

Odnos pacientov s shizofrenijo do antipsihotične terapije

Attitude of patients with schizophrenia towards antipsychotic therapy

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Izvleček

Namen: Zdravnikom vseh medicinskih strok, predvsem v psihiatrični, je dobro znano, da pacienti ne jemljejo zdravil na način, kot so jim bila predpisana. Pri shizofreniji, ki je večinoma kronična bolezen, ima sodelovanje v zdravljenju velik pomen v doseganju in vzdrževanju klinične remisije. Odnos do zdravil lahko napove sodelovanje v zdravljenju in je prepoznan kot napovedni dejavnik v zdravljenju shizofrenije.

Metode: V našo observacijsko raziskavo je bilo vključenih 55 pacientov s shizofrenijo ali shizoafektivno motnjo po kriterijih Mednarodne klasifikacije bolezni 10, ki so prejeli peroralne antipsihotike (N=25) ali depo (v obliki mesečnih injekcij) antipsihotike (N=30). Za primerjavo subjektivnega odnosa do zdravil med obema skupinama je bila uporabljena lestvica Odnos do zdravil–30 (Drug Attitude Invento-

Abstract

Purpose: The failure to take medication as prescribed is a vexing problem for clinicians in all specialties, but especially in psychiatry. Schizophrenia is a chronic illness, so treatment adherence has a major influence on achieving and maintaining clinical remission. The patient's attitude towards medication may predict adherence and is a major prognostic factor. We compared the attitudes toward antipsychotic medication in two treatment groups, schizophrenia patients receiving daily oral antipsychotics and those receiving monthly depot injections.

Methods: Our study included 55 patients with schizophrenia or schizoaffective disorder as determined by the International Classification of Disease 10 (ICD 10). Patients receiving either daily oral antipsychotics (N=25) or monthly depot injections

ry–30 oz. DAI–30). Socialno, zaposlitveno in medosebno funkcioniranje pacientov je bilo primerjano s pomočjo lestvice Globalna ocena funkcioniranja (Global Assessment of Functioning – GAF).

Rezultati: Med pacienti, ki so prejeli peroralne antipsihotike in tistimi, ki so prejeli antipsihotike v depo obliki, ni bilo statistično pomembnih razlik glede celokupnega števila točk na DAI–30 ($p=0.146$). Globalni odnos do zdravljenja je bil v obeh skupinah pozitiven. Med obema skupinama ni bilo statistično pomembne povezave med celokupnim številom točk na DAI–30 in vsakodnevnim funkcioniranjem ($p=0.299$). S faktorsko analizo smo dobili pozitivni in negativni faktor odnosa do zdravljenja.

Zaključek: Ocena odnosa do zdravljenja je pomemben dejavnik v oceni sodelovanja v zdravljenju pacientov s shizofrenijo. Boljše razumevanje pacientovega sprejemanja zdravljenja in njegovega subjektivnega odgovora je potrebno zato, da lahko celoviteje obravnavamo terapevtske komponente, ki so pomembne pri posameznikih s shizofrenijo.

($N=30$) completed the Drug Attitude Inventory–30 (DAI–30) to compare subjective attitudes towards medication. Attitudes toward medication were also compared against social, occupational, and interpersonal functioning as determined by the Global Assessment of Functioning scale (GAF).

Results: There was no statistically significant difference in total DAI–30 score between the patients taking oral antipsychotics and those receiving monthly depot injections ($p=0.146$). General attitudes towards antipsychotic medication were positive in both patient groups. There was no statistically significant co–relation between the DAI–30 total score and everyday functioning between groups ($p=0.299$).

Conclusion: The attitude towards medication is an important factor in treatment compliance in patients with schizophrenia. Attitudes were positive and did not depend on dosing method, indicating that choice of treatment should be based on clinical efficacy as neither dosing method was associated with a greater risk of noncompliance.

INTRODUCTION

Schizophrenia is a chronic illness that requires long-term treatment. Adherence to the prescribed antipsychotic therapy is a crucial factor for a successful treatment outcome. Adherence issues can severely limit the clinical improvement that is achievable even with the best treatment available (1). There is no evidence that the situation has improved over the last 30 years despite the use of new antipsychotics with better tolerability. Patients who fail to take their medication as prescribed are at a greatly increased risk of relapse (2). The prevention of relapse remains a major public health challenge, and improvements in this area can have a great impact on morbidity, mortality, quality of life, and on health care costs (3).

