

ORIGINAL ARTICLE

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**Medication and symptom severity in schizophrenia patients in
COVID-19 pandemic: A cross-sectional study****Asli Kazgan¹, Sevler Yildiz², Osman Kurt³, Sevda Korkmaz⁴**¹Siverek State Hospital, Department of Psychiatry, Sanliurfa, Turkey²Binali Yildirim University, Faculty of Medicine, Department of Psychiatry, Erzincan, Turkey³Firat University, Faculty of Medicine, Department of Public Health, Elazig, Turkey⁴Firat University, Faculty of Medicine, Department of Psychiatry, Elazig, Turkey

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**Abstract**

The present study aimed to determine the possible correlation between medical treatment [oral antipsychotics (OAP), long-acting injectable antipsychotics (LAI), oral + long-acting injectable antipsychotics (OAP + LAI)] and symptom severity, and the compliance of schizophrenia patients with the medication during the COVID-19 pandemic. The study was conducted with 100 schizophrenia patients who applied to the psychiatry outpatient clinic during the pandemic and met the study criteria. Sociodemographic data form, Positive and Negative Symptom Scale (PANSS), and Functional Recovery Scale in Schizophrenia (FRSS) were applied to each participant. The rate of patients who quit current treatment was 19%. A statistically significant difference was determined between the patients on OAP and those on LAI, and between those on OAP and those on OAP + LAI based on the overall scale scores ($p < 0.001$). There were significant differences between the FRSS scores of the patients who discontinued treatment, those who continued medication, and those who switched to depot antipsychotic medication ($p < 0.001$). There was a significant difference between those who discontinued medication and those who continued medication based on the overall scale scores ($p < 0.001$). In the present study, it was determined that the symptoms of patients on only LAI medication and those in OAP + LAI medication were lower, and their functionality scores were higher when compared to the patients on only OAP medication. It was also determined that among the schizophrenia patients who applied to psychiatry clinic during pandemic, those who were on LAI exhibited better functionality and lower symptom burden when compared to other treatment modalities. During the pandemic, it was observed that LAI medication protected the patients better.

Keywords: Schizophrenia, long-acting injectable antipsychotics, oral antipsychotics, COVID-19 pandemic**Introduction**

Deaths and compulsory changes in daily life habits due to COVID-19, observation acute psychiatric symptoms in infected individuals, and difficulties associated with access to physician necessitated the psychological scrutinization of the pandemic [1]. During the COVID-19 pandemic, psychiatric problems such as panic disorder, anxiety and depression could be observed [2]. It could be suggested that schizophrenia patients were among the groups whose psychological health was most affected during this period, and the pandemic was a risky for psychotic exacerbations [3].

It was reported that non-compliance (completely or partially) with medication was 75% in patients with schizophrenia [4]. Compliance problems increase the re-hospitalization as well

as the morbidity and mortality. Compliance problems lead to exacerbations during early onset of the disorder and worsen the prognosis. It was observed that depot antipsychotics developed as an alternative to oral antipsychotics (OAP) since 1960s to solve this problem reduced the positive symptoms, relapses and relapse rates, hospitalizations and non-compliance risk [5-7]. These long-acting injectable antipsychotics (LAI), developed to eliminate non-compliance, eliminated daily doses via biweekly, monthly or quarterly injections [6]. Certain clinical guidelines indicated that LAI was an important option in schizophrenia patients with non-compliance with medication [8, 9]. It could be suggested that compliance with medication is especially important in psychologically challenging periods, and we are concerned that patients may discontinue medication and their complaints may increase even when they stay on medication. Prior to the pandemic, it was seen that the health systems of low and middle income countries faced problems such as limited financial resources, obstacles to accessing health services, insufficient number of medical personnel and difficulty in supplying medicines, and it was reported that people with chronic diseases were most adversely affected by these

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conditions during crisis periods such as the pandemic [10-11]. These adverse conditions can adversely affect treatment adherence and course of disease in chronic diseases such as schizophrenia.

