

Attitudes Toward Antipsychotics Among Outpatient Clinic Attendees With Schizophrenia

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Background: A cross-sectional study was conducted in patients with schizophrenia who regularly attended an outpatient clinic to examine the impact of psychopathology, side effects, and sociodemographic factors on attitudes toward antipsychotics.

Method: Sixty patients with a schizophrenic disorder according to ICD-10 criteria who had a duration of illness over 1 year and whose discharge from an inpatient unit had been at least 6 weeks earlier were investigated. Apart from the registration of demographic data, various rating scales were used: the Positive and Negative Syndrome Scale, the St. Hans Rating Scale for Extrapyramidal Syndromes, the Udvalg for Kliniske Undersogelser (UKU) Side Effect Rating Scale, and the Drug Attitude Inventory (DAI).

Results: Generally, the aspects describing a positive attitude toward antipsychotics on the DAI received a higher degree of assent than those characterizing a negative drug attitude. However, employment status correlated with a poorer global medication attitude on the DAI, and positive symptoms and sedation correlated with greater negative feelings on the DAI subjective negative feelings subscale.

Conclusion: Our results suggest that special attention should be paid to patients who experience positive symptoms or sedation and to those with relative absence of symptoms, who are therefore tempted to stop taking medication.

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Antipsychotic drugs have become a mainstay in the treatment of schizophrenia. However, the optimal use of antipsychotics will not depend on the prescribing physicians alone but also on patients' perceptions, such as their understanding of the effects and side effects of the antipsychotic drugs.

Although many patients show good compliance with drug therapy, at least in the short term, up to one third of outpatients are completely noncompliant and another third have been reported to be only partially compliant with medication.¹ These compliance problems result from a number of different factors, which have been reviewed elsewhere.^{1,2}

Many patients experience antipsychotic drugs as unpleasant and something they would prefer to avoid. This leads to noncompliance and relapse, which can worsen the course and prognosis of the disease.³ Further, symptom exacerbations can lead to antipsychotic treatment resistance and development of chronic psychosis.⁴ Recently, Cramer and Rosenheck⁵ reviewed the literature to assess the extent of compliance with medications for schizophrenia and mood disorders in comparison to physical disorders. The overall compliance rate for antipsychotic medication was 58% and therefore lower than that for antidepressants (65%) and for medications treating physical disorders (76%).

A number of factors appear to affect compliance in patients with schizophrenia. These include the degree of global psychopathology,⁶ response to treatment, and side effects.^{2,7–11} Next to other factors, for instance, the complexity of the treatment regimen,^{12,13} the importance of evaluating the patient's perspective has also been emphasized. Barriers to treatment adherence and collaboration may include patients' subjective responses to antipsychotics¹³ and attitudes toward medication.^{10,14–16}

In the current study, we attempted to examine the influence of psychopathology, antipsychotic-induced side effects, and sociodemographic factors on attitudes toward medication among outpatients with schizophrenia. To this end, we investigated patients who regularly attend our schizophrenia outpatient clinic.

METHOD

We performed a cross-sectional study including 60 patients with schizophrenia between the ages of 19 and 60 years from our specialized outpatient clinic. All subjects had a duration of illness of over 1 year and had been discharged from an inpatient unit at least 6 weeks earlier. The diagnostic criteria of a schizophrenic disorder according to ICD-10, which were applied clinically without using a formal instrument, served as a basis for study inclusion after patients had consented in writing. Apart from the registration of demographic data, various rating scales were utilized: psychopathology was rated by means of the Positive and Negative Syndrome Scale (PANSS),¹⁷ and, to quantify side effects, the St. Hans Rating Scale for Extrapyramidal Syndromes¹⁸ and the Udvalg for Kliniske Undersogelser (UKU) Side Effect Rating Scale¹⁹ were used. The St. Hans Rating Scale for Extrapyramidal Syndromes consists of 4 subscales: an akathisia subscale, a dystonia subscale, a parkinsonian subscale, and a dyskinesia subscale. Each item is scored from 0 to 6. The UKU comprises a total of 48 symptoms, arranged into 4 groups: psychic, neurologic, autonomic, and other side effects. Each symptom is scored on a severity scale from 0 to 3, and the rater assesses whether the report is best attributed to a side effect (rated as unlikely, dubious, or probable) or related to the disease. For the purpose of subsequent statistical analysis, patients with a score of 2 or higher on any item of the St. Hans scale or a score of 1 or higher on any UKU item were considered side effect "cases."

