The Effect of Long-acting Antipsychotic Treatment on the Level on Care Burden in Schizophrenia Patients

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Abstract

Background: Most patients with schizophrenia are unable to fulfill their personal and social responsibilities and these are met by their caregivers. The concept of 'burden' has come to the fore for caregivers. Long-acting injectables have been shown to reduce relapse rates, and provide a better level of functionality, but their effect on caregiver burden has not been investigated.

Objective: Our aim in this study is to investigate the effect of transition from oral to long-acting antipsychotic treatments on caregiver burden. Other factors that may be related to the burden were also discussed.

Setting: This study was performed at Community Mental Health Center of Erzurum Regional Training and Research Hospital.

Methods: Caregivers (n:138) of patients diagnosed with schizophrenia for at least one year and who received oral paliperidone or aripiprazole were evaluated at baseline and 1 year after switching to long-acting injectables.

Main outcome measure: The Zarit Caregiver Burden Scale (ZCBS) and the Clinical Global Impression-Disease Severity (CGI-S) were administered. Demographic characteristics of caregivers and patients were evaluated.

Results: Significant decreases were found in the ZCBS and CGI-S scores after transitioning to long-acting injectable antipsychotics ($p < 0.001$). Caregiver burden was positively correlated with patient's age, CGI-S score, time spent in the same house, duration of illness, and the number of hospitalizations. A significant negative correlation was found among the caregiver's age, educational level, and income ($p < 0.05$).

Conclusion: In the present study, the importance of switching to long-acting injectable antipsychotics, which is a modifiable factor, to reduce caregiver burden was emphasized

Introduction

Schizophrenia is a chronic and devastating disorder and causes impairment in social functions in most patients. Therefore, most patients with schizophrenia cannot fulfill their personal and social responsibilities. The needs of patients in these domains are met by their caregiving relatives who are mostly first-degree ones [1]. The care that should be given causes changes in the dynamics of the family due to the difficulties it involves and causes stress in the family members living with the patient [2–5]. Caregivers who try to maintain a balance between their personal responsibilities such as work, family, and patient care often neglect their physical and mental health [6]. As a result, the concept of 'burden' has come to the fore for caregivers [7].

To determine the correct targets and develop appropriate methods for reducing the burden of caregivers, it is necessary to define the factors related to the burden first. Studies on burden focus on the factors

related to the patient, their caregiver, and social factors [8]. Also, factors including the number of relapses and hospitalizations are also related to the burden [9, 10]. Antipsychotic medications are known to reduce the relapse rate and the number of hospitalizations [11]. But the rate of non-adherence to treatment is rather high in patients with schizophrenia [12, 13]. Studies have shown that the majority of patients with schizophrenia [84%] do not continue oral antipsychotic drug treatment during their follow-up and 40–50% of them do not comply with the treatment in long-term follow-up [14, 15].

The high rate of non-compliance with oral antipsychotic treatment has led to the need for the development of long-acting injectable antipsychotics [16]. Numerous studies have shown that long-acting injectables do reduce relapse rates, the number of hospitalizations, duration of hospitalization, and provide a better level of functioning [17–23]. However, their effect on caregivers' burden has not been adequately investigated. It is important to reduce the burden of care while creating more effective treatment and support programs for patients and their relatives. For this purpose, it is very important to identify the factors related to the burden of care and to determine the treatment strategies to reduce the burden. In this respect, our study mainly aimed to investigate the effect of transitioning to long-acting antipsychotic treatment on the level of care burden in primary caregivers of patients who were switched from oral antipsychotics to long-acting antipsychotic treatments. On the other hand, other factors that may be related to the care burden were also discussed.

Materials And Method

Design and Ethical approval

This study was conducted with patients who were diagnosed with schizophrenia according to DSM-V criteria and who were under follow-up by the Community Mental Health Center of Erzurum Regional Training and Research Hospital and their caregiving relatives. Ethical approval was obtained from the Erzurum Regional Training and Research Hospital's ethics committee for the study (Date: 07.09.2020 Decision No:2020/16-173). Written consents were obtained from the patients and their relatives who agreed to participate in the study. The diagnoses of the patients were made clinically by the psychiatrist. Transition to paliperidone palmitate or aripiprazole long-acting treatment was planned for patients whose clinic statuses were stable with paliperidone and aripiprazole oral treatment. Oral treatments were discontinued on Day 9 of paliperidone palmitate injection and Day 30 of aripiprazole injection. The scales were administered to patients and their caregivers before the long-acting antipsychotic treatments were initiated and one year after the start date.

