ATTITUDES TOWARD ANTIPSYCHOTIC MEDICATION, INSIGHT AND PSYCHOPATHOLOGY IN OUTPATIENTS WITH SCHIZOPHRENIA

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ABSTRACT

OBJECTIVE: Attitude toward antipsychotic medication is considered as one of the main predictors for medication adherence in schizophrenia. The present non-interventional cross-sectional study aims to explore the associations between attitudes toward antipsychotic medication, insight and other clinical variables in outpatients with schizophrenia.

METHOD: Attitudes toward antipsychotic medication, clinical and social variables, socio-demographic and illness-related characteristics were assessed via a set of semi-structured clinical interviews and self-rating scales in a total of 226 patients with schizophrenia on a long-term antipsychotic treatment in community based settings. The associations between attitudes toward medication and severity of psychopathology, insight and medication side effects were examined.

RESULTS: The greater hospitalization rate in the previous year was associated with more severe psychopathology at the time of the study, more pronounced side effects of the therapy and lack of insight. The lack of insight, the presence of more severe negative and depressive symptoms and disease duration less than 5 years correlated significantly with negative attitudes toward antipsychotic medication. The severity of medication side effects was not associated with the drug attitudes.

CONCLUSION: Psychoeducational and psychotherapeutical interventions, along with pharmacotherapy, can be beneficial in forming positive attitudes toward medication and improving medication adherence in schizophrenia, especially in patients with a short duration of the disease.

Key words: schizophrenia, attitudes, antipsychotic therapy, insight, adherence

INTRODUCTION

Medication non-adherence in schizophrenia results in a substantial increase of relapses and readmissions\(^1\), violence and self-harm\(^2\), poorer outcomes\(^3\) and higher treatment costs\(^4\). Yet, about 50% of the patients with schizophrenia show some kind of non-adherence in the course of therapy.\(^5\)

There is a consensus among researchers about the predictive value of negative attitudes toward medication\(^6,7\), lack of insight\(^6\), substance abuse\(^8\) and cognitive impairments\(^5\) for the non-adherence to antipsychotic therapy, whereas the role of a large number of other variables for the adherence rates in schizophrenia remains controversial.

Despite the importance of the attitudes toward medication for the adherence in schizophrenia, little is known about the associations between attitudes and socio-demographic, illness-related and clinical characteristics of the schizophrenic disorder. This problem has been addressed in a few studies focusing on attitudes toward medication in outpatients with schizophrenia, but they differ in design and methodology.\(^9-12\)

AIM

The present study aims to find the correlations between attitudes toward antipsychotic medication and important characteristics of the individuals with schizophrenia (severity of psychopathology, insight, side effects of the therapy) in order to focus more effectively the interventions for improving adherence in schizophrenia.

MATERIAL AND METHODS

A multi-centered, non-interventional, cross-sectional design was chosen for the study. A total of 226 patients with a diagnosed schizophrenic disorder according to the criteria of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision on a long-term antipsychotic...
treatment in outpatient settings were consecutively recruited when approaching the outpatient services in four major cities in this country (Sofia, Plovdiv, Bourgas and Vratsa). Inclusion criteria were a diagnosis of schizophrenia, age above 18 and a signed informed consent. Exclusion criteria were: first episode of psychosis, date of the last hospitalization less than two months prior to the study, change in type or dose of antipsychotic medication within the previous month and substance abuse.

A set of self-rating scales and clinical interviews was used to assess the attitudes toward medication, psychopathology, insight and side effects of the medication in the sample. A Bulgarian translation and reverse translation of all the instruments but BPRS-E was made by two independent researchers for the purpose of the present study. Prior to the study all of the self-rating scales applied were validated in a pilot sample of 30 Bulgarian outpatients with schizophrenia. Insignificant corrections were made under the supervision of a specialist for the patients’ better understanding of the questions.

Socio-demographic and illness-related data of the studied sample was obtained.

ATTITUDES TOWARD MEDICATION
The Drug Attitude Inventory (DAI-10; Hogan et al, 1983) consists of 10 yes/no statements reflecting patients’ experiences and attitudes about medication. DAI-10 is an abbreviated form of DAI-30 and was developed to assess how the subjective attitude toward antipsychotic medication of people with schizophrenia may affect compliance with treatment. The correlation between the DAI versions was high – 0.94.14

A three-factor structure was found for DAI 10 with intra-class correlation coefficient \( r_{ic} = 0.71 \) and test-retest reliability – 0.92.14 The test-retest reliability of DAI 10 in the pilot sample of the present study was 0.96 (one week interval).

