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Differences in Baseline Characteristics of Patients Treated with Olanzapine or Other Antipsychotics in Japanese Patients with Acute Schizophrenia: A 1-Year Observational Study under Routine Clinical Practice in Japan

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Abstract

Objective: Baseline characteristics of acute schizophrenia patients were analyzed to identify differences in the baseline characteristics of patients treated with olanzapine monotherapy compared with those treated with other antipsychotic monotherapies. Methods: This prospective, naturalistic observational study was designed to evaluate discontinuation rates of olanzapine and non-olanzapine antipsychotic monotherapy in Japanese adult patients with acute schizophrenia. Results: A total of 1089 patients were assessed: 578 patients were treated with olanzapine, 487 with non-olanzapine atypical antipsychotics, and 24 with typical antipsychotics. The mean Clinical Global Impression-Severity (CGI-S) Schizophrenia, Brief Psychiatric Rating Scale (BPRS) total, and BPRS positive scores were higher in patients treated with olanzapine compared with most of the non-olanzapine treated patients. The majority of patients with a CGI-S Schizophrenia score of 7 (29/41 patients) as well as patients with a BPRS total score of 90 or higher (14/18 patients) were treated with olanzapine. On the other hand, physicians tended to prescribe antipsychotics other than olanzapine for patients with heavier body weight or diabetes mellitus. Conclusion: The

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present study demonstrated that olanzapine was more likely to be prescribed to patients with more severe schizophrenia symptoms. However, further studies are warranted to reach a definite conclusion.

Keywords

Schizophrenia, Baseline Characteristics, Olanzapine, Antipsychotics

1. Introduction

Atypical antipsychotics have been widely used as a first-line therapy for acute and maintenance phases of schizophrenia. They are essential in the treatment of schizophrenia. However, these medications could be partially ineffective or intolerant for some patients, and a switching strategy is often chosen to address those issues. Today, a number of atypical antipsychotics are available on the market, and selection of antipsychotics is vital to maximize the effectiveness and minimize the risk of undesirable adverse events.

Several studies have investigated the differences in baseline characteristics of patients treated with antipsychotics [1]-[5]. However, Japanese patients with acute schizophrenia treated with antipsychotic monotherapy had not been investigated in a prospective large-scale clinical study with a long-term follow-up period. Previously, we conducted a prospective, naturalistic observational study to evaluate the discontinuation rates of olanzapine and non-olanzapine antipsychotic monotherapies in Japanese patients with acute schizophrenia in a routine clinical practice setting [6]. In the primary evaluation, patients treated with olanzapine monotherapy were found to have a significantly greater chance of continuing the medication than those treated with a non-olanzapine antipsychotic monotherapy, possibly due to the greater efficacy of olanzapine monotherapy and its acceptable tolerability and safety profile. Using this study population, we extended our analysis to a comparison of baseline characteristics of the patients who were treated not only with olanzapine monotherapy but also those treated with other atypical antipsychotic monotherapies (*i.e.*, risperidone, aripiprazole, blonanserin, quetiapine, and paliperidone) as well as typical antipsychotic monotherapies (*i.e.*, haloperidol).

The objectives of the present analysis were 1) to identify specific characteristics of patients with acute schizophrenia who were treated with olanzapine monotherapy, and 2) to identify differences in patient characteristics that might be related to the selection of antipsychotic monotherapy. The findings of the present analysis would be beneficial for selection of antipsychotic treatment.

2. Materials and Methods

2.1. Study Design

This was a prospective, naturalistic multi-center observational study designed to evaluate discontinuation rates of antipsychotic monotherapies in Japanese adult patients with acute schizophrenia. The selection of the medication depended on the investigators, and patients were monitored until discontinuation of the monotherapy or completion of study. Using its cohort data, we investigated the differences between baseline characteristics of patients treated with olanzapine monotherapy and those treated with other antipsychotics.

Oral antipsychotics were prescribed following the dosage and administration approved in Japan. Informed consent was obtained from all patients enrolled in this study. This study was conducted in compliance with guideline of Good Post-marketing Study Practice (GPSP) and the Declaration of Helsinki.