With all this information, we hypothesized that our schizophrenia patients may be adversely affected clinically during the pandemic and that the treatment methods they receive may be a factor in this effect. The present study aimed to determine the correlation between the medical treatment (oral-LAI-oral + LAI) of schizophrenia patients and severity of their symptoms during the COVID-19 pandemic, which was considered particularly difficult for schizophrenia patients. In this period of isolation and restricted access to hospitals, we aimed to analyze whether there was a correlation between the mental state of our schizophrenia patients, their treatment, and compliance with medication during this period.

Materials and Methods

The present study was conducted after the local ethics committee approval and in accordance with the Helsinki Declaration principles. Our study is a cross-sectional study involving 100 randomized patients who were admitted to the Psychiatry Clinic of Firat University Hospital during the COVID-19 pandemic and who were treated in outpatient or inpatient clinic and who met the study criteria and who were diagnosed with schizophrenia by the psychiatrist according to the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) diagnostic criteria. For the study, 116 schizophrenia patients and/or their relatives were interviewed. As the relatives of 3 of the patients did not agree to participate in the study, 7 patients had comorbid obsessive-compulsive disorder and alcohol and substance use disorder and 6 patients had the level of organization do the degree to prevent participation in the study, they were excluded from the study. Inclusion criteria; being between the ages of 18-65, not having COVID-19 infection, not having any other psychiatric disorders and personality disorders other than schizophrenia, not having any neurological or neurodevelopmental diseases, not having alcohol substance use, the signature of the consent form by the patient or his/her guardian. All patients were applied a Sociodemographic Data Form, Positive and Negative Symptom Scale and Functional Recovery Scale in Schizophrenia by psychiatrist in psychiatric outpatient clinic and/or inpatient service. The questionnaire was completed in an average of 25-30 minutes. There is no control group in the study.

Data Collection Instruments

1) Sociodemographic and Clinical Data Form: A sociodemographic and clinical data form developed by the authors based on clinical experiences, the literature review, and the aim of the study was used. It was a semi-structured form that collected sociodemographic data such as age, gender, marital status, educational status, profession, place of residence, income level, family structure, and clinical data such as duration of the disease, and presence of psychosocial stressors at the onset of the disease.

2) Positive and Negative Symptoms Scale (PANSS): The scale is a structured interview form that includes 30 items and seven points, developed by Kay et al. to evaluate the severity of the symptoms in schizophrenia patients [12]. Seven out of the 30 psychiatric parameters were included in the positive symptoms

subscale (P), seven parameters were included in the negative symptoms subscale (N), and 16 parameters were included in the general psychopathology subscale (G). The potential score varies between 7 and 9 for the positive and negative symptom subscales, and between 16 and 112 for the general psychopathology subscale [12]. Kostakoglu et al. [13] conducted the validity and reliability studies in Turkish language. When internal consistency was analyzed, the total Cronbach alpha coefficients of positive and negative syndrome and general psychopathology subscales were found to be similar and higher in comparison to the original study (.75, .77 and .71, respectively) [13].

3) Functional Recovery Scale in Schizophrenia (FRSS): The Functional Recovery Scale in Schizophrenia was developed by the experts in the "Functional Recovery in Schizophrenia Observation Group." It is a 5-point Likert-type scale that includes 19 items that investigate the improvements in functionality regardless of the disease symptoms. The scale is applied as a semi-structured interview. The evaluation is based on the information obtained from both the patient and patient's family. The questions cover a period of one month prior to the interview. Each item is scored between 1 and 5 points and the total score is obtained by adding item scores. The total score varies between 19 and 95. Patients with a score under 58 are considered to exhibit a low level of functional recovery. A functional recovery level between 59 and 66 is considered moderate. Patients with 66 points or above are considered to exhibit a high level of functional recovery. The reliability coefficient of the scale developed by Llorca et al. is 0.90 [14]. Emiroglu et al. [15] conducted the validity and reliability studies in Turkish language. The value of Cronbach's alpha was found to be 0.89 for the Turkish version of FRSS [15].

Statistical Analysis

The study data were analyzed with SPSS (Statistical Package for Social Sciences v. 22; SPSS Inc., Chicago, IL) software. Descriptive categorical study data are presented as frequencies and percentages, and mean $\pm$ standard deviation, median, interquartile ranges (25-75 percentile values) were used to present continuous data. The normal distribution of continuous variables was determined with the Kolmogorov-Smirnov Test. The Mann-Whitney U test was employed to compare the variables that did not display normal distribution between the two groups, and the Kruskal Wallis test was used for the comparison of variables between more than two groups. Spearman correlation test was employed to examine the correlation between continuous variables. The statistical significance level was accepted as $p < 0.05$.

