

COMPLIANCE WITH MEDICATION TREATMENT BY PEOPLE WITH ANXIETY DISORDER*

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ABSTRACT: In this study, the factors related to compliance with the prescribed drugs therapy are verified among people with anxiety disorder. Quantitative, cross-sectional, descriptive study, involving 161 patients from a mental health service in a city of the state of São Paulo, between January 01st and December 31st 2012. Patient histories were reviewed and the Treatment Adherence Measure, Beck Anxiety Inventory and a sociodemographic script were used. Most participants were considered compliant with the drugs. No statistically significant differences were evidenced between compliance and the research variables. The high percentage of participants using benzodiazepines over a long period is highlighted, suffering from moderate and severe anxiety despite the medication compliance and who were unaware of the prescribed medication dose. This study appoints elements that interfere in the safety of the drug treatment for people with anxiety disorder for whom intervention is possible, contributing to improve their treatment.

DESCRIPTORS: Anxiety disorders; Medication compliance; Outpatients.

ADESÃO AO TRATAMENTO MEDICAMENTOSO POR PESSOAS COM TRANSTORNO DE ANSIEDADE

RESUMO: Este estudo verificou os fatores relacionados à adesão de pessoas com transtorno de ansiedade quanto à farmacoterapia prescrita. Estudo quantitativo, transversal, descritivo, realizado com 161 pessoas de um serviço de saúde mental, num município do estado de São Paulo, entre 01 de janeiro e 31 de dezembro de 2012. Utilizou-se revisão de prontuários, Teste de Medida de Adesão ao Tratamento, Inventário de Ansiedade de Beck e roteiro sociodemográfico. A maioria dos participantes foi considerada aderente aos medicamentos. Não foram evidenciadas diferenças estatisticamente significativas entre a adesão e as variáveis investigadas. Destaca-se a alta porcentagem de participantes em uso prolongado de benzodiazepínicos, com ansiedade moderada e severa apesar da adesão aos medicamentos e que desconheciam a dose dos medicamentos prescritos. Este estudo aponta elementos que interferem na segurança do tratamento farmacológico da pessoa com transtorno de ansiedade e que são passíveis de intervenção, contribuindo para a otimização do seu tratamento.

DESCRITORES: Transtornos de ansiedade; Adesão à medicação; Pacientes ambulatoriais.

ADHESIÓN AL TRATAMIENTO MEDICAMENTOSO DE PERSONAS CON TRASTORNO DE ANSIEDAD

RESUMEN: El estudio verificó factores relacionados a adhesión de personas con trastorno de ansiedad a la farmacoterapia prescripta. Estudio cuantitativo, transversal, descriptivo, realizado con 161 personas en servicio de salud mental de un municipio del Estado de São Paulo, del 01 de enero al 31 de diciembre de 2012. Se aplicó revisión de historias clínicas, Test de Medida de Adhesión al Tratamiento, Inventario de Ansiedad de Beck y relevamiento sociodemográfico. La mayoría de participantes calificó como adherente a la medicación. No se evidenciaron diferencias estadísticamente significativas entre adhesión y las variables investigadas. Se resalta el alto porcentaje de pacientes con uso prolongado de benzodiazepínicos, con ansiedad moderada y severa a pesar de adherir al tratamiento, y el desconocimiento de dosis de los medicamentos prescriptos. El estudio detecta factores que interfieren en la seguridad del tratamiento farmacológico del paciente con trastornos de ansiedad, pasibles de intervención, contribuyendo a su optimización..

DESCRITORES: Trastornos de Ansiedad; Cumplimiento de la Medicación; Pacientes Ambulatorios.

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● INTRODUCTION

Anxiety disorders are considered a big problem for the global population. They are associated with high levels of suffering and limitations⁽¹⁾. In an epidemiological study conducted in Brazilian cities, it was identified that anxiety disorders prevailed (17.6%) over other mental disorders⁽²⁾.

Besides provoking significant suffering, these disorders are related to high direct and indirect costs and figure among the most psychiatric disorders in adult life⁽³⁾, demanding early diagnosis and specialized monitoring⁽⁴⁾.

