



Gap between patients with schizophrenia and their psychiatrists on the needs to psychopharmacological treatment: A cross-sectional study

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Abstract

Aim: Psychopharmacological treatment is indispensable in patients with schizophrenia but data on needs, preferences, and complaints about their medications are limited. Moreover, there has been no study to assess the degree of awareness of their psychiatrists (gap in needs) regarding these issues.

Methods: Ninety-seven Japanese patients with schizophrenia (ICD-10) were asked to fill in the questionnaire consisting of multiple-choice questions regarding (a) their needs and complaints about psychopharmacological treatment that they were receiving, and (b) their preference of dosage form, dosing frequency, and timing of dosing. Additionally, their psychiatrists in charge were asked to predict their patients' response to the above questions.

Results: Both the most frequently endorsed need and complaints about the current psychopharmacological treatment were "nothing in particular" ($n = 14$, 16.7% and $n = 17$, 20.2%); merely 23.1% and 15.4% of their psychiatrists correctly predicted these responses, respectively. "Once a day" ($n = 56$, 65.1%), "at bedtime" ($n = 53$, 61.6%), and "tablet" ($n = 51$, 59.3%) were the patients' most favorite dosing frequency, timing, and dosage form, respectively; 59.8% ($n = 49$), 54.9% ($n = 45$), and 64.6% ($n = 53$) of their psychiatrists predicted them.

Conclusions: These findings suggest that there is substantial room for improvement on the side of psychiatrists to capture their patients' needs and complaints about psychopharmacological treatment.

KEYWORDS

adherence, needs, preference, psychopharmacology, schizophrenia

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1 | INTRODUCTION

Schizophrenia is typically a life-long illness, often requiring long-term antipsychotic treatment to prevent relapse.^{1,2} However, adherence to antipsychotic treatment in the maintenance phase has been reported to be generally suboptimal. For example, the proportion of patients who are sufficiently adherent to antipsychotic treatment reportedly declines to approximately half within 1 year and even to one-fourth within 2 years after discharge.³ Such low medication adherence is of serious concern since it increases the risks of negative outcomes such as relapse and hospitalization.^{4,5} To enhance patients' medication adherence, it is critically important to grasp their needs and preferences to medications they are receiving in the first place. Despite its apparent clinical significance, patients' preferences to medications have been one of the understudied topics. In fact, there are only a few studies that examined these issues in patients with schizophrenia.^{6,7}

Furthermore, these previous studies investigated solely on the side of the patients and did not assess the degree of awareness of their psychiatrists regarding these issues. The potential gap between patients' preferences to medications and their psychiatrists' assumption would likely result in poor adherence as well as lack of patients' trust toward their psychiatrists in charge.

To elucidate the patients' needs, preferences, and complaints to psychopharmacological treatment and examine how their psychiatrists correctly assess them, we conducted a cross-sectional study both from subjective and objective perspectives.

2 | METHODS

2.1 | Participants

In- and outpatients with a diagnosis of schizophrenia according to the International Classification of Diseases, 10th edition (ICD-10),⁸ who were 20 years of age or older and capable of providing informed consent were included. This study was conducted at three sites in Tokyo and Saitama, Japan: Ohizumi Hospital, Ohizumi Mental Clinic, and Asakadai Mental Clinic. The study was approved by the institutional review board at each participating site. Prior to study entry, participants provided written informed consent after receiving detailed information about the protocol. The term of schizophrenia was not used in the informed consent document because some of the potential participants or their families may have been unaware of their diagnoses. This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments (Fortaleza, Brazil, October 2013).

2.2 | Cross-sectional assessments

The primary measures were patients' needs and preferences for psychopharmacological treatment, using a questionnaire developed

by the authors that consists of multiple-choice questions regarding (a) their needs (16 items: poor sleep, anxiety, hallucination, tension, depression, emotional withdrawal, poor attention, preoccupation, delusions, stereotyped thinking, poor impulse control, hostility, apathetic social withdrawal, relapse, nothing in particular, and others) and complaints (24 items: nothing in particular, concentration difficulties, increased fatigability, depression, sleepiness, rigidity, hypokinesia, tremor, akathisia, dystonia, increased salivation, reduced salivation, nausea/vomiting, constipation, micturition/polydipsia, orthostatic dizziness, palpitations, weight gain, menstrual problem, galactorrhea, gynecomastia, sexual problem, and medications do not reduce symptoms) to psychopharmacological treatment that they were receiving, and (b) dosing frequency (5 items: once a day, twice a day, three times a day, four times a day, and five times a day or more), timing of dosing (5 items: after breakfast, after lunch, after dinner, at bedtime, and others), and their preference of dosage form (9 items: tablet, liquid, powder, orally disintegrating tablet, sublingual tablet, fast acting injection, long-acting injection, patch, and nothing in particular). Additionally, their treating psychiatrists were asked to predict their patients' responses to the above questions. The patients and their treating psychiatrists were asked to select a single response in this multiple-choice questionnaire.