Results

One hundred patients were included in the study. 56.0% of the participants were male and the average patient age was 37.5 ± 7.9 (min = 23, max = 63). The mean duration of disorder was 11.4 ± 5.5 (min = 3, max = 40) years.

It was found that 46% of the patients were on OAP, 11% were on LAI and 39% were on OAP + LAI medication. Paliperidone palmitate (56%) was the prominent medication among LAI. It was determined that 69% of the patients continued medication during the pandemic, and 19% quit the current oral medication. The medication of the rest was changed.

Only 6% of the patients did not undergo inpatient treatment before the pandemic. Other patients were hospitalized 1-3 times (25%), 2-5 times (27%) or more than 5 times (42%). It was observed that 14% of the patients applied 5-10 times and 3% applied more

than 10 times to the psychiatry clinic. It was found that 65% of the patients did not undergo inpatient treatment during the pandemic, 25% were treated once and 10% were treated twice (Table 1).

Table 1. Participant socio-demographics and clinical data

		n	%
Gender	Male	56	56.0
	Female	44	44.0
	Unmarried	59	59.0
Marital status	Married	31	31.0
	Widowed/divorced	10	10.0
	Town	48	48.0
Residence	City	52	52.0
	Primary education or lower	70	70.0
	Secondary education or higher	30	30.0
Education level	Low	31	31.0
	Middle	69	69.0
	Civil servant	5	5.0
Income level	Worker	8	8.0
	Unemployed	87	87.0
	Yes	53	53.0
Occupation	No	47	47.0
	Yes	96	96.0
	No	4	4.0
Smoking	OAP	46	47.9
	LAI	11	11.5
	OAP+ LAI	39	40.6
Medication modality	Paliperidone palmitate	28	56.0
	Zuklopentilsol	5	10.0
	Risperidone microspheres	11	22.0
Depot medication	Haloperidol decanoate	1	2.0
	Aripiprazole	5	10.0
	Yes	69	69.0
Treatment during the pandemic	Quit oral medication	19	19.0
	Switched to depot medication	6	6.0
	Switched to oral medication	6	6.0
Number of pre-pandemic hospitalizations	1-3	31	31.0
	3-5	27	27.0
	More than 5	42	42.0
Number of psychiatric outpatient clinic applications during the pandemic	1-5	83	83.0
	5-10	14	14.0
	More than 10	3	3.0
Number of hospitalizations in the psychiatric department during the pandemic	N/A	65	65.0
	1	25	25.0
	2	10	10.0

LAI: Long acting injectable, OAP: oral antipsychotics, SD: standard deviation

The median FRSS score of the patients included in the study was 47 (28.5-65.9), the PANSS positive median score was 16 (13-27.5), the PANSS negative median score was 25 (17.5-30.5), the PANSS general psychopathology median score was 38 (30-52.5) and the overall PANSS median score was 82 (63-111.5).

The FRSS scores of male patients ($p = 0.01$) were significantly higher when compared to the scores of female patients, while the positive markers ($p = 0.01$) and general PANSS scores of females ($p = 0.029$) were significantly higher when compared to the scores of males. There was a significant difference between the PANSS positive ($p = 0.007$) and PANSS overall ($p = 0.041$) scores based on marital status. It was observed that this difference was due to the difference between married and widowed/divorced groups in both score types. It was determined that the FRSS scores of the middle income patients were significantly higher than those of the low income patients ($p = 0.039$), and their PANSS overall score was significantly lower ($p = 0.035$). It was observed that there was a significant difference between the FRSS ($p < 0.001$), PANSS positive ($p = 0.035$), PANSS negative ($p = 0.005$) and overall PANSS ($p = 0.016$) scores based on occupation. It was determined that this difference was due to the difference between employed and unemployed patient scores.

It was determined that the FRSS scores of the patients who received psychiatric treatment were significantly higher when compared to those who did not ($p = 0.014$). A statistically significant difference was determined between the overall scale scores of the patients on OAP and on LAI, and between those on OAP and on OAP + LAI ($p < 0.001$) (Table 2).

