MICRO REPORT

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Prescription patterns in patients with schizophrenia in Japan: First-quality indicator data from the survey of "Effectiveness of Guidelines for Dissemination and Education in psychiatric treatment (EGUIDE)" project

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Abstract

Background: Guideline for Pharmacological Therapy for Schizophrenia was published by the Japanese Society of Neuropsychopharmacology in 2015. "Effectiveness of Guidelines for Dissemination and Education in psychiatric treatment (EGUIDE)" project aimed to standardize medical practice using quality indicators (QIs) as indices to evaluate the quality of medical practice. In this study, we have reported the quality indicator values of prescription before the beginning of the guideline lectures in the EGUIDE project to ascertain the baseline status of treating patients with schizophrenia.

Methods: A cross-sectional, retrospective case record survey was conducted, involving 1164 patients with schizophrenia at the time of discharge. We checked all types and dosage of psychotropic drugs.

Results: Forty-three percent of patients had antipsychotic polypharmacy, and substantial concomitant medication was observed (antidepressants; 8%, mood stabilizers: 37%, anxiolytics or hypnotics: 68%).

Conclusions: In the results obtained in this study, we plant to report changes in the effectiveness of education in the EGUIDE project near the future.

KEYWORDS

antipsychotics, EGUIDE project, guideline, quality indicator, schizophrenia

1 | INTRODUCTION

Several guidelines are available for treating patients with schizophrenia.[1-3] In 2015, the Japanese Society of Neuropsychopharmacology published the Guidelines for Pharmacological Therapy of Schizophrenia (GL).[4] The GL recommend second-generation antipsychotic monotherapy and do not recommend concomitant medication (antidepressants, mood stabilizers, and hypnotics). However, it is difficult to assess the extent to which these guidelines have been disseminated in real clinical settings in Japan. In fact, it has been repeatedly reported that polypharmacy with antipsychotics or combination therapy with other psychotropic drugs for schizophrenia prevails in Japan compared with other countries.[5] Another previous report shows almost 30% patients received antipsychotic monotherapy, whereas between 32% and 42% of patients undergo treatment with more than 3 agents.[6,7] Psychotropic polypharmacy may cause several side effects, including life-threatening events such as a cardiovascular attack. Individuals in Japan with severe mental illness suffer premature death and excess mortality.[8] Furthermore, Japanese psychiatrists have too many patients to take enough time per patient in outpatient care.[9] Considering this situation, we initiated the "Effectiveness of Guidelines for Dissemination and Education in psychiatric treatment (EGUIDE)" project in 2016,[4] which aimed to standardize medical practice using quality indicators (QIs) as indices to evaluate the quality of medical practice. In the project, we

designed and conducted a series of training courses[4] and used QIs as indicators to evaluate the extent to which evidence-based medicine in accordance with the GL prevailed among psychiatrists who participated in the training course by following longitudinal alterations in QIs. In this letter, we report the QI values in the first year (before the implementation of the educational program) to ascertain the current status of treating patients with schizophrenia in Japan as the baseline for the longitudinal observations.

2 | MATERIALS AND METHODS

2.1 | Study design

This research was a cross-sectional, retrospective study conducted from October 2016 to December 2016. A total of 44 institutions (23 university hospitals, 12 national/public hospitals, and 9 private hospitals) participated in the EGUIDE project. A total of 11 QIs (Table S1) were calculated based on data on prescriptions for patients with schizophrenia at discharge (April to September 2016) before the first EGUIDE program was conducted (October 2016 to February 2017).

A cross-sectional, case record survey was conducted using a standardized data collection form at each study site, involving a sample of 1164 patients who had been diagnosed with schizophrenia at the time of discharge. The data were collected by the EGUIDE project members. In the EGUIDE project prescription survey, we checked all types and dosages of psychotropic drugs, including antipsychotics, mood stabilizers, antidepressants, and benzodiazepines. We also assessed the use of modified electroconvulsive therapy (mECT) and long-acting injection in these patients.

The following 11 QIs were used in the present study:

QI-1. Antipsychotic monotherapy ratio in patients with schizophrenia

QI-2. Antipsychotic monotherapy ratio without the use of any other psychotropics in patients with schizophrenia

QI-3. No prescription ratio of anxiolytics or hypnotics in patients with schizophrenia

QI-4. Reducing the ratio of the prescribed dosage of anxiolytics or hypnotics in patients with schizophrenia

QI-5. Reducing the ratio of the number of anxiolytics or hypnotics in patients with schizophrenia

QI-6. No prescription ratio of antidepressants in patients with schizophrenia

QI-7. No prescription ratio of mood stabilizers or antiepileptic drugs in patients with schizophrenia

QI-8. Using the ratio of long-acting injections in patients with schizophrenia

QI-9. Clozapine treatment ratio in patients with schizophrenia

QI-10. mECT ratio in patients with schizophrenia

QI-11. No prescription ratio of sulpiride in patients with schizophrenia

Definition of QIs was presented in Table S1.