Some drugs can be used to treat anxiety disorders, among which antidepressants and benzodiazepines are highlighted. The efficacy of benzodiazepines has been well documented in short treatments, but their extended use is contraindicated due to the risk of adverse effects, including addiction⁽⁵⁾.

In recent years, antidepressants, being well tolerated without causing addiction, have been established as the first-line treatment for the different categories of anxiety disorders⁽⁶⁾. Nevertheless, compliance with antidepressants is challenging, as approximately half of the patients interrupt the medication treatment during the first six months⁽⁷⁻⁹⁾. A study conducted in the USA revealed that 57% of the investigated patients diagnosed with anxiety disorder did not comply with the antidepressant therapy⁽¹⁰⁾.

Defining treatment compliance is a complex task as there is no consensus in the literature in this respect. According to the World Health Organization, compliance can be defined as the extent to which a person's behavior coincides with the recommendations agreed up with a healthcare provider⁽¹¹⁾. Nevertheless, studies defend the understanding of patients as active subjects, who participate and take responsibilities in the process of treatment compliance or not⁽¹²⁾.

As verified, the prevalence of anxiety disorders in society is significant, causing personal suffering and social burdens. These disorders tend to be chronic unless they are appropriately treated. Therefore, medication treatment compliance is a theme of interest in the literature, as it can be modified in search of a better prognosis for these patients.

Nevertheless, in a recent literature review⁽¹³⁾ on the theme, it is shown that few studies have investigated predictors of non-compliance with drug treatment in patients with anxiety disorders, and that the identified studies consistently describe high rates of non-compliance in these clients, emphasizing the importance of further research on the theme. Studies appoint that non-compliance with drug therapeutics can be related to a complex range of factors related to the patient (sex, age, ethnic origin, marital status, education and socioeconomic level); to the therapeutic regimen (complex treatment, collateral effects); disease characteristics (absence of symptoms) and relationship with the health team⁽¹⁴⁻¹⁶⁾. Knowledge on the factors interfering in medication compliance is needed for anticipation and careful exploration, with a view to a successful treatment⁽⁷⁾.

In Brazilian literature, no studies on prevalence and factors related to drug compliance have been identified among patients with anxiety disorder. Hence, this study contributes to complete a knowledge gap on this theme in Brazil.

In view of the hypothesis that there are demographic, socioeconomic, clinical and pharmacotherapeutic variables involved in treatment compliance, the objective in this study was to verify, in people with anxiety disorder, possible associations between medication compliance and depressive symptoms, knowledge about the drug prescription and demographic, socioeconomic, clinical and pharmacotherapeutic profile.

● METHOD

A retrospective, cross-sectional and descriptive study with a quantitative approach was undertaken. It was developed at a mental health outpatient service affiliated with the Unified Health System, located in an interior city in the state of São Paulo - Brazil.

The patient population with doctor's appointments scheduled at the place of study between January 01st and December 31st 2012 were eligible for the study if they complied with the following inclusion criteria: having a diagnosis belonging to the group of anxiety disorders (according to ICD-10)⁽¹⁷⁾, established by the physician responsible for the service; having a medical prescription for continuous drug use to treat the disorder; age 18 years or older and being capable of oral communication in Portuguese.

To collect the data on the demographic, socioeconomic, clinical and pharmacotherapeutic profile, the structured interview technique was employed, guided by a questionnaire the authors had developed and the analysis of the patient history after the interviews.

The level of drug treatment compliance (outcome variable) was assessed through the Treatment Adherence Measure (TAM). This test was developed and validated in Portugal⁽¹⁸⁾ in 2001 and adapted to the Brazilian context⁽¹⁹⁾. It consists of seven items, answered on a Likert scale with the respective scores: Always (1), Almost always (2), Frequently (3), Sometimes (4), Rarely (5) and Never (6). The level of compliance is obtained by adding up the item scores and dividing the sum by the total number of items, in which higher scores correspond to a higher compliance level for the respondents.

