

Studying medication adherence in patients with schizophrenia: focus on antipsychotic-related factors

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Background

Antipsychotic medications are considered to be the mainstay treatment for schizophrenia. Overall, 50–75% of patients with schizophrenia will relapse within a year if their antipsychotics are discontinued, compared with just 25% of patients who continue their medications. Thus, understanding drug-related determinants of medication adherence is one of the critical issues for relapse prevention.

Aim

The aim of the present study was to estimate the rate of nonadherence and to assess medication-related extrapyramidal and weight-gain side effects influencing adherence to antipsychotic drugs.

Patients and methods

The present study included 109 patients recruited from Ain Shams University Institute of Psychiatry, Egypt. They were interviewed using the Structured Clinical Interview for DSM-IV (SCID), and diagnosed according to DSM-IV. Demographic data and weight were assessed upon enrollment. They received antipsychotic medication with a dose range of 280–300 mg chlorpromazine equivalent, and were followed up for 6 months. At the end of this period, adherence to medication was assessed using the Brief Adherence Rating Scale and the side effects of antipsychotics; accordingly, we had an adherent ($n=34$) and a nonadherent group ($n=74$). Side effects of antipsychotics were assessed using the Simpson Angus Scale (for extrapyramidal symptoms), Barnes Rating Scale (for akathisia), and Abnormal Involuntary Movement Scale (for dyskinesia). Finally, patients' weights were again measured.

Results

Overall, 68.8% of the patients were nonadherent to their antipsychotic medications. An analysis of the different variables that could affect adherence revealed that females and university graduates significantly were more adherent ($P=0.04$, 0.02 , respectively). We did not find any statistically significant difference between the adherent and nonadherent groups regarding the type of antipsychotics prescribed and weight gained ($P>0.05$). Experiencing motor side effects had significant relation to adherence as the presence of dyskinesia, akathisia, and extrapyramidal symptoms lead to nonadherence ($P=0.014$, 0.017 , 0.00 , respectively). The studied risk factors did not yield any drug-related predictors for nonadherence, probably because of the small sample size.

Conclusion

The rate of nondrug adherence was relatively high. Females and university educated patients were more adherent to treatment. There was no relation between type of antipsychotic prescribed and drug compliance; however, experiencing motor side effects might be a driving component for nonadherence. This information may help clinicians to make proper interventional decisions to maximize drug adherence.

Keywords:

adherence, schizophrenia, treatment, type of antipsychotic

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Introduction

In the fourth century BC, Hippocrates observed that many patients did not adhere to medical advice [1]. Since then, the terminology used to describe this phenomenon has changed but the issue remains the same. As Kemp and David [2] stated, compliance is the extent to which a

patient's behavior, in terms of taking medication or executing lifestyle changes, coincides with medical or health advice. Whereas medication nonadherence is the number of doses that were taken incorrectly, and it includes the following: not filling the prescription, taking an incorrect dose, taking a medication at the wrong time, forgetting to take a prescribed dose, or stopping therapy

too soon [2]. A recent review estimated that 41% of the schizophrenia patients are nonadherent to their antipsychotic medications [3], which may play a major role in determining the frequent relapse and rehospitalization [4]. Long-term antipsychotic treatment is the most effective factor for improving symptom outcomes [5]; therefore, discontinuation of medication is considered to be one of the most relevant outcome measures [6]. Antipsychotic medications are effective in the treatment of acute episodes of psychosis [7], reducing the risk of relapse after response to the first-episode, a cumulative response rate of 87% achieved by 1 year [8].

The course of schizophrenia varies, but most patients have a chronic course with frequent relapses, typically characterized by the exacerbation of psychosis and rehospitalization. Successive relapses can lead to reduction in the degree and duration of the next remission, worsen disability, and increase refractoriness to future treatment. Hence, preventing relapse and maintaining treatment with antipsychotic drugs is mandatory for patients who have schizophrenia [9].

Understanding the determinants of antipsychotic medication adherence in schizophrenia patients is critical as each psychotic relapse can contribute to accrued social toxicity and disability; or as Lieberman and Fenton [10] put it, 'untreated psychosis damages lives'. Nonadherence to medication can have a significant impact on health resources and healthcare costs such as drug budget and costs of unplanned hospitalization [11].

There are overlapping groups of factors influencing adherence to antipsychotics, namely illness-related factors (symptom severity, insight, and comorbidity), socio-demographic variables, family support, attitude to illness, strength of therapeutic alliance, and medication-related variables [12,13].