The following assessments were also performed: Preference of Medicine Questionnaire (POM),⁹ Morisky Simplified Self-Report Measure of Adherence,^{10,11} Perceived Deficits Questionnaire (PDQ), and the Japanese version of the Drug Attitude Inventory-10 (DAI-10)^{12,13} by the patients, and the Positive and Negative Syndrome Scale (PANSS)¹⁴ and VAGUS¹⁵ for insight into illness by their psychiatrists. POM rates how patients evaluate the current medication compared to the previous one by choosing one of the following items: much better, slightly better, about the same, slightly worse, and much worse. The Morisky Simplified Self-Report Measure of Adherence is a self-evaluation scale of adherence. The total score ranges from 0 to 4, and a higher score indicates lower adherence. The VAGUS measures the core dimensions of clinical insight into psychosis, including general illness awareness, symptom attribution, awareness of need for treatment, and awareness of negative consequences attributable to the illness. The VAGUS has a clinician-rated and a self-report scale. The latter version was used for this study. A total score for the VAGUS ranges from 0 to 10 with a higher score indicating greater insight into illness. We translated the questionnaire of the VAGUS into Japanese and carried out back-translation to ensure consistency in its meaning. The VAGUS was translated into Japanese by two investigators and then back-translated into English by another two, who were not aware of the original English version.¹⁶ The scale's developer (Dr Philip Gerretsen) confirmed the back-translated version with regard to accuracy and context. The VAGUS was only performed by those who were already informed of their diagnosis by their psychiatrists. The following information was also collected: age, sex, in- or outpatients, educational background, current medications, duration of illness, duration of treatment, and history of long-acting injection use.



2.3 | Statistical analyses

Statistical analyses were performed using IBM SPSS Version 25.0 (IBM). The concordance rate was evaluated by the rate psychiatrists in charge exactly predicted their patients' responses for each question. Preferences of dosing frequency, timing, and dosage form were compared between patients who showed good medication adherence (ie, 0-2 in the Morisky Simplified Self-Report Measure of Adherence) and those who did not (ie, 3 and 4 in the Morisky Simplified Self-Report Measure of Adherence) by a chi-squared test. Response to the POM questionnaire and their psychiatrist's estimated response was compared by a chi-squared test.

3 | RESULTS

3.1 | Study sample

Table 1 summarizes demographic and clinical characteristics of 97 patients participated in this study. The relatively high mean \pm SD age of 46.6 ± 12.5 years and mean \pm SD duration of illness of 20.3 ± 13.8 years indicated that they were in a chronic stage of the illness. The mean DAI-10 score of 3.4 indicates their positive attitude toward medications, and the mean Morisky Simplified Self-Report Measure of Adherence of 1.6 represented moderate medication adherence. The main antipsychotics prescribed were olanzapine ($n = 18$), risperidone ($n = 17$), aripiprazole ($n = 1$), paliperidone ($n = 8$), aripiprazole long-acting injection (LAI) ($n = 6$), blonanserin ($n = 6$),

TABLE 1 Demographic and clinical characteristics of patients

Characteristics	Values
Age, y	46.6 \pm 12.5
Male sex	49 (54.4)
Inpatients	41 (45.6)
Duration of illness, y	20.3 \pm 13.8
Duration of treatment, y	17.2 \pm 13.6
History of LAI use	26 (28.9)
PANSS	
Total score	72.8 \pm 18.7
Positive symptoms score	16.6 \pm 5.5
Negative symptoms score	19.5 \pm 6.1
General psychopathology score	36.7 \pm 9.3
PDQ total score	25.9 \pm 14.4
VAGUS total score	6.4 \pm 1.7
DAI-10 total score	3.4 \pm 4.9
MMAS-4 score	1.6 \pm 1.2

Note: Values are shown as mean \pm standard deviation (range) or n (%). Abbreviations: DAI-10, Drug Attitude Inventory-10; LAI, Long-acting injection; MMAS-4, Morisky Medication Adherence Scale-4 items; PANSS, Positive and Negative Syndrome Scale; PDQ, Perceived Deficits Questionnaire.

paliperidone LAI ($n = 5$), perospirone ($n = 4$), haloperidol LAI ($n = 3$), risperidone LAI ($n = 2$), haloperidol ($n = 2$), fluphenazine decanoate ($n = 1$), asenapine ($n = 1$), quetiapine ($n = 1$), and chlorpromazine ($n = 1$). Four patients were receiving two antipsychotics, and one patient did not take any medication.