The scale has been widely used in psychiatric practice for almost 30 years. Although DAI is not the optimum for predicting non-adherence, its simple application and the lack of alternatives make it a scale of choice in the studies on drug attitudes and adherence in mentally ill patients.15

INSIGHT
The Schedule for Assessment of Insight (SAI)16 is a semi-structured clinical interview providing an assessment of the three main components of the insight – recognition of illness, realizing the need of treatment and symptom relabelling. Higher total scores indicate better insight. The scale showed significant correlations with other instruments for assessment of insight and severity of psychopathology.17

The factor analysis in the present sample of patients with schizophrenia reveals a three-factor structure of the instrument with Cronbach’s alpha of 0.863 for the first factor, 0.838 for the second factor and 0.592 for the third factor. The inter-rater reliability (kappa) in the pilot sample varied from 0.728 to 0.898 for the subscales and was 0.840 (p < 0.0001) for the scale.

SAI is a reliable, simple and informative instrument for assessment of insight that provides a detailed assessment of particular characteristics of insight, including realizing the need of treatment, what probably modifies the attitudes toward medication.

PSYCHOPATHOLOGY
The expanded version of the Brief Psychiatric Rating Scale (BPRS-E) was applied. BPRS-E is a widely used observer-rated scale consisting of 24 items and is a sensitive and effective measure of psychopathology and treatment related symptom change.

Bulgarian translation and reverse translation of the instrument was made within an international study on the coercion in psychiatry and was applied in a sample of 359 mentally ill inpatients.19

In view of the differences in the literature regarding the factor structure of the scale we conducted a factor analysis that revealed a four-factor structure of BPRS-E with a total percent of explained variance of 48.681. Cronbach’s alpha for the single factors varied from 0.663 to 0.760. The test-retest reliability in the pilot sample was 0.79 for the scale with a range of 0.51 to 0.93 for the single items.

BPRS-E distinguishes reliably between negative and depressive symptoms in patients with schizophrenia which is a priority over other instruments for assessment of psychopathology.20

SIDE EFFECTS
The Liverpool University Narcoleptic Side Effect Rating Scale (LUNSERS021) is a 41-item, 4-point Likert type scale measuring unwanted antipsychotic side effects during the previous month. A higher total score indicates more reported side effects.

Internal consistency of the scale was 0.85 and test-retest reliability – 0.81.21 A ROC-curves analysis demonstrated good distinction between medicated patients and healthy controls with regard to the side effects of the antipsychotic therapy.21

Test-retest reliability in the pilot sample in a one-
week interval was high – 0.86. The study sample of patients with schizophrenia (n = 226) showed significantly higher level of medication side effects compared to the healthy controls without therapy (n = 64) – $t = 7.923; p < 0.001$ (Student’s t-test).

The subjective side effects of the therapy and not the observed ones are essential for the attitudes toward treatment\(^\text{22}\), which, along with the good psychometric characteristics of the instrument, makes it appropriate to the purpose of the present study.

**STATISTICAL ANALYSIS**

Descriptive statistics, statistical variation and correlation analysis (Pearson correlation) as well as t-test and Fisher’s exact test were performed choosing a significance level of $p < 0.05$. The SPSS (version 14.0 for Windows) was used in all cases for statistical analysis.

**RESULTS**

**SAMPLE**

A total of 226 patients with schizophrenia on antipsychotic treatment in outpatient settings were recruited. The socio-demographic characteristics of the sample were quite typical for a population treated for schizophrenia (Table 1).

The mean age of the patients was $42.1 \pm 0.929$ years. Most of them had secondary education, received disability benefits and were single. Mean duration of the illness was $15.7 \pm 0.459$ years, most of the patients received an atypical antipsychotic. Only small proportion of the patients participated in psycho-social rehabilitation programs and more than half of the patients had one or more hospitalizations in the year prior to the study.