Despite that identification of drug-related factors associated to nonadherence will help clinicians to modify their treatment strategies, only few clinical trials have directly examined differences in adherence among patients taking both conventional and atypical antipsychotics. Hence, it was felt appropriate to focus and examine what the antipsychotic-related variables associated with adherence in schizophrenia patients were.

Aim

The aim of the present study was to estimate the rate of nonadherence and to assess medication-related extrapyramidal and weight-gain side effects influencing adherence to antipsychotic drugs.

Hypothesis

We hypothesized that the patients prescribed with atypical antipsychotic medication would have greater adherence to treatment than those receiving conventional antipsychotics, and that motor side effects could be a risk factor affecting nonadherence.

Patients and methods

In this prospective study the patients were enrolled from Ain Shams University Institute of Psychiatry, Egypt, from August 2011 to May 2012. All procedures were reviewed and approved by the Ethical Committee of Ain Shams University. Informed written consent was obtained from each participant before enrollment in the study.

During the study period, a total of 137 patients were recruited fulfilling the inclusion criteria of our study. However, 28 of them (20.4% drop-out rate) were dropped out of the study. One patient died and 27 patients did not attend the follow-up. The remaining 109 patients continued the study.

Participants

Patients were included in this study if they (i) received a diagnosis of schizophrenia disorder according to *Diagnostic and statistical manual of mental disorders*, 4th ed. (DSM-IV) and who were seeking advice from the Institute of Psychiatry; (ii) signed the informed consent before enrollment in the study; and (iii) were aged from 18 to 65 years. Patients were excluded from the study if they had any disorder that clearly interfered with antipsychotics side effect profile, such as having central nervous system lesions, severe hepatic, or renal dysfunction or were on antipsychotic medications before admission.

Assessment of the study group

Patients were assessed at two time points: upon enrollment and 6 months later. We chose these two points based on the results of the pilot study, which concluded that patients were unable to commit to monthly appointments, and hence to minimize the drop rate we chose only two visits. The second visit was determined to be 6 months after enrollment so as not to miss any tardive side effect of antipsychotics, which take at least 6 months to occur and can affect adherence.

Upon enrollment

We conducted a clinical interview on the basis of the Structured Clinical Interview for DSM-IV (SCID) [14] to confirm the diagnosis of schizophrenia. Then, the following data were determined:

- (1) Sociodemographic variables, including age, sex, level of education, occupation, marital status, and residency, were recorded in a sheet designed by the researcher.
- (2) Patients' weights were measured and recorded.
- (3) Patients were prescribed either typical or atypical antipsychotics with a dose range of 280–300 mg chlorpromazine equivalent.

Six months later

The patients were contacted after 6 months; they were assessed by the following in the presence of reliable relative living with the patients to overcome the recall bias of the patients:

- (1) Brief Adherence Rating Scale (a recently developed clinician-administered adherence assessment tool) consists of four items: three questions and an overall visual analog rating scale to assess the proportion of doses taken by the patient in the past month (0–100%). The three questions, about the patient's knowledge of their own medication regimen and episodes of missed medication-taking, are as follows: (i) number of prescribed doses of medication per day; (ii) number of days in the past month when the patient did not take the prescribed dose; and (iii) number of days in the past month when the patient took less than the prescribed dose [15].
- (2) Motor side effects of the antipsychotics medication were recorded on the following three scales:
 - (a) The Simpson Angus Scale was used to determine extrapyramidal symptoms. This scale consists of 10 items measuring gait (hypokinesia; one item), rigidity (six items), and glabellar tap, tremor, and salivation (one item each). The items are scored on a five-point scale (0–4). The scale was developed for the assessment of parkinsonism and related extrapyramidal adverse effects. The total assessment takes about 10 min [16].
 - (b) Barnes Rating Scale (BRS) was used to determine akathisia. BRS comprises items for rating the objective features of motor restlessness, the subjective complaints of restlessness, and the associated distress. There is also a global severity rating on a six-point (0–5) scale, with operational definitions for each scale point. The global item score may be used as an overall severity measure and has a diagnostic threshold, with a score of 2 or more indicating the presence of akathisia [17].
 - (c) Abnormal Involuntary Movement Scale (AIMS) has 12 items, each of which is rated on a five-point severity scale ranging from 0 to 4. Ten items assess abnormal movement in specific body regions (orofacial area, extremities, and trunk) as well as the global severity; two items concern dental conditions that can complicate the diagnosis of dyskinesia to determine involuntary movements [18].
- (3) Patients' weight were measure by using the same or similar devices.

