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Study on independent influencing factors of compliance in patients with schizophrenia treated with paliperidone palmitate injection

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Summary. Introduction. Patients with schizophrenia require long-term treatment, and poor medication compliance during therapy is a common issue. Poor compliance can lead to recurrent fluctuations in the patients' disease course, exacerbate its progressive deterioration, severely impact patients' social functioning and quality of life, and thus represents an increasingly serious public health problem. Long-acting injectable antipsychotics (LAIs) are generally considered one of the most effective treatments in psychiatry, which can reduce the substantial economic burden on patients and society, lowering readmission rates, improving patients' quality of life, and decreasing healthcare costs. This study is a retrospective analysis based on follow-up data from patients with severe mental disorders. **Objective.** The study aims to explore the factors influencing medication compliance in schizophrenia patients treated with paliperidone palmitate injection, providing a basis for developing targeted compliance intervention strategies in clinical practice. The study included schizophrenia patients receiving paliperidone palmitate injection and systematically analyzed the impact of variables such as demographic characteristics, caregiver competence, social functioning, disease duration, and the presence of comorbid chronic conditions on medication compliance. **Conclusions.** Medication compliance in patients with schizophrenia is influenced by the interaction of multiple factors. Among these, age ≥50 years is a core independent risk factor affecting medication compliance, while having a guardian with good caregiving ability serves as an independent protective factor. The impact of a disease duration ≥10 years on compliance approaches statistical significance (p=0.050). A comparison of social functioning across the dimensions of the SDSS revealed that differences in social functioning deficits between the two groups with different levels of medication compliance were only evident in the dimensions of social withdrawal and interest in and concern for the external environment. This suggests that deficits in these specific dimensions of social functioning are also important factors influencing medication compliance in patients.

Key words. Medication compliance, paliperidone palmitate injection, retrospective study, schizophrenia.

Studio sui fattori indipendenti che influenzano la compliance nei pazienti con schizofrenia trattati con paliperidone palmitato a rilascio prolungato.

Riassunto. Introduzione. I pazienti affetti da schizofrenia necessitano di un trattamento a lungo termine e la scarsa aderenza alla terapia farmacologica rappresenta un problema comune. Questa può causare fluttuazioni ricorrenti nel decorso della malattia, aggravarne il progressivo deterioramento, incidere pesantemente sul funzionamento sociale e sulla qualità della vita dei pazienti e costituisce quindi un problema di salute pubblica sempre più grave. Gli antipsicotici a rilascio prolungato (LAI) sono generalmente considerati uno dei trattamenti più efficaci in psichiatria, in grado di ridurre il notevole onere economico a carico dei pazienti e della società, abbassare i tassi di riammissione, migliorare la qualità della vita dei pazienti e diminuire i costi sanitari. Questo studio è un'analisi retrospettiva basata sui dati di follow-up di pazienti con gravi disturbi mentali. **Obiettivo.** Lo studio ha lo scopo di esplorare i fattori che influenzano l'aderenza alla terapia farmacologica nei pazienti affetti da schizofrenia trattati con paliperidone palmitato, fornendo una base per lo sviluppo di strategie mirate di intervento sull'aderenza nella pratica clinica. Lo studio ha incluso pazienti affetti da schizofrenia trattati con paliperidone palmitato e ha analizzato sistematicamente l'impatto di variabili quali le caratteristiche demografiche, la competenza dei caregiver, il funzionamento sociale, la durata della malattia e la presenza di condizioni croniche comorbili sull'aderenza alla terapia farmacologica. **Conclusioni.** L'aderenza terapeutica nei pazienti affetti da schizofrenia è influenzata dall'interazione di molteplici fattori. Tra questi, l'età ≥50 anni rappresenta un fattore di rischio indipendente fondamentale che incide sull'aderenza terapeutica, mentre la presenza di un tutore con buone capacità assistenziali costituisce un fattore protettivo indipendente. L'impatto di una durata della malattia ≥10 anni sull'aderenza si avvicina alla significatività statistica (p=0,050). Un confronto del funzionamento sociale attraverso le dimensioni dell'SDSS ha rivelato che le differenze nei deficit di funzionamento sociale tra i due gruppi con diversi livelli di aderenza alla terapia erano evidenti solo nelle dimensioni del ritiro sociale e dell'interesse e della preoccupazione per l'ambiente esterno. Ciò suggerisce che i deficit in queste specifiche dimensioni del funzionamento sociale sono anche fattori importanti che influenzano l'aderenza alla terapia nei pazienti.

