Adherence to depot versus oral antipsychotic medication in schizophrenic patients during the long-term therapy

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Abstract

Background/Aim. There is a high rate of schizophrenic patients who do not adhere to their prescribed therapy, despite the implementation of antipsychotic long-acting injections and the introduction of atypical antipsychotics. The aim of this study was to investigate the differences in sociodemographic, clinical and medication adherence variables between the two groups of schizophrenic patients on maintenance therapy with depot antipsychotic flufenazine decanoate and oral antipsychotics only as well as a correlation between the therapy with depot antipsychotic fluphenazine decanoate and the two groups of schizophrenic patients on maintenance therapy.

Methods. A total of 56 patients of both genders, aged < 60 years, with the diagnosis of schizophrenia (F20) (ICD-10, 1992) clinically stable for at least 6 months were introduced in this cross-sectional study. The patients from the depot group (n = 19) were on classical depot antipsychotic flufenazine decanoate administering intramuscularly every 4 weeks (with or without oral antipsychotic augmentation) and the patients from the oral group (n = 37) were on oral therapy alone with classical or atypical antipsychotics, either as monotherapy or combined. The Positive and Negative Syndrome Scale (PANSS) was used to assess symptom severity. Item G12 of the PANSS was used to assess insight into the illness. The patients completed the Medical Adherence Rating Scale (MARS) was used to assess adherence to the therapy. A higher MARS score indicates behavior [Medical Adherence Questionnaire (MAQ subscale)] and attitudes toward medication [Drug Attitude Inventory (DAI subscale)] that are more consistent with treatment adherence. The exclusion criteria were determined. The Pearson’s \( \chi^2 \) test was used to compare categorical variables, Student’s \( t \)-test to compare continuous variables and Pearson’s correlation to test the correlation significance; \( p < 0.05 \).

Results. Significant between-group differences in age, illness duration, chlorpromazine equivalents, PANSS score and DAI subscore were found. Item G12 of the PANSS subscore and MARS score correlated significantly negatively. A significant positive correlation between receiving depot antipsychotic and DAI subscore as well as between illness duration and both DAI subscore and MARS score were also found.

Conclusion. Schizophrenic patients on classical depot antipsychotic maintenance therapy might present subpopulation of patients with significantly longer illness duration, more favorable medication attitude and outcome in relation to those on oral antipsychotics alone.

Key words: schizophrenia; therapeutics; pharmaceutical preparations; antipsychotic agents; drug utilization; delayed-action preparations.

Apstrakt

Uvod/Cilj. Postoji visoka stopa šizofrenih bolesnika koji se ne pridržavaju propisane terapije uprkos primeni antipsihotika u obliku injekcija dugog dejstva i uvodenja atipičnih antipsihotika. Cilj ovog rada bio je da se ispitaju razlike u sociodemografskim, kliničkim i varijablama pridržavanja terapije između dve grupe šizofrenih bolesnika na terapiji održavanja depo antipsihotikom flufenazin-dekanoatu i samo oralnim antipsihoticima, kao i da se utvrdi korelacija između pridržavanja terapije i drugih ispitivanih varijabli.

Method. Ova studija preseka obuhvatala je 56 bolesnika oba pola, starosti < 60 godina sa dijagnostom šizofrenije (F20) (MKB-10, 1992) koji su bili klinički stabilni najmanje šest mjeseci. Bolesnici depo grupe (n = 19) bili su na klasičnom depo antipsihotiku flufenazin-dekanoatu koji se daje intramuskularno na četiri nedelje (sa ili bez oralne augmentacije antipsihotikima), a bolesnici oralne grupe (n = 37) bili su samo na oralnoj terapiji klasičnim ili atipičnim antipsihotikom, bilo kao monoterapija ili u kombinaciji. Skala pozitivnog i negativnog sindroma (PANSS) korišćena je za procenu težinom simptoma. Stavka G12 PANSS korišćena je za procenu uvid u bolest. Skala procene pridržavanja lečenja (MARS) koju popunjava bolesnik, upotrebljena je za procenu pridržavanja...
In the treatment of schizophrenia, adherence is identified as the most important modifiable risk factor. Non-adherence patients have an average risk of relapse that is 3.7 times greater than that of good adherence patients. Medication adherence behavior is a multifactorial phenomenon. Meta-analytical studies on risk factors for non-adherence to medication in patients with schizophrenia showed a consistent influence of certain variables (insight and therapeutic alliance, for example), while study results for other variables such as age, gender, marital status, duration of illness are too inconsistent to let drawing a conclusion regarding their influence on adherence behavior.