3.2 | Gap between patients and psychiatrists on needs, preferences, and complaints about psychopharmacological treatment

Approximately half the patients thought their current regimen was much better than the previous one, while 39.4% of their psychiatrists correctly estimated their medication preferences (Table 2).

The most frequently endorsed need for psychopharmacological treatment was "nothing in particular" ($n = 14$, 16.7%), followed by "anxiety" ($n = 13$, 15.5%); only 23.1% ($n = 18$) of their psychiatrists correctly predicted these responses (Table 3).

With regard to complaints about the current psychopharmacological treatment, "nothing in particular" was the most frequent response of the patients ($n = 17$, 20.2%), followed by "sleepiness," "tremor," "constipation," and "weight gain" ($n = 7$, 8.3%); only 15.4% of their psychiatrists accurately estimated these responses.

"Once a day" ($n = 56$, 65.1%) and "at bedtime" ($n = 53$, 61.6%) were the patients' most favorite dosing frequency and timing, respectively; 59.8% ($n = 49$) and 54.9% ($n = 45$) of their psychiatrists predicted them (Table 4). The most popular dosage form for the patients was "tablet" ($n = 51$, 59.3%), which was correctly predicted by 64.6% ($n = 53$) of their psychiatrists.

3.3 | Associations between medication adherence and preferences of dosing frequency, timing, and dosage form

There were no statistical differences in preferences of dosing frequency, timing, or dosage form between patients who showed good medication adherence and those who did not ($P = .19$, $P = .76$, and $P = .56$, respectively).

4 | DISCUSSION

In the present study, the most endorsed need regarding psychopharmacological treatment by patients with schizophrenia was "nothing in particular," suggesting a problem in illness insight; a certain proportion of the participants did not recognize the importance of pharmacotherapy since they were unaware of the symptoms to be improved. In addition, their psychiatrists correctly grasped their patients' needs regarding psychopharmacological treatment in only a quarter of occasions. With regard to the dosing frequency and timing, "once a day" and "at bedtime" were most frequently endorsed. Moreover, they preferred the "tablet" form the most. These

TABLE 2 Preference of current medications according to the POM questionnaire

	Patients' response	Response that their psychiatrists estimated ^a	Concordance rate
Much better	38 (48.1%)	9 (11.0%)	39.4%
Slightly better	22 (27.8%)	48 (58.5%)	
About the same	13 (16.5%)	23 (28.0%)	
Slightly worse	2 (2.5%)	2 (2.4%)	
Much worse	4 (5.1%)	0 (0.0%)	

Abbreviation: POM, Preference of the Medicine questionnaire.

^a $\chi^2_{(9)}=34.3, P < .001$.

TABLE 3 Symptoms patients most wanted to reduce with psychopharmacological treatment

	Patients' response	Response that their psychiatrists estimated	Concordance rate
Nothing in particular	14 (16.7%)	6 (6.9%)	23.1%
Anxiety	13 (15.5%)	10 (11.5%)	
Poor sleep	12 (14.3%)	23 (26.4%)	
Relapse	12 (14.3%)	10 (11.5%)	
Delusions	6 (7.1%)	1 (1.1%)	
Hallucination	4 (4.8%)	11 (12.6%)	
Apathetic social withdrawal	4 (4.8%)	5 (5.7%)	
Poor attention	4 (4.8%)	0 (0.0%)	
Depression	3 (3.6%)	9 (10.3%)	
Emotional withdrawal	3 (3.6%)	0 (0.0%)	
Tension	2 (2.4%)	4 (4.6%)	
Hostility	2 (2.4%)	1 (1.1%)	
Stereotyped thinking	1 (1.2%)	1 (1.1%)	
Poor impulse control	0 (0.0%)	4 (4.6%)	
Preoccupation	0 (0.0%)	1 (1.1%)	
Others	4 (4.8%)	1 (1.1%)	

responses were not always exactly guessed by their psychiatrists. Such under-recognition highlights the need of greater vigilance and active evaluation of patient's attitudes toward the treatment in order to enhance their treatment adherence.