2.2. Patients

The key eligibility criteria for this study were patients who were diagnosed with schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) Text Revision and ≥20 years of age, and who started treatment with oral antipsychotic monotherapy (patients who were treatment-naïve, or who had switched from other antipsychotics or from poly-pharmacotherapy to monotherapy were included), had a Clinical Global Impression-Severity (CGI-S) Schizophrenia score of ≥4 at the start of oral antipsychotic mono-

therapy, and had acute stage of schizophrenia developed within one month prior to starting oral antipsychotic monotherapy.

2.3. Measures and Statistical Methods

Analysis was performed in patients whose case report forms were collected and who were confirmed to meet all the eligibility criteria. The baseline characteristics of patients treated with olanzapine monotherapy (olanzapine group) were compared with those treated with non-olanzapine atypical antipsychotic monotherapy (non-olanzapine atypical antipsychotic group). The baseline characteristics of patients treated with typical antipsychotic monotherapy (typical antipsychotic group), and those treated with individual antipsychotics that included 20 or more patients (*i.e.*, risperidone, aripiprazole, blonanserin, quetiapine, and paliperidone) were summarized using descriptive statistics, however due to small sample size, no statistical comparison with the olanzapine group was conducted.

In the present study, baseline information for analysis was grouped into four categories: 1) demographic and clinical characteristics of patients (*i.e.*, gender, age, history of schizophrenia, inpatient or outpatient status, living status, prior antipsychotic medication use within one month prior to the initiation of antipsychotic monotherapy, CGI-S Parkinsonism score, use of anti-Parkinsonism agents, antidepressants, antiepileptic agents, or mood stabilizers; 2) severity of schizophrenia (*i.e.*, CGI-S Schizophrenia Score, Brief Psychiatric Rating Scale [BPRS] total score, Positive, Negative, and Anxiety-Depression scores); 3) body weight and body mass index (BMI); and 4) history of diabetes mellitus or presence of diabetes mellitus, and blood glucose level.

Differences in baseline patient characteristics between the olanzapine and non-olanzapine atypical antipsychotic groups were compared using Student's t-test for continuous variables, Fisher's exact test for binary variables, or the Monte Carlo method for other categorical variables. Multiplicity adjustments were not performed.

3. Results

A total of 1124 patients from 72 centers in Japan were enrolled and the study was conducted from January 2010 to November 2012, and assessed for baseline characteristics. Thirty-five patients were not eligible for analysis: 26 for inclusion criteria not met (14, age under 20 years old; 12, concomitant use of multiple antipsychotics) and 9 for lack of case report. Thus, data from 1089 patients were analyzed. Among those, 578 patients were treated with olanzapine, 487 with non-olanzapine atypical antipsychotics (including 160 risperidone, 154 aripiprazole, 67 blonanserin, 44 quetiapine, 40 paliperidone) and 24 with typical antipsychotics (including 13 haloperidol) (**Figure 1**).

The baseline demographic and clinical characteristics of patients in each group are summarized in **Table 1**. Overall, 46.0% of the patients in the olanzapine group and 42.7% in the non-olanzapine atypical antipsychotic group were male ($p = 0.293$). For the individual antipsychotic groups, more than half of the patients were male in the paliperidone and typical antipsychotic groups (60.0% and 54.2%, respectively) while the majority of patients were women in the other groups. History of schizophrenia (mean duration) was 14.42 years in the olanzapine group, which was comparable to 14.43 years in the non-olanzapine atypical antipsychotic group ($p = 0.992$). It was the longest in the typical antipsychotic group, with 22.47 years. Although there was no statistically significant difference ($p = 0.117$), the percentage of inpatients in the olanzapine group (61.8%) was higher than that of the non-olanzapine atypical antipsychotic group (56.9%). With the exception of the risperidone group, inpatient percentages for all other individual antipsychotic groups were lower than that of the olanzapine group.