Depot formulations (long-acting injections) of classical (first-generation) antipsychotics were introduced in the 1960s to promote medication adherence. The use of classical depot antipsychotics is less frequent in the last decade, perhaps owing to the introduction of oral atypical antipsychotics. A prospective, observational study of the treatment for schizophrenia by Shi et al. found that only 26% of patients were treated with depot formulations of typical antipsychotics at least once during the designated three-year period. Clinicians use long-acting antipsychotic injections to manage fewer than 1 in 5 patients with schizophrenia having episodes of medication non-adherence despite treatment guidelines for schizophrenia recommend that clinicians strongly consider depot therapy for patients who may be non-adherent to atypical antipsychotic treatment regimens.

Depot antipsychotics are unable to prevent relapse completely; even in clinical trials there are 20%–25% of patients who relapse, despite receiving depot. According to a large, prospective, observational study of schizophrenia patients treated in ten European countries, the European Schizophrenia Outpatient Health Outcomes (EU-SOHO), reported that more than 50% of patients who were initiated on classical depot antipsychotics or were switched to them were treated with depot formulations to help address problems of nonadherence, rather than for lack of efficacy or other reasons. Systematic literature reviews of randomized controlled trials and observational studies of classical antipsychotic long-acting injections vs. oral antipsychotics in schizophrenia suggested that classical depot antipsychotics may improve outcome and significantly reduce relapse rate compared with oral antipsychotics.

Over the past decade, a substantial number of patients switched from classical depot antipsychotics to oral atypical antipsychotics. However, one number of patients remains on first-generation depot antipsychotic therapy long term.

The aim of this study was to investigate the differences in sociodemographic, clinical and medication adherence variables between the two groups of schizophrenic patients on maintenance therapy with depot antipsychotic fluphenazine decanoate (group D) and oral antipsychotics only (group O) as well as correlation between the medication adherence and other examined variables.

**Methods**

A cross-sectional assessment of patients with schizophrenia on maintenance treatment was undertaken. The patients recruited for this study were regular on scheduled outpatient visits for depot administration and/or prescription of oral antipsychotic therapy and remained covered by the same doses of antipsychotic drugs that had been applied at least 6 months before inclusion.

The inclusion criteria were that participants of both genders were aged <60 years, fulfilled International Statistical Classification of Diseases and Related Health Problems, 10th Revision 1992 (ICD; World Health Organization) criterion for schizophrenia (F 20), had been clinically stable for 6 months, were currently prescribed either classical depot antipsychotic therapy or oral antipsychotic therapy alone.

The sample consisted of 56 patients. The patients of the depot group (the group D) (n = 19) were receiving fluphenazine decanoate administering intramuscularly every 4 weeks with or without oral antipsychotic augmentation. The patients of the oral group (the group O) (n = 37) were using antipsychotics either as monotherapy or in combination.

The patients were prescribed oral classical antipsychotics (high potency-fluphenazine and low potency-chlorpromazine or levomepromazine) and atypical antipsychotics (risperidone and clozapine). Concomitant non-antipsychotic psychotropic therapy was administered to the patients included antidepressants or/and mood stabilizers to attain better symptom control, as well as anticholinergics for treating of extrapyramidal unwanted effects.

The dosage of each antipsychotic was converted to its chlorpromazine equivalents.
Apart from the registration of both sociodemographic and clinical data from medical records, the Positive and Negative Syndrome Scale (PANSS) \(^{14}\) was performed to assess symptom severity and the patients completing the Medical Adherence Rating Scale (MARS) \(^{15}\) was used to assess adherence to medication.

The exclusion criteria were the following: a history of drug abuse, evidence of organic brain disorder including mental retardation, severe somatic disease.

Oral and written informed consent was obtained from all participants prior to the participation in the study.

The study was conducted at the Outpatient’s Department of Clinic for Psychiatry, Clinical Centre of Serbia, Belgrade, Serbia, from 2008 to February 2011.

**Assessment**

The PANSS \(^{14}\) is a 30-item (7 positive, 7 negative, and 16 general psychopathology symptom items) observer-rated scale. Each item is rated on a severity scale ranging from 1 (absence of psychopathology) to 7 (extremely severe). A possible range of scores on both Positive and Negative psychopathology subscale is 7–49 and on General psychopathology subscale is 16–112. Item G12 of the PANSS (higher scores indicate worse insight into the illness) was used to assess insight into the illness. Higher PANSS scores indicate greater symptoms.