The findings in the expectation toward pharmacotherapy among patients with schizophrenia have not been consistent in the literature. A survey of 271 patients with schizophrenia in the United States (mean \pm SD age, 38.4 \pm 11.9 years; 163 males (60.0%); 60% were diagnosed with schizophrenia between 15 and 25 years of age) reported improvement in positive symptoms as the most preferred treatment outcome (relative importance score of 10.0), followed by elimination of hyperglycemia (3.6, 95%CI = 2.6-4.6), improvement in negative symptoms (3.0, 95%CI = 1.6-4.3), reduced weight gain (2.6, 95%CI = 1.2-4.0), avoidance of hyperprolactinemia (1.7, 95%CI = 0.9-2.6), improved social functioning (1.5, 95%CI = 0.4-2.5), and avoidance of extrapyramidal symptoms (1.0, 95%CI = 0.3-1.8).⁶ Another study in the United States indicated that primary stakeholders (N = 53) including patients (n = 20), their families (n = 13), mental health providers (n = 20), and policy makers (N = 100) more highly valued productive activity and social activity outcomes than

outcomes associated with medication side effects and deficit symptoms.¹⁷ In contrast, in the present study, "nothing in particular" was the most frequently endorsed response, suggesting their low degree of commitment to the treatment in our sample. One of the possible reasons for their passive attitudes may be a result of different sample characteristics; they had a mean VAGUS score of 6.4 (a score range, 0 to 10) but other studies failed to address insight to the illness. Alternatively, our patients may have been content with their current regimen although the PANSS score indicated at least some degree of psychopathology.

In the present study, "once a day" dosing was liked the most, which was correctly predicted by two-fifth of their psychiatrists. While dosing intervals have conventionally been determined based on peripheral pharmacokinetic half-lives of the drugs, recent evidence suggests the possibility of extended, but regular dosing regardless of their half-lives.^{18,19} Taken together, the dosing interval could be adjusted based on their symptomatology and patient's preferences. With regard to dosage form, one previous study suggested that medication adherence was associated with their preference of dosage form. Levitan and colleagues examined



	Patients' response	Response that their psychiatrists estimated	Concordance rate
Number of current medications			
Too many	25 (29.8%)	35 (39.3%)	60.8%
Too few	2 (2.4%)	1 (1.1%)	
Just right	57 (67.9%)	53 (59.6%)	
Dosing frequency (per day)			
Once	56 (65.1%)	75 (83.3%)	59.8%
Twice	16 (18.6%)	7 (7.8%)	
Three times	8 (9.3%)	5 (5.6%)	
Four times	5 (5.8%)	1 (1.1%)	
Five times or more	0 (0.0%)	2 (2.2%)	
Timing of dosing			
After breakfast	19 (22.1%)	6 (6.7%)	54.9%
After lunch	0 (0.0%)	0 (0.0%)	
After dinner	11 (12.8%)	7 (7.9%)	
At bedtime	53 (61.6%)	75 (84.3%)	
Others	3 (3.5%)	1 (1.1%)	
Dosage form			
Tablet	51 (59.3%)	63 (70.8%)	64.6%
Long-acting injection	10 (11.6%)	10 (11.2%)	
Orally disintegrating tablet	4 (4.7%)	5 (5.6%)	
Fast acting injection	4 (4.7%)	1 (1.1%)	
Liquid	2 (2.3%)	0 (0.0%)	
Powder	2 (2.3%)	0 (0.0%)	
Patch	2 (2.3%)	1 (1.1%)	
Sublingual tablet	1 (1.2%)	0 (0.0%)	
Nothing in particular	10 (11.6%)	9 (10.1%)	

TABLE 4 Preferences of number, frequency, timing, and dosage form of medications

271 schizophrenia patients in the United States and found that adherent patients preferred a daily pill to an equally effective monthly injection ($P = .01$), while non-adherent patients who missed one to four doses per week preferred monthly injection to a pill ($P = .01$).⁶ In our study, with regard to preferences of dosing frequency, timing, and dosage form, there were no statistical differences between patients who showed good medication adherence and those who did not. Compared to the patients in the previous study in the United States,⁶ those in our study were older (46.6 ± 12.5 vs 38.4 ± 11.9) and all Japanese. These socio-demographic differences may impact the patient's dosage form preferences, which should be taken into account in interpreting the data and comparing the results across countries.

