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Treatment adherence and self-stigma in patients with depressive disorder in remission – A cross-sectional study

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Abstract

OBJECTIVE: A wide range of variables may influence the rate of adherence to treatment. These variables can be associated with the disease itself, method of treatment, patient's personality, environmental factors and therapeutic relationship. Self-stigma is one of the possible factors related to poor adherence. The aim of the study was to find out the relationship between current adherence, discontinuation of medication in the past and self-stigma in stable psychiatric outpatients diagnosed with depressive disorder.

METHODS: The study included 72 stable outpatients diagnosed with depressive disorder with a mean age of 49.00 ± 12.56. Disorder severity was assessed using the Clinical Global Impression scale. Adherence was measured by the Drug Attitude Inventory – 10 items (DAI-10) scale and self-stigma by the Internalized Stigma of Mental Illness (ISMI) scale. The data were evaluated in 66 patients. Six patients were excluded because of incompletely filled in questionnaires.

RESULTS: The rate of adherence was not associated with gender, education, employment, family burden (family history) or partner status. Current adherence did not differ between patients who arbitrarily discontinued their medication in the past and those who did not. Adherence was significantly positively correlated with patient's age, age at disease onset and the level of self-stigma.

CONCLUSIONS: The study results suggest that the level of self-stigma and age of the patient can be very important factors associated with adherence in patients with depressive disorder.

ORIGINAL ARTICLE

INTRODUCTION

Treatment adherence is one of the main factors affecting the success of treatment and, consequently, also the quality of life and social adaptation of the patients (Gilmer *et al.* 2004). It is defined as the rate at which patients adhere to treatment recommendations and rules associated with treatment (Bulloch & Patten 2010). Partial or complete non-adherence is associated with worse clinical outcomes including a greater use of emergency care, more hospitalizations and suicides (Vermeire *et al.* 2001). A wide range of variables may influence the level of adherence. These variables can be associated with the disease itself (diagnosis, severity of symptoms and cognitive deficits). Possible factors related to the treatment are adverse effects of medication, overall comfort in therapy, effectiveness of the treatment itself, therapeutic relationship, etc. Influences associated with patient personality may include personality characteristic of the patient, possible self-stigma, rate of hope or prejudices against the disease and its treatment. Environmental factors like negative attitudes of relatives to the disease and treatment, stigmatization or insufficient social support may also interfere with the level of adherence (Sirey *et al.* 2001; Fung *et al.* 2008; Prasko *et al.* 2011; Ustündağ & Kesebir 2013; Latalova *et al.* 2013; Latalova *et al.* 2014; Ociskova *et al.* 2014).

Attitudes of patients to medication can be evaluated by the Drug Attitude Inventory (DAI). Based on the questionnaire results it is possible to predict non-adherence and future drug discontinuation (Brook *et al.* 2003; Tay 2007).

Self-stigma is a gradual process during which a person uncritically adopts the negative evaluation of him/her by society that can disparage the individual (Livingston & Boyd 2010). Self-stigma and fear from stigmatization are associated with lower adherence to medical procedures (Sirey *et al.* 2001; Padurariu *et al.* 2011). Patients who adopt the prejudices about psychiatric patients as their own believe less in the improvement of their mental state, are more depressive and have more negative self-evaluation (Yen *et al.* 2005). Efforts to avoid the labeling lead to denial of the disorder, postponing or avoiding the treatment. It could be the most significant barrier in the way of help (Barney *et al.* 2009).

The aim of the study was to investigate the association between current adherence, discontinuation of medication in the past and self-stigma in stable psychiatric outpatients diagnosed with depressive disorder.

METHODS

The study was offered to all patients diagnosed with depressive disorder who came to medical examination at the psychiatric outpatient clinic in the period from July 1 to September 30, 2013 and who met the following criteria: (a) diagnosis of recurrent depressive disorder based on the criteria of ICD-10 (1992), (b) willingness to fill in certain scales, (c) signed informed consent, (d) age between 18 and 75 years, and (e) compensated psychiatric disorder (the patient is able to attend outpatient appointments, his/her mental condition has not changed in the long term, may not be hospitalized).

Certain patients were not included in the study or excluded (diagnosed with mental retardation, organic mental disorder, bipolar disorder, psychotic disorder or severe physical illness, having acute impairment of their mental state requiring hospitalization, or needing more/changed medication or psychotherapeutic crisis intervention). The patients attended outpatient medical check-ups and were treated with standard medication used for the depression diagnostic group in accordance with the recommended approach.

