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Treatment adherence in schizophrenia. A comparison between patient's, relative's and psychiatrist's opinions

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Introduction. Patients with psychiatric illness typically have great difficulty following a medication regimen, but they also have the greatest potential for benefiting from adherence. Due to the lack of insight in schizophrenia, adherence to treatment is especially important. We try to analyze and compare the opinion on adherence and compliance of psychiatrists, patients with schizophrenia and relatives.

Method. A direct, anonymous survey specifically designed for the project was administered to psychiatrists, patients and relatives from all over Spain through different associations of patients and family legally constituted in Spain. Analysis was done separately for variables corresponding to the three groups.

Results. The psychiatrists (n = 844) considered that 56.8% of their evaluated patients (n = 7.439) were non-compliers in the past month, as opposed to 43.2% of these patients who were considered good compliers (3,215 patients). Ninety-five percent of the patients (n = 938) stated that they took their medication regularly, while 5 % answered no to this question. Eighty-two percent of relatives (n = 796) think that patients regularly take their medication, but 47% state that they sometimes forget to take it.

Conclusions. Treatment adherence should be evaluated in clinical trials and in research on treatment of diseases, particularly in chronic mental diseases such as schizophrenia. It seems clear that only programs aimed at detection and resolution of the problems involved in treatment adherence will be able to improve the mid- and long-term prognosis of patients with schizophrenic disorders.

Key words:
Adherence. Schizophrenia. ADHES project. Compliance.

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Adherencia terapéutica en la esquizofrenia: una comparación entre las opiniones de pacientes, familiares y psiquiatras

Introducción. Habitualmente los pacientes con enfermedades mentales presentan grandes dificultades a la hora de seguir las prescripciones médicas, pero también poseen el mejor potencial para beneficiarse de la adherencia. Debido a la falta de *insight* propia de la esquizofrenia, la adherencia al tratamiento resulta especialmente importante. El trabajo analiza y compara la opinión respecto a la adherencia y el cumplimiento de una amplia muestra de psiquiatras, enfermos diagnosticados de esquizofrenia y sus familiares.

Método. Encuesta directa y anónima diseñada específicamente para este proyecto, administrada a psiquiatras, enfermos y familiares de toda España a través de distintas asociaciones de enfermos y familiares legalmente constituidas en todo el territorio español. El análisis de los datos se llevó a cabo de forma separada para las variables correspondientes a los tres grupos.

Resultados. Los psiquiatras (n = 844) consideran que el 56,8% de sus pacientes evaluados (n = 7.439) fueron incumplidores en el último mes en contraposición al 43,2 % de estos pacientes que se consideran buenos cumplidores (n = 3.215 pacientes). El 95% de los pacientes (n = 938) afirmaron haber seguido la medicación regularmente, mientras que el 5% contestó negativamente a esta cuestión. El 82% de los familiares (n = 796) piensan que los pacientes toman regularmente su medicación, aunque el 47% indica que a veces la olvidan.

Conclusiones. La adherencia al tratamiento debería ser evaluada en ensayos clínicos, así como en las investigaciones de tratamiento de enfermedades, particularmente las enfermedades mentales crónicas tales como la esquizofrenia. Parece evidente que sólo los programas dirigidos a la detección y resolución de problemas relacionados con la adherencia al tratamiento serán capaces de mejorar el pronóstico a medio y largo plazo de los pacientes con esquizofrenia.

Palabras clave:
Adherencia. Esquizofrenia. Proyecto ADHES. Cumplimiento

INTRODUCTION

Surprisingly, historically treatment adherence and compliance have been a secondary topic in medicine. Such a situation was surprising because most authors agree that treatment noncompliance is common, and its impact on the course and prognosis of the different diseases is highly relevant[1].

However, in recent times, there has been a significant increase in the number of studies analyzing compliance in the different conditions, and particularly in mental disorders[2-4].

Compliance and adherence are terms used indistinctly, despite the fact that some authors insist that they should not be considered synonymous. In some reports, compliance is only defined as the extent to which a patient complies with a drug prescription. Adherence would refer to a wider concept, including lifestyle habits, diets, and even an active collaboration attitude of the patient with a set of therapeutic strategies. Most studies are usually aimed at assessing compliance with drug treatment or attendance to scheduled visits, which are easier to evaluate[5].