TABLE 1 Demographics of schizophrenia patients

	n	Age (mean ± SD)	Age (min-max)	ECT
Total	1164	46 ± 15.0	13-88	68
Male	504	44 ± 14.0	17-87	31
Female	660	47 ± 15.7	13-88	37

2.2 | Statistical analysis

We performed all statistics using Microsoft Excel 2019. First, we presented each QI in all subjects in all hospitals. Then, we calculated all QIs in each hospital and presented QIs of 44 hospitals as means ± standard deviations. QIs of three subgroups of 44 hospitals divided by hospitals type (university hospital, national/public hospitals, and private hospitals) were also reported as means ± standard deviations.

3 | RESULTS

Table 1 shows demographics of patients with schizophrenia in this study. The QI values are presented in Table 2. Forty-three percent of patients had antipsychotic polypharmacy, and substantial concomitant medication was observed (antidepressants: 8%, mood stabilizers: 37%, anxiolytics or hypnotics: 68%) in all subjects. We also showed means of QI values of all hospitals and of three hospital types.

4 | DISCUSSION

In this study, we report the QI values before the beginning of the guideline lectures in the EGUIDE project. In this study, 43% of patients received antipsychotic polypharmacy. The results of the present study endorse the previous report that antipsychotic polypharmacy prevails in Japan compared with other countries.[5] In another previous study,[10] the antipsychotic polypharmacy rate in Japan was 57.4%. Possible reasons for the discrepancy between the studies with respect to prescription patterns include different prescribing traditions. Japanese young psychiatrists usually follow and are less likely to amend or challenge traditional prescribing traditions introduced by senior psychiatrist. In this study, many cases are entered from the university hospital (educational institutions). These points may influence this discrepancy results. The major strengths of the EGUIDE project are the large sample size, which includes every region of Japan, the standardized method of data collection, and the longitudinal design. We investigated the effectiveness of the guideline education programs by conducting a prescription survey every year. Based on this baseline report, we will plan to report changes in the effectiveness of education program in the future.

The low percentage of patients with schizophrenia receiving long-acting injections, clozapine therapy, or mECT treatment may

TABLE 2 QI values for patients with schizophrenia in 2016

QI		All		University hospitals		National/public hospitals		Private hospitals	
		n = 1164	44 hospitals Mean ± SD	n = 600	23 hospitals Mean ± SD	n = 281	12 hospitals Mean ± SD	n = 283	9 hospitals Mean ± SD
1	Antipsychotic monotherapy	57.1%	54.6 ± 20.6	57.0%	60.9 ± 19.3	46.1%	43.0 ± 22.5	67.4%	53.8 ± 15.7
2	Antipsychotic monotherapy without other psychotropics	15.5%	14.8 ± 11.7	14.7%	16.6 ± 13.0	13.7%	12.3 ± 10.9	18.8%	13.4 ± 9.3
3	No prescription of anxiolytics or hypnotics	31.7%	29.6 ± 14.6	34.2%	34.5 ± 14.4	27.0%	23.0 ± 14.2	30.9%	26.1 ± 12.4
4	Reducing the ratio of prescribed dosage of anxiolytics or hypnotics	25.4%	26.5 ± 15.4	29.6%	30.9 ± 14.7	19.1%	20.9 ± 16.8	22.7%	22.5 ± 13.1
5	Reducing the ratio of the number of anxiolytics or hypnotics	18.6%	20.5 ± 15.8	22.4%	24.6 ± 14.6	12.5%	15.1 ± 17.3	16.7%	17.3 ± 15.6
6	No prescription of antidepressants	92.3%	92.7 ± 6.7	91.4%	91.0 ± 5.8	92.6%	93.6 ± 7.8	94.0%	95.8 ± 6.8
7	No prescription of mood stabilizers or antiepileptic drugs	62.7%	63.3 ± 14.6	64.9%	65.8 ± 12.1	62.1%	63.8 ± 17.8	58.9%	56.3 ± 15.1
8	Use of long-acting injections	8.3%	7.5 ± 10.1	7.2%	4.9 ± 6.1	10.2%	13.2 ± 16.2	8.9%	6.7 ± 4.8
9	Clozapine treatment for schizophrenia	7.1%	7.1 ± 11.8	5.0%	7.8 ± 9.9	4.7%	7.9 ± 15.4	13.5%	4.1 ± 12.2
10	mECT	5.8%	5.8 ± 8.8	7.0%	6.5 ± 9.3	8.9%	8.2 ± 9.9	0.4%	0.7 ± 2.0
11	No prescription ratio of sulpiride	98.9%	99.4 ± 1.4	98.9%	99.3 ± 1.4	99.2%	99.4 ± 1.5	98.6%	99.6 ± 1.3

largely be influenced by the Japanese medical system because several institutions included in this study were university hospitals, and these hospitals in Japan have a limited hospitalization period. There are several limitations in this study. First, we did not assess symptoms using rating scales. Second, the data were collected from medical records that the collaborating investigators obtained in routine clinical settings, which might impact the results. Third, there is a selection bias, because only 23 university hospitals, 12 national/public hospitals, and 9 private hospitals may not represent prescription patterns of all psychiatrists in Japan. Moreover, the data were obtained exclusively (more than half) from university hospitals (educational institutions), which may make it difficult to generalize the results.