A brief description of the assessment tools

- **Internalized Stigma of Mental Illness (ISMI) scale** consists of 29 items that assess five domains of internalized stigma. These include feelings of alienation and exclusion from society, the degree of consent with the stereotypes about people with mental illness, perception of how other people treat the individual since he/she was diagnosed with a certain disorder, the rate of withdrawal from society, and the degree of resistance to the stigma. The Czech version of the scale was standardized by Ociskova *et al.* (2014 in press).
- **Drug Attitude Inventory (DAI-10)** was designed to assess patients' attitude to medication (Hogan *et al.* 1983). The patient marks each statement as true or false. The statements are about effects of medication, its necessity and voluntariness of its use. It is used to assess the current level of adherence.
- **Clinical Global Impression (CGI) scale** is used for global assessment of the severity of psychopathology (Guy 1976). The first evaluation is performed by the patient's psychologist or psychiatrist using the objective form of the scale CGI. The patient also evaluates himself/herself by the subjective version of CGI, which includes seven levels of severity of the psychopathology.
- **Demographic questionnaire** contains basic information such as gender, age, employment status, pension status, education, age of disease onset, duration of attendance at the outpatient clinic, number of hospitalizations, time since the last hospitalization, number of visited psychiatrists, current medication, discontinuation of medication in the past (recommended by a psychiatrist or arbitrarily).

Statistical analysis

The statistical packages Prism3 and SPSS 17 were used for statistical analysis. Demographic data and mean total scores of the particular scales were assessed using

descriptive statistics. Means, medians, standard deviations, and distribution of data were defined. The means were compared by the t-test. The relationships between particular categories were analyzed using correlation coefficients and linear regression. The relationship between alternative variables (gender, marital status, discontinuation of medication) was verified by the Fisher test.

Backward stepwise regression was used to analyze the significance of the correlations of the particular factors. The 5% level of significance was considered to be acceptable for all statistical tests.

Ethics

The study was approved by the local ethics committee. The research was conducted in accordance with the latest version of the Helsinki Declaration and standards of Good Clinical Practice (GCP) (EMEA 2002). The patients signed informed consent.

RESULTS

Sample description

Seventy-two patients were willing to complete the questionnaire. All of them participated in the study. Detailed analysis was performed on data from 66 patients who completed all the questionnaires. Demographic and clinical data of the sample are shown in Table 1.

Adherence and discontinuation of medication in the whole sample in association with demographic and clinical variables

Current adherence and discontinuation of medication in the past and their correlation with qualitative demographic and clinical variables

There were no statistical differences in current adherence to treatment (assessed by DAI-10) and frequency of admitted discontinuation of medication in the past

Tab. 1. Demographic and clinical data of the whole sample of patients

Variables	Whole sample (n=72)	Patients who filled in all the questionnaires (n=66)
Age	49.00±12.56	48.69±12.93
Age of disease onset	39.22±15.77	38.95±15.46
Gender (M: F)	37 : 35	33 : 32
Family psychiatric burden: no burden / psychiatric disorder / depressive disorder	41 / 17 / 14	37 / 16 / 12
Education: vocational training / secondary school / university	31 / 24 / 17	28 / 21 / 16
Employed / Unemployed	38 / 34	33 / 32
No pension / full disability pension / partial disability pension/ old age pension	31 / 13 / 14 / 14	27 / 12 / 12 / 14
Marital status: single / married / divorced / widowed	17 / 37 / 14 / 4	14 / 36 / 12 / 3
Without a partner / with a partner	26 / 46	22 / 43
Number of psychiatric hospitalizations	2.16±2.40	2.22±2.38
Number of outpatient psychiatrists during treatment	1.96±1.44	2.00±1.49
Objective CGI – severity	3.15±1.53	3.17±1.55
Subjective CGI – severity	3.49±1.70	3.57±1.73
Antidepressants: average dose adjusted to a daily dose of paroxetine	47.52±25.09 mg (n=71)	46.89±26.06 (n=63)
Anxiolytics: average dose adjusted to a daily dose of diazepam	7.21±6.18 mg (n=12)	8.25±5.01 (n=10)
Antipsychotics: average dose adjusted to a daily dose of risperidone	2.38±2.50 mg (n=21)	2.04±1.61 (n=20)
Mood stabilizers: average dose adjusted to a daily dose of lamotrigine	220.5±96.71 mg (n=11)	208.3±82.92 (n=9)
Adherence to medication	5.27±4.07	5.05±3.99
Arbitrary discontinuation of medication in the past	38.9%	39.4%
ISMI – total score	62.83±13.33	62.69±13.38
Alienation	13.20±3.74	13.17±3.77
Stereotype Endorsement	13.76±3.55	13.71±3.55
Discrimination Experience	9.55±2.91	9.52±2.92
Social Withdrawal	12.58±3.70	12.54±3.72
Stigma Resistance	13.76±2.49	13.75±2.51

