

Mental patients and their profile of compliance with psychopharmacological treatment*

DOENTES MENTAIS E SEU PERFIL DE ADESÃO AO TRATAMENTO PSICOFARMACOLÓGICO

LOS ENFERMOS MENTALES Y SU PERFIL DE ADHESIÓN AL TRATAMIENTO PSICOFARMACOLÓGICO

Lucilene Cardoso¹, Sueli Aparecida Frari Galera²

ABSTRACT

Non-compliance with drug-based treatment is a complex and universal phenomenon that develops gradually during psychiatric treatments, and is related to disease aggravation. The purpose of this study was to describe the profile of using a given medication in the clientele of a community mental healthcare service and its characteristics. We performed a retrospective study in the medical records of patients who used Haloperidol Decanoate in a period of 1 year and 8 months. 167 medical records were analyzed. 60% of the patients presented irregular use of medication, which reflects in high risks of relapse and re-hospitalizations. This profile configures low compliance with the prescribed drug treatment, leading to reflections about which factors influence this behavior and which measures could be implemented in the maintenance of extra-hospital treatment for these patients.

KEY WORDS

Mentally ill persons.
Patient compliance.
Treatment refusal.
Community psychiatry.
Psychiatric nursing

RESUMO

A não adesão ao tratamento medicamentoso é um fenômeno complexo e universal que se desenvolve gradualmente no curso dos tratamentos psiquiátricos e está relacionado ao agravamento das doenças. O objetivo deste estudo foi descrever o perfil de utilização de um psicofármaco na clientela de um serviço de saúde mental comunitário e suas características. Realizamos um estudo retrospectivo, nos prontuários de pacientes que fizeram uso de Decanoato de Haloperidol, num período de 1 ano e 8 meses. Analisamos 167 prontuários. O uso irregular da medicação esteve presente em 60% dos pacientes e reflete um grande risco para ocorrência de recaídas e reinternações. Este perfil configura uma baixa adesão ao tratamento medicamentoso prescrito, o que remete a reflexão sobre quais fatores estão influenciando este comportamento e quais medidas podem ser implementadas na manutenção do tratamento extra-hospitalar destas pessoas.

DESCRIPTORES

Pessoas mentalmente doentes.
Cooperação do paciente.
Recusa do paciente ao tratamento.
Psiquiatria comunitária.
Enfermagem psiquiátrica.

RESUMEN

La no adhesión al tratamiento medicamentoso es un fenómeno complejo y universal que se desarrolla gradualmente en el curso de los tratamientos psiquiátricos y está relacionado al agravamiento de las enfermedades. El objetivo de este estudio fue describir el perfil de utilización de un psicofármaco en la clientela de un servicio de salud mental comunitaria y sus características. Realizamos un estudio retrospectivo en los registros de pacientes que usaron el Decanoato de Haloperidol, en un período de 1 año y 8 meses. Analizamos 167 registros. El uso irregular de la medicación estuvo presente en 60% de los pacientes y refleja un gran riesgo para el apareamiento de recaídas y nuevas internaciones. Este perfil configura una baja adhesión al tratamiento medicamentoso prescrito lo que nos lleva a reflexionar sobre cuales serían los factores que están influenciando este comportamiento y cuales serían las medidas que pueden ser implementadas en la mantención del tratamiento de estos sujetos fuera del hospital.

DESCRIPTORES

Enfermos mentales.
Cooperación del paciente.
Negativa del paciente al tratamiento.
Psiquiatría comunitaria.
Enfermería psiquiátrica.

* Extracted from the thesis "Perfil demográfico e clínico de pessoas que fazem uso de Decanoato de Haloperidol", Ribeirão Preto College of Nursing, University of São Paulo, 2006. ¹ Doctoral student of the Psychiatric Nursing Graduate Program at Ribeirão Preto College of Nursing, University of São Paulo, São Paulo, SP, Brazil. lucileneca@yahoo.com.br ² Advisor and Professor of the Psychiatric Nursing and Human Sciences Department at Ribeirão Preto College of Nursing, University of São Paulo, São Paulo, SP, Brazil. sugalera@eerp.usp.br

INTRODUCTION

According to international estimates and those provided by the Ministry of Health, 3% of the population (5 million people) need continuous care due to grave and persistent mental disorders, and another 9% need occasional treatment related to less severe disorders, totaling 12% of the general population of the country – 20 million people⁽¹⁾.

