasons for abuse and misuse of antibiotics. Our findings may help identify interventions for curbing antimicrobial drug resistance and help alleviate the associated disease burden.

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METHODS

Ethics approval

The study was approved by the ethics committee at the involved institution.

Patients and study design

From October 2015-November 2015, we recruited a total of 720 patients from all clinical departments at a Chinese teaching hospital who were treated with antimicrobial drugs (Table 1). A questionnaire survey was administered to assess the level of compliance to the prescribed antimicrobial therapy. The reliability and validity of the questionnaire were tested in preliminary experiments conducted before the start of the survey.

Inclusion criteria were patients who were willing to answer all the questions and who were prescribed oral antimicrobial drugs, and for whom at least half of the duration of therapy was not under the supervision of a doctor or a nurse (patients in China must use antimicrobial agents prescribed by a qualified doctor and should not take any over-the-counter drugs from a pharmacy; in the context of the present study, "antimicrobial drugs" excluded antiviral, antifungal, and antiparasitic drugs). Patient who gave illegible feedback, those who could not read or speak clearly, and those who had a history of severe allergy to an antibacterial drug or drug addiction were excluded (n = 6).

The health team in the hospital consisted of doctors, clinical pharmacists, nurses, and qualified hospital managers. The necessary quality assurance mechanisms were in place and antimicrobial stewardship was strictly regulated during the entire study.

The questionnaire collected information related to 3 key domains: demographic information (eg, age, sex, residential address, and education level), socioeconomic information (eg, marital status, occupation, employment status, and family income), and patients' understanding (eg, basic knowledge about antimicrobial drugs and their side effects, correct timing and dose for antimicrobial drugs, criteria for drug discontinuation, and drug switching).

Criteria for patients' understanding

All participants were required to answer 8 questions[18] (Supplementary Material).

For the first 7 questions, each "no" was awarded a score of 1, whereas no score was awarded in case of a "yes" response. For question 8, answer "oral consumption" or "intramuscular injection" was awarded 1 point, whereas the answer "intravenous injection" was not awarded a score. A total score < 6 indicated poor understanding of antimicrobial drugs, a score between 6 and 8 indicated an average rating (ie, common level), and a total score of 8 points was rated as good.

Table 1
Source of recruited patients according to clinical department

Name	n (%)
Department of Obstetrics and Gynecology	64 (8.96)
Department of Orthopedics	78 (10.92)
Department of Respiratory	30 (4.20)
Department of Gastroenterology	86 (12.04)
International Medical Care Center	12 (1.68)
Ambulatory Care Unit	49 (6.86)
Department of Neurosurgery	57 (7.98)
Department of Thoracic Surgery	55 (7.70)
Department of Ophthalmology	46 (6.44)
Department of Otorhinolaryngology, Head, and Neck Surgery	33 (4.62)
Department of Cardiology	135 (18.91)
Department of Urology	44 (6.16)
Department of General Surgery	25 (3.50)

Outcomes of patient compliance with antimicrobial therapy

Patient compliance to antimicrobial therapy was evaluated using a Chinese version of the Morisky Medication Adherence Scale,[19] which includes 8 questions.

For the first 7 questions, each "no" was awarded a score of 1, whereas no score was awarded for answer "yes." For question 8, the answers "never," "occasionally," "sometimes," "often," and "always" were awarded a score of 2, 1.5, 1, 1.5, and 0, respectively. A total score < 8 indicated noncompliance and a score of 8 indicated good compliance. We also listed potential reasons for poor compliance based on the published literature. All subjects were asked to indicate the reason(s) applicable in their case. Incident rate for each reason was calculated.

Statistical analysis

Data pertaining to continuous variables are expressed as mean ± standard deviation; those pertaining to categorical variables are expressed as frequency or percentage. Continuous variables were compared using Kruskal-Wallis test and χ^2 test was used for categorical variables. Multiple logistic regression analyses was performed to estimate the effect of marital status, family income, and understanding after adjusting for gender and age, and the effect of understanding after adjusting for gender, age, home address, marital status, occupation, education level, employment status, and family income. All analyses were performed with the statistical software package R (R Foundation for Statistical Computing, Vienna, Austria). A 2-sided significance level of .05 was used to evaluate statistical significance.

