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Adherence to antidepressant treatment :What the doctor think and what the patient says

THESE

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RESUME

Il a été montré que l'adhérence à un traitement antidépresseur varie entre 30 et 70%. Le but de cette étude était de comparer, dans un groupe de 144 patients ambulatoires avec un trouble de l'humeur et/ou un trouble anxieux traités avec des antidépresseurs, l'auto-estimation de l'adhérence avec l'estimation de l'adhérence par le médecin, ainsi qu'avec l'alliance thérapeutique. Les scores d'adhérence estimés par les patients et par les médecins étaient significativement différents, les médecins sous-estimant l'adhérence dans 29% des cas et la surestimant dans 31% des cas en comparaison avec l'évaluation des patients. L'adhérence mesurée par les taux plasmatiques des médicaments, malgré qu'elle soit plus élevée que prévue si on se réfère à des études publiées précédemment, était en accord avec les scores auto-estimés par les patients mais pas avec les scores estimés par les médecins. Finalement les scores d'alliance thérapeutique estimés par les patients et par les médecins n'étaient pas liés à l'auto-déclaration d'adhérence.

Adherence to Antidepressant Treatment: What the Doctor Thinks and What the Patient Says

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Abstract

Adherence to antidepressant treatment has been shown to range from 30 to 70%. The aim of this study was to compare the patient's self-report of adherence with the doctors' estimation of adherence and therapeutic alliance in 104 outpatients with mood and/or anxiety disorder treated with antidepressants. The adherence scores estimated by the patients and the doctors were significantly different, the doctors underestimating adherence in 29% of cases and overestimating it in 31% of cases compared to the patients' evaluation. Adherence measured by drug plasma concentration, despite being higher than expected from previously published reports, was in line with the patients' self-reported score but not the doctors' estimation. Finally, the patients' and the doctors' Helping Alliance scores were not related to adherence self-report.

Key words

patient compliance · medication adherence · antidepressive agents

Introduction

Depression is an important cause of disability in the world, with antidepressant drugs representing the mainstay of treatment. As in other chronic disorders, several studies have consistently shown that adherence with antidepressants is poor, ranging from 30 to 70% [1, 2]. Discontinuations are most frequent during the first month of therapy and factors leading to discontinuations are multiple and poorly understood [1]. Many studies have examined the extent of adherence to treatment. However, there exists only few data on the doctor's perception of their patients' adherence, and they demonstrated that doctors were only able to correctly identify non-adherent patients in 2/3 of cases or fared no better than chance (for a review see [2]). The aim of this study is to evaluate the relation between the patients' adherence to antidepressant treatment, their doctors' perception and their therapeutic alliance.

Patients and Methods

200 adult outpatients treated with antidepressants for anxiety and/or mood disorders at the Hôpital de Cery, Prilly-Lausanne, Switzerland were approached for participation in this transversal observational study. 104 patients were included, 96 patients being excluded because of language problems or because they did not agree to participate. Adherence was evaluated with an interview of the patients (by an investigator not involved in their follow-up) and antidepressant blood level measurement. The doctor conducting the interview had access to the patients' medical charts. Blood sampling took place immediately after recruiting and interviewing patients for the study, excluding thus additional drug intake. Patients were informed that the data collected during the study would not be transmitted to their treating physicians. The interview included a validated self-reported medication-taking scale [3]: "Do you ever forget to take your medicine?", "Are you careless at times about taking your medicine?", "When you feel better, do you sometimes stop taking your medicine?", "Sometimes if you feel worse when you take the medicine, do you stop taking it?". Affirmative answers scored one point and led to the calculation of a 0–4 point score, higher scores indicating poorer adherence [3]. In parallel, the treating doctors also evaluated their patient's adherence as a 0–4 point score (0, very good compliance; 4, poor compliance). The interview also included questions on reasons for discontinuation of treatment and on the information received from their treating doctor on the correct time of administration and the possible side-effects of their treatment. The degree of satisfaction with antidepressant treatment was also evaluated with a 4-item questionnaire including global satisfaction, control of the symptoms and intensity of side-effects using 5- and 6-point Likert scales (psychometric scales used to specify the level of agreement to a statement). The strength of the patient-therapist alliance, which is based on the collaboration and bond between therapist and patient, was measured by the patient's and therapist's version of the Helping Alliance questionnaire (HAQ-II), a widely used 19-item questionnaire with each item rated on a 6-point Likert scale [4]. Written informed consent was obtained from all patients. The study was approved by the psychiatry ethics committee of the University of Lausanne, Switzerland. The plasma concentrations of all the antidepressants except for nefazodone and doxepine were measured as previously described [5–8]. Chi-squared test for association, Mann-Whitney U test, Kruskal-Wallis test and/or Spearman correlation were used. All tests were performed with STATA (11.0; StataCorp, USA), and $p \leq 0.05$ was considered as statistically significant.