Study participants Patients, who were followed up for at least one year with a diagnosis of schizophrenia, who were not in an acute exacerbation during the study, who did not have any diagnosis of comorbid organic disease or intellectual disability, and who were 18 years of age or older were included in the study. Family members who helped the patient's daily functioning; conducted their medical follow-up and treatment; met their needs; who primarily gave care to the patient and did not "do this as a professional job"; and who voluntarily agreed to participate as a caregiver were included as a caregiver. One caregiver for each patient was included in the study. In patients with more than one caregiver, the caregiver who was reported to have the most responsibility for the patient was

preferred. Inclusion criteria for the caregivers were: being over 18 years of age, the absence of any comorbidity or intellectual disability that could affect their cognitive or mental functions, and being literate.

Data Collection Tools

Scales Applied to Patients Patient Data Form: Involves questions including the age, gender, employment status of the patient; history of suicide and forensic events, duration of illness, and number of hospitalizations.

Clinical Global Impression Scale (CGI-S): It is a scale that can be used to evaluate the severity of mental disorders, the level of recovery, and drug side effects. The scale has 3 subscales showing the severity of the disease, general improvement, and the level of side effect. In this study, the disease severity subscale (CGIS-S) was used. The scale is scored between 1 to 7 points. The higher the scale scores indicate the higher the severity of the disease.

Scales Applied to Caregivers Caregiver Socio-Demographic Data Form: It involves questions including the caregiver's age, marital status, years of education, income status, and the time they spent with the patient.

Zarit Caregiver Burden Scale (ZCBS): This scale has been developed by Zarit et al. in 1980. It is a scale used to evaluate the difficulties experienced by caregivers of individuals or the elderly who need care. The scale, which can be completed by the caregiver or the researcher, consists of 22 statements that determine the effect of caregiving on the individual's life and is scored between 0 and 66. The items in the scale are generally related to the social and emotional domain, and a high score on the scale indicates a high level of distress experienced. The Turkish reliability and validity study of the scale was performed by Özlü et al [24].

Statistical analysis

The analysis was carried out using the IBM SPSS 20 (Armonk, NY: IBM Corp.) software. The sample size was calculated using the G*power program. Calculations were made at 80% strength and 95% power level. The data were presented as mean, standard deviation, median, minimum, maximum, percentage, and number. The normality of the distribution of continuous variables was examined with a Shapiro Wilk-W test when the sample size was <50, and with a Kolmogorov Smirnov test when the sample size was ≥ 50 . For comparisons of two independent groups, an Independent Samples t-test was used when the normal distribution condition was met, and a Mann-Whitney U test was used when not. For the comparison of the two dependent groups, a Paired Samples t-test was used if the normal distribution condition was met and, and a Wilcoxon test when not. For the comparison of continuous variables with more than two independent groups, an ANOVA test was used when the normal distribution condition was met, and a Kruskal Wallis test when not. After the ANOVA test, post hoc tests were performed using a Tukey test when the variances were homogeneous, and Tamhane's T2 test when not. The Kruskal Wallis test was performed using the Kruskal Wallis one-way ANOVA (K samples) test for post hoc tests. A Pearson Chi-square test (if the expected count >5), Chi-square test (if the expected count was 3–5), and Fisher's Exact test (if the expected count was <3) were used for 2x2 comparisons of categorical variables. For comparisons between categorical variables greater than 2x2, a Pearson Chi-square test was used if the expected value was (>5) and a Fisher-Freeman-Halton test was used if the expected value was <5.

Post hoc tests after the Chi-square test were performed using the Bonferroni method. Pearson correlation analysis was performed for correlation analysis.

Results

This study included 138 patients with a diagnosis of schizophrenia and 138 relatives who gave care to these patients.