Tab. 2. Adherence and discontinuation of medication in correlation with a hereditary psychiatric burden, gender, partner status and discontinuation of medication.

Variable	Adherence to treatment	Statistics – comparison of groups with each other	Frequency of discontinuation of medication in the past	Statistics – comparison of groups with each other
Males (n=33) Females (n=32)	5.46±4.25	Mann-Whitney test; U=446.5; n.s.	36.4% 43.8%	Fisher test: n.s.
No heredity (n=37) With heredity (n=28)	5.30±3.98 4.71±4.05	unpaired t-test; t=0.5809 df=63; n.s.	37.8% 42.9%	Fisher test: n.s.
Education Vocational training (n=28) Secondary school (n=21) University (n=16)	 5.50±3.34 5.05±4.67 4.25±4.19	one-way analysis of variance: F=0.4927 df=64; n.s.	 35.7% 33.3% 56.3%	chi-square, df=2.364, 2: n.s.
Employed (n=32) Unemployed (n=33)	4.313±4.00 5.76±3.90	unpaired t-test: t=1.475 df=63; n.s.	43.8% 36.4%	Fisher test: n.s.
With a partner (n=43) Without a partner (n=22)	5.35±3.64 4.46±4.62	unpaired t-test: t=0.8541 df=63; n.s.	44.1% 31.8%	Fisher test: n.s.
No discontinuation of drugs (n=39) Discontinuation of drugs (n=26)	5.13±4.10 4.92±3.89	unpaired t-test: t=0.2017 df=63; n.s.		

Tab. 3. Correlations of the DAI-10 results with demographic and clinical data (Spearman's r and their statistical significance).

Variable	Correlation with adherence
Age	**0.4225** $p<0.0005$
Age of disease onset	**0.2826** $p<0.05$
Number of psychiatric hospitalizations	- 0.1105 n.s.
Number of outpatient psychiatrists	- 0.0359 n.s
Objective CGI-S	- 0.0884 n.s
Subjective CGI-S	- 0.2305 n.s.
Adjusted dose of antidepressants (n=63)	- 0.0619 n.s
Adjusted dose of mood stabilizers (n=9)	0.06793 n.s.
Adjusted dose of antipsychotics (n=20)	0.2023 n.s
Adjusted dose of anxiolytics (n=10)	0.5433 n.s
ISMI – total score (n=66)	- **0.3608** $p<0.005$
Alienation	**- 0.3616** $p<0.005$
Stereotype Endorsement	- 0.2463 $p<0.05$
Discrimination Experience	- 0.2154 n.s
Social Withdrawal	**- 0.2864** $p<0.05$
Stigma Resistance	**- 0.3209** $p<0.01$

n.s. = non significant

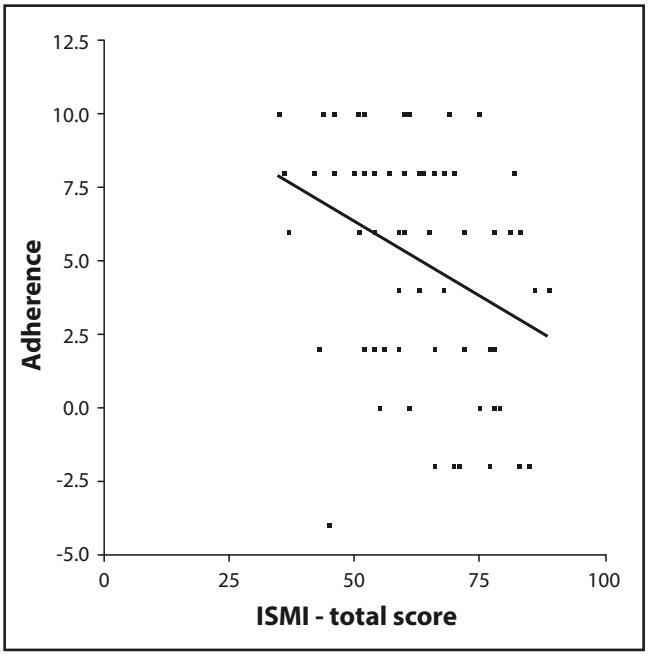

Fig. 1. Linear regression between the total ISMI score and adherence. Linear regression F=8.371, DFn 1000, DFd 63.00; $p<0.01$

between groups divided by gender, heredity, level of education, partnership or (no) discontinuation of medication in the past. Table 2 shows adherence and discontinuation of medication with respect to the hereditary psychiatric burden, gender, partner status and discontinuation of medication in the past.