To identify the presence of anxiety symptoms, Beck's Anxiety Inventory⁽²⁰⁾ was used, previously adapted and validated for Brazil⁽²¹⁾. This symptomatic self-reported questionnaire consists of 21 items with different alternative answers about how the subject has felt, corresponding to different severity levels of the anxiety. The sum of the individual item scores provide a total that, in turn, constitutes a dimension score of the intensity of anxiety, classified as follows: minimum level of anxiety (0-7 points), mild anxiety (8-15 points), moderate anxiety (16-25 points) and severe anxiety (26-63 points).

The participants' level of knowledge on the prescribed drugs was classified using a tool adapted by Stape⁽²²⁾. This tool indicates how to translated into percentages the amount (numbers) of information the patient has and guides the ranking of this knowledge. It presupposes that a person's level of knowledge on each aspect of the drugs (name, dose and usage frequency) can be scored from 0 to 100% and classified at regular intervals, representing the following classes: no knowledge (0%); very little knowledge (0% -| 25%); little knowledge (25% -| 50%); regular knowledge (50% -| 75%) and good knowledge (75% -| 100%).

The participants were invited to participate in the study by telephone or when they attended the service. The interviews took place in reserved rooms to guarantee the privacy of the information. The mean length of the interviews was 30 minutes. The study objectives were explained and, after the participants had verbally consented to participate, they were asked to sign the informed consent form.

The data were typed in an Excel worksheet. Then, data analysis was undertaken in SAS® 9. To verify the association between the independent and the dependent variables in this study, the chi-square test was applied. In this study, significance was set at 0.05 ($p < 0.05$).

Approval for the study was obtained from the Research Ethics Committee under protocol 108/2012.

● RESULTS

Among the 161 (100%) research participants, 77.6% were female, between 41 and 60 years of age (50.3%), white (90.6%) and had a partner (62.1%). The subcategories of anxiety disorder that stood out in quantitative terms were "panic disorder", "mixed anxious and depressive disorder" (21.1% each subcategory) and "generalized anxiety disorder" (20.4%).

As verified, antidepressants were the most prescribed drugs for the study participants (91.3%), followed by anxiolytics (69.5%). Among the antidepressants, the prescription of Sertraline Hydrochloride for 61 participants (37.8%) and Fluoxetine Hydrochloride for 33 (20.4%) are highlighted. The Treatment Adherence Measure revealed that most of the participants complied with the medication treatment (85%).

Using Beck's Anxiety Inventory, it was verified that 50.9% of the participants presented a minimum degree of anxiety. The chi-square test did not reveal a statistically significant difference between

medication treatment compliance and anxiety symptoms ($\chi^2=2.93$; $p=0.230$). Nevertheless, a higher compliance percentage was found among patients with mild depression (92.1%).

Table 1 presents the prevalence rates of medication treatment compliance according to the study participants' demographic and socioeconomic variables.

No statistically significant differences were found between compliance and the investigated demographic and socioeconomic variables, but drug compliance was higher among male participants (86.1%), white (86.3%), without a partner (88.5%) and unemployed (100%).

As observed in Table 2, there was no statistically significant difference between the degree of compliance and the clinical variables investigated.

A higher compliance percentage was found among participants who only received medication treatment (86%), suffered from comorbidities (90.6%), had never been hospitalized to treat the anxiety disorder (85.7%) and did not take other types of drugs (86.3%).

Table 1 – Prevalence rates of medication treatment compliance according to study participants' demographic and socioeconomic variables. Ribeirão Preto, SP, Brazil, 2012