Parole chiave. Aderenza ai farmaci, paliperidone palmitato, schizofrenia, studio retrospettivo.

Introduction

Schizophrenia is a chronic and relapsing disorder that imposes a substantial burden on patients, their families, and society at large[1]. With a global prevalence close to 1%[2], the treatment of schizophrenia requires long-term management. However, poor medication compliance during treatment is a common issue, leading to recurrent fluctuations in the patients' illness course[3], exacerbating its progressive deterioration, and severely impacting patients' social functioning and quality of life[4]. Paliperidone palmitate injection (hereinafter referred to as PP or the long-acting injectable formulation) not only can help improve medication compliance and reduce the incidence of adverse reactions but also further alleviates negative psychological symptoms and social withdrawal[5]. Therefore, this study aims to investigate the compliance of schizophrenia patients treated with the long-acting injectable formulation, analyze its independent influencing factors, and develop targeted intervention strategies for high-risk factors, thereby offering novel insights for clinical preventive interventions.

Materials and methods

General information

This study selected patients receiving long-acting injectable (LAIs) antipsychotics at the outpatient department of the Fengtai District Mental Health Center from 2023 to 2024. A one-year retrospective real-world follow-up was conducted. The Beijing Mental Health Information Management System was used to collect general demographic data of the subjects (including gender, age, marital status, education level, employment status), disease duration, family supervision status, disease insight, and social functioning. The system's follow-up records were used to collect information on the subjects' LAIs treatment, including injection dates, adverse reactions, and disease recurrence. All assessors conducting the Social Disability Screening Schedule (SDSS) evaluations during follow-up underwent standardized training and passed the assessment. This study was approved by the Hospital Medical Ethics Committee (Approval No: Lun Shen [2026] No. 2). In this study, electronic data were processed exclusively by research-designated personnel. All patient-specific personal information was fully anonymized and stripped from the datasets prior to encrypted storage. Only data relevant to the research objectives were retained for subsequent statistical analysis.

Inclusion criteria

The inclusion criteria were: 1) meeting the diagnostic criteria for schizophrenia in the International Classification of Diseases, 10th Revision (ICD-10); 2) age ≥18 years old; 3) patients undergoing follow-up management by community health service centers.

Exclusion criteria

The exclusion criteria were: 1) inability to cooperate with and complete the study follow-up; 2) active use of psychoactive substances; 3) other patients considered unsuitable for inclusion in the study.

Observation indicators

The primary observation indicator was compliance to LAIs antipsychotic treatment among community-dwelling schizophrenia patients. According to the paliperidone palmitate injection package insert: "If more than 6 weeks have elapsed since the previous injection, restart with the recommended initiation regimen". Based on the recommended regimen in the drug's package insert, compliance to LAIs treatment in this study was defined as all intervals between consecutive injections during the study period being less than 6 weeks. Subjects meeting this criterion were classified into the good compliance.

Treatment non-compliance was defined as one or more intervals between injections exceeding 6 weeks during the study period, including two scenarios: 1) resumption of LAIs treatment with re-initiation of the loading dose regimen; 2) discontinuation of LAIs treatment. Subjects meeting these criteria were classified into the non-good compliance.

Adverse drug reactions (ADRs) in the study subjects were assessed by specialized associate chief psychiatrists or above in the LAIs outpatient clinic, with reference to the ADR criteria specified in the paliperidone palmitate package insert. Additionally, independent influencing factors for compliance to paliperidone palmitate injection treatment in schizophrenia patients were analyzed.

Statistical methods

All data in this study were organized and analyzed using SPSS23.0 statistical software. Categorical data were expressed as number (percentage) [n (%)], and intergroup comparisons were performed using the χ^2 test. After passing the normality test, continuous data conforming to a normal distribution were expressed as mean±standard deviation ($X \pm SD$), and intergroup comparisons were conducted using the independent t-test. Variables with a statistically significant p-value <0.05 identified in univariate analysis were included in multivariate regression analysis to further explore influencing factors. The significance level for this study was set at $\alpha = 0.05$, with $p<0.05$ considered statistically significant.

