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Depot Versus Oral Antipsychotics in Patients with Schizophrenia: Which is Better on Side Effects, Functional Improvement, and Life Satisfaction

Şizofreni Hastalarında Depo Antipsikotiklere Karşı Oral Antipsikotikler: Yan Etki, İşlevsel İyileşme ve Yaşam Doyumu Üzerinde Hangisi Daha İyi?

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ABSTRACT

Objective: Schizophrenia is a chronic mental disorder that reduces quality of life, causes deterioration in social and occupational functioning, and requires continuous care for psychosocial rehabilitation. The aim of this study was to investigate functional improvement, life satisfaction, and drug side effects in patients with schizophrenia and schizoaffective disorder using depot antipsychotics, oral antipsychotics, or both.

Methods: The study included 162 patients with clinically stable schizophrenia and schizoaffective disorder who were regularly followed up at the Rize Community Mental Health Center for at least 1 year. The Satisfaction with Life Scale (SLS), Glasgow Antipsychotic Side-Effect Scale (GASS), and Functional Remission of General Schizophrenia (FROGS) scale were administered to patients with available sociodemographic and clinical data.

Results: There were significant differences between the groups with respect to age at onset, number of hospitalizations, and gender. The mean GASS score of patients using both depot and oral antipsychotics was significantly higher than that of those using only depot antipsychotics. There was no significant difference between the groups in terms of mean SLS, total FROGS scores, and sub-dimension FROGS scores.

Conclusion: It was concluded that it would be appropriate to prefer depot antipsychotics in the presence of poor prognostic factors such as medication non-adherence, frequent hospitalization, and lack of insight. There is a need for multicenter prospective studies with longer follow-up of patients for side effects, life satisfaction, quality of life, and functional improvement to achieve more significant results.

Keywords: Schizophrenia, side effects, depot antipsychotics, life satisfaction

ÖZ

Amaç: Şizofreni, yaşam kalitesini düşüren, sosyal ve mesleki işlevsellikte bozulmaya neden olan, psikososyal rehabilitasyon için sürekli bakım gerektiren kronik bir ruhsal bozukluktur. Bu çalışmanın amacı, sadece depo antipsikotikler, sadece oral antipsikotikler veya her ikisini birden kullanan şizofreni ve şizoaffektif bozukluk hastalarında fonksiyonel iyileşme, yaşam doyumu ve ilaç yan etkilerini araştırmaktır.

Yöntemler: Çalışmaya Rize Toplum Ruh Sağlığı Merkezi'nde en az bir yıldır düzenli olarak takip edilen, klinik olarak stabil şizofreni ve şizoaffektif bozukluk tanılı 162 hasta dahil edildi. Sosyo-demografik ve klinik verileri mevcut olan hastalara Yaşam Doyumu Ölçeği (SLS), Glasgow Antipsikotik Yan Etki Ölçeği (GASS) ve Genel Şizofrenide İşlevsel İyileşme Ölçeği (FROGS) uygulandı.

Bulgular: Gruplar arasında başlangıç yaşı, hastaneye yatış sayısı ve cinsiyet açısından anlamlı fark vardı. Hem depo hem de oral antipsikotik kullanan hastaların ortalama GASS skoru, sadece depo antipsikotik kullananlara göre anlamlı olarak yüksekti. SLS, FROGS toplam puanları ve FROGS alt boyut puan ortalamaları açısından gruplar arasında anlamlı fark yoktu.