The problem of adherence in psychiatry is worsened by the chronic nature of mental diseases, disease unawareness, and the high degree of stigmatization associated with mental disorders. There is some agreement in considering that non-adherence has serious implications in patients with mental disorders: poorer prognosis, increased hospital admissions, increased relapse or recurrence rates, higher suicidal rates, and poorer quality of life[7-12]. Different instruments have been developed to evaluate adherence[13-19].

Among mental diseases, the highest figures of non-adherence or non-compliance are found in schizophrenic disorders, due to their unique characteristics. Poor insight, negative attitudes toward treatment, prior history of non-adherence, toxic abuse, short duration of disease, poor therapeutic alliance, and an inadequate planning of discharge in the event of hospitalization have been reported to be predictors of poor adherence[7-12,20,21].

As the significance of adherence in the course of schizophrenia or other mental disorders has already been established[22], research is now aimed at more precise identification of predictors of total or partial non-adherence and, in a still incipient way, at development of strategies contributing to a better adherence. There are still few publications in this field, in which effective clinical interventions that may be implemented by psychiatric departments to reduce treatment non-adherence are investigated[23].

This was why the ADHES project (Adherencia Terapéutica en la Esquizofrenia, Treatment Adherence in Schizophrenia) was conducted in Spain. More than 800 Spanish psychiatrists participated in it (22nd-28th March, 2005), providing information on approximately 7,000 patients. During the same week, 938 patients and 796 relatives were directly surveyed on treatment adherence. The aim was to ascertain the characteristics of adherence of Spanish patients with schizophrenia treated by this group of psychiatrists and to survey affected relatives and patients on treatment compliance, while designing in parallel approaches to improve adherence. ADHES is a mid- and long-term project. The main results obtained in the sample of psychiatrists, patients and relatives and the working methods used are presented here.

MATERIAL AND METHOD

Psychiatrists

A direct survey, specifically designed for the ADHES project. The psychiatrists answered a total of 10 questions regarding the following characteristics of their patients diagnosed of schizophrenia: suspicion that they had forgotten to take the treatment some day during the past month; suspicion that the patient did not adhere to the prescriptions on his/her own will; if yes, whether patient was unable to perceive a worsening after missing treatment; whether environment conditions or relatives may make adherence difficult; whether use of toxic substances is suspected; whether they think that patient should be constantly reminded of the need for the prescribed medication; whether patient has shown a lack of awareness of disease that may lead to irregular compliance; whether there are cognitive disorders that impair adherence; whether patient has felt embarrassed or annoyed for having to take medication daily; and finally, whether when patient has felt better, he/she has sometimes thought that the medication was not necessary, and therefore discontinued medication taking it.

Patients

A direct, anonymous survey was specifically designed for the ADHES project and administered to patients from all over Spain who came to the patient's and family' association legally constituted in Spain. Surveys were provided to such associations and directly collected from them by the project staff. The questionnaire consisted of seven questions referring to whether the patients took their medication regularly, if they ever forgot it, if they even voluntarily skipped it, if they took the medication only when they were ill, if they felt worse if they stopped taking it, if they considered the medication was beneficial for their condition, and finally, if need for daily treatment was annoying.

Relatives

A direct, anonymous survey specifically was designed for the ADHES project and administered to patients from all over Spain who came to the patient's and family' association

legally constituted in Spain. Surveys were provided to such associations and directly collected from them by the project staff. The questionnaire consisted of seven questions referring to whether the patients took their medication regularly, if they ever forgot it, if they ever voluntarily skipped it, if they suspected that patient was hiding a negative attitude toward medication, if they thought that the patient considered the medication as beneficial, if administration had become a frequent family discussion subject, whether a treatment not requiring daily administration would be more convenient.

DATA ANALYSIS

Analysis was separately performed for variables corresponding to the three groups (psychiatrists, patients, relatives). A first descriptive analysis was made of the study population, and the overall results for each population were collected in a second stage of analytical study. Means, standard deviations, and percentages were given for all variables, with a maximum admitted error of ± 3.5, and a 95.5% confidence levels (two sigma). Once cleared and coded, data were recorded in Barwin statistical software for quantitative analysis. Tabulation results have been expressed as absolute and relative frequency distributions (contingency tables).