Fifty percent (n: 69) of the patients who received care were females and 50% (n: 69) were males. Seventy-four percent (n: 102) of the patients switched from paliperidone oral treatment to monthly long-acting injectable paliperidone palmitate treatment, 26% (n: 37) from aripiprazole oral treatment to monthly long-acting injectable aripiprazole. Oral treatments were discontinued on Day 9 of paliperidone palmitate injections and on Day 30 of aripiprazole injections.

The data regarding the patients' mean duration of illness, number of hospitalizations, employment status, suicidal history, and forensic event histories are shown in Table 1.

Table 1
Sociodemographic characteristics of the patients included in the study

N:138	Min-Max	Mean $\pm$ SD
Age	21–75	45.17 $\pm$ 11.59
Duration of illness (years)	3–45	17.14 $\pm$ 11.20
Number of hospitalizations	1–35	7.41 $\pm$ 5.28
	Frequency	Percent
Gender		
<i>Male</i>	69	50
<i>Female</i>	69	50
Working status		
<i>Unemployed</i>	133	96.4
<i>Student</i>	5	3.6
Suicidal history		
<i>No</i>	99	71.7
<i>Yes</i>	39	28.3
Forensic case history		
<i>No</i>	87	63.0
<i>Yes</i>	51	37.0

Fifty-four point three percent (n: 75) of the caregivers who participated in the study were females and 45.7% (n: 63) were males. Of the caregivers, 37% (n: 51) were siblings of the patient, 23.9% (n: 33) were parents, 10.9% (n: 15) were spouses, and 28.3% (n: 39) were second degree relatives. The characteristics of the caregivers including educational status, marital status, employment status, and the time they spent with the patient are given in Table 2.

The correlation analysis between the care burden and the characteristics of the patients revealed statistically significant positive relationships between the care burden and the CGI-S score, the age of the patient, the duration of the disease, and the number of hospitalizations (Table 3a). When the relationship between the demographic variables of the patient and the burden was evaluated, it was found that the care burden was not related to gender, but it was correlated with being unemployed or being a student (Table 3b).

Table 3
a. Correlation analysis of caregiver burden and characteristics of the patients

Tablo 2. Sociodemographic characteristics of the caregivers		
N:92	Min-Max	Mean $\pm$ SD
Age	20–72	34.39 $\pm$ 14.13
Educational status (years)	1–15	6.54 $\pm$ 3.82
Living in the same house (years)	3–60	18.85 $\pm$ 11.47
Hours spent together in a day	8–18	12.96 $\pm$ 3.95
Monthly income per person (TRY)	500–2000	1059.78 $\pm$ 649.64
	Frequency	Percent
Gender		
<i>Male</i>	63	45.7
<i>Female</i>	75	54.3
Marital Status		
Single	30	21.7
Married	102	73.9
Widowed	6	4.3
Working status		
Unemployed	15	10.9
Irregularly employed	15	10.9
Employed	66	47.8
Housewife	24	17.4
Retired	18	13.0
Degree of relationship		
Parent	33	23.9
Spouse	15	10.9

**denotes statistical significance ($p < 0.001$)

Tablo 2. Sociodemographic characteristics of the caregivers					
Sibling	51	37.0			
Other	39	28.3			
	CGI-S	Age of patient	Duration of illness	Number of hospitalizations	
Caregiver burden	.182	.430	.742	.369	r
	.033*	.000**	.000**	.000**	p
CGI-SI: clinical global impression scale; r: pearson correlation coefficient; p: significance *denotes statistical significance (p < 0.05) **denotes statistical significance (p < 0.001)					
Table 3b. Comparison of caregiver burden and the categorical characteristics of the patients					
Patient's	ZCBS Mean	p			
	± SD				
Gender					
Male	79.7 ± 9.23	0.669			
Female	80.57 ± 14.10				
Working status					
Unemployed	80.86 ± 11.42	0.000**			
Student	60.8- ±6.57				
ZCBS: Zarit Caregiver Burden Scale					
**denotes statistical significance (p < 0.001)					

When the relationship between caregiver burden and caregiver characteristics was evaluated, it was found that there were statistically significant negative correlations between burden and the age of the

caregiver, the education level of the caregiver, and the monthly income per person. A statistically significant positive relationship was found between the burden and the duration of the patient and the caregiver living in the same house and the duration of time spent together during a day (Table 4a).