Sonuç: İlaç uyumsuzluğu, sık hastaneye yatış ve içgörü eksikliği gibi kötü prognostik faktörlerin varlığında depo antipsikotiklerin tercih edilmesinin uygun olacağı kanısına varıldı. Daha anlamlı sonuçlar elde etmek için yan etkiler, yaşam memnuniyeti, yaşam kalitesi ve fonksiyonel iyileşme açısından hastaların daha uzun süre takip edildiği çok merkezli prospektif çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Şizofreni, yan etki, depo antipsikotik, yaşam doyumu

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INTRODUCTION

Schizophrenia is a chronic mental disorder characterized by positive symptoms, such as delusions and hallucinations, as well as negative symptoms, such as social withdrawal and cognitive impairment, creating a great burden on patients, their families, and society and leading to disabilities (1). Schizophrenia reduces the quality of life, causes deterioration in social and occupational functionality, and requires continuous care for psychosocial rehabilitation (2,3). Antipsychotic drugs used to alleviate acute symptoms and prevent long-term relapse are the mainstay of treatment for schizophrenia (4). Pharmacological treatment for schizophrenia should be individually tailored to the needs and preferences of the patient. In addition to ameliorating psychotic symptoms and preventing relapse, it should aim to improve the patient's psychosocial functionality level, independence, and quality of life, considering treatment adherence of the patient and drug side effects (5).

Various studies have found a medication non-adherence rate of 40-80% in patients with schizophrenia who are prone to forget the drug dose or deliberately discontinue the drug (6,7). The most common causes of medication non-adherence include poor insight, drug side effects, belief that the drug will worsen the disease, lack of motivation, and cognitive loss (6).

It is very important to avoid the high risk of relapse after the first psychotic episode of schizophrenia because subsequent episodes impair the quality of life of patients and harm their psychosocial functionality (3,8). It has been observed that patients with schizophrenia who regularly use their medications have low rates of emergency admission and hospitalization and that early intervention reduces long-term negative outcomes and preserves functionality (9).

Considering medication non-adherence, the use of depot antipsychotics for long-term control of psychotic symptoms is increasing, and studies comparing oral antipsychotics with depot forms have come to the fore (10-12). Recent studies have indicated lower non-adherence to treatment with long-acting antipsychotic depot injections (8,13). Studies have also investigated the attitudes of patients, their relatives, and healthcare professionals toward depot antipsychotics. Adequately informing patients about depot antipsychotics and establishing therapeutic cooperation between clinician and patient for drug selection appears to be important (8).

The aim of this study was to investigate functional improvement, life satisfaction, and drug side effects in patients with schizophrenia who were followed up at Rize Community Mental Health Center (CMHC) and were using only depot antipsychotics, oral antipsychotics, or both.

MATERIALS AND METHODS

Procedure and Participant

Before starting the research, the necessary ethical approval was obtained from the Human Research Ethics Committee of Rize Provincial Directorate of Health (approval number: E-64247179-799). Participants were informed about the study and signed consent forms were obtained. The study included 162 patients who were diagnosed with schizophrenia and schizoaffective disorder according to the DSM-5 diagnostic criteria and were followed up at the Rize CMHC for at least 1 year. The eligibility criteria were as follows: regular attendance at follow-up visits, regular use of medications, use of only oral antipsychotics, only depot antipsychotics, or both, clinical stability, and consent to participate in the study.

The study employed a comparative cross-sectional design to investigate functional improvement, life satisfaction, and drug side effects among patients with schizophrenia who were administered depot antipsychotics, oral antipsychotics, and both for at least 6 months. A comparative cross-sectional study design is a quantitative research approach that involves comparing data collected from two or more distinct groups (patients with schizophrenia using different types of antipsychotics) at a single point in time. The data for this study were collected between July 2021 and December 2021.

The clinical stability of participants was assessed using the Clinical Global Impression (CGI) scale, with a CGI score of 5 or less indicating clinical stability (14). Those with cognitive impairment, neurological diseases such as epilepsy, a history of head trauma, and mental retardation were excluded from the study.

Tools

A sociodemographic data form, Satisfaction with Life Scale (SLS), Glasgow Antipsychotic Side-Effect Scale (GASS), and Functional Remission of General Schizophrenia (FROGS) scale were administered to participants by the CMHC chief physician who followed up with them, namely the researcher.