The percentages of patients with antipsychotic use within one month prior to the start of monotherapy in the olanzapine group (37.9%) was comparable to the 37.2% observed in the non-olanzapine atypical antipsychotic group ($p = 0.849$).

The mean CGI-S Parkinsonism score in the olanzapine group was 0.8, which was the same as that in the non-olanzapine antipsychotic group (0.8, $p = 0.758$), but lower than that in the typical antipsychotic group (1.6). Moreover, the percentages of patients with use of any anti-Parkinsonism agent in the olanzapine group (8.7%) were significantly lower than those in the non-olanzapine atypical antipsychotic group (13.3%, $p = 0.017$). The highest percentage of patients using an anti-Parkinsonism agent was seen in the typical antipsychotic group (41.7%).

There was no statistically significant difference between the percentages of patients who used an antidepressant, antiepileptic agent, or mood-stabilizer in the olanzapine group and the non-olanzapine atypical

Table 1. Baseline demographic and clinical characteristics of patients.

		Olanzapine (n = 578)		Non-olanzapine atypical antipsychotics												Typical antipsychotics overall (n = 24)	
				Overall* (n = 487)		Risperidone (n = 160)		Aripiprazole (n = 154)		Blonanserin (n = 67)		Quetiapine (n = 44)		Paliperidone (n = 40)			
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gender	Male	266	(46.0)	208	(42.7)	72	(45.0)	59	(38.3)	27	(40.3)	18	(40.9)	24	(60.0)	13	(54.2)
	Female	312	(54.0)	279	(57.3)	88	(55.0)	95	(61.7)	40	(59.7)	26	(59.1)	16	(40.0)	11	(45.8)
	p-value[F)]	0.293															
Age (years)	n	574		484		160		152		67		43		40		24	
	Mean (SD)	46.1	(15.6)	47.1	(15.9)	47.3	(16.0)	46.0	(15.5)	47.0	(16.4)	50.3	(16.9)	46.0	(15.6)	49.2	(14.0)
	p-value[M)]	0.295															
History of schizophrenia (years)	n	404		305		95		106		39		29		22		10	
	Mean (SD)	14.42	(14.11)	14.43)	(13.80)	15.46	(14.40)	13.06	(12.93)	12.57	(12.38)	17.60	(15.09)	15.22	(16.07)	22.47	(10.69)
	Median	10.00		10.00		10.00		8.54		10.25		12.00		6.13		19.29	
	Min - max	0.0 - 55.0		0.0 - 60.0		0.0 - 60.0		0.0 - 45.5		0.1 - 42.8		0.3 - 53.5		0.1 - 45.0		10.0 - 44.1	
	p-value[S)]	0.992															
Inpatient or outpatient status	Inpatient	357	(61.8)	277	(56.9)	113	(70.6)	83	(53.9)	26	(38.8)	24	(54.5)	18	(45.0)	10	(41.7)
	Outpatient	221	(38.2)	210	(43.1)	47	(29.4)	71	(46.1)	41	(61.2)	20	(45.5)	22	(55.0)	14	(58.3)
	p-value[F)]	0.117															
Living status	Single-person household	43	(7.4)	37	(7.6)	7	(4.4)	10	(6.5)	10	(14.9)	4	(9.1)	5	(12.5)	3	(12.5)
	Living with family	163	(28.2)	166	(34.1)	38	(23.8)	60	(39.0)	29	(43.3)	16	(36.4)	17	(42.5)	11	(45.8)
	Living with non-family members	14	(2.4)	6	(1.2)	2	(1.3)	0	(0.0)	2	(3.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Others	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Unknown	357	(61.8)	277	(56.9)	113	(70.6)	83	(53.9)	26	(38.8)	24	(54.5)	18	(45.0)	10	(41.7)
	p-value[M)]	0.284															
Antipsychotics use within 1 month prior to the initiation of monotherapy	Yes	219	(37.9)	181	(37.2)	48	(30.0)	63	(40.9)	25	(37.3)	16	(36.4)	21	(52.5)	14	(58.3)
	No	359	(62.1)	306	(62.8)	112	(70.0)	91	(59.1)	42	(62.7)	28	(63.6)	19	(47.5)	10	(41.7)
	p-value[F)]	0.849															
CGI-S Parkinsonism Score**	n	401		325		108		106		48		30		20		15	
	Mean (SD)	0.8	(1.5)	0.8	(1.4)	0.9	(1.5)	0.8	(1.3)	0.8	(1.5)	0.8	(1.4)	0.8	(1.3)	1.6	(2.0)
	p-value[S)]	0.758															
Use of any anti-Parkinsonism agents**	Yes	50	(8.7)	65	(13.3)	27	(16.9)	13	(8.4)	14	(20.9)	3	(6.8)	4	(10.0)	10	(41.7)
	No	528	(91.3)	422	(86.7)	133	(83.1)	141	(91.6)	53	(79.1)	41	(93.2)	36	(90.0)	14	(58.3)
	p-value[F)]	0.017															