Statistical analyses

All data were recorded and statistical analyses were carried out using the statistical package for the social sciences (SPSS, 17th version) [19]. The results were tabulated, grouped, and statistically analyzed using the suitable statistical parameters. For description analysis, data were expressed as mean values and SD. We also used the paired *t*-test for comparison between means of the different groups of patients. Student's test was used to test for the significance of an independent variable in experiments where there were only two levels of this variable (to compare between two independent means). The Pearson χ^2 -test was used to detect whether there was a significant association between different categorical

variables. Logistic regression analysis is an approach of modeling the relationship between a categorical variable *y* and one or more variables denoted by *X*. For all tests, a significance level of *P* less than 0.05 was predetermined. *P* value was used to indicate the level of significance (*P* > 0.05: insignificant; *P* < 0.05: significant).

Results

Demographic data and treatment characteristics

A total of 109 patients (77 men, 32 women) with a DSM-IV diagnosis of schizophrenia were included in this study. Their mean age was 32.2 ± 9.0 years. The majority of patients were single (68.8%), whereas 24.8% were married and 6.4% were divorced. Around 62% had received school education (primary, preparatory, secondary, and technical schools), 26.6% were university graduates, and ~12% patients were illiterate. Overall, 57% of the patients were unemployed, whereas about 43% were employed. Regarding place of residency, most of the patients (82.6%) were living in urban areas, whereas only 17.4% were living in rural areas.

Assessment of patients' adherence

Patients' adherence was assessed using the Brief Adherence Rating Scale 6 months after enrollment, which revealed that about two-thirds (68.8%) of the patients were nonadherent whereas only one-third (31.2%) were adherent; we then subdivided the 109 patients into adherent and nonadherent groups accordingly and compared between the two groups using different variables.

Sociodemographic variables

The adherent group could not be distinguished from the nonadherent group in terms of marital status, occupational status, and place of residency. However, sex and educational level showed a statistically significant relation with adherence, with women significantly more adherent than men (*P* = 0.02) and university graduates significantly more adherent than school educated and illiterate patients (*P* = 0.04) (Table 1).

Treatment-related variables

Motor side effects of antipsychotics: 6 months later, 4.5% of our patients experienced dyskinesia, 11% suffered akathisia, and the most common side effect was extrapyramidal symptoms (EPS) experienced by 52.3% of our patients. The side effects were more observed in nonadherent patients as 7% experienced dyskinesia, 16% akathisia, and 66.6% extrapyramidal symptoms with significant association existing with nonadherence (*P* < 0.05).

Weight gained: Patients' mean weight (in kg) on recruitment was 85.5 ± 7.6 kg. On measuring weight 6 months later, using similar weighting device, the mean weight was 91.9 ± 9.7 kg. A paired-sample *t*-test was conducted to compare the difference in weight on the two occasions. We found a statistically significant increase in mean of weight (*t* = 13.7, *P* < 0.0005). The mean increase in

weight scores was 6.44 kg. It is obvious from Table 2 that nonadherent patients gained more weight (about 8 kg) than did the adherent patients (about 5.5 kg) in the 6 months after enrollment, yet the difference between them regarding weight was not statistically significant ($P > 0.05$).

Type of antipsychotic: The majority of patients were prescribed atypical antipsychotics (65.1%), followed by typical antipsychotics (27.5%), and only 7.3% were prescribed both typical and atypical antipsychotics. There was no statistically significant difference between the adherent and nonadherent groups regarding type of antipsychotic prescribed ($P > 0.05$) (Table 2).

Risk factors correlated with nonadherence

To evaluate the predictive value for the motor side effects of antipsychotics we performed logistic regression analysis. We used patient adherence after 6 months as the

dependent factor and used motor side effect variables akathisia (BRS for akathisia), dyskinesia (AIMS), and EPS, which showed statistically significant relations as a risk factor.

We chose variables that show significant difference in the univariate analysis. The logistic regression analysis showed EPS ($P = 0.083$), dyskinesia ($P = 0.668$), and akathisia ($P = 0.998$), reflecting that motor side effects were nonpredictive to nonadherence despite the significant difference in the univariate (Table 3).