The patients' subjective response to antipsychotics and their attitudes toward medication were assessed by means of the Drug Attitude Inventory (DAI),¹⁴ a self-report questionnaire consisting of statements about the perceived effects and benefits of antipsychotics with which the patient can agree or disagree. It is divided into 7 factors: (1) *subjective positive feelings* related to antipsychotics (e.g., feeling happier), (2) *subjective negative feelings* attributed to the drugs (e.g., feeling tired and sluggish), (3) *health/illness-dependent drug intake*: patients' model of health (e.g., believing it is unnatural to take medication), (4) patients' *confidence in physician* (e.g., believing it is up to the doctor when one stops taking medication), (5) *control*: patients' attitude toward the locus of control in taking medication (e.g., feeling pressured to ingest medication), (6) *prevention*: patients' belief in the effect of antipsychotics in forestalling relapse (e.g., antipsychotics can prevent one's getting sick), and (7) *harm*: patients' concerns with potential toxic effects (e.g., believing medication is a slow-acting poison). Each item of the DAI is scored as 1 or 2, depending on whether the answer selected by the patient indicates a negative or positive view of medication.

The ratings of psychopathology and side effects were performed by the treating physician, while the DAI was rated by an independent rater.

Statistical Analysis

The subscales of the PANSS and the DAI were computed according to the instructions of the developers. In addition, the raw subscores of the DAI were converted to a range from 0 to 100 by linear transformation. Descriptive summary statistics for the total sample were calculated for sociodemographic and clinical patient characteristics, psychopathology (PANSS), drug attitude (DAI), and anti-psychotic-induced side effects (St. Hans scale, UKU). Potential relations of drug attitude (DAI) with patient characteristics, psychopathology, and side effects were studied using multiple linear regression analysis, with DAI subscales as the dependent variable. To reduce the number of dependent variables tested, the total set of 7 DAI subscales was condensed to 3: positive feelings and effects (including the original subscales 1, 4, and 6), negative feelings and effects (including the subscales 2, 5, and 7), and health/illness-dependent drug intake (consisting of the original subscale 3). This grouping of subscales was verified by a factor analysis of the 7 original subscales resulting in 2 factors (54% explained variance), one comprising the first group of subscales and the other comprising the second group of subscales, while the last subscale loaded on both factors.

The linear regression consisted of a 2-step procedure to reduce the number of independent variables considered in an individual analysis. In a first step, only patient characteristics (trait variables) were used as independent variables: age, sex, duration of illness, marital status, and employment (including sheltered work with at least 20 hours/week). Statistically significant variables were selected by stepwise backward variable elimination. In a second step, the statistically significant variables of the first step plus the PANSS subscales and side effects (St. Hans scale, UKU) were entered as independent variables. The same variable selection procedure as above was used. Side effects considered were akathisia, parkinsonism, dyskinesias, sedation, depression, weight gain, diminished sexual desire, other sexual dysfunctions, and hypersalivation.

RESULTS

The demographic characteristics of the study sample are summarized in Table 1. The majority of patients were male, and their mean age was 34 years with a mean duration of illness of approximately 9 years. Regarding psychopathology (PANSS), patients had relatively few positive symptoms and low-to-moderate negative symptoms. One quarter (N = 15) of the patients were treated with traditional antipsychotics, the other 75% (N = 45), with second-generation drugs.