We should strive to improve polypharmacy in the treatment of schizophrenia in Japan. Based on the results obtained in this study, we plan to report changes in the effectiveness of education in the EGUIDE project in the future.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS
KIchi and HH were critically involved in data collection and data analysis and wrote the first draft of the manuscript. KW and KIna were critically involved in the study design and contributed to the interpretation of the data and the writing of the manuscript. NHase, YY, TY, KM, and JM were involved in the data analysis and contributed to the interpretation of the data. TT, KIwa, TK, TH, Hiroki Yamada, NS, TN, NT, KN, SO, MU, EK, HYamamori, HT, TS, RF, TI, JF, TO, KOhi, YM, YT, NHashi, JI, KOga, and Hisashi Yamada were involved in the participant recruitment process and data collection and contributed to the interpretation of the data. RH supervised the entire project, collected the data and was critically involved in the design, analysis, and interpretation of the data. All authors contributed revising the manuscript critically for important intellectual content and gave final approval of the version to be published and had agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA REPOSITORY
The data are not publicly available due to privacy and ethical restrictions (ie, we did not obtain informed consent on the public availability of raw data).

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD
The entire study protocol was approved by the ethics committees of the National Center of Neurology and Psychiatry and each participating university/hospital/clinic.

INFORMED CONSENT
Written informed consent was obtained from all participants (psychiatrists) after a complete explanation of the procedures by the principal researcher at the study facility. Patients were able to opt out of the purpose and procedures of the study and to refuse study participation. Public availability of raw data was not planned in the research protocol approved by an Institutional Reviewer Board. We did not obtain informed consent of the public availability.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL
The study protocol has been registered in the University Hospital Medical Information Network Registry (UMIN000022645).

ANIMAL STUDIES
N/A

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REFERENCES
1. Castle DJ, Galletly CA, Dark F, Humberstone V, Morgan VA, Killackey E, et al. The 2016 Royal Australian and New Zealand College of Psychiatrists guidelines for the management of schizophrenia and related disorders. Med J Aust. 2017;206(11):501–5.
2. Crockford D, Addington D. Canadian Schizophrenia guidelines: Schizophrenia and other psychotic disorders with coexisting substance use disorders. Can J Psychiatry. 2017;62(9):624–34.
3. Hasan A, Falkai P, Wobrock T, Lieberman J, Glenthoj B, Gattaz WF, et al. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia, part 1: update 2012 on the acute treatment of schizophrenia and the management of treatment resistance. World J Biol Psychiatry. 2012;13(5):318–78.
4. Takaesu Y, Watanabe K, Numata S, Iwata M, Kudo N, Oishi S, et al. Improvement of psychiatrists' clinical knowledge of the treatment guidelines for schizophrenia and major depressive disorders using the 'Effectiveness of Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)' project: a nationwide dissemination, education, and evaluation study. Psychiatry Clin Neurosci. 2019;73(10):642–8.
5. Yang S-Y, Chen L-Y, Najoan E, Kallivayalil RA, Viboonma K, Jamaluddin R, et al. Polypharmacy and psychotropic drug loading in patients with schizophrenia in Asian countries: fourth survey of Research on Asian Prescription Patterns on antipsychotics. Psychiatry Clin Neurosci. 2018;72(8):572–9.
6. Okuma YNT, Ito H. Antipsychotics prescribing patterns of with schizophrenia in Japan: using the national database of health insurance claim information and specified medical checkups. Jpn J Clin Psychopharmacol. 2013;16:1201–15.
7. Yoshio T, Inada T, Uno J, Miwa T, Kitagawa K, Miyahara Y, et al. Prescription profiles for pharmacological treatment of Japanese inpatients with schizophrenia: comparison between 2007 and 2009. Hum Psychopharmacol. 2012;27(1):70–5.

8. Kondo S, Kumakura Y, Kanehara A, Nagato D, Ueda T, Matsuoka T, et al. Premature deaths among individuals with severe mental illness after discharge from long-term hospitalisation in Japan: a naturalistic observation during a 24-year period. BJPsych open. 2017;3(4):193–5.

9. Hori H, Yamato K. Assessment of current clinical practices for major depression in Japan using a web-based questionnaire. Neuropsychiatr Dis Treat. 2019;15:2821–32.

10. Dong M, Zeng L-N, Zhang Q, Yang S-Y, Chen L-Y, Najoan E, et al. Prescription of antipsychotic and concomitant medications for adult Asian schizophrenia patients: findings of the 2016 Research on Asian Psychotropic Prescription Patterns (REAP) survey. Asian J Psychiatry. 2019;45:74–80.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.