Results and Discussion

The present results are based on the data of 104 patients: 55 (53%) men (43 ± 11 years old) and 49 (47%) women (39 ± 11 years old), mean weight of 74 ± 16 kg, 51 (50%) smokers. 88 patients (85%) took other medication(s), among them 8 (8%) took 2 antidepressants. The antidepressant treatments with their median daily dose are described in **Table 1**. The median treatment duration was 12 months [$n=87$; interquartile range (IQR), 5–26 months]. Clinical diagnosis was available for 102 patients and is described in **Table 1**. 31 (30%) of patients suffered from anxi-

* Both authors contributed equally to this study.

ety disorders, 38 (37%) from mood disorders and 33 (32%) from both.

The self-report of adherence yielded a score of 0 points (very good adherence) for 32 patients (31%), 1 point for 38 patients (37%), 2 points for 23 patients (22%) and 3 points for 11 patients (11%). No patients had a self-estimated score of 4 points (poor adherence). The median score for all patients was 1. The most frequent yes-answered questions were about carelessness (52%) and forgetfulness (46%), whereas discontinuation of treatment when feeling better (15%) or worse (2%) was less frequent. Self-reported adherence scores were shown to be a useful method to identify non-adherent patients as compared to the microprocessor-based medication event monitoring system (MEMS), a system which records the precise time of opening of the tablet container [9]. Patients with mood disorders reported a better adherence compared to patients with anxiety disorders, with 82% of patients with mood disorder ($n=38$) reporting a score of 0 or 1 vs. 52% of patients with anxiety disorder ($n=31$; $\chi^2=7.1$; $p=0.008$). The self-reported adherence scores increased with the median treatment duration, except for patients with the lowest adherence (9 months for 0-point score, 12 months for 1-point, 23 months for 2-point and 5 months for 3-point; $p=0.04$).

The adherence was estimated by the doctors for 99 patients. It yielded a score of 0 point for 23 patients (23%), 1 point for 46 patients (46%), 2 points for 20 patients (20%), 3 points for 8 patients (8%) and 4 points for 2 patients (2%). The median adherence score estimated by the doctors was 1 point. The distribution of the adherence scores estimated by the patients and the doctors was significantly different (Fig. 1a; $p=0.009$) even though the scores were correlated ($\rho=0.32$; $p=0.0012$). The 2 scores matched for 39 patients; whereas the doctors overestimated the score compared to the patients in 29 cases and underestimated it in 31 cases. This relatively poor estimation is in agreement with the few published reports on this subject (for a review see [2]).

The self-estimation of the global satisfaction with the medication indicated that 9 patients (9%) were dissatisfied to very dissatisfied, 63 patients (61%) were satisfied to very satisfied and 32 patients (31%) were neither satisfied nor dissatisfied. Concerning the control of the symptoms, 12 patients (12%) reported that their medication did not help at all, 56 patients (54%) reported a little or moderate help and 36 patients (35%) a large or enormous help. Among the 104 patients, 48 (46%) declared having side effects, which were estimated as being very light to light (30%), moderate to average (68%) and severe (2%). The most frequent reported side-effects were loss of libido ($n=18$), tiredness ($n=14$), gastrointestinal problems ($n=12$), sudation and hot flushes ($n=10$), dry mouth ($n=8$), weight gain ($n=7$) and headache ($n=6$). None of these estimations was related to the self-reported adherence score ($p>0.3$). In addition, 31 patients (30%) estimated that their doctor did not inform them sufficiently about the importance of the dose, frequency and time of administrations; whereas 60 patients (58%) estimated that they were not sufficiently informed about the possible side-effects. Both answers were not related to the self-reported adherence score or the degree of satisfaction from treatment ($p>0.1$). During the interview, 16 patients (15%) declared having discontinued the antidepressant, and most of them (8 out of 11 answers) did not inform their doctor. Among these 16 patients, 6 (38%) had a self-reported adherence score of 3 points, vs. 5 of 88 patients (6%) still taking their treatment ($\chi^2=28.4$, $p<0.0005$).

