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Non-compliance with Antipsychotic Medication and Symptom Profiles in Schizophrenia

Zack Zdenek Cernovsky[1,*], Lamidi Kola Oyewumi[2, *], Harold Merskey[1], Larry Craig Litman[1]

[1]Department of Psychiatry, University of Western Ontario (Also Known as Western University), London, Canada
[2]Department of Psychiatry, Department of Biomedical and Molecular Sciences, and Department of Psychology, Queen's University, Kingston, Canada

Email address

zcernovs@uwo.ca (Z. Z. Cernovsky), oyewumik@queensu.ca (L. K. Oyewumi)

[*]Corresponding author

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Abstract: This article presents analyses of de-identified archival data on the incidence of noncompliance with antipsychotic medication in a sample of 104 patients with schizophrenia (average age 38.2 years, SD=9.9; 41 men, 63 women). Statistical calculations were performed to determine the correlates of episodes of noncompliance leading to a relapse and re-hospitalization within one year of treatment. The data set included 87 symptoms relevant for studies of schizophrenia as well as numerous socio-demographic variables and data on the patient's history of illness. Noncompliance was associated with symptoms of autism (r=.32, p=.001), widespread delusions (r=.25, p=.01), persistent persecutory delusions (r=.28, p=.004), and a relatively poor premorbid adjustment (r=.33, p=.001). The adjusted R^2 from a multiple regression suggested that the four variables accounted for 18% of variance in our noncompliance data.

Keywords: Schizophrenia, Noncompliance, Autism, Delusions

1. Introduction

As stated by Koulayev's team in 2017, the failure of patients to regularly take medication as prescribed by the physician remains an unsolved and economically expensive problem for healthcare systems around the world [1]. It is a particularly serious problem in the patients with schizophrenia. Almost all patients not treated with any form of antipsychotic medication usually relapse within three years [2]. Various reasons are given by the patients with schizophrenia to justify their medication noncompliance. For example, patients may cite the side effects of their medications such as reduced motor speed, weight gain, indigestion, dysphoria, and reduced creativity. According to the study published in 2018 by Geretsegger, Pichler, Gimpl et al. [3], the risk of partial adherence or non-adherence is to be expected in two-thirds of patients with schizophrenia.

A Canadian study of noncompliance by Ruscher, De Wit, and Mazmanian [4] reported that 65.8% of 148 psychiatric patients had changed the way they took their medication (such as the dosage or timing) without discussing it with their psychiatrist and 47.3% reported that at some time in the past they had stopped taking their medication without talking to their psychiatrist. While some schizophrenic patients in that study praised the positive effects of medication such as anxiety reduction, control of psychotic symptoms, and increase in energy, some complained about muscular problems, or dryness in the mouth, or "feeling slowed down." Ruscher's team [4] found that patients with elementary education significantly less often changed their medication regimen than patients with secondary or postsecondary education. Those who previously discontinued their medication were significantly more often inpatients than outpatients at the time of the study. The number of previous admissions, length of hospitalization, sex, age, and marital status were not correlated to noncompliance with medication. A study on very large samples published in 2016 by Czobor, Van Dorn, Citrome, at al. [5] showed that reduced adherence to pharmacological treatment was associated with substance use (p=0.0003), higher levels of hostility (p=0.0002), and impaired insight (p<0.0001).

The cases of noncompliance followed by re-hospitalization are of special clinical importance. For this reason, the present study evaluated clinical and sociodemographic correlates of noncompliance followed by re-hospitalizations within one year. The purpose of this exploratory analysis was to search for variables associated with noncompliance that could serve as clinical risk markers. In particular, the aim of this study was to examine if noncompliance is associated with highly specific symptom profile patterns within the schizophrenia spectrum or with certain socio-demographic variables. Similar large scale computerized studies involving hundreds of relevant variables as potential predictors were made possible by the pioneering work of Johan Landmark, a Canadian psychiatrist of Norwegian origin, by means of his Manual for Diagnosing Schizophrenia [6].

2. Materials and Methods

This study was based on de-identified archival data that consists of ratings of 87 symptoms for diagnosing schizophrenia and data on numerous socio-demographic variables. The data were compiled by Johan Landmark and included coded information on noncompliance with psychiatric medications [6]. The present study was carried out on 104 of Canadian patients (41 men, 63 women) for whom compliance data were available and who, at the time, met the DSM-III diagnostic criteria for schizophrenia. Their age ranged from 20 to 65 years (average of 38.2 years, SD=9.9). The data included only patients stabilized on fluphenazine.

Noncompliance was defined as not taking the prescribed antipsychotic drugs, as reported by patients themselves, their relatives, or medical staff. In particular, the statistical analyses dealt with noncompliance that resulted in a relapse and re-hospitalization within one year. The incidence of this phenomenon was quantified as follows: no known episode (score = 1), one known episode (score = 2), two known past episodes (score = 3), and more than two such episodes (score = 4).

The following socio-demographic and clinical data were also included in the analysis: age, gender, marital status, educational level, number of own children, number of different addresses in the last 5 years, number of siblings, history of alcohol abuse, history of drug abuse, age at first hospitalization, type of onset (acute versus insidious), total number of months spent in psychiatric hospitals, and ratings of premorbid adjustment (good=1, fair=2, marginal=3, poor=4). Included were also the data on the present occupation, highest occupational position ever held, and the father's highest occupational position. In each of these three variables, the occupational status was coded as in Hollingshead and Redlich [7]. The data were analysed with the SPSS.