Mental disorders with chronic evolution, characterized by continuous poly-medication treatment, are marked by instability in the manifestation and treatment of the pathology. In the course of the disease, mental patients and their relatives experience periods where the symptoms are controlled and reduced, alternating with moments of crisis, psychiatric relapses and the consequent re-hospitalization of the patients⁽²⁾.

In general, periods in which symptoms are reduced and controlled are possible due to an efficient drug-based treatment, associated to non-medication treatment (psychotherapy, operative group, psychoeducational programs, family therapy, home visits, occupational therapy, development of skills, assisted medication, rehabilitation programs, support groups, therapeutic monitoring, among others⁽³⁾). However, in this context, the mental patient's compliance with the medication-based treatment is often low. Non-compliance with medication is observed in about 50% of the people undergoing mental treatment, and this is responsible for many serious consequences, in addition to being the main cause of psychiatric morbidity and re-hospitalizations⁽⁴⁾.

Non-compliant behaviors regarding drug-based treatment are complex and universal phenomena. In the course of psychiatric treatment, non-compliance develops gradually and is related to the aggravation of the diseases⁽⁵⁾. In certain cases, as a consequence of relapse, the recovery time often becomes longer and the clinical response is inferior to the treatment⁽⁶⁾.

Concepts for compliance vary widely in literature, but the term can be defined as *the utilization of prescribed medication or other procedures in at least 80% of the time, observing times, doses and treatment length*⁽⁷⁾. This is a behavior determined by the dynamics of multiple factors, which also makes it difficult to define measurement instruments and effective interventions to supplant it⁽⁸⁾.

Recent studies about compliance associate the use of specific drugs in patients with different psychiatric diagnoses. These studies indicate that the behavior in situations of non-compliance to drug treatment is determined by different factors⁽⁹⁾. Mental patients and their relatives, during the maintenance of drug treatment, are influenced by specific and complex situations, which make the generalization of the findings difficult for other conditions than those

studied. However, this is a relevant theme, since there are cases when over 85% of the patients may be non-compliant during a given period in the course of their disease, and suffer the consequences of such behavior along with their relatives⁽¹⁰⁾. It is known that the risks of hospitalization and relapse are lower in patients considered compliant with psychopharmacological treatment when compared to patients who do not comply with treatment⁽⁵⁻⁶⁾.

Recent studies suggest that the risk of relapse is around 3.5 to 10% every month, approximately^(5,11), and they point to non-compliance to psychopharmacological treatment as the main reason for the occurrence of relapse in non-hospitalized patients⁽¹²⁾. The permanence of the symptoms due to poor compliance makes it difficult to elaborate therapeutic and psychological approaches, interaction between the healthcare team and the patient, and it even hinders the patient's social reintegration. The factors that can influence compliance are related to socio-demographic conditions, the therapeutic plan, the nature of the disease and the relationship between patients and healthcare professionals, among others^(9,13).

Among these factors, the following are worth noting: non-acceptance of the disease and disbelief in the benefits of treatment, the occurrence of side effects due to the utilization of the drugs, the lack of insight, the severity of the disease, alcohol and drug abuse, acceptance of the disease and fear of re-hospitalizations (relapse), treatments with deposit medication, low complexity of the therapeutic scheme and the establishment of a therapeutic alliance between the healthcare professional and the patient⁽¹⁴⁾.

Different methods (direct and indirect) have been used to characterize the compliance of the patient to the prescribed treatment. Direct methods are characterized by the detection of the medication or the products of their metabolism in the patient's biological fluids. Indirect procedures include measurements performed through interviews with the patient, information obtained from healthcare professionals and the patients' relatives, results of treatments or prevention activities, filling prescriptions and counting pills⁽¹³⁾. However, there is still no method that guarantees the simultaneous approach of all possible daily factors that can influence treatment compliance.