Response of the psychiatrists, relatives and patients group was obtained with a survey sent by post mail.

RESULTS

Psychiatrists

A total of 844 psychiatrists filled out the questionnaire. The psychiatrists mostly worked in public health sites (66%), 12% in acute units and 10% in long stay units. Almost half of those who responded to the questionnaire (43%) had worked as a professional from 11 to 20 years, and thus had extensive clinical experience. These psychiatrists provided information on 7,439 patients (table 1).

A total of 56.8% of these psychiatrists (a total of 4,224 patients) considered that his/her patient was not a good complier in the past month, as opposed to 43.2% who thought that non-compliance did not occur during that four-week period (3,215 patients). On the other hand, 70.7% of psychiatrists (with responses representing 5,260 patients of the total sample) considered that the patient omitted taking the prescribed medication on his/her own accord. A total of 63.3% of surveyed clinicians thinks that their patients (a total of 4,708) are unable to perceive a worsening in their health after the first few days in which the prescribed treatment is missed.

Most of the psychiatrists (73.7%) think that their 5,479 patients surveyed need some person (physician, relative, etc.) to remind them that they must take their medication to have good compliance. As regards comorbidity with alcohol or

Table 1 Answers by psychiatrists

844 psychiatrists/n = 7,439 patients	Yes (n/%)	No (n/%)
Do you suspect that your patient has forgotten to take medication as prescribed any day during the past month?	4,224 (56.8)	3,215 (43.2)
Do you think that your patient has ever decided to stop taking the medication (or has taken excess medication) on his/her own accord?	5,260 (70.7)	2,179 (29.3)
If any of the previous answers was yes, do you think that your patient is unable to perceive a worsening of his/her health status after the first few days of missed treatment?	4,708 (63.3)	2,731 (36.7)
Does your patient have, or has ever had, an irregular daily routine. or does he/she live or has ever lived under conditions (relatives, environment...) that may make difficult an adequate daily compliance with treatment?	4,542 (61.1)	2,897 (38.9)
Do you suspect your patient to be using or to have recently used alcohol or drugs?	3,271 (44)	4,168 (56)
Do you think your patient needs the family, psychiatrist... to remind him/her to take the medication for he/she to take it as prescribed?	5,479 (73.7)	1,960 (26.3)
Does your patient show, or has ever shown, a lack of awareness of the disease that could lead to irregular compliance with medication?	6,198 (83.3)	1,241 (16.7)
Has your patient cognitive impairment problems (impaired memory, disorganization...) that could make daily medication compliance difficult?	3,448 (46.4)	3,991 (53.6)
Has your patient ever felt embarrassed or annoyed for having to take tablets every day for his/her disease?	4,760 (64)	2,679 (36)
When your patient has felt better, did he/she ever think that medication was not necessary and stopped taking it?	5,391 (72.5)	2,048 (27.5)

drug use, 3,271 patients (44% of psychiatrists) would have a dual schizophrenia/toxic abuse pathology, as compared to 4,186 patients with no such dual condition (56% of psychiatrists).

According to 83.3% of surveyed psychiatrists (representing information about 6,198 patients), the patient has sometimes shown lack of awareness of the disease, and this has been the main reason for non-compliance. An additional 46.4% think that their 3,448 patients have evidence of a cognitive impairment that could make adherence difficult. Finally, 72.5% of these Spanish clinicians state that when their patients have felt better, they have sometimes thought that medication was not necessary and discontinued it.

Patients

A total of 938 patients aged 16 to 80 years completed the survey. Sixty percent of them had ages ranging from 22 to 45 years. Ninety-five percent stated that they took their medication regularly, while 5% answered no to this question. Thirty-five percent admitted that they «frequently forget» some dose, as compared to 65% of patients who say they never miss their doses. Forty-two percent of patients stated that they had sometimes skipped the medication on their own accord, while 58% said they had not (tables 2 and 3). Sixty-six percent of patients admitted that they felt worse when not taking the medication, and 34% state that their condition is not worse when they do not comply with drug treatment. Medication is assessed as beneficial by 90% of patients, and only 10% think that it is not beneficial. Sixteen percent say that they only take medication when feeling ill, as opposed to 84% who do not act this way. Forty-five percent of patients find it annoying to take daily medication for their disease, while 55% state that drug intake causes them no inconvenience.