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Use of any antidepressants**	Yes	31	(5.4)	28	(5.7)	8	(5.0)	8	(5.2)	1	(1.5)	5	(11.4)	3	(7.5)	3	(12.5)
	No	547	(94.6)	459	(94.3)	152	(95.0)	146	(94.8)	66	(98.5)	39	(88.6)	37	(92.5)	21	(87.5)
	p-value[F)]		0.790														
Use of any antiepileptic agents**	Yes	79	(13.7)	66	(13.6)	18	(11.3)	25	(16.2)	5	(7.5)	9	(20.5)	3	(7.5)	6	(25.0)
	No	499	(86.3)	421	(86.4)	142	(88.8)	129	(83.8)	62	(92.5)	35	(79.5)	37	(92.5)	18	(75.0)
	p-value[F)]		1.000														
Use of any mood stabilizers**	Yes	11	(1.9)	17	(3.5)	3	(1.9)	7	(4.5)	2	(3.0)	4	(9.1)	1	(2.5)	0	(0.0)
	No	567	(98.1)	470	(96.5)	157	(98.1)	147	(95.5)	65	(97.0)	40	(90.9)	39	(97.5)	24	(100.0)
	p-value[F)]		0.125														

*Including patients treated with perospirone (n = 16) and zotepine (n = 6); **At initiation of monotherapy; CGI-S, Clinical Global Impression-Severity of Illness; SD, standard deviation. S)Student's t-test; F)Fisher's exact test; M) Monte Carlo method (vs. olanzapine group).

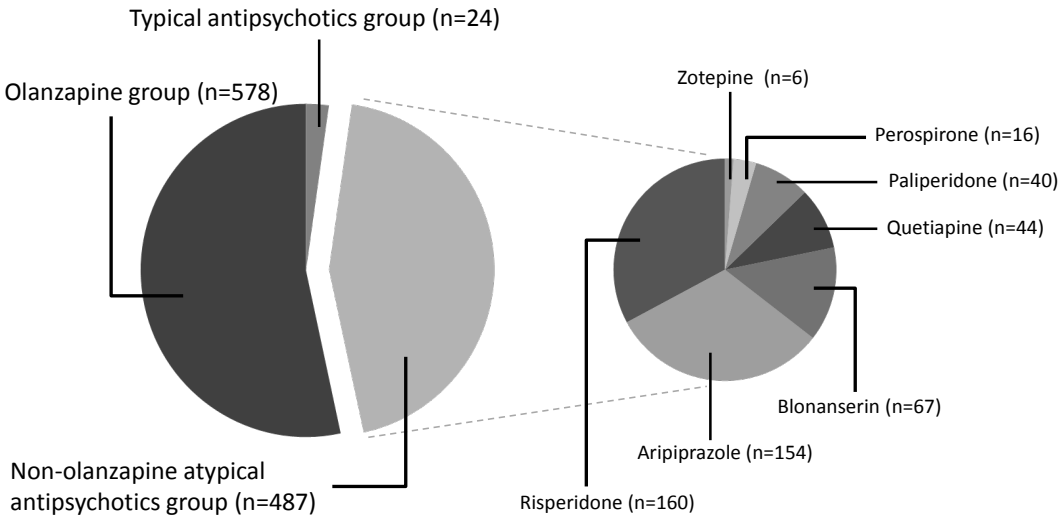

Figure 1. Number of patients in each treatment group.

antipsychotic group. The percentages of patients who used an antidepressant or antiepileptic agent in the typical antipsychotic groups were numerically higher than those in the olanzapine group. On the other hand, there were no significant differences observed for age and living status (single or living together with family or other individuals).