The MARS \(^{15}\) is patient completed scale. It contains 10 questions that require a Yes or No answer and indicates both problematic behaviors with the questions from the Medical Adherence Questionnaire (MAQ) \(^{16}\), a 4-item questionnaire regarding ways in which patients may fail to take their prescribed medication (forgetting, carelessness, stopping the drug when they feel better, and stopping the drug because they believe in makes them feel worse), along with attitudes toward medication, from 6 items based on the Drug Attitude Inventory (DAI) \(^{17}\) regarding taking medication only when being sick, being controlled by medication, clearer thoughts on medication, prevention of getting sick by medication, feeling weird, like a zombie on medication and feeling tired and sluggish on medication. The DAI provide rating of participants’ attitude at the time of assessment; no time frame is specified in the MAQ, which is a potential limitation of the measure.

Higher MARS scores indicate behavior and attitudes that are more consistent with treatment adherence.

The Statistical Package for Social Science (SPSS) for Windows, Version 13.0 was used for the analysis. Comparison of categorical variables of the two study groups was performed using the Pearson's \(\chi^2\) test and comparison of continuous variables was performed using the Student’s \(t\)-test. The Pearson’s correlation was used to test the correlation significance. For all tests, a level of \(p = 0.05\) (two-sided) was considered significant.

**Results**

The sociodemographic and clinical characteristics of the group D and the group O of patients are summarized in Table 1. The patients of the group D were significantly older and had significantly longer illness duration in comparison with the patients of the group O.

Table 1 presents average doses of antipsychotic medications and mean chlorpromazine equivalent doses as well as percentages of patients using concomitant psychotropic medication in the groups D and O. Significantly lower doses of clozapine were prescribed to the patients from the group D and the patients from the same group were treated with significantly higher antipsychotic doses in chlorpromazine equivalents in relation to the patients from the group O. No patient in the group D was treated with risperidone and haloperidol and \(l\) could not be computed.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Depot administration</th>
<th>Oral administration</th>
<th>(\chi^2)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categorical variables</td>
<td>(n = 19)</td>
<td>(n = 37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>9 (47.3)</td>
<td>23 (62.2)</td>
<td>0.599</td>
<td>0.439</td>
</tr>
<tr>
<td>female</td>
<td>10 (52.7)</td>
<td>14 (37.8)</td>
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<td></td>
</tr>
<tr>
<td>Marital status</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>married</td>
<td>2 (10.5)</td>
<td>3 (8.1)</td>
<td>1.077</td>
<td>0.584</td>
</tr>
<tr>
<td>single</td>
<td>15 (79.0)</td>
<td>26 (70.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>divorced / widow</td>
<td>2 (10.5)</td>
<td>8 (21.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live arrangement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>alone</td>
<td>2 (10.5)</td>
<td>3 (8.1)</td>
<td>0.000</td>
<td>1.000</td>
</tr>
<tr>
<td>Work situation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>working</td>
<td>6 (31.6)</td>
<td>8 (21.6)</td>
<td>0.239</td>
<td>0.625</td>
</tr>
<tr>
<td>Continuous variables</td>
<td>(\bar{x})</td>
<td>SD</td>
<td>(\bar{x})</td>
<td>SD</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>44.4</td>
<td>8.0</td>
<td>34.9</td>
<td>8.8</td>
</tr>
<tr>
<td>Years of education</td>
<td>11.7</td>
<td>1.9</td>
<td>12.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Duration of treatment (yrs)</td>
<td>20.2</td>
<td>7.5</td>
<td>10.9</td>
<td>7.5</td>
</tr>
</tbody>
</table>

\(n\) – number of patients, \(\%\) – percentage of patients, \(\bar{x}\) – mean value, SD – standard deviation

The proportion of patients using anticholinergic drugs was significantly higher in the group D of patients in relation to the group O of patients.

The mean total PANSS, insight item G12 of the PANSS, MARS as well as MAQ and DAI subscales of MARS scores were shown in Table 3. Considerably lower mean total PANSS score, Positive, Negative and General psychopathology subscores in the group D of patients in comparison with the group O of patients were found. The average DAI subscale of MARS score was significantly higher in the group D of patients in relation to the group O of patients.