Table 4

b. Comparison of caregiver burden and the categorical characteristics of the caregivers

Table 4a. Correlation analysis of caregiver burden and characteristics of the caregivers						
	Age	Education year	Monthly income per person	Living in the same house (years)	Hours spent together in a day	
Caregiver burden	– .268	– .546	– .660	.489	.696	r
	.001*	.000**	.000**	.000**	.000**	p
r: pearson correlation coefficient; p: significance						
*denotes statistical significance (p < 0.05)						
**denotes statistical significance (p < 0.001)						
	ZCBS Mean ± SD	p				
Gender						
Male	79.67 ± 10.38	0.676				
Female	80.52 ± 13.07					
Marital Status						
Single	70.2 ± 7.58	0.000**				
Married	83.59 ± 11.22					
**denotes statistical significance (p < 0.001)						

When the relationship between the caregiver burden and the demographic variables of the caregiver was assessed, it was found that there was no statistically significant correlation between the burden and the gender of the caregiver. The burden was significantly higher in married caregivers and spouses, and the burden was highest in retired caregivers. It was found that there was no significant difference in burden between caregivers who were unemployed and those who were housewives (Table 4b, Table 4c).

When the relation between the burden and the oral antipsychotic treatment and long-acting injectable antipsychotics was evaluated, a significant decrease was found in the ZCBS and CGI scores after switching to long-acting injectable antipsychotics ($p < 0.001$) (Table 5).

Table 5
Comparison of ZCBS and CGI-SI scores before and one year after long-acting antipsychotic use

	Mean $\pm$ SD	p value	Z value
ZCBS-1	80.13 $\pm$ 11.88	0.000	-10.182
ZCBS-2	45.24 $\pm$ 9.52		
CGI-SI-1	6.46 $\pm$ 0.5	0.000	.000
CGI-SI-2	3.43 $\pm$ 0.65		
ZCBS-1: Zarit Caregiver Burden Scale scores when using Oral Antipsychotic Treatment			
ZCBS-2: Zarit Caregiver Burden Scale scores 1 year after the start of Long Acting Antipsychotic Treatment			
CGI-SI-1: Clinical Global Impression Scale scores while using Oral Antipsychotic Treatment			
CGI-SI-2: Clinical Global Impression Scale scores 1 year after the use of Long Acting Antipsychotic Therapy			

Discussion

In this study, unlike other studies on the subject, the change in caregiver burden in caregivers of schizophrenia patients with the transition from oral treatment to long-acting injectable antipsychotics was evaluated. Other factors that could affect caregiver burden were also addressed.

Considering the studies evaluating the relationship between the gender of the caregiver and burden, it is seen that patient care is generally undertaken by women [25–27]. Similarly, female caregivers were constituting the majority in this study. It has been reported that the cultural structure of societies may have an impact on this. Considering our country and the geography in which our study was conducted, it is seen that the traditional family structure is more dominant, women generally undertake patient care [28].

In our study, no difference was found between female and male caregivers in terms of care burden. When looking at the studies related to caregiver burden, there exist studies showing that the burden is higher in female caregivers [27, 29, 30] and there are also studies showing no difference between genders [9, 31]. Literature reviews show that a large sample size could suggest a higher burden in women.

In the present study, no relationship was found between caregiver burden and patient gender, in line with most of the literature [9, 31]. In this study, a statistically significant positive correlation was found between patient age and burden. In the literature, while some studies found a significant relationship

between burden and patient age [9], some studies reported no relationship between the two [8, 32]. Considering that even healthy people increase the burden of additional diseases on their families with age, this may be an expected result.