The baseline CGI-S Schizophrenia and BPRS scores are summarized in **Table 2**. The mean CGI-S Schizophrenia score was significantly higher in the olanzapine group than that in the non-olanzapine group (4.9 vs. 4.8; p = 0.015). Although there were no statistically significant differences (p = 0.108 and p = 0.225, respectively), mean BPRS total and BPRS positive scores in the olanzapine group (60.3 and 16.5, respectively) were numerically higher than those in the non-olanzapine atypical antipsychotic group (58.5 and 16.1, respectively). For the individual antipsychotics groups, the scores in the olanzapine group were numerically higher compared with most of the other groups, with the exception of the risperidone group. The scores between the olanzapine and risperidone groups were comparable. On the other hand, mean BPRS Negative and Anxiety/Depression scores were comparable between groups. The majority of patients with a CGI-S Schizophrenia score of 7 (29 of 41 patients) as well as patients with a BPRS total score of 90 or higher (14 of 18 patients) were treated with olanzapine monotherapy. Moreover, the majority of patients with a BPRS positive score of 25 or higher (19 of 31 patients) were also treated with olanzapine monotherapy.

Baseline body weight and BMI are summarized in **Table 3**. With the exception of the quetiapine group, the mean body weight of patients in the olanzapine group (57.70 kg) was numerically lower than those in the

Table 2. Baseline CGI-S and BPRS scores.