RESULTS

Questionnaires were distributed to 720 subjects; of these, 714 subjects provided complete data and were included in the analysis. Out of 714 patients from various departments in a Chinese teaching hospital (Table 1), 621 (86.97%) patients had a total score < 8, which indicated noncompliance, whereas only 93 (13.03%) patients showed good compliance (Fig 1).

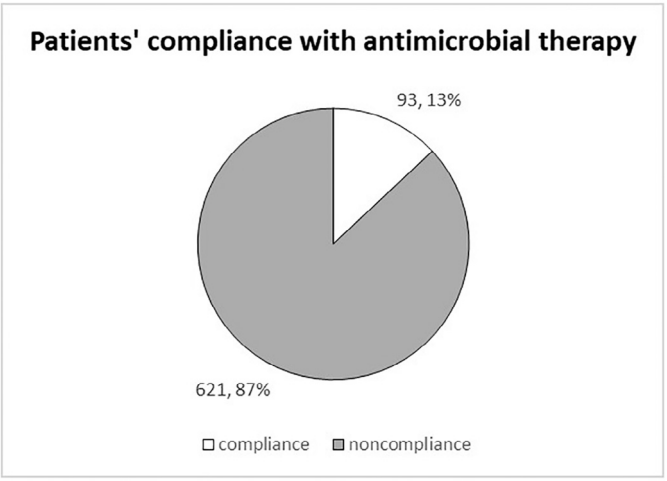

Fig 1. Proportion of study population with compliance and noncompliance to antimicrobial therapy. 621 patients (87%) had a total score < 8 (noncompliance) and 93 patients (13%) scored 8 (compliance).

Table 2
Reasons for noncompliance to antimicrobial therapy

Reasons	n	Incident rate, %
Unaware of the consequences of taking antimicrobial drugs without the doctor's advice	273	38.2
Take too many drugs varieties, forget correct order and dosage	289	40.5
Clinical pharmacists do not specify the administration method and dose	177	24.8
The smell and the shape of the drugs is difficult to accept	135	18.9
Fear of adverse effects caused by long-term use	437	61.2
Long-term administration	248	34.7
Too busy in study or work	382	53.5
Drug prices too high to afford	214	30.0
Do not know the exact effect of the drugs prescribed by the doctor	168	23.5
Inadequate knowledge about the illness and take the drugs passively	172	24.1
Lack of confidence in young doctors	82	11.5
Effect of drug wanes after a period of time	229	32.1
Drug manuals are too technical to understand	154	21.6
The prescribed doses are difficult to comply with (such as the need to break the tablet into 2 pieces)	88	12.3
Patients are too worried about the adverse effects described in the drug manual	252	35.3
Do not need to continue treatment once the condition improves	299	41.9
Patients consider that their condition does not require medication, and that they will recover by themselves	275	38.5
Preference for secret recipe or food therapy	52	7.3
Gullible to advertising, television broadcasting, or other means of promotion	123	17.2
New package of the drugs	67	9.4
Lack of attention from family members	109	15.2

Reasons for noncompliance to antimicrobial therapy are listed in Table 2. In a majority (61.2%) of participants, fear of adverse effects caused by long-term use was the main reason attributed to poor compliance. Other main reasons for noncompliance were: "too busy in study or work" (53.50%), "symptoms improved" (41.90%), and "complexity of the treatment" (40.50%).

The results of the Kruskal-Wallis test analyses are presented in Table 3. Analysis revealed that age, marital status, family income, and patients' understanding of treatment were significantly associated with compliance.

The results of logistic regression analysis showing the association between compliance and variables such as marital status, family income, and understanding are presented in Table 4. The odds ratio (OR) and 95% confidence intervals (95% CIs) of compliance after adjusting for these factors were similar to those in the nonadjusted model. The higher the family income, the better the understanding; further, subjects with a nonsingle status were more likely to be compliant.

We further explored the potential nonlinearity of the relationship between understanding and compliance. After adjusting for gender, age, home address, marital status, occupation, education level, employment status, and family income, understanding level of "common" and "good" remained independently predictive of increased risk of compliance by 0.77-fold (OR, 0.77; 95% CI, 0.42-1.42; $P = .40$) and 0.13-fold (OR, 0.13; 95% CI, 0.07-0.24; $P < .0001$), respectively, compared with "poor" understanding (OR = 1) (Table 5).