Sociodemographic data form: The sociodemographic data form was prepared by the researcher to investigate sociodemographic characteristics such as age, gender, economic status, educational level, marital status, and employment status, as well as clinical characteristics including age of onset, disease duration, number of hospitalizations, suicide attempt, family history, etc.

Satisfaction with Life Scale: The scale consists of 5 items. The Turkish validity and reliability study was conducted by Dağlı and Baysal (15) in 2016, and the correlation coefficient of the scale was found to be 0.92.

Glasgow Antipsychotic Side-Effect Scale: The scale developed in order to evaluate the side effects of antipsychotic drugs consists of 22 items. The Turkish validity and reliability study of the scale was performed by Aslan et al. (16).

Functional Remission of General Schizophrenia: FROGS is a 5-point Likert-type scale consisting of 19 items to evaluate improvements in functionality independent of disease symptoms. The administration of the scale was carried out in the form of semi-structured interviews. The Turkish validity and reliability study of the scale was performed by Emiroğlu (17), who reported a reliability coefficient of 0.90 for the scale.

Statistical Analysis

The SPSS version 26 statistical software package was used for data analysis. One-Way ANOVA was used to determine whether there were differences between the GASS, SLS, and FROGS scores of participants who used only injectable drugs, only oral drugs, or both. Pearson correlation analysis was used to determine the correlations between these variables. Regression analysis was performed to determine to what extent GASS scores predicted SLS and FROGS scores. The level of statistical significance was set at 0.05 for all analyses.

RESULTS

The demographic information of the participants is given in detail in Table 1. When the groups were compared in terms of sociodemographic variables, a significant difference was found in terms of disease onset age [$F(2,159)=3.81$, $p<0.05$), number of hospitalizations [$F(2,159)=3.14$, $p<0.05$), and gender [$\chi^2(2,162)=7.89$, $p<0.05$). However, there was no significant difference between the groups according to other variables ($p>0.05$).

A One-Way ANOVA was performed to compare the effect of three different groups (long acting: depot, oral, combination) on SLS, GASS, and FROGS scores (Table 2). A One-Way ANOVA revealed a statistically significant difference in GASS scores between at least two groups [$F(2,159)=4.15$, $p<0.05$, $\eta^2=0.05$). Tukey's HSD test for multiple comparisons found that the mean value of GASS was significantly different between combination ($M=14.81$, standard deviation (SD)=7.93) and long-acting ($M=9.39$, $SD=5.23$). However, One-Way ANOVA revealed that there was not a statistically

Table 1. Comparison of sociodemographic and clinical data between groups

	Long acting (depot), (n=18)		Oral, (n=74)		Combination, (n=70)		p
	M	SD	M	SD	M	SD	
Age	45.67	12.66	44.01	11.90	43.60	9.96	0.784[a]
Disease onset age	27.89	10.45	22.92	6.45	22.86	7.07	0.024[a]
Disease duration	17.78	12.59	21.07	10.42	20.67	11.55	0.530[a]
Number of hospitalizations	1.44	1.69	2.76	3.47	3.69	4.03	0.046[a]
BMI	29.78	4.43	29.07	4.54	29.64	4.63	0.701[a]
	n	%	n	%	n	%	
Gender							
Female	8	44.4	16	21.6	10	14.3	0.019[b]
Male	10	55.6	58	78.4	60	85.7	
Marital status							
Single	9	50.0	48	64.9	44	62.9	0.451[b]
Married	6	33.3	21	28.4	16	22.9	
Divorced	3	16.7	5	6.8	10	14.3	
SES							
Low	2	11.1	14	18.9	11	15.7	0.772[c]
Middle	16	88.9	56	75.7	56	80.0	
High	0	0.0	4	5.4	3	4.3	
Job status							
Unemployed	13	72.2	41	55.4	29	41.4	0.073[b]
Employee	4	22.2	13	17.6	15	21.4	
Retired	1	5.6	20	27.0	26	37.1	
Psychiatric diagnosis							
Schizophrenia	18	100.0	70	94.6	63	90.0	0.280[c]
Schizoaffective	0	0.0	4	5.4	7	10.0	
Suicide attempt							
Yes	1	5.6	15	20.3	18	25.7	0.169[b]
No	17	94.4	59	79.7	52	74.3	
Psychiatric diagnosis in the family							
Yes	7	38.9	37	50.0	35	50.0	0.673[b]
No	11	61.1	37	50.0	35	50.0	
Other disease							
No	13	72.2	59	79.7	60	85.7	0.367[b]
Yes	5	27.8	15	20.3	10	14.3	