It was observed that there was a significant difference between the scale scores of the patients who were compliant with medication and those who were not during the pandemic ($p < 0.001$). It was observed that this difference was due to the difference between those who discontinued medication, those who continued medication, and switched to depot medication for the FRSS scores, and only the difference between those who discontinued oral medication and who continued medication for all other scores (Table 2).

It was observed that there was a significant difference between the scale scores of the patients who received inpatient treatment before the pandemic and who did not ($p < 0.001$). In general psychopathology sub-dimension scores, this difference was only due to the difference between those who were hospitalized more than 5 times and those hospitalized 1-3 times, and in other scale scores, the difference was due to the difference between those hospitalized more than 5 times and those hospitalized 1-3 times, and those hospitalized more than 5 times and those who hospitalized 3-5 times (Table 2).

During the pandemic, it was observed that there was a significant difference between all scores except the negative markers score based on outpatient admissions ($p < 0.05$). This difference was only due to the difference between those who applied 1-5 times and those who applied 5-10 times. It was observed that there was a significant difference between all scores based on inpatient treatment during the pandemic ($p < 0.001$). It was found that this difference was due to the difference between those who did not receive inpatient treatment and those who received inpatient treatment once, and between those who did not receive inpatient

treatment and those who received treatment twice (Table 2).

A positive significant relationship was determined between age and duration of the disease. It was observed that there was a significant negative correlation between the FRSS and PANSS scores. It was observed that there was a significant positive correlation between the PANSS sub-dimension scores and the overall PANSS score (Table 3).

Discussion

The review of the findings on one of the aims of the study, namely the correlation between the medication type and symptom severity, would demonstrate that the patients who were on OAP exhibited the lowest functionality and highest PANSS scores. The functionality of the patients who were on LAI was significantly higher when compared to those who were on OAP, and the functionality of those who were on OAP + LAI was higher when compared to those who were on OAP. Similarly, all PANSS scores of patients who were on LAI were significantly lower than those who were on OAP, and the scores of those who were on OAP + LAI were significantly lower when compared to those who were on OAP. Thus, it was observed that LAI medication protected the patients better. Our findings are consistent with most of the literature that shows the efficacy of LAI in schizophrenia patients compared to OAP's regardless of the stage of the disease. LAI's are effective in improving both positive and negative symptoms [16-18]. In a study conducted with second-generation LAI's, major improvements were recorded in patients' PANSS negative scores and depressive symptoms, global functionality and severity of suicidal thoughts within 5 years of diagnosis [19]. In a longitudinal observational study, it was found that the patients treated with LAI's had lower scores on PANSS positive and negative subscales compared to patients treated with OAP's after 6 months of treatment [20]. In a metaanalysis performed by Leucht et al. [21] it was reported that depot injections in schizophrenia patients can prevent recurrence of hallucination attacks. LAI's, compared to OAP's, are associated with better drug compliance, fewer transfer and fewer relapses, significantly lower re-hospitalization rate, and a significantly longer re-hospitalization period in schizophrenia patients [22, 23]. Compliance with medication directly affects functionality. In the present study, the functionality of patients who continued the psychiatric treatment was significantly higher than those who were not treated.

It was reported that LAIs ensure a stable plasma concentration and facilitate the sustainability of the treatment [6]. Furthermore, LAIs were reported to reduce the frequency of adverse events such as akathisia, dysphoria and medication-induced deficit syndrome due to the principle of the lowest effective dose, facilitate medication follow-up; and thus, increase the quality of life of the patients [24]. It was considered significant that although the present study patients were mainly on OAP, all patients who discontinued medication were on OAP before. This finding suggested that controlling the compliance of patients on OAP to medication and/or the adverse effects of the treatment was a problem for both relatives of the patients, the patients and physicians. Oral medication requires regular daily intake. Difficulties that may arise in the procurement and access to medication during the pandemic could have caused patients to discontinue the medication since the application intervals are quite long in LAI when compared to OAP.

