

Adherence to antipsychotic medication in indigenous patients with schizophrenia

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Original article

ABSTRACT

Introduction

Non-adherence to antipsychotic medication remains a complex problem in the treatment of schizophrenia patients, especially in indigenous population.

Objective

The aim of the study was to assess the differences in drug adherence, measured by the attitude towards the antipsychotics among Aymara and Non-Aymara patients with schizophrenia.

Method

The sample consisted of patients receiving treatment in the Mental Health Public Services in Bolivia (32.8%), Peru (33.6%) and Chile (33.6%). We used the Drug Attitude Inventory (DAI-10); the Barnes Akathisia Scale (BAS), as a measure of side effects, and the Positive and Negative Syndrome Scale (PANSS) to assess the severity of the disorder.

Results

The findings showed that Aymara patients present less adherence than Non-Aymara people; however, these differences were not significant ($t = 1.29$; $p = 0.19$). The severity of the disorder, as well as the age, showed a significant association with adherence, revealing that younger patients and with greater symptoms presented a more negative attitude toward the drugs.

Discussion and conclusion

The lack of significant differences between the groups responds to three possible reasons: 1. This sample of indigenous patients is integrated on Mental Health Services that offer a clear biomedical approach where drug therapy is the primary treatment. 2. It is possible that these indigenous patients are changing their conception of mental disorder, and 3. A significant number of families have migrated to urban areas. These migratory dynamics have promoted the loss of traditions and customs of the ethnic group, which gradually adopts new and intercultural lifestyles. Professionals should be warned about applying stereotypes regarding the relationship between ethnicity and antipsychotics.

Key words: Indigenous, schizophrenia, adherence, medication.

RESUMEN

Introducción

La falta de adherencia a la medicación antipsicótica sigue siendo un problema en el tratamiento de pacientes con esquizofrenia, más aún en población indígena.

Objetivo

Evaluar las diferencias en la adherencia farmacológica, medida a través de la actitud hacia los antipsicóticos, entre pacientes aymara y no-aymara con esquizofrenia.

Método

La muestra estuvo compuesta por pacientes que recibían tratamiento en los Servicios Públicos de Salud Mental de Bolivia (32.8%), Perú (33.6%) y Chile (33.6%). Se utilizó el Inventario de Actitud hacia la Medicación (DAI-10); la Escala Barnes de Acatisia (EBA) como medida de efectos secundarios y la Escala para el Síndrome Positivo y Negativo de la Esquizofrenia (PANSS) para evaluar la severidad del trastorno.

Resultados

Los pacientes aymara presentan una menor adherencia que los pacientes no-aymara, sin embargo, estas diferencias no fueron significativas ($t = 1.29$; $p = 0.19$). La severidad del trastorno y la edad mostraron una asociación significativa con la adherencia, observándose que pacientes más jóvenes y con mayor sintomatología presentan una actitud más negativa hacia los fármacos.

Discusión y conclusión

Se discute cómo las dinámicas migratorias han promovido la pérdida de tradiciones y costumbres propias de la etnia promoviendo la adopción de estilos de vida nuevos y cada vez más interculturales, e incluso cambiando su concepción de la enfermedad mental. Los profesionales tratantes deben estar conscientes de no aplicar estereotipos en cuanto a la relación etnia-antipsicóticos.

Palabras claves: Indígenas, esquizofrenia, adherencia, medicación.

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INTRODUCTION

Antipsychotic medication has shown to reduce symptomatology and relapses associated with schizophrenia.¹ Despite these benefits, non-adherence rates in patients range from 20% to 89%,²⁻¹⁰ being this the biggest obstacle in the management of the disorder.²

Adherence is defined as "the extent to which the behavior of a patient, in relation to medication taken the diet followed or lifestyle changes, corresponds to the recommendations agreed to the health professional".¹¹ On the other hand, the term "therapeutic compliance" is related to a more passive and submissive behavior of the patient to comply with a medical order or prescription. The lack of participation in the definition, according to Dilla¹² et al. (2009) would evidence the lesser use of the term compliance although in the clinic both concepts are used interchangeably.¹³

Adherence to the pharmacological treatment in schizophrenia is a complex phenomenon with multiple factors, summarized in four: socio-demographic variables; variables related to the disorder itself (type of schizophrenia, severity, course of the disorder); treatment-related variables (frequency and intensity of side effects, length of treatment) and, finally, variables that have to do with the values and attitudes of the patient (attitude toward the disease).^{8,14,15} Patients who do not maintain an adequate pharmacological adherence present about 10 times more risk of relapse and four times more risk of hospitalization than those with an adequate adherence.¹⁶ The latter one has consequences for both the patient and the society.¹⁷⁻²⁰ Previous studies have found that young male patients with low socioeconomic status, belonging to a minority, with poor social functioning and difficulties in establishing an adequate therapeutic alliance present more challenges in achieving adherence to the treatment.^{8,21} It has likewise been observed that the cultural context and ethnicity also have an important influence. Thus, African-American and Mexican-American patients showed lower adherence (19 days and 18 days less, respectively) than white patients in a study conducted in Texas.^{22,23} In this same framework Diaz et al.,²⁴ in 2005, found that African-American and monolingual Latino patients also presented worse adherence than Caucasians. Similar results were found in San Diego.²⁵ The latter leads to the conclusion that adherence to antipsychotic medication varies among ethnic groups.¹