Relatives

A total of 796 first-degree relatives of patients diagnosed of schizophrenia completed the questionnaire. Eighty-two percent of relatives think that patients regularly take their medication, but 47% state that they sometimes miss taking it. Medication has been sometimes missed by patients on their own decision according to 52% of relatives, while 48% state that non-compliance was not due to patient decision (tables 4 and 5). Sixty-three percent of relatives do not think that patients are hiding any negative attitude toward drug treatment (while 37% think they do). According to 72% of relatives, patients assess the medication as beneficial for themselves. In 71% of cases, taking medication regularly does not provoke discussions within the family, but 29% of relatives say that this question usually causes arguments. A total of 76% of the relatives think it would be more convenient to have a treatment that would only have to be administered once every several weeks (tables 4 and 5).

Table 2 Answers from patients regarding the degree of treatment compliance

n = 938	Yes (n/%)	No (n/%)
Frequently takes his/her treatment	891 (95)	47 (5)
Frequently forgets to take medication	328 (35)	610 (65)
Sometimes missed medication on his/her own accord¡	394 (42)	544 (58)

Table 3 Answers from patients regarding their attitude toward the medication prescribed by the psychiatrist

n = 938	Yes (n/%)	No (n/%)
Has felt worse when not taking the medication	619 (66)	319 (34)
Assesses medication as something beneficial for him/her	844 (90)	94 (10)
Only takes the medication when he/she feels ill	150 (16)	788 (84)
Finds it annoying to have to take medication for his/her disease every day	422 (45)	516 (55)

OVERALL COMPARISON

Joint evaluation of responses in the three groups (fig. 1) shows marked differences: psychiatrists think that 56% of their patients ever miss their medication, an opinion shared by 47% of relatives, but only by 35% of patients. The results show even more marked differences in answers to the

Table 4 Answers from relatives regarding the degree of treatment compliance by the patient

n = 796	Yes (n/%)	No (n/%)
Thinks that his/her relative usually takes medication	653 (82)	143 (18)
Thinks that his/her relative sometimes misses medication	374 (47)	422 (53)
Thinks that his/her relative has sometimes stopped taking medication on his/her own accord	414 (52)	382 (48)

Table 5 Answers from relatives regarding patient attitude toward the medication prescribed by psychiatrist

n = 796	Yes (n/%)	No (n/%)
Suspects that patient hides a negative attitude toward medication	295 (37)	501 (63)
Thinks that patient assesses medication as something beneficial for him/her	573 (72)	223 (28)
Daily intake of medication has become a frequent source of arguments	231 (29)	565 (71)
It would be more convenient to have a treatment that is only administered once every several weeks	605 (76)	191 (24)

question as to whether some non-compliance was due to the patient's will. Seventy percent of psychiatrists answered yes to this question, as compared to 42% of patients.

DISCUSSION

Adequate management of a disease such as schizophrenia requires long-term treatment. This treatment allows for controlling symptoms, preventing relapse, decreasing suicidal attempts, and increasing the quality of life of patients, amongst others. Short and long-term treatment compliance represents one of the mainstays on which this potential for adequate management of the disease is based[24]. Conventional and atypical antipsychotics have been shown to be helpful, but schizophrenia continues to be undertreated, and the degree of patient adherence to the different treatments is low[25,26].

Despite the multiple methods used and described (attendance to visits, pill count, drug monitoring, clinical interviews, relative opinion, etc.), adequate quantification of treatment compliance or adherence is difficult[27]. Patients with schizophrenia add some difficulties because of the symptoms and impairment caused by the disease, the resulting difficulty in clinical follow-up, the side effects of treatments, the need for daily medication during long time periods, the stigma of disease, etc.[28]. Small treatment deviations may have a significant impact on the course of a disorder. Partial lack of adherence may represent a more relevant problem than treatment refusal[29]. According to Spanish clinicians, non-compliance occurs in one out of every two of their patients, and results in most cases from the direct will of patients, who stop taking their medication.