A statistically significant negative correlation was found between the burden and the age of the caregiver. In the literature, while the burden increases with the age of the caregiver in Asian countries, it decreases in countries such as the US and Mexico [6, 33, 34]. In a previous study conducted in our country, it was found that the burden increased with the age of the caregiver, in contrast to the results of our study [35]. Our findings, on the other hand, are consistent with those found in a study conducted with caregiving parents of individuals with mental illness [36, 37]. This may be related to the possibility of younger caregivers having more additional social roles, such as having a job, raising children, and caring for aging parents, than older caregivers. Another explanatory situation might be that elderly caregivers are more experienced in accepting the disease and the sick individual and developing coping strategies.

Although there are conflicting research results regarding the educational level of the patient's caregiver and burden, the results of this study were consistent with the other study conducted in our country. It was shown in our study that as the caregiver's years of education increase, the burden of caregivers tends to decrease. It may be related to the change in people's perception of psychiatric diseases as the level of education increases and the level of stigmatization decreases [38]. No doubt that this can be evaluated more objectively in a study to be conducted on the effect of stigmatization level on caregiver burden.

In this study, it was shown that the burden of the caregiver decreased with the increase in the monthly income level and the decrease in the time spent with the patient. This result was found to be consistent with other studies conducted in our country [35]. A low level of income makes it difficult to access healthcare services and to meet basic care needs in the follow-up and treatment of the disease, which is thought to increase the burden of caregivers. At the same time, it can create a perception of an increased burden by decreasing access to social and cultural areas and increasing the time spent with the patient.

Although most of the patients in our study are unemployed, we also have patients who are students. Because students have their own independent time, it can be suggested that they have less care burden than unemployed caregivers.

In the present study, a positive correlation was found between burden and duration of illness and number of hospitalizations. These findings are consistent with those of previous studies on this subject [9, 27, 38].

When the working status of the patients is evaluated, most of our patients do not work. But there is a significant difference between our patients who are students and who are unemployed. It was observed that the caregiver burden of the relatives of students was significantly lower than that of the unemployed caregivers. The requirement of a certain level of functioning to maintain school makes this probable.

When we look at the effect of the transitioning from oral antipsychotic treatment to long-acting injectable antipsychotics, which is considered as the main purpose of this study, it was found that this type of treatment significantly reduced the burden. This is a factor that can easily be changed by healthcare professionals according to other factors. With the change of this factor, other factors such as the number of hospitalizations and recurrence rate that affect the burden are also affected positively and the burden decreases in various ways.

Studies show that despite the benefits of antipsychotics in the treatment of schizophrenia, the rate of non-adherence to treatment is still high [12, 13]. Non-adherence to treatment is an important problem that is very common in clinical practice and may require re-hospitalization [39]. In the first year after discharge, the rate of patients who discontinue oral antipsychotic treatment reaches up to 50%. Treatment compliance is less than 30% in the second year [40]. The use of long-acting antipsychotics in schizophrenia provides advantages in ensuring compliance with treatment and maintenance of effective therapy [41]. Relapse rate in first-episode schizophrenia is 70% in patients with treatment non-compliance and 25% in patients with treatment compliance [42, 43]. In another study, the relapse rate at 1-year follow-up was 42% for those who used oral antipsychotics and 27% for those who used depot antipsychotics [44]. A significant difference was also found in the duration of hospital stays between oral drug use and depot therapy [45].

It has been reported that the rate of medication non-adherence reported by caregivers in schizophrenia patients is also high, and that poor adherence to antipsychotics is associated with care burden [46].

Many studies have shown that long-acting injectable antipsychotics are associated with better treatment compliance [47–50]. In light of this information, it can be argued that long-acting antipsychotic treatment may decrease care burden by increasing treatment compliance. Accordingly, it was found in this study that switching from oral antipsychotic treatment to long-acting injectable antipsychotics significantly reduced the care burden.

This study included a patient population receiving the long-acting injectable formulation of two different active ingredients. Since the number of patients was not homogeneous in both groups, it could not be determined whether the caregiver burden could be reduced according to the active ingredients of the drugs. With the elimination of this limitation, the caregiver burden can also be evaluated with regard to the active substance in future studies.

Despite the advantages of long-acting antipsychotic injectables, the proportion of psychotic patients treated with such medications appears to be low, with national and regional differences around the world [51]. Our study results are supportive of increasing the prevalence of long-acting antipsychotic use and thus reducing caregiver burden.

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