The most frequently reported antipsychotic-induced side effects (St. Hans scale, UKU) included depression (43% [N = 26]), sedation (42% [N = 25]), hypersalivation (42% [N = 25]), parkinsonism (38% [N = 23]); conven-

Table 1. Patient Characteristics^a

| Characteristic | Value |
|--|---------------|
| Patients, N | 60 |
| Age, mean ± SD, y | 34.1 ± 10.2 |
| Sex, %, F/M | 18/82 |
| Duration of illness, mean ± SD, y | 9.2 ± 9.4 |
| Time since discharge, mean ± SD, y | 23.6 ± 40.2 |
| Psychopathology score, mean ± SD | |
| PANSS positive subscore | 10.3 ± 3.4 |
| PANSS negative subscore | 14.9 ± 6.5 |
| PANSS total score | 50.5 ± 14.2 |
| Antipsychotic treatment, N (%) | |
| Traditional antipsychotics | 15 (25) |
| Second-generation antipsychotics | 45 (75) |
| Daily dose, mean ± SD, mg | |
| Traditional antipsychotics (CPZ equivalents) | 359.6 ± 227.0 |
| Risperidone | 3.8 ± 1.4 |
| Sertindole | 8.0 |
| Olanzapine | 11.0 ± 4.6 |
| Clozapine | 286.4 ± 101.4 |
| Zotepine | 225.0 ± 35.4 |
| Housing, N (%) | |
| Lives with original family | 25 (42) |
| Lives with own family | 7 (12) |
| Lives alone | 17 (28) |
| Lives in a small group home | 8 (13) |
| Other | 3 (5) |
| Marital status, N (%) | |
| Single | 43 (72) |
| Married/stable partnership | 13 (22) |
| Divorced/separated | 4 (7) |

^aAbbreviations: CPZ = chlorpromazine, PANSS = Positive and Negative Syndrome Scale.

tional antipsychotics: 53% [8/15], novel: 33% [15/45]), weight gain (37% [N = 22]; conventional antipsychotics: 13% [2/15], novel: 44% [20/45]), diminished sexual desire (30% [N = 18]), and sexual dysfunctions (25% [N = 15]). Mild-to-moderate akathisia was assessed in 22% (N = 13) of the patients, and dyskinesia, in 12% (N = 7). As expected, there was a higher incidence of extrapyramidal side effects in the group treated with conventional antipsychotics, while weight gain was considerably more frequent in subjects treated with novel antipsychotics. Because of the small number of patients treated with conventional antipsychotics in this sample, no significance tests were performed.

Table 2 shows an overview of the patients' attitudes toward antipsychotic medication, as assessed by means of the 30-item version of the DAI. Generally, the subscales describing positive aspects of antipsychotics (positive feelings and effects, prevention, confidence in physician) received much higher scores and thus a higher degree of assent than subscales characterizing negative aspects of medication, thereby giving indications of compliance problems (negative feelings and effects, harm, control, health/illness-dependent drug intake). However, 1 of the latter group of subscales obtained higher scores than the other components of this category: approximately one third of the patients indicated health/illness-dependent drug use.

Table 2. Drug Attitude Inventory (DAI) Scores (N = 60)^a

| Subscale | Mean | SD | Proportion of Patients With a Score Above 50 | |
|--|------|------|--|------|
| | | | N | % |
| (I) Subjective positive feelings | 69.8 | 31.5 | 41 | 68.3 |
| (II) Subjective negative feelings | 27.8 | 25.8 | 6 | 10.0 |
| (III) Health/illness-dependent drug intake | 38.3 | 35.2 | 20 | 33.3 |
| (IV) Confidence in physician | 88.1 | 28.4 | 50 | 83.3 |
| (V) Control | 7.5 | 20.2 | 1 | 1.7 |
| (VI) Prevention | 91.7 | 26.3 | 54 | 90.0 |
| (VII) Harm | 20.0 | 20.8 | 4 | 6.7 |
| Total score (most positive attitude = 100, most negative attitude = 0) | 82.9 | 14.1 | 56 | 93.3 |

^aRaw subscores of the DAI were converted to a range of 0 (no agreement) to 100 (total agreement) by linear transformation.