Adherence and its correlations with quantitative demographic and clinical data

Current adherence to treatment assessed by the Drug Attitude Inventory (DAI-10) was significantly positively correlated with patient age and age of disease onset. Although it did not correlate with the number of hospitalizations, overall severity of disease (objectively or subjectively assessed), number of outpatient psychiatrists visited by patients and doses of medication. The DAI-10 results correlated with demographic and clinical data are shown in Table 3.

The relationship between adherence and self-stigma

The total score of self-stigma was significantly negatively correlated with current adherence to the treatment (Table 3). The greater was the degree of self-stigma in the patient, the lower was his/her adherence to the

treatment (Figure 1). Adherence correlated negatively with Alienation, Social Withdrawal and Stigma Resistance (ISMI subscores). Linear regression between the ISMI total score and adherence is shown in Figure 1.

If the rate of adherence to stepwise regression analysis was defined as the dependent variable (measured by DAI-10) and independent variables were the age, age of disease onset and total ISMI score, these three variables explain 28.2% of the variance in adherence. In the next step, the patient age and total ISMI score were detected as two independent factors. If the age increases by one year, the DAI-10 score increases by 0.131 points. If the total ISMI score increases by 1 point, the adherence decreases by 0.089 points.

Discontinuation of medication in the past

Patients who admitted discontinuation of medication in the past did not differ in the age or age of disease onset from patients who had not discontinue medication by their choice (Table 4). These groups also did not differ in the gender ratio, education, partner status, family burden or disease severity. The comparison of patients who discontinued or did not discontinue drugs in the past is shown in Table 4.

The rate of self-stigma, current adherence to treatment and discontinuation of medication in the past

When comparing the degree of self-stigma (assessed by the ISMI) between patients who had discontinued medication in the past and those who had not there was no significant difference between the groups (Table 4). There was also no significant difference in adherence among patients who had previously discontinued medication and those who had not.

Adherence, self-stigma and comorbidity with personality disorders

Twenty-seven patients (41.5%) were diagnosed with personality disorder (PD). There were 4 patients with dependent PD, 4 with avoidant PD, 3 with anancastic PD, 2 with borderline PD, 3 with histrionic PD, 2 with narcissistic PD, 2 with depressive PD, 1 with paranoid PD, 1 with schizoid PD and 5 with mixed PD. Patients with personality disorder had significantly lower

Tab. 4. Comparison of patients who discontinued or did not discontinue drugs in the past.

Variable	No discontinuation of medication in the past (n=39)	Discontinuation of medication in the past (n=26)	Statistical comparison
Age	48.23±13.19	49.38±12.77	unpaired t-test; t=0.3499 df=63; n.s.
Age of disease onset	38.59±15.59	39.50±15.55	unpaired t-test: t=0.2308 df=63; n.s.
Gender M : F	21 : 18	12 : 14	Fisher test: n.s.
Family burden yes : no	16 : 23	12 : 14	Fisher test: n.s.
Education: vocational training / secondary school / university	18 / 14 / 7	10 / 7 / 9	chi-square, 2.364, 2: n.s.
Employed / Unemployed	18 /21	14 / 12	Fisher test: n.s.
Lives with / without a partner	24 / 15	19 / 7	Fisher test: n.s.
Objective CGI – severity	3.44±1.52	2.77±1.53	unpaired t-test: t=1.728 df=63: n.s.
Subjective CGI – severity	3.87±1.66	3.12±1.77	unpaired t-test: t=1.753 df=63; n.s.
Adherence to medication	5.13±4.10	4.92±3.89	Mann-Whitney test: U=485.5; n.s.
ISMI – total score	63.62±13.65	61.31±13.12	unpaired t-test: t=0.6783 df=63; n.s.

Tab. 5. Comparison of patients without personality disorder with those with personality disorder.