A significant negative correlation between item G12 of the PANSS subscore and MARS score \( (r = -0.326, p = 0.014) \) was found. A significant positive correlation between receiving depot therapy (the group D = 1, the group O = 0) and DAI subscore \( (r = 0.364, p = 0.006) \), as well as between illness duration and both DAI subscore \( (r = 0.483, p = 0.000) \) and MARS score \( (r = 0.313, p = 0.019) \) were also found using the Pearson’s Correlation.

**Discussion**

According to the results obtained in this study, the schizophrenic patients on typical depot antipsychotic maintenance treatment (the group D) had the following significant differences in relation to the schizophrenic patients on oral antipsychotics only (the group O): older age, longer illness duration, lower symptom severity, higher antipsychotic doses and more favorable attitude to treatment. A significant positive correlation between better insight and medication adherence, between receiving depot treatment and attitude toward medication and between illness duration and both attitude toward medication and medication adherence (medium strength of the relationships) were also found.

Fluphenazine decanoate, as maintenance treatment in the group D of patients and haloperidol decanoate were the most frequently used classical depot antipsychotics in the previous decades in our environment, in addition to atypical risperidone long-acting injection. Also, fluphenazine decanoate and haloperidol decanoate are still most available for the greatest number of patients. Second-generation antipsychotics prescription is most frequent in the last decade. For these reasons, significantly older age and longer illness duration of the group D of patients in comparison to the group O of patients, could be expected results.

The majority of patients included in the study were treated with more than one kind of antipsychotic drugs, including concurrent use of oral and depot antipsychotics.

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**Table 2**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Medication</th>
<th>Depot administration (n = 19)</th>
<th>Oral administration (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>( \bar{x} )</td>
<td>SD</td>
</tr>
<tr>
<td>Fluphenazine decanoate</td>
<td>19 (100)</td>
<td>25 mg /4w.</td>
<td>0</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>5 (26.3)</td>
<td>2.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>5 (26.3)</td>
<td>82.4</td>
<td>37.1</td>
</tr>
<tr>
<td>Continuous</td>
<td>Levomepromazine</td>
<td>3 (15.8)</td>
<td>33.3</td>
</tr>
<tr>
<td>Clozapine</td>
<td>3 (15.8)</td>
<td>75.0</td>
<td>0</td>
</tr>
<tr>
<td>Chlorpromazine equivalents</td>
<td>19 (100)</td>
<td>588</td>
<td>194</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>3 (15.8)</td>
<td>(15.7)</td>
<td>2</td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td>5 (26.3)</td>
<td>(26.3)</td>
<td>2</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>7 (36.8)</td>
<td>(36.8)</td>
<td>4</td>
</tr>
</tbody>
</table>

n – number of patients, % – percentage of patients, \( \bar{x} \) – mean dose of the medication (mg/day), SD – standard deviation

**Table 3**

<table>
<thead>
<tr>
<th>Psychometric scales</th>
<th>Depot administration (n = 19)</th>
<th>Oral administration (n = 37)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PANSS (^a)</td>
<td>70.0</td>
<td>14.1</td>
<td>84.6</td>
<td>19.9</td>
</tr>
<tr>
<td>POS (^b)</td>
<td>12.4</td>
<td>3.3</td>
<td>15.2</td>
<td>5.4</td>
</tr>
<tr>
<td>NEG (^c)</td>
<td>22.5</td>
<td>5.3</td>
<td>27.1</td>
<td>6.9</td>
</tr>
<tr>
<td>GEN (^d)</td>
<td>34.9</td>
<td>6.7</td>
<td>42.2</td>
<td>10.2</td>
</tr>
<tr>
<td>G12 item (^e)</td>
<td>2.7</td>
<td>1.1</td>
<td>3.2</td>
<td>1.3</td>
</tr>
<tr>
<td>MARS (^f)</td>
<td>8.5</td>
<td>1.4</td>
<td>7.7</td>
<td>2.4</td>
</tr>
<tr>
<td>MAQ (^g)</td>
<td>3.0</td>
<td>0.7</td>
<td>2.8</td>
<td>1.1</td>
</tr>
<tr>
<td>DAI (^h)</td>
<td>5.2</td>
<td>0.7</td>
<td>4.2</td>
<td>1.3</td>
</tr>
</tbody>
</table>