Variables	Compliance		χ^2 ⁽¹⁾	p-value
	Yes	No		
	n (%)	n (%)		
Sex			0.03	0.845
Male	31 (86.1)	5 (13.9)		
Female	106 (84.8)	19 (15.2)		
Age ranges			0.73	0.693
1st quartile (19-40 years)	34 (87.1)	5 (12.9)		
2nd quartile (41-60 years)	67 (82.7)	14 (17.3)		
3rd quartile (61-80 years)	36 (87.8)	5 (12.2)		
Skin color			1.80	0.179
White	126 (86.3)	20 (13.7)		
Non-white	11 (73.3)	4 (26.7)		
Marital status			0.91	0.339
With partner	83 (83)	17 (17)		
Without partner	54 (88.5)	7 (11.5)		
Occupation			0.40	0.191
Retired	21 (84)	4 (16)		
Unemployed	14 (100)	0 (0)		
Contracted worker	29 (85.2)	5 (14.8)		
Self-employed worker	18 (72)	7 (28)		
Housewife	55 (87.3)	8 (12.7)		
Education			0.06	0.970
No education	33 (84.6)	6 (15.4)		
Primary (finished/unfinished)	55 (85.9)	9 (14.1)		
Secondary (finished/unfinished) or higher	49 (84.4)	9 (15.6)		
Monthly family income			0.04	0.944
Up to 3 minimum wages	60 (85.7)	10 (14.3)		
Three minimum wages or higher	58 (85.2)	10 (14.8)		

⁽¹⁾ Critical score on chi-square test

Table 2 – Prevalence rates of medication treatment compliance according to study participants' clinical variables. Ribeirão Preto, SP, Brazil, 2012

Variable	Compliance		p-value $\chi^2^{(1)}$
	Yes	No	
	n (%)	n (%)	
Length of diagnosis			0.08 0.956
Up to 5 years	49 (85.9)	8 (14.1)	
6 to 10 years	64 (84.2)	12 (15.8)	
11 years or more	24 (85.7)	04 (14.3)	
Treatment types			0.85 0.355
Drugs only	123 (86)	20 (14)	
Drugs + others	14 (77.7)	04 (22.3)	
Clinical comorbidities			1.45 0.228
Yes	39 (90.6)	04 (9.4)	
No	98 (83)	20 (17)	
Use of other drugs			0.15 0.695
Yes	74 (84)	14 (16)	
No	63 (86.3)	10 (13.7)	
Other mental disorder			0.03 0.861
Yes	32 (84.2)	06 (15.8)	
No	105 (85.3)	18 (14.7)	
Hospitalization for anxiety treatment			0.51 0.474
One or more	11 (78.5)	03 (21.5)	
None	126 (85.7)	21 (14.3)	

⁽¹⁾ Critical score on chi-square test

Concerning the participants' knowledge on the prescribed drugs, a higher knowledge level was found regarding the administration frequency of the drugs, as 118 (73.2%) participants presented "good knowledge", because they correctly informed the administration frequency of 76 to 100% of the prescribed drugs. As verified, 55 (34.1%) participants could not inform the dose of the drugs they were taking.

Table 3 shows that there was no significant association between drug treatment compliance and the participants' level of knowledge on the drug name ($p=0.142$), dose ($p=0.448$) and administration frequency ($p=0.295$).

Among the participants with knowledge levels superior to 50% for all aspects investigated, drug treatment compliance was more frequent.

In this study, it was observed that the total number of drugs ($p=0.649$), number of pills per day ($p=0.752$), number of times the drug is administered per day ($p=0.765$), purchase of the drug when missing from the public network ($p=0.449$) and family support ($p=0.532$) were not associated with drug treatment compliance (Table 4).

It was identified that the subjects undergoing monotherapy presented a higher percentage of compliance (89.1%). A higher frequency of drug treatment compliance was found among participants who took five or less pills per day (85.3%), who administer the drug once a day (86.2%), who had never experienced shortage of the drug in the public network (88.5%) and who mentioned family support (86.4%).

Table 3 – Prevalence of drug treatment compliance and knowledge level on the name, dose and administration frequency of the drugs the study participants took. Ribeirão Preto, SP, Brazil, 2012

Variables	Compliance		$\chi^2^{(1)}$	p-value
	Yes	No		
	n (%)	n (%)		
Knowledge level on drug name(s)			2.15	0.142
0 – 0.5	32(78)	9(22)		
0.51 – 1.0	105(87.5)	15(12.5)		
Knowledge level on drug dose(s)			0.57	0.448
0 – 0.5	86(83.4)	17(16.6)		
0.51 – 1.0	51(87.9)	7(12.1)		
Knowledge level on drug frequenc(y)(ies)			1.09	0.295
0 – 0.5	27(79.4)	7(20.6)		
0.51 – 1.0	110(86.6)	17(13.4)		