Study results

Univariate analysis of patients' medication compliance

This study enrolled a total of 225 participants, of whom 135 had poor treatment compliance and 90 had good treatment compliance. Comparative analysis of the general demographic and clinical characteristics between the two groups showed that age, educational level, caregiver care capacity, and disease duration were key factors affecting treatment compliance (table 1). The results indicated that participants aged ≥50 years, those with an educational level of senior high school or below, those with incompetent caregivers, and those with a disease duration of ≥10 years were more likely to have poor treatment compliance. In addition, participants with poor treatment compliance had significantly higher scores on the SDSS, which suggested a correlation between treatment compliance and the social functional status of the participants.

Multivariate analysis of patients' medication compliance

With patients aged <50 years, those with a disease duration <10 years, those with a junior college education or above, and those without caregiver care capacity as the reference group, we performed a multivariate logistic regression analysis to explore factors associated with compliance to LAIs in patients with schizophrenia (table 2). The results showed that age ≥50 years was an independent risk factor for LAIs compliance in these patients, whereas having a caregiver with adequate care capacity was an independent protective factor (both $p<0.05$). Furthermore, a disease duration of ≥10 years approached statistical significance in its impact on compliance ($p=0.050$). In contrast, educational level and SDSS scores were not significantly associated with compliance to long-acting injectable antipsychotics.

Table 1. Baseline characteristics of general data in PCG and GCG patients with schizophrenia receiving LAI injections.

Characteristics	Overall	PCG	GCG	p
	n=225	n=135	n=90	
Gender, n (%)				
Male	115 (51.11)	70 (51.85)	45 (50.00)	0.892
Female	110 (48.89)	65 (48.15)	45 (50.00)	
Age, n (%)				
<50 years old	64 (28.44)	19 (14.07)	45 (50.00)	<0.001
≥50 years old	161 (71.56)	116 (85.93)	45 (50.00)	
Marriage, n (%)				
Married	149 (66.22)	87 (64.44)	62 (68.89)	0.585
Divorced/Widowed/Single	76 (33.78)	48 (35.56)	28 (31.11)	
Educational level, n (%)				
Senior high school or below	163 (72.44)	111 (82.22)	52 (57.78)	<0.001
Junior college or above	62 (27.56)	24 (17.78)	38 (42.22)	
Guardian's Caregiving Capacity, n (%)				
With capacity	68 (30.22)	48 (35.56)	20 (22.22)	0.047
Without capacity	157 (69.78)	87 (64.44)	70 (77.78)	
Disease duration				
<10 years	32 (14.22)	9 (6.67)	23 (25.56)	<0.001
≥10 years	193 (85.78)	126 (93.33)	67 (74.44)	
Comorbidity				
Yes	151 (67.11)	87 (64.44)	64 (71.11)	0.369
No	74 (32.89)	48 (35.56)	26 (28.89)	
SDSS (median (IQR))	8.0 (6, 9)	8 (7, 9)	7 (5.2, 9)	0.048

Table 2. Multivariate logistic regression analysis of LAIs adherence in patients with schizophrenia.

Factor	OR (95% CI)	p
Age		
<50 years old	0.23 (0.11-0.46)	<0.001
≥50 years old	RG	RG
Disease duration		
<10	0.39 (0.15-0.99)	0.050
≥10	RG	RG
Educational level		
Senior high school or below	1.92 (0.93-3.95)	0.074
Junior college or above	RG	RG
Guardian's Caregiving Capacity		
With capacity	2.20 (1.12-4.48)	0.025
Without capacity	RG	RG
SDSS (Per 1-Point Increase)	0.94 (0.83-1.04)	0.248

Legend: RG= reference group; SDSS= Social Disability Screening Schedule.

Analysis of social disability

The SDSS is adapted from the Disability Assessment Schedule (DAS) developed by the World Health Organization (WHO) and is primarily designed to assess the degree of social functional impairment in patients with psychiatric disorders. It has been widely adopted as a core assessment tool in numerous community-based psychiatric epidemiological surveys. Based on social function evaluation data retrieved from the Beijing Mental Health Information Management System, this study performed statistical analyses on SDSS assessment results associated with medication compliance in the study participants.