\(^a\) The Positive and Negative Syndrome Scale; \(^b\) Subscale of positive symptoms from the PANSS (higher scores indicate greater symptoms); \(^c\) Subscale of negative symptoms from the PANSS; \(^d\) Subscale of general psychopathology from the PANSS; \(^e\) Item G12 of the PANSS (insight into the illness) (higher scores indicate worse insight into the illness); \(^f\) The Medical Adherence Rating Scale; \(^g\) Medical Adherence Questionnaire; \(^h\) Drug Attitude Inventory; \( \bar{x} \) – mean score, SD – standard deviation
Prolonged polypharmacy with antipsychotic drugs is prevalent in clinical practice although, according to relevant guidelines, it may be considered only in some cases of treatment-resistant patients. However, it is believed that the use of two or more antipsychotic drugs concomitantly (co-prescribing) optimises symptom control, enables the reduction of positive as well as of negative symptoms and avoids high doses of single drugs, thus reducing potential adverse effects.

The group D of patients had a significantly higher mean chlorpromazine equivalent dose (588 +/- 194) than the group O of patients (373 +/- 384) which is in accordance with the findings from similar study. Prescription of oral antipsychotics (clozapine or low potency neuroleptics when necessary) in the group D of patients influenced the results relating to chlorpromazine equivalent doses in this study. One difficulty in determining the lowest effective maintenance dose for depot antipsychotics is the delay in relapse of symptoms after a dosage reduction because a significant level of drug remains in the tissues for weeks to months after drug discontinuation.

Concomitant medication use in the patients included in our study ranges from 11% to 37% for anticholinergics, 5% to 16% for antidepressants and 5% to 26% for mood stabilizers. Higher percentages of the patients from the group D were treated with both antidepressants and mood stabilizers in relation to the patients from the group O, but the differences were not considerable. The frequency of anticholinergic use as proxy indicator of extrapyramidal side-effects was significantly higher in the group D of patients in comparison with the group O of patients, possibly accounting for a significantly higher dose (chlorpromazine equivalents) prescription in the D group in relation to the group O. The results of Larsen and Gerlach's study regarding the at-tention towards treatment, side-effects, mental state and quality of life of chronic schizophrenic out-patients on maintenance treatment with depot neuroleptics showed that hypoknia and hyperkinesia were the adverse effects least noticed by the patients, but most noticed by the treating physician, while the opposite was the case with psychic side-effects (dullness/tiredness). However, 88% of the patients included in that study who reported no side-effects had at least one. The neglect of this dimension may lead to non-compliance.

A consistent correlation between the presence or severity of side-effects and the degree of adherence could not be found in a systematic review. Although intolerance is a major cause of antipsychotic drug discontinuation in schizophrenia, it often accounts for fewer discontinuations than the lack of efficacy. In a cross-sectional study of Patel et al. on adherence to depot versus oral antipsychotic medication, beliefs and attitudes have been more important than side effects in predicting self-reported adherence and influencing factors thereof.

The findings of our study relating to psychopathology (significantly lower symptom severity of total as well as positive, negative and general psychopathology in the group D of patients in regard to the group O of patients) suggested a more favorable course of the illness of the group D of patients compared with the group O of patients. Several other studies showed that antipsychotic drugs that are administered in a depot injection are associated with lower rates of relapse and hospital admission than medications that are administered orally, because of the greater likelihood that the patient will receive medication. Meta-analytical study of David and Adams showed that depot antipsychotic preparations appear useful in relapse prevention when utilized for patients with difficulties in medication compliance, despite limitations of the analysis. However, data is still limited in this area.

The two groups of patients included in our study did not differ in the level of insight into the illness that was described as a strong predictor of adherence to medication, despite significant differences in symptoms severity. This result points out once again how much is difficult to attain full insight into the disorder in patients with schizophrenia irrespective illness duration, reduction of severity of other symptoms and phase of treatment. However, insight correlated significantly with medication adherence, according to the results of our study. The group D of patients had better insight, but not significantly in relation to the group O of patients and both patients groups had intermediate level of insight. In considering these findings, we should take into account the following: firstly, item G12 of the PANSS (used in this study for assessment of insight into the illness) addresses only to an improvement in understanding illness as well as medication consequences and secondly, the patients included in the study were continuously attending outpatient’s service for depot administration and/or prescription of oral antipsychotic therapy which implies better insight into disorder in regard to those not attending scheduled outpatients visits. We can speculate that the majority of the participants on oral antipsychotics were started and maintained on oral antipsychotics because of their better insight and adherence. However, because of the cross-sectional nature of the study design, it is not possible to ascertain the insight of the participants when they were started on their medication. In addition, patient who uses his/her medication because it improves well-being does not necessarily need to have insight into the disorder. This might explain why Nageotte et al. found that 38% of patients were compliant despite the fact that they did not believe themselves to be ill. Hogan et al. demonstrated that patients’ experience of and adherence to antipsychotic regimens depended on how they felt on medication, rather than what they knew or believed about it.