Table 3
Association between patient demographic characteristics, socioeconomic factors, and patient compliance to antimicrobial therapy

Characteristic	Compliance	Noncompliance	*P* value
Gender			.10
Male	37 (39.78)	303 (48.79)	
Female	56 (60.22)	318 (51.21)	
Age, y			.004*
> 60	25 (26.88)	183 (29.47)	
45-60	20 (21.51)	221 (35.59)	
< 45	48 (51.61)	217 (34.94)	
Home address			.16
Rural	40 (43.01)	316 (50.89)	
City	53 (56.99)	305 (49.11)	
Education level			.26
Under high school	37 (39.78)	286 (46.05)	
Bachelor's degree or above	56 (60.22)	335 (53.95)	
Marital status			.003*
Unmarried, divorced, or widowed	28 (30.11)	290 (46.70)	
Married	65 (69.89)	331 (53.30)	
Occupation			.17
Cadres	17 (18.28)	80 (12.88)	
Self-employee	14 (15.05)	93 (14.98)	
Worker	15 (16.13)	98 (15.78)	
Farmer	6 (6.45)	95 (15.30)	
Others	41 (44.09)	255 (41.06)	
Employment status			.57
Unemployed	35 (37.63)	247 (39.77)	
Retired	25 (26.88)	187 (30.11)	
Employed	33 (35.48)	187 (30.11)	
Family income, RMB			.004*
< 2000	12 (12.90)	150 (24.15)	
2001-3500	17 (18.28)	163 (26.25)	
3501-5000	29 (31.18)	158 (25.44)	
> 5000	35 (37.63)	150 (24.15)	
Understanding			<.001*
Poor	22 (23.66)	296 (47.67)	
Common	26 (27.96)	253 (40.74)	
Good	45 (48.39)	72 (11.59)	

NOTE. Values are presented as n (%).
RMB, renminbi (1 RMB = $0.1532).
*Indicates a statistically significant between-group difference.

DISCUSSION

Although several strategies have been made to control abuse and misuse of antibiotics by both medical staff and patients, spread of bacterial resistance and poor patient compliance continue to be a global concern. In this study, 86.97% of all patients showed noncompliance with antimicrobial drugs (total score < 8); only 13.03% showed good compliance (total score = 8), which is lower than the rates reported from previous studies conducted overseas.[8,11] Assessment of the key causes of noncompliance to antimicrobial therapy in China is of great importance.

The key reasons for lack of compliance included patients' fear of adverse effects caused by long-term use, preoccupation with study or work, tendency to quit treatment upon improvement in condition, prescription of too many drug varieties to remember the correct order and dosage, long duration of treatment, lack of affordability of the high drug prices, preference for secret recipe or food therapy, lack of confidence in young doctors, lack of attention from family members, inadequate instructions from the clinical pharmacists

regarding the administration method and dose, inadequate knowledge about the illness, and even the smell and the shape of the drugs. These reasons are similar to those reported from some previous studies.[11,12,20] Besides, on multivariate regression analysis, age, marital status, family income, and understanding showed a significant association with the total compliance score ($P < .05$). A previous study identified increasing age as an independent factor associated with nonadherence.[21] Poor compliance in elderly patients may be attributable to forgetfulness and decline in memory. Further, elderly individuals have been shown to be more likely to be influenced by advertisements,[20] and our study shows that some elderly patients have a preference for secret recipes or food therapy. In a study by Salami and Oluboyo,[22] unmarried status was shown to be associated with poor therapy compliance, which is in line with our results. The high cost of medicines is a major barrier and a vast majority of patients tend to belong to the economically disadvantaged section of the society[23]; therefore, the lower the income the worse is the compliance. An interesting observation in our study is that there was no significant association of gender, home address, education level, occupation, and employment status with compliance. In other words, a highly educated woman, living in a city, and who has an enviable job would not automatically comply with her physician's therapeutic regimen. Lack of knowledge about antibiotics is a critical determinant of nonadherence, which is independent of the education level in the community.[24] After adjusting for all confounding factors, understanding remained an independent predictor of increased risk of compliance by 0.13-fold (OR, 0.13; 95% CI, 0.07-0.24; $P < .0001$), compared with poor understanding (OR = 1). Therefore, to improve compliance, it is important to improve patients' understanding of the treatment.