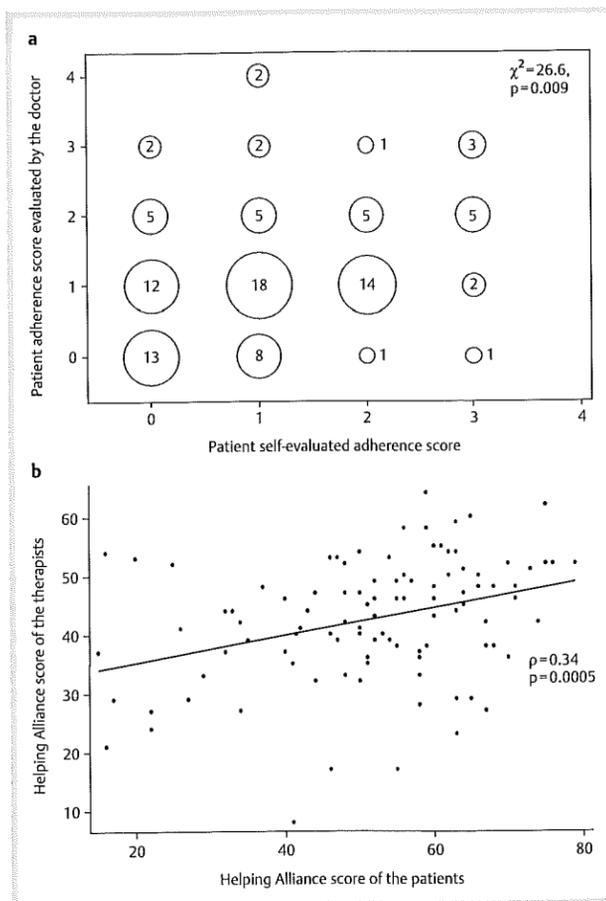


Fig. 1 Distribution of the adherence scores estimated by the patients and by the doctors for 99 patients with antidepressant treatment **a**. Helping Alliance scores of the patients and of the doctors for 103 patients with antidepressant treatment **b**.

The antidepressant blood concentration was measured for 101 patients, and 7 patients (7%) had undetectable or very low plasma concentrations (in relation to the dose and the interval since the last intake: $<10\%$ of the expected concentration [10]), suggesting very poor or non-adherence. Their self-report of adherence was significantly different from the rest of the patients (median scores 3 and 1, respectively; $p=0.02$). 4 of these 7 patients (57%) had a self-reported score of 3 points, vs. 7 of the other 94 patients (7%; $\chi^2=16.6$, $p=0.001$). In addition, 31 patients (30%) were considered as possibly partially non-adherent (concentration of antidepressant and/or its main metabolite inferior to 1/3 of the expected trough concentration for the dose [10] and/or if the patients declared having discontinued their treatment). Their self-report of adherence was also significantly different from the rest of the patients (median scores 2 and 1, respectively; $p\leq 0.00005$). 8 of these 31 patients (26%) had a self-reported score of 3 points, vs. 3 of the other 71 patients (4%; $\chi^2=24.7$, $p\leq 0.00005$). On the other hand, the adherence scores estimated by the doctors were not significantly different between patients with undetectable or very low plasma concentrations vs. the others, or between patients with partial adherence vs. the others ($p\geq 0.1$). Thus, the self-reported adherence score is more in accordance with the information obtained with the blood concentration than the doctors' estimation of adherence. Still, the observation of partial adherence deduced from

Table 1 Clinical diagnosis according to ICD-10 ($n=102$; patients might have up to 4 diagnoses) and antidepressant treatment ($n=104$) of patients.