Variable	Without personality disorder (n=38)	With personality disorder (n=27)	Statistical comparison
Age	51.92±12.67	44.15±12.11	unpaired t-test: t=2.482 df=63; ***p*<0.05**
Age of disease onset	42.79±15.10	33.56±14.56	unpaired t-test: t=2.465 df=63 ***p*<0.05**
Objective CGI – severity	3.08±1.53	3.30±1.59	unpaired t-test: t=0.5552 df=63; n.s.
Subjective CGI – severity	3.26±1.69	4.00±1.73	unpaired t-test: t=1.716 df=63; n.s.
Adherence to medication	5.84±3.58	3.78±4.16	unpaired t-test: t=2.140 df=63; ***p*<0.05**
ISMI – total score	59.61±12.29	67.04±13.87	unpaired t-test: t=2.278 df=63; ***p*<0.05**
Discontinuation of medication in the past	42.1%	37.0%	Fisher test: n.s.

degrees of adherence and higher levels of self-stigma than patients without personality disorder. A comparison of patients with personality disorder with those without this comorbidity is shown in Table 5.

DISCUSSION

Older depressed patients exhibited higher adherence to treatment than younger patients. It probably reflects the fact that older patients can cope easily with the need to use drugs. This result is similar to studies by Hinkin *et al.* (2004) and Barclay *et al.* (2007) who also found out that adherence increased with patient age. However, their studies were not focused on individuals with depression but HIV-positive patients. The present study also found that patients in whom the disease started at a later age had a higher degree of adherence to treatment. Adherence was not associated with patients' education. We found no study focused on depressive patients. In a study by Khanam *et al.* (2014) investigating patients with hypertension, increased adherence was associated with higher education. In the present study, individuals with secondary and upper education prevailed. There were just a few patients without secondary education. The ratio of types of education could distort the results of adherence analysis by education. Furthermore, patients with personality disorder exhibited lower adherence to treatment than patients without personality disorder. This finding is consistent with a study by Colom *et al.* (2000) performed in euthymic bipolar patients. It may be caused by personality disorder patients' lower confidence in psychiatrists, instability in the therapeutic relationship or greater need to rebel against authorities. However, we did not focus on this topic in our research so we cannot predict any behavior based on our results.

We found no relationship between adherence and partner status. In their study, Matas *et al.* (1992) demonstrated better adherence in patients living with a partner. The difference may be due to the different population studied. While they examined patients with schizophrenia and bipolar disorder, our study focused on patients with major depressive disorder.

Probably the most important finding of our study related to its primary goals is that lower adherence to treatment was associated with higher rates of self-stigma. This result is consistent with findings of other authors who examined the relationship between adherence and self-stigma in a population of elderly depressed outpatients (Sirey *et al.* 2001). Surprisingly, higher rates of self-stigma were not associated with more frequent discontinuation of medication in the past. It is possible that the discontinuation of medication is associated with the former fear of adverse effects of drugs or bias, rather than with the belief that the need to use drugs contributes to the stigmatization. Furthermore, our study confirmed that patients with personality disorder showed higher rates of self-stigma than those without the condition. A possible explanation is that comorbid personality disorder may contribute to the greater severity of disease and subjective worse experience.

Another surprising finding was that patients who had deliberately discontinued drugs did not manifest lower current adherence to treatment, higher rates of self-stigma or comorbid personality disorder. These results could be explained by the fact that patients gain experience after months or years of treatment, which reduces their fear of drugs and so they gradually realize the benefits of pharmacotherapy. Discontinuation of medication by their will was admitted equally by females and males. These results are in accordance with the conclusions of other authors who studied adherence to psychotropic medications in the general population (Bulloch and Patten 2010).

Limitations of the study

One limitation of the study is that data about adherence and self-stigma were collected using questionnaires and could be modified by different motivation of patients. Some patients did not fill in the questionnaires completely, so they had to be excluded from some analyzes. The diagnoses of major depressive disorder and personality disorders were assessed by a psychiatrist based on the diagnostic criteria and confirmed by two other experienced psychiatrists. On the other hand, they were not evaluated by a structured interview, which could have improved the objectivity of the diagnosis, especially in personality disorders.

CONCLUSION

The study results suggest that the rate of self-stigma may be a significant factor that is associated with poorer adherence of patients with major depressive disorder. If these findings are confirmed by further studies, a great perspective for increasing adherence may be strategies for reduction of self-stigma, which can be implemented by systematic psychoeducation of patients.

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