		Olanzapine (n = 578)		Non-olanzapine atypical antipsychotics										Typical antipsychotics	
				Overall* (n = 487)		Risperidone (n = 160)		Aripiprazole (n = 154)		Blonanserin (n = 67)		Quetiapine (n = 44)		Paliperidone (n = 40)		Overall (n = 24)	
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
CGI-S schizophrenia score	n	578		487		160		154		67		44		40		24	
	Mean (SD)	4.9	(0.9)	4.8	(0.9)	5.0	(0.9)	4.7	(0.8)	4.7	(0.8)	4.9	(0.9)	4.9	(0.9)	4.7	(0.8)
	p-value[S)]	0.015															
	4	240	(41.5)	230	(47.2)	63	(39.4)	83	(53.9)	34	(50.7)	19	(43.2)	17	(42.5)	11	(45.8)
	5	165	(28.5)	137	(28.1)	42	(26.3)	43	(27.9)	23	(34.3)	12	(27.3)	12	(30.0)	9	(37.5)
	6	144	(24.9)	108	(22.2)	52	(32.5)	24	(15.6)	9	(13.4)	11	(25.0)	9	(22.5)	4	(16.7)
	7	29	(5.0)	12	(2.5)	3	(1.9)	4	(2.6)	1	(1.5)	2	(4.5)	2	(5.0)	0	(0.0)
BPRS total score	n	354		308		103		101		49		22		21		14	
	Mean (SD)	60.3	(15.5)	58.5	(14.2)	61.8	(15.4)	58.4	(13.2)	54.9	(13.2)	59.0	(13.1)	56.0	(11.8)	54.3	(15.2)
	p-value[S)]	0.108															
	≥20, <30	2	(0.3)	2	(0.4)	0	(0.0)	1	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	≥30, <40	25	(4.3)	23	(4.7)	5	(3.1)	4	(2.6)	7	(10.4)	2	(4.5)	2	(5.0)	2	(8.3)
	≥40, <50	70	(12.1)	57	(11.7)	20	(12.5)	22	(14.3)	8	(11.9)	3	(6.8)	3	(7.5)	3	(12.5)
	≥50, <60	82	(14.2)	97	(19.9)	28	(17.5)	31	(20.1)	19	(28.4)	6	(13.6)	8	(20.0)	5	(20.8)
	≥60, <70	81	(14.0)	60	(12.3)	16	(10.0)	22	(14.3)	7	(10.4)	8	(18.2)	6	(15.0)	2	(8.3)
	≥70, <80	54	(9.3)	40	(8.2)	18	(11.3)	12	(7.8)	6	(9.0)	1	(2.3)	2	(5.0)	1	(4.2)
	≥80, <90	26	(4.5)	25	(5.1)	13	(8.1)	8	(5.2)	2	(3.0)	2	(4.5)	0	(0.0)	1	(4.2)
	≥90, <100	10	(1.7)	3	(0.6)	2	(1.3)	1	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	≥100, <110	4	(0.7)	1	(0.2)	1	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
BPRS positive score	n	354		308		103		101		49		22		21		14	
	Mean (SD)	16.5	(4.9)	16.1	(4.8)	17.5	(4.7)	16.0	(4.5)	14.5	(4.9)	15.6	(4.7)	15.1	(4.3)	13.5	(5.2)
	p-value[S)]	0.225															
	<5	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	1	(1.5)	0	(0.0)	0	(0.0)	0	(0.0)
	≥5, <10	28	(4.8)	28	(5.7)	6	(3.8)	9	(5.8)	5	(7.5)	3	(6.8)	2	(5.0)	3	(12.5)
	≥10, <15	100	(17.3)	87	(17.9)	23	(14.4)	28	(18.2)	21	(31.3)	5	(11.4)	5	(12.5)	5	(20.8)
	≥15, <20	120	(20.8)	114	(23.4)	35	(21.9)	43	(27.9)	14	(20.9)	10	(22.7)	10	(25.0)	4	(16.7)
	≥20, <25	87	(15.1)	67	(13.8)	34	(21.3)	18	(11.7)	7	(10.4)	3	(6.8)	4	(10.0)	1	(4.2)
	≥25, <30	19	(3.3)	11	(2.3)	5	(3.1)	3	(1.9)	1	(1.5)	1	(2.3)	0	(0.0)	1	(4.2)
BPRS negative score	n	354		308		103		101		49		22		21		14	
	Mean (SD)	10.4	(3.8)	10.6	(3.5)	10.7	(3.8)	10.6	(3.4)	10.5	(3.6)	10.0	(3.3)	11.0	(2.1)	12.0	(3.3)
	p-value[S)]	0.493															
	<5	29	(5.0)	14	(2.9)	4	(2.5)	5	(3.2)	3	(4.5)	1	(2.3)	0	(0.0)	0	(0.0)

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	≥5, <10	107	(18.5)	110	(22.6)	37	(23.1)	37	(24.0)	18	(26.9)	7	(15.9)	6	(15.0)	3	(12.5)
	≥10, <15	166	(28.7)	136	(27.9)	42	(26.3)	43	(27.9)	20	(29.9)	12	(27.3)	14	(35.0)	7	(29.2)
	≥15, <20	49	(8.5)	48	(9.9)	20	(12.5)	16	(10.4)	8	(11.9)	2	(4.5)	1	(2.5)	4	(16.7)
	≥20, <25	3	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	≥25, <30	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
BPRS anxiety/ depression score	n	354		308		103		101		49		22		21		14	
	Mean (SD)	12.6	(4.9)	12.0	(4.0)	11.8	(4.6)	12.4	(3.8)	11.8	(3.3)	11.6	(3.9)	12.3	(3.8)	12.8	(3.9)
	p-value[S)]	0.093															
	<5	17	(2.9)	5	(1.0)	3	(1.9)	0	(0.0)	1	(1.5)	0	(0.0)	0	(0.0)	0	(0.0)
	≥5, <10	80	(13.8)	82	(16.8)	37	(23.1)	22	(14.3)	9	(13.4)	8	(18.2)	3	(7.5)	3	(12.5)
	≥10, <15	145	(25.1)	151	(31.0)	37	(23.1)	53	(34.4)	30	(44.8)	10	(22.7)	15	(37.5)	6	(25.0)
	≥15, <20	77	(13.3)	54	(11.1)	19	(11.9)	20	(13.0)	9	(13.4)	3	(6.8)	1	(2.5)	4	(16.7)
	≥20, <25	29	(5.0)	16	(3.3)	7	(4.4)	6	(3.9)	0	(0.0)	1	(2.3)	2	(5.0)	1	(4.2)
	≥25, <30	6	(1.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[*]Including patients treated with perospirone (n = 16) and zotepine (n = 6). CGI-S, Clinical Global Impression-Severity of Illness; BPRS, Brief Psychiatric Rating Scale; SD, standard deviation. [S)]Student's t-test (vs. olanzapine group).