Better knowledge and understanding of non-compliance and the universe of the mental patients can provide healthcare professionals with resources that are more adequate to the maintenance of the psychiatric treatment and better tools to prevent relapses related to this phenomenon. Since nursing is directly linked to treatment and daily routine of the patient, it can promote the establishment of a therapeutic alliance, support and maintenance of treatment, in addition to identifying everyday occurrences that may interfere in the patient's compliance. This is a signifi-

In the course of
psychiatric treatment,
non-compliance
develops gradually and
is related to the
aggravation of the
diseases.

cant field for all healthcare professionals, as it influences the whole personal, professional and social universe of the treatment of mental patients.

OBJECTIVE

This study aimed to describe the utilization (compliance) profile of a drug in the clientele of a community mental healthcare service and its characteristics.

METHOD

This is a cross-sectional, retrospective study, using all medical records of patients who used the following drug: haloperidol decanoate (HD), from October 29, 2003 to June 30, 2005 (one year, eight months), at the Mental Healthcare Center - *Núcleo de Saúde Mental (NSM)* in the city of Ribeirão Preto, Brazil.

Place

The Mental Healthcare Center *Núcleo de Saúde Mental (NSM)*, an outpatient clinic that is part of the Teaching Healthcare Center *Joel Domingos Machado* of Faculdade de Medicina de Ribeirão Preto - Universidade de São Paulo - USP - Brazil (CSE-FMRP-USP). This is an outpatient Psychiatric and Psychological clinical service for people over 18 years old, living in the western district of the city, after being referred there by the healthcare units. The actions developed by the aforementioned services are: psychiatric-medical service; nursing services (appointments); psychological monitoring; speech pathology care and therapy groups. According to the NSM's routine, the patient receiving care at the center can receive the prescribed drugs for free at the CSE-FMRP-USP pharmacy, or buy it instead. The patients usually choose to receive the prescribed medication for free at the CSE-FMRP-USP. Therefore, upon receiving the drugs, one of the employees of the service or an accompanying partner escorts the patient to the nursing room, where the medication is administered by the nurse or a nursing technician, according to the medical prescription. Every time the NSM patient receives medication, this requirement is registered in the computerized databanks of the pharmacy. For this reason, we decided to use the registry of the

Chart 1: Utilization profile of utilization of haloperidol decanoate, according to the intervals between administrations and the risk of relapse. Ribeirão Preto - SP, 2007.

Medication usage	Prescribed interval between administrations	Risk of relapse
Regular use	Up to 27 days	Low
Regular use according to prescription	28 to 31 days	Low
Irregular use	32 to 73 days	Increased
Abandonment or suspension of the treatment	Over 73 days	Highly increased

We used SPSS software, v. 10.00, for data analysis. The distance between the patient's home and the service was estimated using AutoCAD software, version 2000. Data analysis was performed with central tendency measures and

aforementioned pharmacy to identify the clients receiving care at the NSM who received at least one provision of haloperidol decanoate during the studied period.

Sample

Medical records of patients of both genders were included in this study, who were regularly registered at the healthcare service, with at least one record of receiving haloperidol decanoate in the pharmacy of the service, from October 29, 2003 to June 30, 2005. The registry of drugs provision at the NSM pharmacy was used to identify the records of clients who used haloperidol decanoate.

Procedures

After the patients who received the medication at the service were identified, the authors started data collection in the respective medical records, using a questionnaire with the following variables: *age, gender, marital status, number of children, education, date of the first haloperidol decanoate prescription, records of adverse effects, type of adverse effect registered, records of alterations in the prescription, type of alteration, first diagnosis registered, records of interurrences, type of interurrences, hospitalization records, number of recorded hospitalizations, date and amount of all occasions on which the patient received the haloperidol decanoate at the pharmacy, approximate distance between the patient's home and the service, and average intervals between each time the patient received the medication.*

The following rules were followed to classify the subjects of this research according to the medical intervals in which they received the medication: *the indicated haloperidol decanoate posology is equal to ten to twenty times the oral dose of haloperidol or another equivalent neuroleptic drug, administered intramuscularly in four-week intervals⁽¹⁵⁾. Patients who suddenly interrupt haloperidol treatment have 25% more chance of relapse in six weeks⁽¹⁶⁾. That is, when the patient stops taking the prescribed dose, the following 42 days (six weeks) are a period of risk for relapse.*

Therefore, the sample subjects were classified according to the utilization profile of the drug, according to Chart 1, as follows:

statistical correlation tests. All the studied variables were compared with the average intervals in which the patients received the medication, applying Kruskal Wallis (H) and chi-square (χ^2) statistical tests.