Rather than being idiosyncratic and unpredictable, the decision to take medication can be viewed as a rational decision made by weighing perceived benefits

against adverse effects (4). The patients' perception of benefits would follow from awareness of the illness and therapeutic benefits as gauged by personal experiences of clinical improvement, residual symptoms, and noxious side effects (2). Disadvantages of medication include side effects, stigma, cost, and inconveniences associated with having to take psychiatric medication (5). Some patients with schizophrenia report experiencing subjective sensations of change after only a few doses of antipsychotics. They often complain about not feeling like themselves or feeling like “zombies”, about not being able to “think straight”, or being limited in terms of activity. These complaints are not always specifically related to antipsychotic drugs. The phenomenon has received various names, including pharmacogenic depression, subjective dysphoric response, neuroleptic dysphoria, and neuroleptic depression (6). The best term

is “subjective response” as it denotes subjective interpretation of physiological changes following the administration of medication (7).

The drug attitude construct could be regarded as a convenient proxy measure of the risk–benefit decision and as a possible predictor of medication adherence (4). Although the impact of subjective response on treatment adherence has been emphasized, both subjective response and attitude towards medication have been shown to have prognostic value and are linked with treatment response, quality of life, drug abuse, and suicide (6, 8). In many cases, the attitude and insight of family members and others regarding the treatment of the mental disorder also significantly influence patients' adherence.

As with any subjective response, measuring attitude is not an easy task (1). One of the best validated scales to measure general attitudes of psychiatric patients toward medication is the Drug Attitude Inventory (DAI) (9). The predictive value of DAI is supported by several clinical studies that evaluated the relationship between patient attitude or subjective response and treatment adherence, mainly in patients receiving first or second generation antipsychotics (4, 10, 11).

The main objective of our study was to compare attitudes of patients with schizophrenia treated with oral antipsychotics versus patients receiving depot antipsychotics. We expected to find that patients receiving oral antipsychotics would exhibit a more positive drug attitude because this method of administration is not linked with the negative perceptions connected with injections and lack of choice.

MATERIAL AND METHODS

The patients were recruited from an outpatient clinic during their regular monthly check-ups at the University Clinical Centre Maribor, Department of Psychiatry, and at the University Psychiatric Hospital, Ljubljana, Slovenia between October and December 2009. The primary inclusion criterion was at least two months clinically stabilized schizophrenia or schizoa-

ffective disorder according to the International Classification of Disease 10 (ICD 10) (12). Patients whose medical history included substance dependency were excluded. Finally, written informed consent was obtained from 55 patients (31 males and 24 females) of 68 eligible candidates. Thirty patients (13 males and 17 females) were receiving injections of depot antipsychotics and 26 patients (11 males and 14 females) were taking oral antipsychotics. The study was approved by the Slovenian Ethics Committee for Research in Medicine.

Drug attitude was assessed with the 30-item Drug Attitude Inventory (DAI) (9). The DAI is an inventory comprised of 30 self-report items measuring a wide range of attitudes and beliefs about psychotropic medication. The scale has a predictive value for non-adherence and covers six categories: subjective positive, subjective negative, health and illness, physician control, prevention, and harm. These items are presented as self-report statements with which a patient either agrees (scored as +1) or disagrees (scored as -1). The final score is the algebraic sum of positive and negative points. A positive total score means positive subjective response and a negative total score means a negative subjective response. The DAI-30 has been shown to have test-retest reliability, high internal consistency, and both discriminative and predictive validity (13).

The Global Assessment of Functioning (GAF) scale is used to assess psychological, social, and occupational functioning during the course of the mental disorder (14). Limitations caused by physical or environmental factors are excluded. Patient function was rated from 1 to 100, where the highest scores indicate excellent functioning in a broad spectrum of activities and an ability to completely master everyday challenges without symptoms, while the lowest scores imply a constant danger of severely injuring oneself or others, or a persistent inability to maintain minimal personal hygiene. In the American classification DSM IV (Diagnostic and Statistical Manual of Mental Disorders IV), GAF is included in the assessment of a mental disorder (14).

Multivariate analysis (MANOVA) was used to detect differences between the two samples and factor analysis (Varimax) was used for variable reduction. The data were computed using the computer package SPSS, Version 12.0 for Windows.

RESULTS

Both treatment groups had similar demographic and clinical characteristics (Table 1). No statistically significant differences were found between patients receiving depot antipsychotics and those receiving oral antipsychotics with respect to age, educational background, duration of illness, number of previous hospitalizations, employment status, and body weight. Although more female patients were included, the distribution between the two groups was balanced (oral group, 54% female; injection group, 56 % female; $p=0.961$). The majority of patients in

both groups (91%) had been diagnosed with paranoid schizophrenia.