Discussion

Antipsychotic medications represent the cornerstone of pharmacological treatment for patients with schizophrenia. Although these agents have been shown to improve psychopathology, reduce relapse, and improve functioning

Table 1 Demographic variables: adherence versus nonadherent patients with schizophrenia

	N (%)		Test	P value
	Nonadherent (n=75)	Adherent (n=34)		
Age in years (mean ± SD)	32.28 ± 9.3	32.26 ± 8.6	t=0.008	0.99
Sex			$\chi^2 = 5.191$	0.02
Male	58 (75.3)	19 (24.7)		
Female	17 (53.1)	15 (46.9)		
Marital status			Fisher's exact=1.013	0.69
Single	51 (68)	24 (32)		
Married	18 (66.7)	9 (33.3)		
Divorced	6 (5.7)	1 (241.1)		
Education			Fisher's exact=10.186	0.04
Illiterate	11 (84.6)	2 (15.4)		
School	51 (76.1)	16 (23.9)		
University	13 (44.8)	16 (55.2)		
Occupation			$\chi^2 = 0.313$	0.57
Unemployed	44 (71)	18 (29)		
Employed	31 (66)	16 (34)		
Place of residency			$\chi^2 = 0.002$	0.968
Urban	62 (68.9)	28 (31.1)		
Rural	13 (68.4)	6 (31.6)		

Numbers in bold to show the significant results to discriminate it from nonsignificant findings.

Table 2 Treatment related variables: adherence patients versus nonadherent

	N (%)		Test	P value
	Nonadherent (n=75)	Adherent (n=34)		
Weight gained in 6 months (kg) (mean ± SD)	8.21 ± 13.2	5.52 ± 4.9	t=1.14	0.25
Type of medication			Fisher's exact=1.32	0.567
Typical antipsychotics	23 (30.7)	7 (20.6)		
Atypical antipsychotics	47 (62.7)	24 (70.6)		
Both typical and atypical antipsychotics	5 (6.7)	3 (8.8)		
Motor side effects			$\chi^2 = 6.012$	0.014
Dyskinesia	5 (7)	1 (2.9)		
Akathisia	12 (16)	0 (0)	$\chi^2 = 6.11$	0.017
Extrapyramidal symptoms	50 (66.6)	7 (20.6)	$\chi^2 = 19.9$	0.00

Numbers in bold to show the significant results to discriminate it from nonsignificant findings.

Table 3 Logistic regression test of potential factors for nonadherent medications

Factors	B	SE	Wald	Significance	Exp(B)
Extrapyramidal symptoms	-3.589	2.07	2.99	0.083	0.02
Abnormal involuntary movement	-1.147	2.67	0.18	0.668	3.15
Akathisia	20.935	8727.1	0.00	0.998	0.00

(DSM-IV-TR), nonadherence to treatment with antipsychotics is a frequent phenomenon [3]. Improving adherence to treatment with antipsychotic medication in patients with psychotic disorders is a complex task [20]. Thus, identifying risk factors associated with nonadherence is an important initial step because modifiable risk factors might become targets for future interventions. The estimated nonadherence rates in patients with schizophrenia range from 50 to 72% [12,21].

In our study, we reported that 68.8% ($n = 75$) of the patients were nonadherent to their antipsychotic treatment. Our estimates of nonadherence are slightly higher (59.1%) than that reported by Coldham *et al.* [22], who followed 186 patients with schizophrenia for 1 year, and that of Kissling [23], who had indicated that over 60% of patients with schizophrenia were noncompliant with their medications; however, lower rates of nonadherence (33%) were reported by Kamali *et al.* [24]. The differences in the reported rates of nonadherence depend on the definition adopted, the method used to assess adherence, and the inclusion criteria of the patients' population.

There is a lack of prospective studies on factors that predict medication adherence. Hence, our study aimed to estimate the rate of adherence, and then to compare adherent with nonadherent regarding different drug-related variables.

Sociodemographic variables

Many efforts have been made to identify predictive factors for medication nonadherence, focusing on sociodemographic variables [3,25]. Most studies did not show a relation between medication adherence and sociodemographic variables such as sex [12,26–30], age, or occupational status [12,29]. Our study yielded significant relation between adherence and both sex and educational level. Female patients were found to be more adherent ($P = 0.04$) than males, which is in agreement with the results of a few studies that reported this positive relationship to female sex [12,26,27]. This may be attributed to the greater likelihood of women to be caregivers and thus with an incentive to take their medication.