This study was approved by the Ethics Committee of Centro de Saúde Escola *Joel Domingos Machado* of Faculdade de Medicina de Ribeirão Preto - University of São Paulo - USP - (protocol #0158/CEP/CSE-FAMRP-USP).

RESULTS

From October 29, 2003 to June 30, 2005, 180 mental patients, clients of the community healthcare service, received haloperidol decanoate at the pharmacy on at least one occasion. Thirteen of the aforementioned records were not found at the service. Therefore, 167 records were analyzed, with 22.8% (38 records) having no information about the patient's marital status; 31.1% (52 records) had no information about the number of children of the patient and 49.7% (83 records) had no data about the patient's education.

Demographic characteristics

Of all patients, 55.8% (N=129) were single; 48.7% (N=115) had no children and 57.1% (N=84) had incomplete elementary education. There were no records of patients with college education. Among the 167 medical records analyzed, 50.9% were male, between 19 and 83 years old, with an average age of 43 years. Most patients (55.1%) lived between 1 and 3 Km away from the healthcare service and only 4.8% of the patients lived further than 6 Km away. The shortest distance between the healthcare service and the

patient's household was approximately 5 meters, and the highest was 24.5 Km. Average distance was 3 Km.

The demographic characteristics did not present a statistically significant relation with the average intervals of the events when the patients received the medication, as identified in the sample.

Profile of medication usage

Most patients were prescribed up to three ampoules of haloperidol decanoate (78.4%), to be administered every 30 days (95.8% of the cases). Only five patients had an immediate haloperidol decanoate prescription, probably related to adjustments of the prescribed doses, or a situation where a patient received the medication followed by treatment abandonment. One patient had a prescription for 20-day intervals between administrations of haloperidol decanoate, and another patient for 21-day intervals. No patient was prescribed administration intervals superior to 30 days. The average intervals in which the patients received the medication varied between 7 and 444 days.

In Table 1, it can be observed that, for most patients (51.5%), intervals in which they received the medication averaged between 32 and 73 days, indicating an irregular use of the drug and increased risk of relapse. When patients who received the medication in a period over 73 days are added, 60% of the sample was classified as using the medication irregularly, with increased risks for the occurrence of relapse.

Table 1 - Association between the average intervals in which the patients received haloperidol decanoate in the pharmacy at the institution and length of treatment. Ribeirão Preto, SP - 2007

Length of treatment with H.D. (full years)	Classification of the average intervals in which the patients received the drug, in days				Total (%)
	≤ 27 days	28 to 31 days	32 to 73 days	> 73 days	
0 - 2	21	19	29	8	77 (46)
3 - 5	8	12	43	5	68 (41)
6 - 8	2	3	13	1	19 (11)
Over 8	2	-	1	-	03 (02)
Total (%)	33 (19.8)	34 (20.3)	86 (51.5)	14 (8.4)	167 (100)

Treatment characteristics

On average, the studied patients had been undergoing haloperidol decanoate psychopharmacological treatment for the past three years, with 46% of those receiving treatment for less than two years, 41% from three to five years and only three patients for more than 8 years, according to Table 1.

A statistically significant association ($p \leq .001$) was found between the length of treatment and the average

intervals in which the patients received the drug, as observed in Table 1.

In tables 2 and 3, we can observe that increased prescribed doses of haloperidol decanoate and the schizophrenia diagnosis, respectively, had a tendency of association, which should be further explored in another study. During the treatment, 69 patients had their haloperidol decanoate dose increased.