Attitude towards medication was measured using the DAI-30 scale. Patients in both groups had an overall positive attitude towards antipsychotic treatment. Patients receiving depot antipsychotics had a mean DAI-30 total score of 12.7 (SD=11.8), and those receiving oral antipsychotics had a mean DAI-30 total score of 16.7 (SD=7.7); there were no statistically significant differences in total DAI-30 scores between both groups [$F(1,53)=2.17$; $p=0.146$]. Statistically significant differences were found on only three items: DAI-2 [$F(1,53)=6.72$; $p=0.012$], DAI-8 [$F(1,53)=5.77$; $p=0.019$], and DAI-23 [$F(1,53)=4.29$; $p=0.043$]. Patients receiving oral antipsychotics had a more positive attitude towards medication on item DAI-2 (“for me, the good things about medication outweigh the bad”), and were more convinced that

Table 1. Demographic and clinical characteristics of schizophrenia outpatients receiving either depot or oral formulations of antipsychotics.

Variable	Depot antipsychotics N=30	Oral antipsychotics N=25	p value
Gender (male:female)	13:17	11:14	0.961
Age (years)	49.3 ± 10.1	44.2 ± 14.3	0.129
Education (years)	11.2 ± 4.0	11.9 ± 2.6	0.419
Duration of illness (months)	233.9 ± 117.6	187 ± 138.6	0.181
Number of hospitalizations	5.6 ± 4.8	5.9 ± 6.5	0.885
Type of antipsychotic			
First generation	24	3	0.027
Second generation	6	22	
Subtype of schizophrenia			
Paranoid	29	21	
Undifferentiated	0	3	
Residual	1	1	
Body weight (kg)	79.0 ± 13.8	81.7 ± 16.6	0.504
Employment status			
Retired	26	19	0.158
Employed	4	4	
Student	0	2	
DAI-30 total sum Mean ± SD	12.7 ± 11.8	16.7 ± 7.7	0.146
GAF total sum Mean ± SD	69.9 ± 6.9	69.7 ± 10.2	0.949

taking medication was their own free choice (DAI-8), whereas patients receiving depot antipsychotics were more convinced that taking medication would prevent them from having a breakdown (DAI-23).

Patients treated with depot antipsychotics had an average GAF total score of 69.9 (SD=6.9) and those treated with oral antipsychotics scored 69.7 (SD=10.2). There were no statistically significant differences between the groups in overall functioning according to GAF [$F(1,53)=0.004$; $p=0.949$]. No statistically significant correlations were found between total DAI-30 scores and total GAF scores [$Rao(2,52)=1.24$; $p=0.299$].

With Varimax rotation, the factors of subjective positive attitude towards medication and factors of subjective negative attitude were revealed (Table 2). A 2-factor solution was extracted as parsimonious. Items assessing negative attitudes and expectations towards medication comprised Factor 1 (statements 3, 16, 25, 28) and items assessing positive attitude and expectations towards medication comprised Factor 2 (statements 6, 9, 15, 18, 21, 26). The third factor was non-specific.

DISCUSSION

The Drug Attitude Inventory (DAI), a self-report test with high reproducibility and predictive validity, was used to assess the attitudes toward antipsychotic treatment of patients taking daily oral therapy and those receiving depot injections. Our initial premise was that oral antipsychotics would lead to a more positive drug attitude due to the negative connotations of injection and perceived lost of control. This is particularly surprising since these patients were receiving mostly second-generation oral antipsychotics with better tolerability profiles, while depot antipsychotics belonged mostly to the group of first-generation antipsychotics. Nevertheless, our results confirm the findings of other studies that did not find a difference in attitude between patients treated with first-generation versus those treated with second-generation antipsychotics (11, 15, 16). These data suggest that treatment choices should be made on the basis of efficacy. Indeed, as this test is a predictive indicator for noncompliance, these data suggest that noncompliance is not a major consideration in dosing choice.

Comparative data documenting different attitudes towards oral and depot formulations are lacking. Jae-

Table 2. Factor analysis (factor loading) for the DAI-30 items.