Table 3. Baseline body weight and body mass index.

		Olanzapine (n = 578)		Non-olanzapine atypical antipsychotics										Typical antipsychotics	
				Overall[*] (n = 487)		Risperidone (n = 160)		Aripiprazole (n = 154)		Blonanserin (n = 67)		Quetiapine (n = 44)		Paliperidone (n = 40)		Overall (n = 24)	
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Body weight (kg)	n	313		217		80		69		36		16		11		5	
	Mean (SD)	57.70	(11.99)	59.62	(14.88)	58.87	(14.09)	62.02	(15.41)	60.09	(16.45)	52.70	(12.52)	59.75	(12.21)	66.48	(21.71)
	Median	57.00		57.00		57.00		60.00		57.00		53.63		63.00		67.60	
	Min - max	0.101															
BMI (kg/m^2)	n	288		204		78		62		36		14		11		5	
	Mean (SD)	21.99	(3.85)	23.03	(4.76)	22.87	(4.26)	24.16	(5.49)	23.18	(4.85)	19.88	(3.12)	21.75	(3.70)	24.72	(7.05)
	Median	21.50		22.41		22.24		23.20		23.06		20.54		20.63		24.24	
	Min - max	14.1 - 37.5		13.8 - 43.0		16.6 - 42.7		16.3 - 40.6		16.9 - 43.0		13.8 - 25.0		15.9 - 27.6		16.4 - 33.4	
	p-value[S)]	0.008															
	≥18.5	49	(8.5)	32	(6.6)	11	(6.9)	8	(5.2)	6	(9.0)	4	(9.1)	2	(5.0)	1	(4.2)
	≥18.5, <25	177	(30.6)	117	(24.0)	46	(28.8)	32	(20.8)	21	(31.3)	10	(22.7)	6	(15.0)	2	(8.3)
	≥25, <30	54	(9.3)	39	(8.0)	16	(10.0)	13	(8.4)	7	(10.4)	0	(0.0)	3	(7.5)	1	(4.2)
	≥30	8	(1.4)	16	(3.3)	5	(3.1)	9	(5.8)	2	(3.0)	0	(0.0)	0	(0.0)	1	(4.2)

[*]Including patients treated with perospirone (n = 16) and zotepine (n = 6); SD, standard deviation; BMI, body mass index. [S)]Student's t-test (vs. olanzapine group).

non-olanzapine atypical antipsychotic group (59.62 kg, p = 0.101). The mean BMI of patients in the olanzapine group (21.99 kg/m^2) was significantly lower than those in the non-olanzapine atypical antipsychotic group (23.03 kg/m^2, p = 0.008). With the exception of the quetiapine and paliperidone groups, the mean BMI for the olanzapine group was lower than each of the other non-olanzapine atypical antipsychotic groups. Moreover, fewer patients with BMI of 30 kg/m^2 or higher were treated with olanzapine (8/25 patients).

Only one patient with diabetes mellitus was treated with olanzapine and no patient with diabetes mellitus was treated with quetiapine. On the other hand, the percentage of patients with diabetes mellitus in the non-olanzapine atypical antipsychotic group was 8.4%, which was statistically significantly higher than those in the olanzapine group (p < 0.001). Percentages of patients whose blood glucose levels categorized as diabetic type were 0.3% (2/578 patients) in the olanzapine group and 0% (0/9 patients) in the quetiapine group, however 3.7% (18/487 patients) in the non-olanzapine atypical antipsychotic group which was significantly higher than those in the olanzapine group (p < 0.001).