The SDSS comprises 10 evaluation dimensions: occupational functioning, marital role, parental role, social withdrawal, extrafamilial social functioning, reduced intrafamilial activity, family role, personal self-care, interest in and concern for the external world, and a sense of responsibility and planning. In the present study, the SDSS was utilized to evaluate the social functional status of study participants. Given that three of these dimensions – occupational functioning, marital role, and parental role – are strongly correlated with demographic characteristics, the present study excluded these three dimensions and retained only the seven core dimensions (including social withdrawal and extrafamilial social functioning) to eliminate potential confounding effects of demographic variables on the assessment results of core social functions. Each dimension is rated on a 3-point scale (0-2), with the scoring criteria defined as follows: 0= no abnormality or only minor deficits that do not result in subjective complaints or functional problems; 1= definite social functional impairment; 2= severe social functional impairment. The total score of the retained seven core dimensions ranges from 0 to 14, with higher scores reflecting more severe social functional impairment in patients.

Further subgroup analysis was performed following the results of the multivariate logistic regression analysis. Nonparametric tests were employed to compare the scores of each dimension of the SDSS between the two groups (PCG and GCG) (table 3). Given the non-normal distribution of the scores, they were presented as median (interquartile range) [M (IQR)]. The test level was set at α=0.05, where $p<0.05$ was considered to indicate a statistically significant intergroup difference. Higher SDSS scores indicate more severe social functional impairment in the corresponding dimension for patients. Based on the characteristics of SDSS scores, distinct and statistically significant intergroup differences were identified in the dimensions of social withdrawal and interest in and attention to the external world among the two patient groups.

Table 3. Comparison of each variable in SDSS between the PCG and the GCG.

Factor (median [IQR])	Overall	PCG	GCG	p
	n=225	n1=135	n2=90	
Social withdrawal	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.001
Social function outside the family	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.489
Insufficient activities within the family	1 (1, 1)	1 (1, 1)	1 (0, 1)	0.241
Family function	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.633
Personal self-care	1 (0, 1)	1 (0, 1)	1 (0, 1)	0.079
Interest and concern towards the outside world	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.005
Responsibility and planning	1 (1, 2)	1 (1, 2)	1 (1, 1)	0.187

Discussion

Schizophrenia, as a chronic psychiatric disorder, is characterized by recurrent disease fluctuations when patients exhibit poor treatment compliance, which exacerbates the progressive deterioration of the condition and severely impairs patients' social functioning and quality of life[6]. Improving medication compliance in this patient population remains a challenge that requires collaborative efforts from multiple perspectives. In our study, we categorized patients receiving LAI treatment into good compliance and poor compliance groups for statistical analysis, aiming to further explore key independent influencing factors for treatment compliance in schizophrenia patients and to develop targeted strategies for clinical care and preventive interventions.

This study, through multidimensional analysis, has identified the core factors influencing the adherence of schizophrenia patients to long-acting injectable treatment – specifically age ≥50 years, insufficient caregiver capacity, and their distinct association with social functioning deficits – providing a solid evidence-based foundation for developing personalized adherence intervention strategies in clinical practice.

The above analysis indicates that enhancing patients' treatment compliance can also facilitate the implementation of targeted community management measures tailored to patients' baseline conditions[7]. For example, simplify medication regimens and strengthen targeted follow-up for elderly patients; regularly assess treatment confidence in patients with prolonged disease duration so as to avoid treatment fatigue[8]. Additionally, medication compliance can be improved by enhancing patients' social functioning. For instance, address social withdrawal by organizing community activities to boost patients' motivation for social interaction, and combined with medication reminder mechanisms[9]; for families, conduct collaborative medication management training to encourage family members to engage in medication supervision[10]. By adopting a multi-faceted intervention approach, the treatment effectiveness and quality of life of patients can be comprehensively enhanced.

In summary, we need to further explore effective intervention strategies targeting poor treatment compliance in patients with schizophrenia. It is hoped that through multidisciplinary collaboration across medicine, psychology, sociology, and other disciplines, we can conduct in-depth exploration of the mechanisms underlying poor compliance, enhance patients' social functioning and psychological well-being, thus developing a more profound understanding of the unmet needs of patients with poor compliance, and provide them with more precise and effective interventions and treatment plans.

Conflict of interests: the authors have no conflict of interests to declare.

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