⁽¹⁾ Critical score on chi-square test

Table 4 – Prevalence levels of drug treatment compliance and total number of drugs taken, number of pills per day, number of times the drug is taken per day, purchase of drug when missing from public network and family support. Ribeirão Preto, SP, Brazil, 2012

Variables	Compliance		$\chi^2^{(1)}$	P-value
	Yes	No		
	n (%)	n (%)		
Total number of drugs			0.86	0.649
1 drug	33(89.1)	4(10.9)		
2 drugs	73(84.8)	13(15.2)		
3 or more drugs	31(81.5)	7(18.5)		
Number of pills per day			0.09	0.752
< or = 5	128(85.3)	22(14.7)		
6 to 10	9(81.8)	2(18.2)		
Number of times drug is taken per day			0.08	0.765
Once	50(86.2)	8(13.8)		
Twice or more	87(84.4)	16(15.6)		
Buys drug when missing from the public network			1.60	0.449
Yes	57(83.8)	11(16.2)		
No	18(78.2)	5(21.8)		
Never short in the network	62(88.5)	8(11.5)		
Support from family and/or friends			0.38	0.532
Yes	89 (86.4)	14 (13.6)		
No	48 (82.7)	10 (17.3)		

⁽¹⁾ Critical score on chi-square test

● DISCUSSION

In this study, the most prescribed drugs were antidepressants, followed by anxiolytics. This result is in accordance with the literature recommendations for the drug treatment of anxiety, as antidepressants are the first-line drugs⁽⁶⁾.

Nevertheless, a high percentage of participants (69.5%) using benzodiazepines was identified, even six months after starting the treatment with antidepressants. This fact is a source of concern, as the use of benzodiazepines is contraindicated over a long period due to the possibility of abuse, intoxication, harmful use, dependence and abstinence⁽⁵⁾. The high prescription of benzodiazepines may be associated with the prescribers' limited knowledge on current treatment recommendations, lack of response to first-line treatments or the patient's preference⁽²³⁾.

This study identified a high percentage (85%) of medication treatment compliance among the participants. In this respect, a study identified that most participants abandoned the medication therapy at the start of the treatment⁽²⁴⁾. In this research, the participants were being treated for anxiety disorder for more than six months. One possible explanation for the high compliance percentage in the population can be the use of an indirect assessment measure, with a greater probability of overestimating the compliance⁽²⁵⁾.

It is also highlighted that, when the TAM was applied, the participant was asked about drug compliance to treat the anxiety disorder, and not specifically about antidepressants. This information is relevant when considering that 6.5% of the interviewees used anxiolytics, and may have considered the compliance with these drugs in their answers. The literature evidences that some people perceive that the benzodiazepines produce gratifying and rapid therapeutic effects, favoring compliance⁽²⁶⁾.

The drug compliance was high, among the participants with mild anxiety symptoms as well as with moderate and severe anxiety. In patients complying with the drug treatment, the compliance can partially explain the presence of minimal or mild anxiety symptoms. As for the high percentage of patients with moderate or severe anxiety symptoms, it is important to consider the possibility of treatment resistance, that is, the patient uses appropriate doses of the drug but does not present the desired response, and a significant part of the patients do not respond satisfactorily to the first-line pharmacological agents⁽²⁷⁾.

Medication treatment resistance affects about one out of three patients with anxiety disorder. Thus, many patients continue with clinically significant residual symptoms⁽²⁸⁾. These aspects strengthen the importance of assessing anxiety symptoms in patients being treated for anxiety disorders in order to adapt the therapeutic schedule. In addition, including psychosocial strategies is relevant to obtain better results⁽²⁹⁾.

Although no statistically significant differences were found between adherence and the variables investigated in this research, it was verified that medication treatment compliance was higher among male patients. The relation between gender and compliance has not been consistently demonstrated in the literature yet. Nevertheless, studies have been conducted with patients using antidepressants and other types of drugs that also revealed greater compliance in male patients⁽³⁰⁻³¹⁾.