3. Results

In the analyses of data, episodes of noncompliance followed by re-hospitalizations within one year were found in 31.7% of the patients (i.e., 33 of 104). Most patients in this subgroup (18 of 33, or 17.3% of the 104 patients) were known to have had only one such episode, five (i.e., 4.8%) had two, and 10 (i.e., 9.6%) had more than 3 such episodes.

Subsequent analyses evaluated the Pearson correlations of the key variable (frequency of noncompliance followed by re-hospitalization within one year) to the 87 symptoms relevant for the diagnosis of schizophrenia, and to sociodemographic variables. The criterion of significance was set to .01, 2-tailed.

The episodes of noncompliance were not significantly related to any of the social and demographic variables except for the ratings of premorbid adjustment ($r=.33$, $p=.001$): more compliant patients had better premorbid ratings. Only 3 symptoms (of the list of 87) were correlated with noncompliance: autism ($r=.32$, $p=.001$), widespread delusions ($r=.25$, $p=.01$), and persistent persecutory delusions ($r=.28$, $p=.004$). In the present study, schizophrenic “autism” was defined as a detachment from reality and a predominance of inner life, ranging from simple but clinically pathological distractibility to a complete stuporous state, with a tendency to cut off socioemotional contact with the environment [6]. The patient may consider his fantasies as the only real world and may view the reality as perceived by the mainstream of the society as an illusion (see Landmark [6]).

The widespread delusions included those of grandeur (involving fame, fortune, unusual skills or achievements), somatic delusions, those of persecution as well as those consisting in inappropriate explanations for daily experiences, thoughts, or behaviours (e.g, hypnotism, telepathy). Some of these involved a feeling that own behaviour, will, emotions, or thoughts were manipulated, influenced, obstructed, or interfered with in strange ways by others via X-rays, radar, or psychic forces, see pages 36 to 39 in Landmark [6]. Persistent persecutory delusion were those of longstanding nature and focussing around the concept of being harmed, grossly mistreated or at an imminent risk of being harmed or mistreated.

The subsequent statistical procedure included all four potential predictor variables (autism, premorbid adjustment, widespread delusions, and persistent persecutory delusions) in a multivariate analysis, calculating the regression equation for noncompliance. The multiple correlation coefficient (R) was .47 ($p<.001$). The adjusted R^2 suggested that these four variables accounted for 18% of variance in the noncompliance data. The variables "persistent persecutory delusion" and "widespread delusions" contributed very little to the equation after the other two predictors were included. When only the premorbid adjustment and autism were included, the Multiple R was .41 ($p<.001$) and the adjusted R^2 suggested that 15% of variance was accounted for. The contribution of these two remaining independent variables was significant ($p<.01$, 2-tailed).

4. Discussion

It appears from these statistical results that patients retrospectively identified as noncompliant with a subsequent relapse requiring re-hospitalization were preponderantly those suffering from symptoms of autism, a less good premorbid adjustment, and widespread or persecutory delusions. Poor premorbid adjustment is suggestive of difficulties in following rules, such as those about medication. Poor adaptation to the treatment regimen might be a part of the overall syndrome. Widespread delusional beliefs and particularly those of persecutory nature are clinically often assumed to be involved in medication noncompliance in psychiatric outpatients. With respect to the correlation of non-compliance with autism, it is noteworthy that some clinicians held autism to be the central problem in schizophrenia (see Stroemgren [8]). As implied by the definition of autism used in the present study, the autistic patient may disregard external events, including medical recommendations about the medication, as an unimportant intrusion. The multivariate analyses carried out in the present study suggest that autism combined with poor premorbid adjustment may be potentially the most important markers for evaluating the risk of noncompliance with subsequent re-hospitalizations. Ideally, future studies should use a more exact noncompliance measurement such as the number of days of not taking the medication.

Surprisingly, the present study did not replicate the finding by Ruscher's team [4] of more frequent noncompliance in patients with more extensive education. In previous statistical calculations by Cernovsky, Landmark, and Helmes [9] of the relationship between educational level and noncompliance, these two were clearly uncorrelated (Pearson r=.00), perhaps because the focus was on cases of noncompliance followed by a re-hospitalization. Although better educated patients probably indeed more frequently change their medication without discussing it with their psychiatrists (72% of those with secondary and 65.6% with postsecondary education, but only 16.7% of those with elementary education, see data in Ruscher et al. [4]), this tendency is not reflected in re-hospitalizations (correlation of .00 to educational level in our study). The present study also failed to replicate the finding by Czobor et al. [5] which isolated substance abuse, high level of hostility, and impaired insight as potential predictors of non-adherence to treatment.

These discrepancies in results highlight the potential practical advantages and disadvantages of the particular definition of noncompliance as used in the present study, for applied clinical research.

The major limitation of the present study is its reliance on reports of noncompliance by patients, their relatives, or by medical staff. Studies which use plasma levels as measures of nonadherence to pharmacotherapy are likely to provide more precise results, see the publication in 2018 by Geretsegger, et al. [3].

5. Conclusions

In this sample of 104 patients, noncompliance with medication was associated with symptoms of autism, poor premorbid adjustment, widespread delusions, and persistent persecutory delusions. Patients with poor premorbid adjustment and autism may be those at the highest risk for noncompliance with prescribed medication.

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Conflict of Interest Statement

The authors declare that they have no competing interests.

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