[a]: ANOVA, [b]: Chi square, [c]: Fisher's exact test, M: Mean, SD: Standard deviation, BMI: Body mass index.

significant difference in SLS and FROGS scores between the two groups (p>0.05).

Pearson correlation analysis was performed before performing hierarchical multiple regression analysis. The predictor variables that had significant relationships with the outcome variables were included in the regression analysis. Predictive variables (e.g., antidepressants and mood stabilizers) that did not have significant relationships with the outcome variables were not included in the regression model.

A hierarchical multiple regression was run to determine if the addition of age and GASS score improved the prediction of SLS scores (Table 3). First, age was entered in the model, which resulted in a beta coefficient of 0.11. Age accounted for approximately 0.07% of the variance in SLS [$F(1,160)=12.18$, $p<0.01$, $R^2=0.07$). The second step of the regression analysis involved entering GASS into the regression equation along with age. Age had a beta value of 0.11 and GASS had -0.22. Age and GASS for approximately 0.20% of the variance in SLS ($F(2,159)=20.30$, $p<0.001$, $R^2=0.20$).

DISCUSSION

This study compared patients with schizophrenia and schizoaffective disorder using only oral antipsychotics, only depot antipsychotics,

Table 2. One-Way ANOVA results

	Group	n	M	SD	F	p	η^2	Difference
GASS	Long acting[a]	18	9.39	5.23	4.15	0.018	0.05	c>a
	Oral[b]	74	12.41	7.92				
	Combination[c]	70	14.81	7.93				
SLS	Long acting	18	15.44	3.36	1.39	0.252	0.02	
	Oral	74	14.76	4.83				
	Combination	70	13.73	4.77				
FROGS	Long acting	18	58.50	16.07	1.01	0.367	0.01	
	Oral	74	56.57	13.26				
	Combination	70	54.21	12.29				
Social functioning	Long acting	18	19.56	5.58	1.42	0.245	0.02	
	Oral	74	18.76	5.00				
	Combination	70	17.69	4.70				
Health and treatment	Long acting	18	12.94	4.01	0.09	0.918	0.00	
	Oral	74	12.80	3.11				
	Combination	70	12.63	3.30				
Daily life	Long acting	18	20.44	5.49	1.11	0.333	0.01	
	Oral	74	19.85	4.31				
	Combination	70	19.01	3.97				
Occupational functionality	Long acting	18	5.56	2.12	1.00	0.372	0.01	
	Oral	74	5.16	1.98				
	Combination	70	4.89	1.76				

GASS: Glasgow Antipsychotic Side Effect Scale, SLS: The Satisfaction with Life Scale, FROGS: Functional Remission of General Schizophrenia Scale, M: Mean, SD: Standard deviation.

Table 3. Hierarchical multiple regression prediction of SLS from age and GASS

	B	SH	B	t	p	R^2
Model 1						
Constant	9.47	1.45		6.51	<0.001	0.07
Age	0.11	0.03	0.27	3.49	0.001	
Model 2						
Constant	12.21	1.45		8.41	<0.001	0.20
Age	0.11	0.03	0.27	3.85	<0.001	
GASS	-0.22	0.04	-0.36	-5.15	<0.001	

Outcome variable: SLS, Model 1 $F(1,160)=12.18$, $p<0.01$. Model 2 $F(2,159)=20.30$, $p<0.001$, SLS: Satisfaction with Life Scale, GASS: Glasgow Antipsychotic Side Effect Scale.