**ATTITUDES TOWARD ANTIPSYCHOTIC MEDICATION**

The attitudes toward medication and the subjective effects of the antipsychotic medication in the sample were rather positive (Fig 1).

The mean of the total score of the inventory was $4.20 \pm 0.305$ which implies that patients had rather positive experience with the antipsychotic therapy and positive attitudes toward medication.

### Table 1. Socio-demographic characteristics in the sample (n = 226)

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Male n (%)</th>
<th>Female n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Female</td>
<td>132 (58.4)</td>
<td>132 226 (58.4)</td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>94 (41.6)</td>
<td>94 226 (41.6)</td>
<td></td>
</tr>
<tr>
<td><strong>education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- primary</td>
<td>37 225 (16.4)</td>
<td>37 225 (16.4)</td>
<td></td>
</tr>
<tr>
<td>- secondary</td>
<td>52 225 (39.6)</td>
<td>52 225 (39.6)</td>
<td></td>
</tr>
<tr>
<td>- secondary vocational</td>
<td>45 225 (20.0)</td>
<td>45 225 (20.0)</td>
<td></td>
</tr>
<tr>
<td>- higher</td>
<td>54 225 (24.0)</td>
<td>54 225 (24.0)</td>
<td></td>
</tr>
<tr>
<td><strong>employment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- employed</td>
<td>33 226 (23.5)</td>
<td>33 226 (23.5)</td>
<td></td>
</tr>
<tr>
<td>- unemployed</td>
<td>53 226 (23.5)</td>
<td>53 226 (23.5)</td>
<td></td>
</tr>
<tr>
<td>- receiving disability benefits</td>
<td>124 226 (54.9)</td>
<td>124 226 (54.9)</td>
<td></td>
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<tr>
<td>- old-age pensioner</td>
<td>4 226 (1.8)</td>
<td>4 226 (1.8)</td>
<td></td>
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<tr>
<td>- student studying</td>
<td>8 226 (3.5)</td>
<td>8 226 (3.5)</td>
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<tr>
<td><strong>Marital status</strong></td>
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<tr>
<td>- married cohabiting</td>
<td>40 226 (17.7)</td>
<td>40 226 (17.7)</td>
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<tr>
<td>- single</td>
<td>126 226 (55.8)</td>
<td>126 226 (55.8)</td>
<td></td>
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<tr>
<td>- divorced</td>
<td>47 226 (20.8)</td>
<td>47 226 (20.8)</td>
<td></td>
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<tr>
<td>- widowed</td>
<td>13 226 (5.8)</td>
<td>13 226 (5.8)</td>
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<td><strong>housing</strong></td>
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<tr>
<td>- one’s own</td>
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<td>93 225 (41.3)</td>
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<td>- common property</td>
<td>14 225 (6.2)</td>
<td>14 225 (6.2)</td>
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<td>1 225 (0.4)</td>
<td>1 225 (0.4)</td>
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<td>- supervised home</td>
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<td>- unsettled</td>
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</table>
Attitudes toward Antipsychotic Medication, Insight and Psychopathology in Outpatients with Schizophrenia

Positive total score of the scale showed 78.6% of the patients (0.786 ± 0.027), which predicts high adherence level to the prescribed therapy.

More severe subjective negative effects of antipsychotic medication were reported by patients with short duration of the disorder (up to 5 years) (F = 5.627; P = .019) and more positive attitudes toward medication showed patients with illness duration more than 5 years (F = 6.815; P = .010). Other socio-demographic and illness-related factors did not display significant correlations with the attitudes toward medication.

**INSIGHT**

Mean value of the total score of the scale for assessment of insight was 7.40 ± 0.250 with highest possible score of 14. Patients realized best the need of treatment and had difficulties to recognize the psychotic symptoms as pathological.

Higher illness duration correlated with better insight (F = 7.774; P = .001). The absence of hospitalizations in the previous year together with higher illness duration determined better insight (F = 2.510; P = .043).

**PSYCHOPATHOLOGY**

The severity of the psychopathology in the studied sample was mild to moderate (37.61 ± 0.508). Higher was the positive symptomatology (11.92 ± 0.266) followed by the negative and depressive symptoms (9.94 ± 0.234 and 8.25 ± 0.196 respectively).