Table 2 - Association between the average intervals in which the patients received haloperidol decanoate in the pharmacy at the institution and the increased prescribed H. D. dose. Ribeirão Preto, SP - 2007

Classification of the intervals, in full days	Increased prescribed dose		Total
	Yes	No	
≤ 27 days	8	25	33
28 to 31 days	9	25	34
32 to 73 days	45	41	86
>73 days	7	7	14
Total	69	98	167

χ^2 :11.79/ $p \leq .008$

Among the 167 subjects studied, 114 (68.2%) had schizophrenia as their only diagnosis or as a main diagnosis, added to others, as shown in Table 3.

Table 3 - Association between the average intervals in which the patients received haloperidol decanoate in the pharmacy at the institution and the schizophrenia diagnosis. Ribeirão Preto, SP - 2007

Classification of the intervals, in full days	Schizophrenia diagnosis		Total
	No	Yes	
≤ 27 days	16	17	33
28 to 31 days	9	25	34
32 to 73 days	20	66	86
>73 days	8	6	14
Total	53	114	167

χ^2 :11.734/ $p \leq .008$

Regarding the psychiatric diagnosis, we identified that 112 (67.1%) patients had only one diagnosis; 42 (25.1%) had two diagnoses, 11 (6.6%) had three diagnoses and 2 (1.2%) had four diagnoses. Therefore, 112 (67.1%) patients

had only one diagnosis, while 55 (32.9%) presented comorbidities. Table 4 presents a general overview of the diagnosis of the studied sample, and briefly describes the occurrence of comorbidities.

Table 4 – Distribution of the relative frequencies of the main diagnosis and comorbidities among the patients who received haloperidol decanoate in the pharmacy of the service. Ribeirão Preto, SP - 2007

Diagnosis	N (%)	N per main diagnosis and percentages (%)	
Schizophrenia	83 (49.7)	114	(68.2)
Schizophrenia + 1 diagnosis	25 (15.0)		
Schizophrenia + 2 diagnoses	4 (2.4)		
Schizophrenia + 3 diagnoses	2 (1.2)		
Mood disorders	15 (9.0)	21	(12.6)
Mood disorders + 1 diagnosis	4 (2.4)		
Mood disorders + 2 diagnoses	2 (1.2)		
Neurotic disorders	6 (3.6)	11	(6.6)
Neurotic disorders + 1 diagnosis	5 (3.0)		
Personality disorders	2 (1.2)	11	(6.6)
Personality disorders + 1 diagnosis	5 (3.0)		
Personality disorders + 2 diagnoses	4 (2.4)		
Mental retardation	2 (1.2)	5	(3.0)
Mental retardation + 1 diagnosis	3 (1.2)		
Mental retardation + 2 diagnoses	1 (0.6)		
Organic disorders	4 (2.4)	5	(3.0)
Organic disorders + 1 diagnoses	1 (0.6)		
Total (%)	167 (100.0)	167	(100.0)

The occurrence of adverse effects was identified in 67 (40.1%) patients. However, this variable did not present a significant association with the average intervals in which

the patients received the medication. With the analysis of each type of adverse effect, in separate, the neuroleptic impregnation occurred in 15 patients during treatment,

with nine having shivers and nine complaining of headaches. Eighteen patients complained of insomnia.

Of all the 167 patients studied, 83.2% presented *intercurrences*, usually varied and concomitant: 63.5% received care on occasional appointments, 53.3% missed scheduled appointments, 34.7% needed emergency appointments in another mental healthcare service, 34.1% abandoned treatment and monitoring at the service at some moment. Of all 167, 13 patients attempted suicide at least once, eleven were medically discharged and three died (non-specified deaths). No statistically significant association was found between the average intervals in which the patients received haloperidol decanoate and the occurrence of these *intercurrences*.

Most patients (57.5%) had at least one hospitalization recorded in their registries since they were admitted in the service. The patient with the highest number of recorded hospitalizations accounted for 44 occurrences. The variable *hospitalization occurrence* had no statistically significant relation with the average intervals in which the patients received the medication in this study.

DISCUSSION

Irregular use of medication was observed in 60% of the patients receiving treatment at the healthcare service. Since most patients were prescribed haloperidol decanoate in 30-day intervals, it was expected that most of them would have received their medication regularly, within the 28-31 day period, which would indicate compliant behavior and low risk of relapse, which did not occur. These findings are similar to others found in studies about compliance to drug treatment, where 50% of the patients do not comply to treatment with psychopharmaceutical substances^(3-4,6).