Clinical diagnosis (ICD 10)	Number	Frequency	
mood disorders	71	70%	
bipolar disorders (F 31)	3	3%	
depression (F 32)	39	38%	
recurrent depression (F 33)	29	28%	
anxiety disorders	64	63%	
phobic disorders (F 40)	11	11%	
anxiety disorders (F 41)	27	26%	
obsessive-compulsive disorders (F 42)	21	21%	
posttraumatic stress disorders (F 43)	2	2%	
somatoform disorders (F 45)	13	13%	
antidepressant treatment	Median dose (range) [mg/d]	Number	Frequency
selective serotonin reuptake inhibitors		79	76%
citalopram	40 (10–60)	31	30%
including citalopram and mirtazapine		4	
including citalopram and reboxetine		1	
paroxetine	20 (10–80)	18	17%
including paroxetine and sertraline		1	
fluoxetine	40 (20–60)	13	13%
sertraline	100 (25–200)	13	12%
including sertraline and mirtazapine		1	
including sertraline and paroxetine		1	
fluvoxamine	125 (100–300)	4	4%
escitalopram	20	1	1%
other antidepressants		20	19%
venlafaxine	225 (75–750)	11	11%
including venlafaxine and mirtazapine		1	
mirtazapine	30 (15–60)	12	6%
including above-mentioned co-prescriptions		6	
nefazodone	450 (400–500)	2	2%
reboxetine	6 (4–8)	2	1%
tricyclic antidepressants		4	4%
clomipramine	115 (105–125)	2	2%
amitriptyline	25	1	1%
trimipramine	150	1	1%
doxepine	25	1	1%

blood concentrations and self-report after a median of 12-month treatment in only 30% of patients is a relatively low value compared to the literature [1,2] and can be considered as very conservative. This overestimation of adherence might have been caused by a selection bias, non-adherent patients having refused more frequently to be included in the study than adherent patients.

The Helping Alliance scores of the patients and the therapists are significantly correlated (Fig. 1b, $\rho=0.34$, $p=0.0004$). The median values (range) are 54 (43–63) for the patients and 44 (37–50) for the therapists. Except for an association between the Helping Alliance therapist score and the doctors' evaluation of adherence ($\rho=-0.22$, $p=0.03$), Helping Alliance scores were neither correlated with the patients' self-reported adherence, nor the doctors' evaluation of adherence, nor the plasma concentrations ($p\geq 0.2$). Patients with a better global satisfaction with their medication had higher Helping Alliance scores, with a median value of 58 for satisfied to very satisfied patients vs. 49 for dissatisfied patients and 50 for neither satisfied nor dissatisfied ($p=0.02$). Similar results were observed for the therapist scores (44, 40 and 46.5, respectively; $p=0.02$). Patients who estimated to be well informed about possible side-effects had higher Helping Alliance scores than the others (57 vs. 50.5; $p=0.02$), while a similar trend was observed for the information on dose,

frequency and time of administration ($p=0.05$). On the other hand, the therapist scores were not found to be different ($p>0.1$). Thus, the Helping Alliance score does not seem to be related to adherence but to the satisfaction and information received. It should be mentioned that this study was conducted in an academic training institution, in which therapists may change as often as once every 6 months, and this circumstance might have affected the patient-therapist alliance. Because of this specific setting, generalization of these data to other settings might not be possible. On the other hand, the frequency of change of therapists is unlikely to have contributed to a major extent to the adherence to treatment measured in the present study as a fast decline in adherence within the first 3 months of therapy has been constantly shown in several studies [1,2].

In conclusion, the estimations of adherence to antidepressant treatment by patients and doctors were significantly different, though slightly correlated. Neither score was related to satisfaction with the medication, control of the symptoms or side-effects. A simple self-reported adherence score was shown to be an easy and useful method to identify non-adherent patients. However, because patients were informed that data collected during the study would not be transmitted to their treating physicians, the reliability of the self-reported adherence score remains to be determined in the absence of such a non-disclo-

sure assurance. The strength of the patient-therapist alliance seemed more closely related to the satisfaction with the medication and the information received on medication and side-effects than to adherence, thus highlighting the need of patient education on compliance. Finally, adherence measured by drug plasma concentration, despite being higher than expected, was in line with the patients' self-reported score but not with the doctors' estimation. Because antidepressant treatment is a long-term treatment and compliance a very important issue, therapeutic drug monitoring could be useful to estimate patient's compliance and/or in case of non-response [10].

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Conflict of Interest



The authors declare no conflict of interest.

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