More severe depressive symptoms in the studied patients with schizophrenia were associated with female gender (F = 7.617; P = 0.006) and the absence of caregivers (F = 4.003; P = 0.047). The positive symptoms correlated significantly with the number of hospitalizations in the previous year (F = 5.948; P = 0.003).

**SIDE EFFECTS**

The side effects of antipsychotic medication were minimal in the sample (0.874 ± 0.022). Higher side effects were reported on the subscales for extrapyramidal (0.63 ± 0.04), anticholinergic (0.58 ± 0.04) and psychic (lack of concentration, impaired memory, lack of emotions, vivid dreams etc.) side effects – 0.84 ± 0.043.

Two or more hospitalizations in the previous year were associated with more subjective side effects (F = 4.497; P = 0.013). University education together with illness duration less than 5 years determined more subjective side effects (F = 4.689; P = 0.004).

**CORRELATIONS BETWEEN INCLUDED VARIABLES**

Table 2 presents the correlation analysis including attitudes toward antipsychotic medication and studied clinical characteristics.

<table>
<thead>
<tr>
<th>Attitudes toward medication</th>
<th>Psychopathology</th>
<th>Insight</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective positive effects</td>
<td>-.183</td>
<td>.421</td>
<td>.002</td>
</tr>
<tr>
<td>Subjective negative effects</td>
<td>-.128</td>
<td>.210</td>
<td>-.011</td>
</tr>
<tr>
<td>Total score of DAI</td>
<td>-.199</td>
<td>-.104</td>
<td>.343</td>
</tr>
</tbody>
</table>

**Table 2. Correlations between treatment attitudes and studied variables (n = 226)**

Pearsons correlations; p < 0.05; p < 0.01; p < 0.001;

DAI – Drug Attitude Inventory.
scales for depression (r = -.150; P = .028) and negative symptoms (r = -.241; p < 0.001).

The side effects were associated with the subjective negative effects of antipsychotic treatment (r = .343; p < 0.001), but not with the attitudes nor with the total score of the scale.

**DISCUSSION**

The present study explores the attitudes toward antipsychotic medication in outpatients with schizophrenia on a long-term antipsychotic treatment. The adherence behavior issue in schizophrenic patients in the community and the treatment attitudes have not yet been studied in this country, which makes it difficult to compare the findings to the Bulgarian psychiatric practice.

The findings revealed rather positive attitudes toward antipsychotic medication in the studied sample. Shorter illness duration was associated with more negative attitudes toward medication whereas the longer duration of the illness correlated with more positive attitudes toward medication and better insight.

Improvement of insight in the course of the schizophrenic disorder may be due to psychoeducation and forming awareness of illness, whereas patients with short illness duration rarely accept the presence of psychiatric disease and the need of treatment. This could be the explanation of the association found between negative drug attitudes and shorter illness duration in the sample.

The correlations of the attitudes and subjective effects of the antipsychotic therapy with the insight have been reported by other researchers. Presence of insight, ability to recognize the psychotic symptoms and acceptance of the need for treatment are logically related to more positive attitudes and perceived benefits from the treatment.

The presence of mild to moderate psychopathology in the studied outpatients with chronic schizophrenic disorder included positive symptoms (residual symptoms probably), negative and depressive symptoms. The symptoms of depression correlated with the absence of caregivers, which underlines once again the need of social support for individuals with schizophrenia.

A negative correlation was found between the severity of psychopathology and the attitudes toward medication. Although some researchers indicate the positive symptoms as predicting negative attitudes toward medication, our findings are similar to those of another study that reported a correlation between the found deficits (negative symptoms) and the negative attitudes toward medication. Generally, the improvement of the depressive, negative and/or positive symptoms is associated with more positive attitudes of the patient toward antipsychotic treatment. This supports the concept that the perceived benefits of the treatment determine the attitudes toward treatment.

The antipsychotic side effects correlated with the subjective negative effects of the therapy, but not with the global attitudes toward treatment. An explanation of the finding could be the report of Lambert et al. that the attitudes toward medication are more influenced by the perceived benefits from treatment than by the side effects of the therapy.

As pointed out by Velligan et al., the attitudes toward treatment are not equal to a dose taken. The patient may have positive attitudes toward treatment but other factors, e.g. financial difficulties, cognitive impairment, may impede the appropriate medication intake. And vice versa, despite the negative attitudes toward medication, a lot of patients continue with their therapy as prescribed.