or both in terms of drug side effects, life satisfaction, and functional improvement. The analysis of the sociodemographic data revealed no significant difference between the groups with respect to age, marital status, employment status, perceived socio-economic level, suicide attempt, and family history of psychiatric illness. All three groups had higher body mass indexes than the normal ranges. The groups were similar with regard to comorbid diseases such as hypertension, obesity, diabetes, and hypercholesterolemia. This is consistent with previous reports showing an increased risk of cardiovascular and metabolic diseases in patients with schizophrenia (18). The comparison of the groups showed a significant difference in terms of age at onset, number of hospitalizations, and gender. The analyses revealed a higher number of hospitalizations in the group using both depot and oral antipsychotics compared with those using only depot antipsychotics, with an earlier age of onset. This may be related to the addition of depot antipsychotics to treatment in the presence of poor prognostic factors such as early onset, frequent hospitalization, and clinicians' tendency to use multiple antipsychotics (19).

This study showed that the mean GASS score of patients using both depot and oral antipsychotics was significantly higher than that of patients using only depot antipsychotics; however, there was no significant difference in regard to using only oral antipsychotics. The higher number of patients using two or three antipsychotics in combination in the group using only oral antipsychotics may have affected the results. Given these data, we concluded that the use of multiple antipsychotics increases the incidence of side effects regardless of the depot or oral form (1). It is known that more side effects can lead to medication non-adherence (6). Medication non-adherence appears to lead to a vicious cycle in the disease process by causing exacerbation of symptoms and hospitalization (20). Therefore, it should be noted that the use of multiple antipsychotics increases the incidence of side effects and adversely affects medication adherence rather than curing the disease.

This study demonstrated no significant difference between the groups with respect to mean SLS, total FROGS scores, and sub-dimension FROGS scores. Studies have shown low rates of long-term improvement both clinically and socially, although most of the patients initially respond well to antipsychotic treatment and especially positive symptoms are controlled (3,11). In particular, discontinuation of antipsychotic treatment leads to relapses, with an increased risk of self-harm or harming others, social isolation, reduced social and occupational functionality, loss of self-esteem, and decreased quality of life (3,21). This is associated with increased caregiver burden, frequent hospitalization, and increased healthcare costs (22). The absence of difference between our study groups in terms of SLS, FROGS total scores, and FROGS subscale scores, the regular use of the drugs by the patients regardless of the drug group, regular follow-up at the CMHC, and the relatively good therapeutic relationship established with the patients may have resulted in a certain level of functional improvement with the control of disease symptoms. Moreover, the long disease duration may have caused the patients to accept the disease and adapt to the treatment over the years. Providing psychoeducation about the disease process and regular drug use, observing and monitoring drug use, administering drugs once daily if necessary, reviewing the side effects of the patient experiencing discomfort due to drug side effects, and switching to depot antipsychotics can increase medication adherence and contribute to improving the quality of life and social functionality (3).

Depot antipsychotics developed to reduce medication non-adherence have some advantages and disadvantages over oral antipsychotics (22). Depot antipsychotics provide advantages such as maintaining stable blood levels of drugs, reducing the need for daily reminders to patients, avoiding gastrointestinal absorption problems and liver first-pass effects, and preventing accidental or intentional overdoses. Even if the patient misses an injection, a sudden drop in the blood level of an antipsychotic drug can be prevented, provided the clinician has sufficient time to intervene. Injections can also increase therapeutic interaction because they are administered by a healthcare professional at regular intervals (2,23). On the other hand, slower titration, a longer time to reach steady-state, and long-term cumulative side effects can be considered disadvantages of depot antipsychotics (24).