In our study population, self-prescription of antimicrobial drugs was quite common, as was the practice of switching from 1 antimicrobial drug to another on the basis of the self-perceived efficacy of the drugs. Similarly, premature cessation of treatment by patients as soon as they begin to feel better to avoid long-term harm to their health, is another reason for poor compliance. This is likely attributable to poor awareness and lack of basic knowledge about antimicrobial drugs. A close association was observed between the level of understanding of the patient and his/her compliance to antimicrobial therapy ($P < .05$). Clinical pharmacists are uniquely positioned to help promote rational use of antimicrobial therapy owing to their knowledge of the physicochemical and pharmacologic properties of drugs, their dosage, adverse effects, and interaction with other drugs. A more proactive role in the clinical application of antimicrobial drugs, by determining the most suitable antimicrobial drug for each patient, ensuring the initial dose, the administration method, frequency of administration, maximal dose, and other similar issues will help promote patient compliance.[25,26]

Moreover, education level of bachelor's degree or above and employment status of senior professional and technical personnel cadres did not show a significant correlation with patient compliance. Our results vary from those of a previous study, which showed education level as the only significant correlate of patient compliance.[10] This inconsistency might imply that traditional school education has failed to adequately equip the community with the requisite knowledge about proper use of antibiotics.[24] Education measures are also required to promote participation of patients in the therapeutic process.[27] Besides, establishment of active surveillance systems for antibiotic use and enforcement of appropriate legislative measures are required. We should endeavor to give full rein to both the invisible hand of the market and the visible hand of the government to improve compliance.

The main value addition made by this study is that it identified various risk factors for noncompliance in a Chinese setting, which may help inform clinical practice. However, there are several limitations to this study. First, the study was conducted in a Chinese teaching hospital; the results presented herein may not be representative. For this reason, we will conduct multicenter research in collaboration with more units in future. In addition, our questionnaires did not include objective methods (eg, pill count), and our results may have been influenced by subjective factors. However, we performed multivariate regression analysis to control the influence of potential confounding variables; our results indicate that understanding is an independent predictor of increased risk of compliance.

Table 4
Risks factors for antibiotic noncompliance (multivariate regression analysis)

Exposure	Unadjusted	Adjusted*
Family income, RMB		
< 2000	1	1
2001-3500	0.77 (0.35-1.66) .50	0.72 (0.33-1.57) .41
3501-5000	0.44 (0.21-0.89) .0217	0.40 (0.20-0.82).0125
> 5000	0.34 (0.17-0.69).0025	0.33 (0.16-0.66) .0019
Marital status		
Unmarried, divorced, or widowed	1	1
Married	0.49 (0.31-0.79) .0031	0.51 (0.31-0.81) .0049
Understanding		
Poor	1	1
Common	0.72 (0.40-1.31) .28	0.71 (0.39-1.29) .26
Good	0.12 (0.07-0.21) < .0001	0.12 (0.07-0.21) < .0001

NOTE. Values are presented as β (95% confidence interval) *P* value or odds ratio (95% confidence interval) *P* value. Outcome variable: compliance; exposure variables: family income, marital status, and understanding.
RMB, renminbi (1 RMB = $0.1532).
*Adjusted for gender and age.

CONCLUSIONS

Our study highlights the continuing trend of poor compliance to antimicrobial therapy at a Chinese teaching hospital. A range of factors and reasons were cited by the respondents that included factors related to patients, medical personnel, and the pharmaceutical industry. Financial constraints, family attention, poor knowledge and communication skills of medical staff (including clinical pharmacists), aggressive promotion, advertising and marketing by the pharmaceutical industry, and factors related to the drugs themselves (eg, smell, shape, and packaging) were the main causes of noncompliance reported by the respondents.

Table 5
Multivariate logistic regression: Understanding associated with compliance

Understanding	Unadjusted	Adjusted I*	Adjusted II†
Poor	1	1	1
Common	0.72 (0.40-1.31) .28	0.71 (0.39-1.29) .26	0.77 (0.42-1.42) .40
Good	0.12 (0.07-0.21) < .0001	0.12 (0.07-0.21) < .0001	0.13 (0.07-0.24) < .0001

NOTE. Values are presented as β (95% confidence interval) *P* value or odds ratio (95% confidence interval) *P* value. Outcome variable: compliance; exposure variable: understanding.
*Adjusted I model adjusted for gender and age.
†Adjusted II model adjusted for gender, age, home address, marital status, occupation, education level, employment status, and family income.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ajic.2018.01.008.

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