Medication adherence was taken as continuous variable in our study, having in mind that it is a dynamic phenomenon and could change during a long-term treatment of schizophrenia. The patients on depot antipsychotic therapy had significantly better experience toward medication in comparison with the patients on oral antipsychotic therapy in this study. There are few data examining patient satisfaction or attitudes regarding depot antipsychotics. The meta-analysis of Walburn et al. showed that in 10 out of 12 studies, a positive opinion towards depot antipsychotics was expressed. Five out of six studies that compared depot with oral antipsychotically administered medication, be-
ics showed patient preference for depots, although, patients tended to state a preference for the formulation that they were taking at the time. In a study by Patel et al., the attitudes regarding current formulation were influenced by illness duration, extrapyramidal symptoms and insight but not by formulation (depot vs oral).

Despite considerably better medication attitude of the group D of patients in relation to the group O of patients in this study, the patients on depot therapy had less than a significantly better medication-taking behavior and adherence to the therapy in comparison with the patients on oral maintenance therapy. The patients from both study groups had intermediate level of compliance with medication. The first two questions of the MAQ subscale (assessing medication-taking behavior) of MARS related to unintentional non-compliance, regarding forgetfulness and carelessness (often confusing for patients) might influence the results of the study referring to compliance behavior. However, there are findings showing the lack of correlation between medication attitudes and medication-taking behavior of the patients as well as that patient’s attitudes to medication may be completely different from their actual medication-taking behavior. Having in mind the frequent need for concurrent prescribing of oral medication in patients with schizophrenia on depot antipsychotic therapy, findings regarding medication-taking behavior seem to be important not only for patients on oral therapy alone, but also for the patients receiving depot maintenance therapy.

The findings from this study relating to medication adherence in the patients with schizophrenia on maintenance treatment, obtained by examination of certain variables, show the complexity of this issue. Compliance behavior remains problematic in both the patients receiving classical depot antipsychotics and those using oral antipsychotics only. They are needed prospective longitudinal studies on medication adherence in patients with schizophrenia on depot antipsychotics, from the introduction of depot therapy and the course of the treatment process.

There are several limitations of the present study which included a heterogeneous sample of 56 participants. This number is relatively low (particularly in the group D as a reflection of the lower frequency of the use of classical depot antipsychotics) for analysis of between-group differences. However, between-group differences in some variables which were examined in this study were significant even with this low numbers per group.

The patients included in this study had to be clinically stable for at least six months and to regularly attend outpatient’s service before inclusion. These inclusion criteria probably influenced our results because these patients maybe stressed the importance of factors that positively influenced medication adherence, but data of non-attender’s and non-compliers were hard to obtain.

Both patients groups were mixed regarding the type of antipsychotics which were prescribed (both atypical and typical antipsychotics were prescribed either as monotherapy or in combination in the group O of patients and clozapine or low-potency antipsychotics in one number of patients in the group D). That probably influenced the finding addressing medication attitude, having in mind different profile of adverse effect of typical vs atypical antipsychotics.

The group D included the patients with additional oral medication (antipsychotics or and concomitant non-antipsychotic psychotropic drugs). For these reasons, a significantly better medication attitude of the group D compared to the group O could not address to depot therapy in particular. Further, the group O included the patients who had been either on depot in the past or at least offered them. The views of such patients on depot medication would complete the picture.

Future investigations designed as prospective clinical studies, with larger sample including patients covered by antipsychotic depot monotherapy and subject groups matched by sociodemographic and clinical characteristics could decrease limitations of our study.

**Conclusion**

In comparison with schizophrenic patients on oral maintenance therapy alone, patients on classical depot antipsychotic maintenance treatment were significantly older, had longer illness duration, were treated with higher antipsychotic chlorpromazine equivalents doses, had more often prescribed anticholinergics, had lower severity of psychopathology and more favorable attitude toward medication.

Insight into the disorder and medication adherence, treatment with typical depot antipsychotics and attitude to medication as well as illness duration and both medication adherence and attitude to treatment were significantly correlated.

This study was completed with the idea of applicability in everyday clinical practice, given that classical depot antipsychotics are still frequently used in a population of schizophrenic patients on maintenance therapy in Serbia.

**References**


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