Table 2. Comparison of FRSS and PANSS scores based on various parameters

		FRSS		Positive markers		Negative markers		General psychopathology		Overall PANSS score	
		Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p	Median (IQR)	p
Gender	Male	58.5 (34-69.5)	0.01	15 (12-24)	0.01	23 (17-28)	0.088	35.5 (30-50)	0.155	74 (59.5-104.5)	0.029
	Female	42.5 (24.5-56.5)		21.5 (13.5-32)		27 (19.5-31.5)		47 (30-55)		92.5 (68.5-116.5)	
Marital status	Unmarried	44 (24-64)	0.077	18 (13-30) ^{a,b}	0.007	26 (19-29)	0.233	41 (30-53)	0.105	84 (66-111) ^{a,b}	0.041
	Married	55 (42-69)		14 (11-18) ^a		21 (16-33)		34 (28-51)		69 (57-105) ^a	
	Widowed/divorced	34 (24-68)		27 (16-36) ^b		30 (24-33)		49.5 (35-58)		112 (65-124) ^b	
Residence	Town	46 (27.5-62.5)	0.537	16.5 (12-27)	0.761	25 (17-31.5)	0.481	36 (30-52.5)	0.738	83 (60-110.5)	0.896
	City	49.5 (29.5-67)		16 (13-28.5)		24 (18-30)		42 (30-52.5)		76 (65.5-112.5)	
Education level	Primary education or lower	45 (29-60)	0.062	16.5 (13-27)	0.627	26 (19-31)	0.191	41.5 (30-53)	0.598	84.5 (65-108)	0.441
	Secondary education or higher	61.5 (28-72)		15 (12-29)		21 (17-30)		35 (30-52)		70.5 (62-113)	
Income level	Low	41 (24-58)	0.039	23 (15-30)	0.055	27 (23-33)	0.034	48 (34-56)	0.051	99 (75-113)	0.035
	Middle	55 (35-68)		16 (12-25)		22 (16-30)		36 (29-51)		73 (59-111)	
Occupation	Civil servant	74 (58-78) ^{a,b}	<0.001	13 (12-15) ^{a,b}	0.035	16 (13-18) ^{a,b}	0.005	36 (28-46)	0.067	66 (53-74) ^{a,b}	0.016
	Worker	72 (68-75) ^a		12 (10.5-16.5) ^a		17.5 (13-22.5) ^a		30 (27-35)		62.5 (50-71.5) ^a	
	Unemployed	44 (25-60) ^b		18 (13-29) ^b		26 (20-31) ^b		43 (30-53)		87 (65-113) ^b	
Smoking	Yes	41 (24-62)	0.025	22 (13-30)	0.081	27 (20-31)	0.076	47 (32-54)	0.056	100 (65-115)	0.057
	No	54 (40-69)		16 (12-23)		21 (16-30)		36 (28-48)		73 (61-94)	
Psychiatric medication	Yes	49.5 (30-66)	0.014	16 (13-27)	0.09	24 (17-30)	0.118	37.5 (30-52)	0.094	76 (62.5-109)	0.074
	No	24 (21.5-29)		28.5 (21.5-34.5)		30 (28.5-31)		53 (47-56.5)		115 (100-119)	
Medication modality	OAP	30 (23-43) ^a	<0.001	27 (19-34) ^a	<0.001	28 (26-32) ^a	<0.001	51 (46-58) ^a	<0.001	108 (91-122) ^a	<0.001
	LAI	72 (66-78) ^b		12 (11-13) ^b		16 (12-24) ^b		26 (24-30) ^b		51 (50-65) ^b	
	OAP+ LAI	63 (52-69) ^b		13 (11-16) ^b		20 (16-25) ^b		31 (27-35) ^b		66 (59-74) ^b	
Depot medication	Paliperidone palmitate	62 (58-71.5)	0.612	13 (11.5-15.5)	0.774	19 (15.5-23)	0.416	30 (27.5-34.5)	0.698	64 (57.5-69.5)	0.532
	Zuklopentilol	69 (69-71)		11 (10-16)		18 (16-25)		31 (28-32)		57 (57-82)	
	Risperidone microspheres	64 (52-70)		13 (11-16)		20 (16-34)		26 (23-37)		65 (51-74)	
	Haloperidol decanoate	69 (69-69)		10 (10-10)		11 (11-11)		25 (25-25)		46 (46-46)	
	Aripiprazole	70 (69-72)		13 (11-15)		23 (22-24)		33 (30-36)		74 (63-76)	
Treatment during the pandemic	Yes	58 (43-69) ^a	<0.001	13 (12-19) ^a	<0.001	22 (16-27) ^a	<0.001	34 (28-46) ^a	<0.001	69 (59-91) ^a	<0.001
	Quit oral medication	24 (22-30) ^b		32 (27-36) ^b		31 (28-36) ^b		57 (52-61) ^b		117 (113-125) ^b	
	Switched to depot medication	53.5 (41-64) ^a		19.5 (16-23) ^{a,b}		23.5 (16-31) ^{a,b}		37 (31-46) ^{a,b}		82 (69-100) ^{a,b}	
	Switched to oral medication	40.5 (38-45) ^{a,b}		24.5 (17-30) ^{a,b}		27.5 (17-32) ^{a,b}		50 (48-60) ^{a,b}		104.5 (94-119) ^{a,b}	
Number of pre-pandemic hospitalizations	1-3	64 (55-71) ^a	<0.001	13 (11-16) ^a	<0.001	17 (14-24) ^a	<0.001	31 (26-41) ^a	<0.001	65 (51-73) ^a	<0.001
	3-5	60 (33-69) ^a		15 (13-27) ^a		22 (17-28) ^a		36 (30-53) ^{a,b}		74 (63-108) ^a	
	More than 5	34.5 (24-44) ^b		23 (16-33) ^b		30 (26-33) ^b		49 (37-56) ^b		105 (84-122) ^b	
Number of psychiatric outpatient clinic applications during the pandemic	1-5	55 (30-69) ^a	0.039	15 (12-27) ^a	0.015	23 (17-30)	0.173	35 (28-51) ^a	0.006	73 (60-108) ^a	0.01
	5-10	40.5 (27-43) ^b		22.5 (18-28) ^b		27.5 (23-33)		50.5 (45-60) ^b		106 (85-116) ^b	
	More than 10	35 (23-40) ^{a,b}		24 (23-40) ^{a,b}		27 (26-28)		52 (41-60) ^{a,b}		112 (90-119) ^{a,b}	
Number of hospitalizations in the psychiatric department during the pandemic	N/A	60 (48-69)	<0.001	13 (11-16)	<0.001	21 (16-28)	<0.001	32 (28-38)	<0.001	68 (57-82)	<0.001
	1	24 (23-35)		28 (23-33)		28 (27-31)		53 (48-59)		111 (104-122)	
	2	23.5 (20-28)		36 (34-39)		31 (27-33)		51.5 (47-54)		118.5 (115-124)	