Table 3. Effect of Sociodemographic Variables, Clinical Variables, and Antipsychotic-Induced Side Effects on Drug Attitude (multiple linear regression analysis)^a

| DAI Subscales (dependent variable) | Independent Variables ^b | Direction of Effect ^c | β (SE) | p Value ^d |
|--|------------------------------------|----------------------------------|-------------|----------------------|
| Positive feelings and attitudes ^e | Employment | ↓ | -13.1 (6.6) | .054 |
| Negative feelings and attitudes ^f | PANSS positive symptoms | ↑ | 1.5 (0.7) | .022 |
| | Sedation | ↑ | 15.8 (4.8) | .002 |
| | Dyskinesia | ↓ | -13.3 (7.3) | .073 |
| Health/illness-dependent drug intake | Duration of illness | ↓ | -1.2 (0.5) | .012 |
| | Akathisia | ↓ | -12.9 (6.5) | .051 |
| | Sedation | ↑ | 20.0 (9.0) | .030 |
| Total score | Employment | ↓ | -11.7 (4.2) | .008 |

^aAbbreviations: DAI = Drug Attitude Inventory, PANSS = Positive and Negative Syndrome Scale.

^bAll variables except for duration of illness and PANSS score are dichotomous, with coding of 0 = no, 1 = yes.

^cArrows indicate whether higher values of independent variables are associated with higher (↑) or lower (↓) DAI scores.

^dParentheses around p values indicate statistical nonsignificance.

^eComprises the DAI subscales subjective positive feelings, prevention, and confidence in physician.

^fComprises the DAI subscales subjective negative feelings, control, and harm.

The effects of sociodemographic characteristics, psychopathology, and antipsychotic-induced side effects on drug attitude were analyzed by multiple linear regression. The results are summarized in Table 3. None of the independent variables studied had a statistically significant effect (p < .05) on positive feelings and attitudes regarding antipsychotics. There was, however, a trend toward a significant association with employment status (p = .054): subjects in a regular or sheltered work setting had less positive feelings toward their medication than unemployed patients.

Negative feelings and attitudes toward antipsychotics were increased by positive symptoms (p = .022) and by the side effect sedation (p = .002) and were possibly reduced, at a trend level, by dyskinesia (p = .073).

The attitude that medication is needless as long as they feel asymptomatic (the subscale health/illness-dependent

drug intake) was more common in patients experiencing sedation as a side effect ($p = .03$) but less frequent (trend level, $p = .051$) in patients suffering from motor akathisia. Moreover, health/illness-dependent drug intake behavior decreased with increasing duration of illness ($p = .012$). The DAI total score, measuring attitudes toward medication in general, was significantly lower in employed patients ($p = .008$).

Type of antipsychotic medication (conventional vs. second-generation antipsychotics) did not show a significant effect on any of the drug attitude variables in the linear regression. In a univariate analysis, patients treated with conventional antipsychotics even showed a slightly more positive attitude toward their medication than patients treated with novel antipsychotics ($p = .058$ for DAI total score, *t* test; no statistical significance for any of the subscores).

DISCUSSION

Since antipsychotic maintenance treatment in the relapse prevention of schizophrenia is generally accepted,²⁰ medication compliance has become a focus of increasing concern. Apart from a possible lack of insight into the disease,²¹ a limited understanding of the effects and side effects of antipsychotic drugs may contribute to reduced compliance.²²

Generally, drug compliance in patients with schizophrenia has been reported to be predicted by the patients' subjective responses to and attitudes toward antipsychotics.^{10,14-16} Hence, we were interested in documenting the impact of psychopathology, antipsychotic-induced side effects, and sociodemographic and illness-related factors on attitudes toward medication. We chose to study regular attendees of a specialized outpatient clinic. The advantage of this approach is that it targets exactly the group of patients one is interested in when evaluating the long-term management of patients with schizophrenia. On the other hand, selecting a sample in this way clearly limits the generalizability of the collected data, since early noncompliers, who usually stop attending outpatient clinics, are not included. However, as PANSS scores and sociodemographic factors show, this was a patient group with some residual symptoms living in a stable social environment. Therefore, we believe that our sample is comparable with stable outpatients treated in similar outpatient settings in other countries.