Nevertheless, attitudes toward antipsychotic medication have been pointed out as the main predictor for adherence levels in patients with schizophrenia, which underlines the need of interventions aiming to create and support positive treatment attitudes in patients with schizophrenia as non-adherence rates in this patients are high.

On the one hand, creating positive attitudes toward treatment depends on the choice of an appropriate antipsychotic therapy as the balance between perceived benefits and disadvantages from treatment is crucial for the attitudes toward treatment. On the other hand, the positive treatment attitudes in the sample correlated with better insight and less negative and depressive symptoms. Similar results reported Helldin et al., who found that during remission patients with schizophrenia have higher quality of life, better insight and more positive treatment attitudes, as well as drug attitudes (as measured by the Drug attitude inventory DAI).

Along with the pharmacotherapy, these aspects of the schizophrenic disorder (insight, psychopathology) may be improved by psychoeducational and psychotherapeutic interventions (cognitive-behavioural, motivational techniques), which corroborates the importance of the psycho-social rehabilitation for individuals with schizophrenia.

A shortcoming of the present study is the absence of follow-up which could provide information for the stability of treatment attitudes over time and the relevance of the conclusions. Furthermore, we
also examined the correlations between the studied variables, which does not identify the factors determining the attitudes toward medication in patients with schizophrenia.

Nevertheless, present study provides data for the severity of psychopathology, subjective side effects of antipsychotic treatment, insight and attitudes toward treatment, while explaining the correlations between treatment attitudes and the studied clinical variables in a sample of patients with schizophrenia on a long-term antipsychotic treatment in outpatient settings.

CONCLUSIONS

The role of the attitudes toward antipsychotic medication as a predictor for adherence in patients with schizophrenia points out the need of focused interventions for creating positive treatment attitudes. The associations found between attitudes toward treatment, psychopathology and insight imply the possibility of application of psychotherapeutic interventions, along with a careful choice and monitoring of the antipsychotic treatment, for the creation of positive treatment attitudes and enhancement of adherence in schizophrenia. The need of psychosocial rehabilitation for improvement of the outcome in individuals with schizophrenia in the community has been underlined.

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ГОТОВНОСТЬ К АНТИПСИХОТИЧЕСКОЙ ТЕРАПИИ, ИНСАЙТ И ПСИХОПАТОЛОГИЯ СРЕДИ ВНЕБОЛЬНИЧНЫХ ПАЦИЕНТОВ С ШИЗОФРЕНИЕЙ

И. Василева, В. Миланова

РЕЗЮМЕ

ЦЕЛЬ: Готовность к антипсихотической терапии считается одним из основных предикторов для содействия в медикаментозной терапии при шизофрении. Настоящее неинтервенционное многоцентровое кросс-секционное исследование ставит себе целью выяснить взаимосвязи между готовностью к антипсихотической терапии, инсайтом и другими клиническими переменными среди внебольничных пациентов с шизофренией.

МЕТОДЫ: С помощью комплекта полуструктурированных клинических интервью и самооценочных шкал сделаны оценка готовности и субъективного ответа на нейролептическую терапию, оценка различных клинико-социальных характеристик, как и оценка социо-демографических анамнестических данных 226 пациентов с шизофренией. Исследованы зависимости между готовностью к лечению и тяжестью психопатологии, наличие инсайта и наличие побочных эффектов терапии у пациентов, подвергнутых долгосрочной антипсихотической терапии.

РЕЗУЛЬТАТЫ: Более высокое число госпитализированных пациентов за прошедший год связывается с тяжестью психопатологии к моменту исследования, с выраженным побочным эффектом терапии и с ухудшенным инсайтом. Отсутствие инсайта, более тяжелая негативная депрессивная симптоматика и давность заболевания до 5 лет коррелируют с негативной готовностью к антипсихотической терапии. Тяжесть побочных эффектов нейролептиков не показывает корреляцию с готовностью к терапии.

ЗАКЛЮЧЕНИЕ: Психообучающие и психотерапевтические интервенции наряду с фармакотерапией могут быть полезными в целях позитивного отношения к лечению, особенно среди пациентов с небольшой давностью заболевания.