As regards education, the results of our study support those of a prior research by King [28] who observed a significant association between education and nonadherence, as our university graduate patients were more adherent to medications than were patients with lower level of education ($P = 0.02$). In contrast, other investigators [12,30,31] found that education is not correlated to the therapeutic compliance. This may be attributed to the fact that better education could mean better access to illness-related information as the educational status may be correlated to the ability to understand and comprehend the psychological education given by the treating team.

We found no connection between compliance and age, which is in agreement with the results of some previous investigations [26,29,30,32]; there are contradictory evidence concerning adherence and age as studies conducted by Ziguras *et al.* [27], King [28], and Linden

et al. [12] showed that compliance improves with age and that being young was significantly correlated with poor medication compliance; one interpretation could be that patients accumulate experience with their psychotic illness and that they learn that there is a connection between relapse and interruption of drug intake. In contrast, Insel *et al.* [33] stated that older patients may fail to adhere to treatments because of cognitive deficits, impairment in memory, and executive performance; furthermore, they are often prescribed multiple treatments. Many researches [12,30,31], including ours, found that marital status was not a risk factor for nonadherence. However, a study by Stanković *et al.* [29] found significant difference between compliant and noncompliant patients regarding marital status.

If compliance is related to knowledge, occupational status should also influence compliance. However, similar to the results obtained by Linden *et al.* [12] and Stanković *et al.* [29], we found no significant difference in this respect.

Cultural issue may contribute to nonadherence to medication in patients with schizophrenia, and interventions to improve adherence should be culturally appropriate [3,34,35]. This issue was targeted by Sweileh *et al.* [35], who tried to examine how religious beliefs and practice can affect attitude toward medication in Palestinian patients with schizophrenia; they concluded that this important dimension should be considered by psychiatrists working with schizophrenia patients. In the Arab world, families of patients with schizophrenia suffer from stigmatization [36]; such a problem seems to be a barrier for treatment. Thus, clinicians should assess the effect of stigma on their standard interview of patients with mental illness and accordingly reduce its impact on patient's life [37].

Treatment-related variables

Another important result is the influence of the type of antipsychotic medication, side effects, and weight gain on compliance.

Our study found that 30 (27.5%) patients were on typical antipsychotics, 71 (65.1%) patients were on atypical antipsychotics, and eight (7.3%) patients were on both typical and atypical antipsychotics; these results were similar to those obtained in a study by Gilmer *et al.* [38] on 1800 patients, finding that 26.8% were on typical antipsychotics, 58.8% were on atypical antipsychotics, and only 14.5% were on polypharmacy. A study conducted by Gianfrancesco *et al.* [39] showed different results, concluding that 84.7% of patients were on atypical antipsychotics and only 15.3% were on typical antipsychotics. In addition, a study by Valenstein *et al.* [40] on 49 003 patients revealed that 53% received conventional agents and 47% received atypical agents; this difference from our study may be attributed to this study's dependence on data from 1998 to 1999, when atypical use was still to some extent limited in comparison with the current use.

Our study failed to demonstrate differences in compliance between patients taking typical or atypical antipsychotics or both. Our finding was in line with the

findings of Stanković *et al.* [29] and Cabeza *et al.* [41] who showed that the type of antipsychotic medication was not significantly different between compliant and noncompliant patients, and also with the findings of a study by Freudenreich *et al.* [42], who demonstrated no difference in drug attitudes of patients taking first or second generation antipsychotics, including clozapine.

Until now, it is far from conclusive whether adherence with atypical antipsychotics is significantly better than with typical ones [29]. There seems to be a trend toward higher adherence rate with atypical antipsychotics because patients might find these medications' side effect profiles to be more acceptable than the side effect profiles of the older, conventional agents [43,44], which was observed in several studies describing greater treatment adherence in patients taking second-generation versus first-generation antipsychotics [44–48].

There are also studies that do not confirm the previous results [38,40,42,49–51]. Some authors have maintained that subjective response is more likely to be positive with atypical neuroleptics [44]. These discrepancies may be accounted for by differences in methods, including differences in adherence measures, definitions of adherence, specific medications included in the study, frequency of assessments, and treatment settings.