In this respect, a study that summarized data from systematic reviews about compliance found that the effect of gender on compliance is not sufficiently clear, as heterogeneous results are found in the systematic reviews and there is a lack of consistent explanations on how gender can influence compliance⁽³²⁾.

Compliance was superior among unemployed patients. Literature does appoint unemployment as a factor of treatment abandonment though⁽³²⁻³³⁾. Studies are needed that clarify how employment can influence compliance, considering particularities related to types of work, environment and work relations⁽³⁴⁾. Therefore, it is suggested that future studies on the theme consider these aspects, with a view to clarifying their influence on medication treatment compliance in patients with anxiety disorder.

A lesser percentage of drug compliance was verified among participants previously submitted to psychiatric internment. It is important to highlight that the internment should facilitate the patient's active participation in the treatment, promote treatment compliance and education for self-care and develop effective planning before discharge⁽³⁵⁾.

What the use of other drugs is concerned, participants who did not use other types of drugs (86.3%) showed greater compliance. This finding is supported in the literature, which reveals that the simultaneous use of multiple drugs can negatively affect the compliance with the medication therapy⁽³⁶⁾, as the complexity of the therapeutic regimen negatively influences the compliance⁽³²⁾ and does not favor patients' knowledge about the drug prescription.

In this research, the high percentage of patients with clinical comorbidities is highlighted. It is important to mention the trend of patients with anxiety disorder to seek help for physical complaints. In these situations, a differential diagnosis is needed and the appropriate treatment for anxiety disorders as well as for clinical comorbidities⁽²⁾.

Patients' appropriate knowledge on the drugs they take is a fundamental factor for compliance⁽³⁷⁾. In this study, participants who showed knowledge levels of more than 50% about the name, dose and administration frequency of the drugs revealed a higher compliance frequency. The large percentage of participants with 0% of knowledge about the medication dose stands out. It is fundamental for the patients to know the dose of the drugs they are using, in view of the severe consequences an excessive drug dose can cause, especially in patients with anxiety disorder to whom antidepressants and anxiolytics are prescribed.

The higher frequency of compliance among participants who mentioned family support is emphasized. The support networks are important to cope with difficulties, especially with regard to chronic illnesses, in which extended difficulties need to be overcome⁽³⁸⁾ and drug compliance is linked to the patient's satisfaction with family members' engagement in care⁽³⁹⁾. Therefore, the family should be included and advised from the start, so that its participation in the treatment, in the control of relapses and in the improvement of communication can favor the preservation of stability⁽⁴⁰⁾.

● CONCLUSION

In this study, most participants complied with the drug treatment. The use of the indirect method to assess compliance may have contributed to this result.

No statistically significant association was found between drug compliance and the research variables. Nevertheless, the highest compliance frequency was found among the male participants, white, without a partner, unemployment, who were only receiving the medication treatment, with comorbidities, not submitted to internment to treat the anxiety disorder, in monotherapy, who had never experienced the lack of the drug in the public network and who mentioned family support.

The large percentage of participants with moderate and severe anxiety should be highlighted, despite the drug compliance, indicating possible treatment resistance and the need to screen these individuals with a view to adapting the medication scheme and implement psychosocial therapies, promoting treatment maintenance.

One concerning result identified in the study was the large percentage of patients using benzodiazepines, even six months after the start of the treatment with antidepressants, going against current recommendations for medication treatment of people with anxiety disorders. The extended use of benzodiazepines can add problems for anxiety patients, as it exposes them to the risk of tolerance and addition. Therefore, with this knowledge, nursing needs to play an active role in the assessment, orientation and discussion with the theme and patients about the drug prescription, with a view to defending the best treatment options.

A higher frequency of compliance was verified among participants with greater knowledge on their therapeutic scheme. Nevertheless, a large percentage of them did not know the medication dose being used. These data appoint the importance of offering educative strategies that promote greater safety

and co-participation in the medication treatment.

Considering that drug compliance is necessary to achieve better treatment outcomes, this study contributes by appointing relevant aspects the health professionals should systematically investigate and take into account in care delivery to patients with anxiety disorder under medication treatment.

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