The length of treatment appears to be a possible factor that influences the irregular use of the medication, since this variable presented a tendency of association with this behavior. Possibly, over the years, the patient loses the motivation to use the medication regularly and continuously.

Among patients treated with conventional neuroleptic drugs, 40% stop taking their medication in their first year of treatment and 75% stop taking this medication within two years. Often, the cost of the treatment (adverse effects, complexity of the therapeutic scheme, long-term compliance) are considered more negative by the patients than having to live with the cost of the disease (distortions of thoughts, perception and affection; difficulty of social acceptance), which can sometimes lead to low compliance with drug therapy⁽¹⁷⁾.

This is a concerning finding, which reveals the necessity to organize of organization of the services to stimulate and aid in the maintenance of this type of treatment. Prescription of a deposit drug alone, indicated for patients with

difficulties in complying, does not seem to guarantee the regular use of the medication, as observed in the findings. The irregular use of the medication by these patients indicates a behavior of increased risk for the occurrence of relapse and its consequences. For these cases, it is known that the continuity of the drug treatment, with the aid of non-drug therapies, permits the promotion of psychosocial rehabilitation, minimization of risks and relief of family stress. When it is effective, the maintenance of the treatment can control psychotic symptoms by preventing consecutive relapse and hospitalizations⁽³⁾.

The purpose of this maintenance is to promote healthcare that is closer to the patients' daily routine, and therefore to aid in the rearrangement of their psychosocial capacities and potentials in the course of the disease. For this reason, psychosocial rehabilitation is also extremely important in the treatment of this clientele, which needs more involvement in their own self-care. However, psychosocial treatment, which has the purpose of helping patients and relatives to cope with everyday difficulties and organize the patients' lives⁽³⁾, needs to be in harmony with the continuity of the drug treatment.

An important characteristic in this study sample was the predominance of the schizophrenia diagnosis among patients who use deposit medication. Recent studies with schizophrenic patients suggest that the risk of relapse is around 3.5 to 10% per month, approximately^(5,11), and indicate non-compliance with drug treatments as the main reason for the occurrence of relapse among non-hospitalized patients^(12,18). Since this is a complex mental disorder, usually with a chronic evolution, healthcare professionals need to develop more qualified monitoring to treat these patients.

In spite of several therapeutic modalities being available nowadays, either psychopharmacological (with new and potent antidepressants, anxiolytics, mood stabilizers and antipsychotics) or psychosocial (with very efficient psychotherapeutic techniques), many patients do not respond satisfactorily to the treatment, being resistant and even refractory to the treatment⁽⁴⁾.

The permanence of the symptoms due to poor compliance makes the interaction between the healthcare team and the patient difficult, much like therapeutic and psychosocial approaches. In addition, it also hinders the patients' social reintegration. Factors that can influence compliance are certainly related to the socio-demographic conditions, the therapeutic plan, the nature of the disease, the relationship between the patient and the healthcare team, among others^(7,13). However, the complex dynamics among so many factors limit accurate measurement of this population with low compliance to drug treatments.

In this research, although the secondary data source (the medical records) has also limited the apprehension of more information that could influence the utilization behavior of the medication by the mental patients, this pro-

cedure is pertinent because it continuously documents the course of disease treatment in this population. These are records about the patients and their treatment and, as such, they are important for research and reflection about the necessities of the clients and the healthcare they are offered. It is worth noting that the healthcare professionals should always be conscious of how to fill out this information, the registration of their clients and the maintenance of these data in order to collaborate for a better comprehension of the necessities of this clientele.

FINAL CONSIDERATIONS

The study allowed us to conclude that the profile of irregular use of the prescribed medication characterized the studied sample, representing a great risk for relapse and re-hospitalizations among the mental patients. This profile configures low compliance to the prescribed drug treatment, leading to a reflection about which factors influence

this behavior and which measures can be implemented to maintain the extra-hospital treatment of these people.