The side effects of antipsychotics, particularly extrapyramidal side effects, may play a major role in determining adherence [52]. Our patients were assessed on possible side effects, 6 months after discharge using three scales: Simpson Angus Scale, BRS, and AIMS. Obtained data showed that only five (4.5%) patients suffered from tardive dyskinesia. This result is in contrast to the European Schizophrenia Outpatient Health Outcomes (SOHO) study, which showed that out of a total of 9298 patients, the prevalence rate of tardive dyskinesia was 9.2% [53]. However, different rates were shown in a study by Woerner *et al.* [54], 20% had tardive dyskinesia in the first year of the study. A study by Bakker *et al.* [55] found higher prevalence of tardive dyskinesia as 55 (28.4%) patients suffered from it. This higher prevalence may be attributed to the nature of the patient sample, which was a representative sample of long-stay patients with chronic severe mental illness. The lower rates of tardive dyskinesia shown in our study are explained by the type of antipsychotic used, as 65% of the patients were using atypical antipsychotics, which are well known to have lower tendency to cause tardive dyskinesia than are typical antipsychotics.

Similarly, the present study revealed a low prevalence of akathisia as only 12 (11%) patients suffered from akathisia, which is in agreement with the study conducted by Bakker *et al.* [55], which concluded that only 8.8–10.4% of their patients suffered from akathisia. In contrast, several studies describe greater rates of akathisia (>30%) in their sample [56,57]. This may be attributed to the fact that our patients could not tolerate akathisia for a long time and usually stopped the drug or sought medical advice.

EPS were the most common motor side effect in our sample as about half (52/109; 52.3%) of the patients suffered EPS at the time of follow-up. These findings were replicated by the study by Bakker *et al.* [55].

In contrast, Abouzaid *et al.* [58] conducted a large-scale study to assess economic burden associated with EPS in a Medicaid population with schizophrenia; a total of 4621 patients were identified, of whom 583 (12.6%) had EPS. In addition, a study by Janno *et al.* [56] found that 23.2% of patients had neuroleptic-induced parkinsonism. The high prevalence of EPS in our sample may be attributed to ethnic variations.

Some authors assume that unwanted medication effects have no influence on compliance [26,42,59,60]. Patients became noncompliant as they experience more side effects however this wasn't the case. This paradoxical phenomenon of fewer side effects in noncompliant patients was explained by Linden *et al.* [12], who reported that compliant patients take more medication and therefore have more side effects, whereas noncompliant patients take their drugs irregularly with a low rate of drug exposure and thus have fewer side effects. Our study showed that motor side effect was significantly associated with poor adherence toward antipsychotic drugs among our patients with schizophrenia in the univariate analysis. This is in agreement with other studies that have found a significant relationship between extrapyramidal side effects and adherence to medication [48,61,62], suggesting that noncompliance is a result of burdensome side effect. However, our results of logistic regression analysis were disappointing as the predictive power of the studied risk factors did not yield any significance that may be partly explained by the small sample size.

We compared patients' weight during admission and 6 months after discharge to measure the gained weight during this period. We found that nonadherent patients had gained about 8 kg; the adherent patients had gained about 5.5 kg, and yet we failed to find significant relation between weight gain and adherence. Our results are in agreement with those of a study by Gray *et al.* [63], which found no significant relation between adherence and medication side effects including weight gain, and are in disagreement with Weiden *et al.* [64], who found no such association and mentioned that obese individuals were more than twice as likely as those with a normal BMI to report missing their medication.

Side effect burdens are often viewed as important reasons for noncompliance [65]; distress due to side effects was associated with nonadherence among patients with schizophrenia. An underestimation of the influence of side effects on compliance will often lead to treatment failures that are erroneously attributed to treatment resistance. Clinicians need to comprehensively assess and monitor side effect profiles of antipsychotic medications regardless of class assignment.

Conclusion and recommendations

We conclude that there is no relation between adherence and type of antipsychotic prescribed; however, experiencing

motor side effects is associated with nonadherence. Females and university educated patients are more adherent to treatment. As the approach to nonadherence has multifaceted aspects, we need to focus on other aspects influencing discontinuation of antipsychotic medication. The effective management of medication side effects is important to maximize drug adherence.

Strength

This study has several unique features and strengths. As far as we know it is one of the few studies in Egypt that explored adherence to antipsychotics among schizophrenia patients. It is a prospective study on patient adherence to antipsychotics treatment in Egyptian schizophrenia patients using a thorough assessment for the predictors of dropouts. It is part of departmental projects exploring different aspects related to medication nonadherence. This part is concerned with drug-related variables.

Limitations

The study was limited by the small sample size, and relatively short follow-up period. Unfortunately, we did not include other medication side effects such as hyperprolactinemia and metabolic syndrome. It was important to assign the duration of illness as a factor; in addition, we did not examine the patients' belief and attitude to medication and the impact of stigma on drug compliance.

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Conflicts of interest

There are no conflicts of interest.

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