p<0.001* FRSS: Functional Recovery Scale in Schizophrenia Patients, PANSS: Positive and Negative Syndrome Scale, LAI: Long acting injectable

Table 3. The correlations between age, duration of the disease and scale scores

		Age	Duration of the disease	FRSS	Positive markers	Negative markers	General psychopathology
Duration of the disease	r	.853					
	p	.000					
FRSS	r	.032	-.053				
	p	.750	.601				
Positive markers	r	.015	.063	-.848			
	p	.880	.531	.000			
Negative markers	r	.019	.192	-.717	.667		
	p	.848	.056	.000	.000		
General psychopathology	r	-.037	.038	-.786	.825	.650	
	p	.718	.707	.000	.000	.000	
Overall PANSS score	r	-.012	.085	-.865	.917	.822	.940
	p	.907	.398	.000	.000	.000	.000

p<0.001* r: correlation coefficient, PANSS: Positive and Negative Syndrome Scale, FRSS: Functional Recovery Scale in Schizophrenia

In the literature, it was reported that several OAP led to lower patient compliance with medication when compared to LAI [25] and LAI cause lower risk of non-compliance with medication [26]. Our findings were consistent with the literature.

It is common for schizophrenia patients to not comply with medication. Intramuscular long-acting antipsychotic injection is one of the most commonly employed treatment options in patients who present non-compliance risk. Depot antipsychotics are often employed in daily practice in addition to oral medication. In the present study, consistent with the literature, the rate of coadministration of depot antipsychotics and oral antipsychotics was 39%. Previous studies reported that 40% of LAIs were co-administered with oral antipsychotics [27, 28].