The most frequently observed side effects in our sample were similar to those previously reported by Weiden et al.²³ Sedation was the only one that adversely affected attitudes toward medication. Patients experiencing this side effect tended to stop taking medication when feeling asymptomatic. Corresponding to the findings of other researchers,^{5,24} positive symptoms were also associated with negative attitudes toward antipsychotics. If our finding is

confirmed, we hypothesize that sedation may contribute to irregular drug ingestion, which in turn leads to an increased degree of psychopathology and secondarily to a decreased awareness of the disease. Consequently, a deceptive subjective feeling of well-being may reduce a patient's subjective need to rely on medication. However, in our sample, the health/illness-dependent drug intake decreased with increasing duration of illness, which may be the result of an increase of insight into the illness over time. This result emphasizes the necessity to actively inform and educate patients about the course of the illness.

Regarding extrapyramidal side effects, dyskinesia correlated with less negative feelings on the DAI subjective negative feelings subscale. This finding may be caused by the higher likelihood of tardive dyskinesia in treatment-compliant patients. On the other hand, tardive dyskinesia has been reported to be subjectively less distressing for patients than other extrapyramidal side effects.²¹ Since akathisia influenced DAI scores only at a trend level, the discrepancy of this finding with other published evidence^{8,25,26} will not be discussed further. We were not able to find any further correlation between extrapyramidal side effects and drug attitude, as described by others.^{25,27} Since second-generation antipsychotics are less likely to lead to extrapyramidal symptoms,²⁸ this result may be related to the frequent use of these drugs (75%) in our patients. We found no relationship between other side effects—such as sexual dysfunctions or weight gain, which have been proposed to be related to poor compliance²⁹—and attitude toward antipsychotics. This may be interpreted as an effect of the intensive care provided in our specialized outpatient clinic, which allows staff to attend to side effects quickly and to actively elicit and respond to patients' concerns. On the other hand, the fact that extrapyramidal side effects and other side effects played a relatively small role in the drug attitudes of our patients may also be a reflection of sample selection, as outlined above. Apart from this, there have been a number of reports^{1,16,30-33} that have failed to confirm associations between side effects and noncompliance or negative subjective responses to drug treatment. As discussed previously, this may be due to the fact that discussions about adverse effects can improve the doctor-patient relationship, thereby indirectly enhancing compliance.³⁴

Regarding a possible connection between sociodemographic factors and drug attitude, we found an association between employment and negative feelings toward medication. This is in agreement with the report of Gaebel and Pietzcker.²⁸ We hypothesize that patients who are working feel better and may be more likely to stop medication because of relative absence of symptoms.

Regarding the type of antipsychotic medication (conventional vs. second-generation), no association with the patients' drug attitude was observed in the present study. However, these results were derived from a post hoc

analysis, since the present study was not designed to investigate such an effect.

In general, the majority of our patient sample indicated having a positive attitude toward their medication. If DAI scores, as suggested by the authors of the instrument,¹⁴ represent an indirect indicator for compliance, we can deduce that two thirds of our patients have satisfactory compliance, since only 33% reported taking medication only when ill. This level of compliance may be viewed as unusually high, as it has been suggested that up to 60% of patients with schizophrenia are noncompliant.^{35,36} The absence of an objective measure of actual compliance may be seen as a weakness of this investigation, although the evaluation of compliance was not the main focus of this study. The variability in levels of compliance between different studies is very likely determined by selection processes in the patient populations assessed. The sample investigated in this study consisted of clinically stable patients who regularly attended an outpatient clinic.

Since attitudes toward psychotropics may not only differ between individuals but may also vary over time, we emphasize the importance of closely monitoring the defining features of attitudes, which include side effects and employment status, to prevent potential compliance problems. Additionally, it is important to keep in mind that patients who feel very healthy also represent a high-risk group in terms of noncompliance and warrant extra caution.

Drug names: chlorpromazine (Thorazine and others), clozapine (Clozaril and others), olanzapine (Zyprexa), risperidone (Risperdal).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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