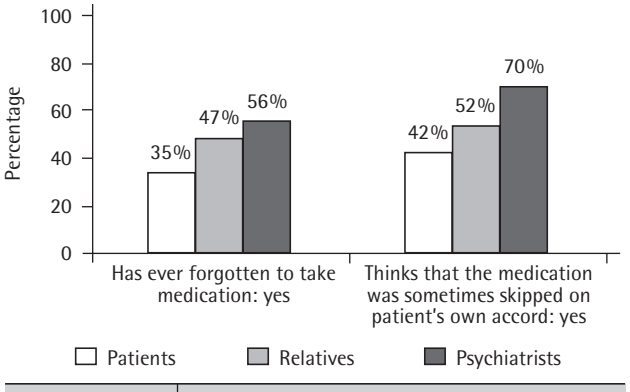

Figure 1 *Overall comparison between answers given by psychiatrists, patients and relatives.*

Psychiatrists

The psychiatrists surveyed were asked their opinion on specific patients they had known for years, and whose overall behavior and adherence they could therefore assess. Many clinical trials assessing compliance only last 8 or 12 weeks, 6 months at the most, despite the fact that compliance continues to decline over time, as reported by various studies[3,12]. Psychiatrists think that lack of compliance has serious consequences: hospitalization, relapse, suicidal risk. Our sample of professionals clearly indicates the significance of non-compliance as a factor triggering relapse and hospitalization. A recent study in which a systematic review was made of the relationship between schizophrenia and suicide[8] found that factors with a robust relationship with a suicidal behavior in schizophrenic patients included: prior affective disorders, prior suicidal attempts, use of drugs, and poor treatment adherence. In the reviewed studies, lack of adherence was defined as non-compliance with medication or non-attendance to scheduled visits.

Patients and relatives should be aware of the importance of treatment compliance, this being very difficult to do. The implications of a lack of adherence are sometimes only detected when psychotic symptoms recur or increase. Our study suggests that patients tend to minimize low compliance, as shown by a comparison with the opinion of relatives. The non-compliance rate reported by relatives is lower than that given by psychiatrists, but the value is closer to that obtained from patients. Patients sometimes think that skipping a dose or some days of medication does not represent non-compliance with treatment[30]. When directly questioned, patients tend to deny compliance problems. Velligan[4] studied 68 schizophrenic patients, and at 3 months, while pill counts indicated an adherence rate of 40% only, and plasma levels decreased compliance to 23%, 55% of patients stated that they considered themselves compliers. A detailed study has been conducted in some cases of agreement between the opinion of clinicians, patients, and relatives[31]. In the first study, conducted on a sample of 1,369 patients, the patients considered themselves as significantly more compliant as compared to the opinion of their psychiatrists. Byerley[32], using an electronic method called

Medication Event Monitoring System (MEMS), 62% of patients did not meet the adherence criterion (70% or more of prescribed doses): psychiatrists considered that only 5% of the sample were non-compliers.

Adequate information and a realistic expectation about the possibilities of treatment are essential. Problems with treatment compliance do not only affect particularly difficult or refractory patients, but patients with a good social support and apparently attending medical visits with some regularity. It is difficult for a patient with schizophrenia to become aware of the increased risk of relapse occurring when he discontinues treatment totally or partially.

Limitations

Only psychiatrists willing to collaborate in a study of these characteristics participated in the ADHES project. The same applies to the other two groups surveyed, which also came from associations of patients' relatives, and were thus especially sensitive to these problems. Hospitalized patients were not included, but many patients in the sample have been admitted during the course of their condition. No specific diagnostic systems were consistently used by the participating psychiatrists; however, it should be noted that these were patients with a long course of the condition, and thus with an apparently high stability in diagnosis.

The results of our study support the notion that treatment adherence or compliance should be evaluated in clinical trials and in research on treatment of diseases, particularly in chronic mental diseases such as schizophrenia. It seems clear that only programs aimed at detection and resolution of the problems involved in treatment adherence (patients, treatments, care, etc.) will be able to improve the mid and long-term prognosis of patients with schizophrenic disorders.

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