One of the possible reasons for the gap between patients' preferences to medications and their psychiatrists' assumptions may be suboptimal communication between them. The patients in our study could be considered to be moderately symptomatic (mean \pm SD PANSS score of 72.8 ± 18.7) and in a chronic phase of the illness with durations of illness and treatment of 20.3 ± 13.8 years and 17.2 ± 13.6 years, respectively. These

patients likely passively receive the treatment and may not disclose their complaints of their ongoing treatment to their psychiatrists even when they do not feel comfortable with their regimen. Another potential reason may be that their insight into illness may have been much lower than their psychiatrists assumed. In fact, both of the most endorsed needs for psychopharmacological treatment and the most frequent response to complaints of their medication were "nothing in particular." On the other hand, "sleepiness," "hallucination," "anxiety," "relapse," and "depression" were the five most frequent responses when their psychiatrists were asked to estimate their patients' needs, which suggests psychiatrists were overly optimistic with regard to their patients' insight into illness and motivation toward the treatment.

There are several limitations in the present study. First, the sample size was small and all participants were Japanese, which may limit the generalizability of the data to other populations. Second, due to its cross-sectional design, the associations that we found in the present study do not necessarily indicate causality. Prospective studies are warranted to replicate the preliminary

TABLE 5 Complaints about psychopharmacological treatment

	Patients' response	Response that their psychiatrists estimated	Concordance rate
Nothing in particular	17 (20.2%)	9 (10.2%)	15.4%
Sleepiness	7 (8.3%)	13 (14.8%)	
Tremor	7 (8.3%)	5 (5.7%)	
Weight gain	7 (8.3%)	4 (4.6%)	
Constipation	7 (8.3%)	2 (2.3%)	
Akathisia	6 (7.1%)	7 (8.0%)	
Medications do not reduce symptoms	6 (7.1%)	2 (2.3%)	
Concentration difficulties	5 (6.0%)	4 (4.6%)	
Menstrual problem	5 (6.0%)	1 (1.1%)	
Increased fatigability	4 (4.8%)	21 (23.9%)	
Increased salivation	3 (3.6%)	1 (1.1%)	
Reduced salivation	3 (3.6%)	1 (1.1%)	
Polyuria/polydipsia	3 (3.6%)	0 (0.0%)	
Orthostatic dizziness	2 (2.4%)	0 (0.0%)	
Hypokinesia	1 (1.2%)	8 (9.1%)	
Rigidity	1 (1.2%)	2 (2.3%)	
Depression	0 (0.0%)	4 (4.6%)	
Dystonia	0 (0.0%)	2 (2.3%)	
Palpitations	0 (0.0%)	1 (1.1%)	
Gynecomastia	0 (0.0%)	1 (1.1%)	
Nausea/vomiting	0 (0.0%)	0 (0.0%)	
Micturition disturbances	0 (0.0%)	0 (0.0%)	
Galactorrhea	0 (0.0%)	0 (0.0%)	
Sexual problem	0 (0.0%)	0 (0.0%)	

findings of this study. Third, the relationship between the patients and their treating psychiatrists, which could have affected the degree of trust between them,²⁰ was not evaluated in the present study. Moreover, the therapeutic alliance seems to play an important role for medication adherence.²¹ In addition, the most frequent response of "nothing in particular" may have indicated that the patients included in this study were not interested in their treatment in the first place. Finally, the multiple-choice questions about needs and preferences to medications developed for the purpose of this study require validation for use in future investigations; low concordance rates in Tables 3 and 5 may be a reflection of many choices to choose from.

In conclusion, the present study has revealed variations in the needs and preferences for psychopharmacological treatment among individual patients with schizophrenia. Moreover, their treating psychiatrists do not always sufficiently assess their patients' attitudes to psychopharmacological treatment. In order to improve patients' adherence to the treatment to mitigate negative outcomes in the treatment of schizophrenia, more interactive discussion regarding their ongoing treatment between patients and their treating psychiatrists may be needed.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

KT designed the study, recruited the subjects, analyzed the data, and wrote the first draft of the manuscript. RY and TS designed the study, analyzed the results, and wrote the manuscript. MM wrote the manuscript. HU designed the study, recruited the subjects, analyzed the data, and wrote the first draft of the manuscript. All authors have made substantial contributions to the conception, participated in drafting the article or revised it critically for important intellectual content, and read and approved the final version of the manuscript.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

The institutional review board of Ohizumi Hospital approved the study.

INFORMED CONSENT

All of the participants provided written informed consent.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

The IRB did not grant the deposit of raw data in a publicly accessible data archive or repository at the time of approval since the procedure was not included in the study protocol or informed consent document.

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