Item number	Item content	Factor 1 (negative)	Factor 2 (positive)
DAI-3	I feel strange, "doped up", on medication.	0.797	
DAI-16	I can't concentrate on anything when I am taking medication.	0.751	
DAI-25	Things that I could do easily are much more difficult when I am on medication.	0.703	
DAI-28	I can't relax on medication.	0.712	
DAI-6	I am more aware of what I am doing, of what is going on around me, when I am on medication.		0.720
DAI-9	Medication makes me feel more relaxed.		0.786
DAI-15	I get along better with people when I am on medication.		0.703
DAI-18	I feel more normal on medication.		0.777
DAI-21	My thoughts are clearer on medication.		0.706
DAI-26	I am happier and feel better when I am taking medication.		0.814

ger and Rossler (2010) were the first to directly compare the psychiatrists', patients', and relatives' attitude towards depot antipsychotics in the same study (3). One of their main findings was that, in general, patients had a more negative attitude towards depot injections than psychiatrists and relatives. However, other studies found that patients generally had positive attitudes towards depot antipsychotics (17, 18). Historically, long-acting depot formulations were reserved for more chronically ill patients with a clear history or high risk of non-adherence (1). In our study this was not the case since we found no differences in the duration of illness or in the number of hospitalizations between patients receiving oral or depot antipsychotics. Some studies now suggest that depot antipsychotics should play a greater role in the early course of the illness, including first-episode patients (19). There is still inadequate attention paid to strategies that may enhance acceptance and adherence to medication, including the more extensive use of depot antipsychotic administration (20). Nevertheless, there are many psychiatrists who support the advantages of depot antipsychotics but do not consider them to be advantageous over oral formulations (3). In clinical practice, only 20 % to 35 % of patients are offered antipsychotic depot treatment, despite the fact that a considerable number of patients would accept a depot drug as a long-term treatment option (3, 10, 20).

In our study, better overall functioning was not predictive of better drug attitude in any patient group; the results of other studies support our findings (4, 15). The average GAF score is an objective evaluation of clinical course and social functioning as assessed by the clinician. Average scores were nearly equal in both groups, and in the good to high range. This finding suggests that patients in our study had mild symptoms and only modest difficulties in social, occupational, and educational functioning but were otherwise functioning well and capable of maintaining meaningful interpersonal relationships (14). Drug attitudes in both groups were generally positive, in general agreement with several previous

studies (4, 21, 22). Since positive drug attitude was predominant in both groups, we suggest that better functioning might lead to a more positive perception of medication.

Factor analysis of the DAI-30 identified two uncorrelated factors; the first one tapped into the perception that medication has negative effects and unpleasant symptoms ("feeling strange", "doped up", "unable to concentrate", "doing things with difficulties", "not being able to relax"), and the second into the perception that medication is helpful ("better awareness of the surroundings", "feeling more normal", "better communication with others", "having clearer thoughts", "feeling much better and happier"). Studies using the shorter version of the inventory (DAI-10) have described a similar factor structure (4, 15). Factor analysis supports the hypothesis of Freudenreich and colleagues (2004) that drug attitude is not a continuum from negative to positive; rather, they are two clearly defined dimensions of drug attitude (4).

Studies that employ convenience sampling have certain limitations. Our findings cannot be generalized beyond the sample of stable, well-functioning outpatients with schizophrenia. Fine differences in patient symptomology were not taken into account. For example, the dominant dimensions (positive, negative, or cognitive) were not assessed, although almost all patients were diagnosed as paranoid schizophrenics. Similarly the antipsychotic side effects, especially extrapyramidal effects so common to first generation antipsychotics, were not assessed by validated rating scales of motor functioning. Some of the symptoms of schizophrenia, especially cognitive impairment, disorganization, and the presence of suspicions and hostility, may negatively influence a patient's willingness to comply with treatment (23). Our survey did not probe deeply into these factors so the possibility of bias remains. Antipsychotic side effects could also influence noncompliance and reluctance to accept treatment of schizophrenia, and the DAI focuses on general aspects of medication benefits and drawbacks, not on noxious responses to specific medications. Indeed, the

medicinal regime was not factored into the analysis because of the sample size. All these issues require a large patient sample.

CONCLUSION

Treatment adherence of patients with schizophrenia is difficult to measure in clinical practice so we test whether the DAI could detect potential non-adherence, particularly when medication is not outright rejected. Relapse-prevention strategies should include drug attitude assessments to choose the most appropriate medication and other comprehensive approaches

for improving treatment adherence of patients with schizophrenia. The DAI-30, or the shorter and simpler DAI-10, may be used for assessing patients' attitude and subjective responses as a means of strengthening therapeutic compliance. We suggest that, in functional outpatients, clinical efficacy rather than the risk of non-compliance should be the primary factor in deciding between oral therapy and depot injections.

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