In the study, patients with a psychiatric hospitalization history during the pandemic had the best functionality scores. It was natural to expect that good functionality would not require the psychiatric hospitalization of the patients and/or reduce the number of hospitalizations. It was determined that as the number of hospitalizations increased, patient PANSS scores decreased and FRSS scores increased. This could be due to the fact that the hospitalized patients were usually on oral medication. Previous studies reported that patients who were on LAI medication experienced lower number of hospitalizations and relapse [29]. In the present study, the most common depot medication was paliperidone palmitate, followed by risperidone microsphere, zuclopenthixol decanoate and aripiprazole equivalent and haloperidol decanoate. In a prospective, grading, and blind study published in 2015, 764 patients diagnosed with schizophrenia within the first 5 years of disease were compared based on paliperidone palmitate (376) and OAP (388) administration, and the relapse was observed significantly later in the paliperidone palmitate group when compared to the oral antipsychotic group, and there was a relative decrease of 29.4% in the risk of relapse [30]. Since the present study was a cross-sectional study, relapse

rates were not analyzed. Relapse conditions could be compared in future follow-up studies. In a meta-analysis, no difference was reported between the PANSS scores except for a single study where risperidone revealed superior results when compared to paliperidone palmitate [31]. Although there was a difference between symptom and functionality scores of the patients on LAI, it was not statistically significant. To determine these differences, larger sample groups are required.

The study findings demonstrated that the functionality of the patients at the time of application was significantly higher in males when compared to females, in employed patients when compared to unemployed patients, and in middle-income patients when compared to low income patients. While it is known that employment and marriage are associated with high functionality [32], PANSS overall and subscale scores of the married, male, and employed patients were significantly lower in the present study.

A possible association between COVID-19 and psychotic symptoms due to an unknown immune mechanism has been mentioned, and coronavirus infection itself could exacerbate symptoms in schizophrenia patients [33, 34]. Thus, past or present coronavirus infection was an exclusion criterion in the present study.

During the COVID-19 pandemic, it could be suggested that difficulties could have been experienced in drug procurement due to medical export restrictions. The fact that certain hospitals could not provide routine healthcare due to the pandemic, and the closure of several psychological health clinics and community psychological health centers could have led to difficulties experienced by schizophrenia patients such as access to physicians and healthcare services. Furthermore, the psychological effects of social isolation implemented to prevent the spread of COVID-19 could be devastating for individuals. Furthermore, this could lead to exacerbation/relapse in schizophrenia patients who experience

difficulties in managing stressors when compared to the general population. In a study that investigated the impact of social isolation induced by COVID-19 pandemic on the psychological health of schizophrenia inpatients, it was reported that inpatients with schizophrenia experienced higher psychological stress and more severe anxiety and depression levels [3]. Broad social support would improve the recovery and social integration of schizophrenia patients [35]. While patients with schizophrenia already interact within a more limited social environment when compared to the general population, social isolation could have a particularly negative impact on these individuals. This could lead to new psychiatric patients, as well as psychotic exacerbations in current patients. Medical treatment could be vital for the patients in this process.

The employment of the cross-sectional model in the study could have prevented a better understanding of the causality between the study variables. Therefore, future experimental and longitudinal studies that would better predict the causality could help understand the correlations between treatment modalities and symptom status better. Also, due to the cross-sectional nature of the current study, data on functionality improvements, reduction of the clinical symptoms, and variations in hospitalization rates were not scrutinized in detail. The inclusion of patients with concomitant diseases could be considered as another limitation of the present study due to the possibility that concomitant physical diseases and treatments could affect the treatment and follow-up of the patients.

Conclusion

In conclusion, in the present study, it was determined that the functionality of the schizophrenia patients who applied to psychiatry clinic during the pandemic and were on LAI medication was better and they experienced lower burden of symptoms when compared to other medication modalities. Although LAI administration, which has been more popular in the treatment of schizophrenia, increases face-to-face contact during the pandemic, it would be wise to maintain LAI medication since they provide better stabilization and compliance when compared to oral medication based on the present study findings.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

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Ethical approval

This research was approved by the Firat University Medical Faculty Research Ethics Committee (No. 2020/17) and conducted in compliance with the ethical principles according to the Declaration of Helsinki.

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Türkçe referanslarınızı ingilizce düzenleyiniz