To us, healthcare professionals, such a result demonstrates that the healthcare offered is still far from ideal and needs to be enhanced. One of the strategies could be the improvement of the interpersonal relationship in the maintenance of the psychiatric treatment, so as to promote better relations of the patients with their bodies, their social circle, their families and their current capabilities. For nursing, a profession that is characteristically interactive and systematic during care, this pathway is necessary to solve problems and maintain treatment, as long as integrity, autonomy and freedom of the clients are respected.

Health should not be seen only as the result of intervention processes in the disease, but also of interventions that may offer strategies to the individuals and their social midst to promote, recover and maintain their state of health inserted in the particular context and daily routine of each and every one.

REFERENCES

1. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Saúde mental no SUS: os centros de atenção psicossocial [texto na Internet]. Brasília; 2004. [citado 2007 nov. 23]. Disponível em: http://www.ccs.saude.gov.br/saude_mental/pdf/SM_Sus.pdf
2. Whitehorn D, Richard JC, Kopala LC. Hospitalization in the first year of treatment for schizophrenia. *Can J Psychiatry*. 2004; 49(9):635-8.
3. Shirakawa I. Aspectos gerais do manejo do tratamento de pacientes com esquizofrenia. *Rev Bras Psiquiatr*. 2000;22 Supl 1:56-8.
4. Gray R, Wykes T, Gournay K. From compliance to concordance: a review of the literature on interventions to enhance compliance with antipsychotic medication. *J Psychiatr Ment Health Nurs*. 2002;9(3):277-84.
5. Davis JM, Chen N. Choice of maintenance medication for schizophrenia. *J Clin Psychiatry*. 2003;64 Suppl 16:24-33.
6. Bechelli LPC. Antipsicóticos de ação prolongada no tratamento de manutenção da esquizofrenia. Parte I - Fundamentos do seu desenvolvimento, benefícios e nível de aceitação em diferentes países e culturas. *Rev Lat Am Enferm*. 2003;11(4): 507-15.
7. Leite SN, Vasconcellos MPC. Adesão à terapêutica medicamentosa: elementos para a discussão de conceitos e pressupostos adotados na literatura. *Cad Saúde Coletiva*. 2003;8(3):775-82.
8. Rigueira Garcia AL. Cumplimiento terapéutico: ¿qué conocemos de España?. *Aten Primaria*. 2001;27(8):559-68.
9. Kurita GP, Pimenta CAM. Adesão ao tratamento da dor crônica e o locus de controle da saúde. *Rev Esc Enferm USP*. 2004;38 (3):254-61.
10. O'Connor PJ. Improving medication adherence: challenges for physicians, payers, and policy makers [editorial]. *Arch Intern Med*. 2006;166(17):1802-4.
11. Csernansky JG, Schuchart EK. Relapse and rehospitalisation rates in patients with schizophrenia: effects of second generation antipsychotics. *CNS Drugs*. 2002;16(7):473-84.
12. Hamann J, Cohen R, Leucht S, Busch R, Kissling W. Shared decision making and long-term outcome in schizophrenia treatment. *J Clin Psychiatry*. 2007;68(7):992-7.
13. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther*. 2001;26(5):331-42.
14. World Health Organization (WHO). Adherence to long-term therapies: evidence for action [text on the Internet]. Geneva; 2003 [cited 2007 nov. 23]. Available from: http://www.who.int/entity/chp/knowledge/publications/adherence_report/en/index.html
15. Nyberg S, Farde L, Halldin C. Delayed normalization of central D2 dopamine receptor availability after discontinuation of haloperidol decanoate: preliminary findings. *Arch Gen Psychiatry*. 1997;54(10):953-8.
16. Glazer WM, Kane JM. Depot neuroleptic therapy: an underrated treatment option. *J Clin Psychiatry*. 1992;53(12): 426-33.
17. Perkins DO. Adherence to antipsychotic medications. *J Clin Psychiatry*. 1999;60 Suppl 21:25-30.
18. Yamada K, Watanabe K, Nemoto N, Fujita H, Chikaraishi C, Yamauchi K, et al. Prediction of medication noncompliance in outpatients with schizophrenia: 2-year follow-up study. *Psychiatry Res*. 2006;141(1):61-9.