4. Discussion

The present study was a large prospective, naturalistic multi-center observational study providing data on the baseline characteristics of more than 1000 Japanese patients with acute schizophrenia. Of those patients, 578 were treated with olanzapine monotherapy, 487 with non-olanzapine atypical antipsychotic monotherapy, and only 24 with typical antipsychotic monotherapy. We analyzed the cohort data to identify differences in the baseline characteristics between the patients with olanzapine monotherapy and those with other antipsychotic monotherapies.

It is thought that the severity of schizophrenia is related to the severity of positive symptoms. The mean CGI-S Schizophrenia score as well as mean BPRS total and positive scores for patients treated with olanzapine and risperidone were higher than those treated with other antipsychotics. Most of the patients with severe symptoms, characterized by a CGI-S Schizophrenia score of 7 or a BPRS total score of 90 or higher, were treated with olanzapine monotherapy. A large-scale observational study (SOHO study, 8519 patients) conducted in 10 European countries also showed that olanzapine was frequently administered to patients with severe symptoms [1]. Moreover, with the exception of risperidone, olanzapine was administered more often to inpatients than other antipsychotics in the present study. Our primary evaluation showed that discontinuation due to the lack of efficacy was significantly less frequent for olanzapine monotherapy than for non-olanzapine antipsychotic monotherapies [6]. Moreover, a previous study conducted in Japan showed that adherence of olanzapine and risperidone were superior to quetiapine and aripiprazole for acute treatment of psychosis in hospitalized patients [7]. Taken together, these results suggest that it would be reasonable to select olanzapine monotherapy, a highly efficacious antipsychotic, for such patients with severe symptoms of schizophrenia or hospitalized patients who might have difficulties in recovering from severe symptoms.

On the other hand, olanzapine was less likely to be prescribed to patients with heavier body weight and those with higher BMI. Similar results were reported in the SOHO study [1]; where patients treated with olanzapine monotherapy had a lower baseline mean BMI compared with those treated with other antipsychotics. One of the potential adverse events of olanzapine is weight gain, so physicians might have hesitated to prescribe olanzapine to patients with heavier body weight to avoid that risk. On the other hand, as a post-marketing surveillance of olanzapine reported that patients with lower body weight gained more weight than other patients following olanzapine administration [8], individual differences in changes of body weight during antipsychotic treatment should also be taken into account. The selection of antipsychotics should be made based on the risk-benefit balance. When olanzapine is selected, body weight of the patient should be regularly monitored as well as other metabolic variables. For patients with diabetes mellitus or higher blood glucose levels, antipsychotics other than olanzapine and quetiapine were more likely to be selected, most likely because olanzapine and quetiapine are contraindicated in patients with diabetes mellitus in Japan [9] [10].

The mean CGI-S Parkinsonism score in patients treated with olanzapine was lower than those treated with risperidone and typical antipsychotics, moreover the proportion of patients who used anti-Parkinsonism agents was lower than those treated with other antipsychotics. On the other hand, the mean CGI-S Parkinsonism score was the highest in patients treated with typical antipsychotics, and anti-Parkinsonism agents were frequently prescribed to those patients. Olanzapine has a relatively low risk of extrapyramidal adverse events, thus concomitant use of anti-Parkinsonism agents may not be necessary for olanzapine treated patients.

5. Limitations

This was a non-randomized, naturalistic observational study in which treatment decisions were made by investigators. Although the present study showed essential clinical data analyzing the baseline characteristics of more than 1000 patients with acute schizophrenia in a routine clinical practice setting, it was difficult to generalize our data for patients treated with typical antipsychotics because typical antipsychotics were administered to only 24 patients.

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Disclosure of Interest

MT was a past employee of Eli Lilly Japan K.K.; SF, JF and LA are employees of Eli Lilly Japan K.K.; MI received honoraria from Eli Lilly Japan K.K.

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