Although depot antipsychotics have been suggested to play an important role in increasing medication adherence, preventing relapses, and reducing hospitalizations in patients with schizophrenia (2), a study found that depot antipsychotics added to oral antipsychotic treatment did not provide any benefit in terms of treatment adherence (25). Furthermore, a recent study showed a higher rate of multiple antipsychotic use, longer length of hospital stay, and higher hospitalization frequency in patients with poorer treatment adherence (19). Because we did not investigate the effect of depot antipsychotics on treatment adherence in our study, it is not possible to speculate on this issue. However, our study showed a higher number of hospitalizations in patients using both depot and oral antipsychotics, suggesting that clinicians tended to add depot antipsychotics to oral treatment in cases of frequent hospitalization, medication non-adherence, and relapses.

Although depot antipsychotics are preferred when oral treatments fail or are inadequate, there are studies providing very robust evidence for the use of depot antipsychotics as first-line therapy (2,3,26). Some studies have stated that clinicians avoid using depot antipsychotics even in cases of medication non-adherence (27). A study reported that health professionals found depot antipsychotics stigmatizing, worried about serious side effects, considered the increasing cost, thought that patients would not accept depot antipsychotic treatment, and assumed that the therapeutic relationship would deteriorate (28). On the other hand, a review reported that 18-40% of patients preferred depot antipsychotics rather than regularly taking oral antipsychotics every day (29). In this regard, we believe that it is important to consider factors such as the clinical findings of the patient, frequency of hospitalization, age of onset, level of insight, and the patient's preference when selecting oral or depot drugs. Because this study demonstrated no significant difference between the groups with regard to life satisfaction and functional improvement, we suggest that depot antipsychotics be used only in case of medication non-adherence or based on the patient's preference, considering the requirement for administering depot antipsychotics by a healthcare professional and increasing cost. Similarly, a recent study comparing oral second-generation antipsychotics and the depot form of risperidone reported no difference between the two drug groups in terms of recovery and no advantage of the depot form in patients with early-stage

schizophrenia, recommending the use of depot antipsychotics only in cases of medication non-adherence and patient preference (29).

This study also showed that age and GASS total score were predictors of life satisfaction. The increase in age had a positive effect on life satisfaction, and high GASS scores were associated with lower life satisfaction. The study result showing that age was a predictor of life satisfaction may be related to the acceptance of the disease by the patients over the years. A higher number of side effects negatively affect the life satisfaction of patients. Therefore, avoiding the use of multiple antipsychotics is also essential for life satisfaction.

Study Limitations

The positive aspects of this study may include regular follow-up of the patients at the CMHC for at least 1-year, regular use of medications by them, a well-established therapeutic relationship with the treatment team, timely administration of injections, and clinical stability in terms of positive psychotic symptoms. The limitations of this study are the cross-sectional evaluation of patients by a single researcher, the inability to distinguish between first- and second-generation antipsychotics, and the absence of a sufficient sample size to compare the oral and depot forms of the drug with the same active ingredient.

CONCLUSION

This study demonstrated no difference between the groups with respect to life satisfaction and functional improvement, thereby suggesting the use of depot antipsychotics in the presence of poor prognostic factors such as medication non-adherence, frequent hospitalization, and lack of insight. Data regarding the effects of depot antipsychotics on functional improvement, quality of life, and life satisfaction and their use in cases of medication non-adherence and in early-stage patients are still limited and contradictory. There is a need for multicenter prospective studies focusing on early-stage patients with a longer follow-up period for side effects, life satisfaction, quality of life, and functional improvement to achieve more significant results.

Ethics

Ethics Committee Approval: Before starting the research, the necessary ethical approval was obtained from the Human Research Ethics Committee of Rize Provincial Directorate of Health (approval number: E-64247179-799).

Informed Consent: Participants were informed about the study and signed consent forms were obtained.

Authorship Contributions

Concept: İ.K.A., M.A., Design: İ.K.A., Supervision: B.K., Materials: İ.K.A., B.K., Analysis or Interpretation: M.A., B.K., Literature Search: İ.K.A., M.A., B.K., Writing: İ.K.A., B.K., Critical Review: B.K.

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