Although the aforementioned studies have been carried out in the United States, there is little literature in Latin America supporting a link between adherence to antipsychotic drugs and belonging to ethnic minorities. However, there are some experiences in the region with psychosocial interventions that improve adherence of patients with schizophrenia, such as the incorporation of social skills training, psychological rehabilitation, integrated treatment and psychoeducation.²⁶⁻³⁰

This article is an observational cross-sectional study that aims to describe the level of adherence to pharmacological treatment in patients with schizophrenia belonging to the indigenous Aymara ethnic group, and compare it with the level of adherence of Non-Aymara patients. The effect of the socio-demographic variables on the adherence to treatment was also studied. To achieve the objective, the Drug Attitude Inventory (*Inventario de Actitud hacia la Medicación, DAI-10*)³¹ as well as the Barnes Akathisia Scale (BAS, *Escala Barnes de Acatisia EBA*),³² were used as a measure of side effects and the Positive and Negative Syndrome Scale (PANSS)³³ was used to assess the severity of the disorder.

Both groups of patients, Aymara and Non-Aymara, receive treatment in the Mental Health Services in Bolivia, Peru and Chile. The Aymara community has a population of approximately two million living in the highlands of the Andes. However, recent Aymara generations have massively migrated from rural villages to larger cities with better job prospects.³⁴⁻³⁷

The Aymara worldview arranges the world in three dimensions: social relationships and with "deities" and the relationship with nature. These three dimensions are intimately intertwined and fully integrated into landscapes and nature in general. It can be said that their way of understanding the universe is enunciated around "cyclical" processes of nature itself and the ritual calendar that they have adapted themselves to the rhythms of nature.

The Aymara do not see themselves as masters of nature, but rather as an intrinsic part of it, fundamental to the maintenance (ritual, educational, economic) of the desired harmony. The Aymara narrative principle that conceives "good living" as a harmonious walk is possible by a concept of culture historically understood in a dynamic and cohesive way.³⁵

If this dynamic conception of the Aymara tradition is considered, it can be said that its behavior will be related to the need to preserve and maintain balance and harmony. If one can speak of an Aymara ethics, it would fundamentally imply a practice and a community experience, unlike the ethics that has become hegemonic in the West, which is based on individualism and personal achievement. This is how urban environments often break with the conception of balance and harmony proper to the Andean worldview.³⁸

In the hypothesis of the study we expect to find a difference related to the adherence toward medication between groups and the effect of socio-demographic variables. In this way Aymara patients, who consider that the disease is generated by a lack of balance caused by the evil spirits or a sin of the affected person, will show a lower adherence towards the antipsychotic medication, this also given because the treatment in this community involves the consumption of herbs and the performance of rituals.^{39,40}

METHOD

Participants

The sample consisted of patients with schizophrenia receiving treatment in three mental health centers: Tacna (Peru), La Paz (Bolivia) and Arica (Chile).

Aymara and Non-Aymara patients were included. Both groups lived in the same urban areas and were attended by the same mental health centers, presenting similar socio-demographic characteristics, such as low educational and job levels. Related to each mental health center that participated in the study, these presented similar characteristics in terms of size, type of treatment given to patients, type of caregivers and free care. The Aymara patients spoke Spanish and their native language. In patient recruitment, the first author reviewed the lists of patients attending each center in each city and the research team made evaluations over a three-month period in each country. Aymara patients were identified by their surnames as established by the legislation on indigenous peoples in the three countries, or by self-definition. Subjects were invited to participate when attending to their monthly control visits as they received outpatient treatment. Patients who were in psychotic crisis or those who already had a sensory or cognitive disorder were excluded. The final sample included 253 patients who agreed to participate, diagnosed with schizophrenia according to the CIE-10⁴¹ by their treating psychiatrist (33.6% from Chile, 33.6% from Peru and 32.8% from Bolivia). The interviews were made from May 2012 to February 2013.

Measures

The study was approved by the Ethics Committee of the University of Tarapacá and by the National Health Service of Chile (*Servicio Nacional de Salud de Chile*). Two external psychologists, supervised by the principal investigator, carried out the evaluations of the patients with a duration of 30 and 40 minutes approximately. These involved an interview to collect demographic and clinical information, as well as the application of the questionnaires detailed below. Prior to the start of the interview, an informed consent was requested. The objectives of the study, as well as the voluntary nature of participation were explained to them. No compensation was offered for participating in the study.

The study complies with the ethical principles contained in the Declaration of Helsinki (2008) of the World Medical Association.

Instruments

Drug Attitude Inventory (DAI-10):³¹ A 10-item self-report scale that was developed to assess attitudes, experiences, and beliefs about antipsychotic drugs. DAI-10 is considered

a good predictor of adherence in the treatment of patients with schizophrenia.^{31,42} Scores range from -10 (very bad attitude) to 10 (best possible attitude). A final positive score indicates a positive attitude toward medication and a final negative score indicates a negative attitude. Patients with a score from six to 10 are considered as adherent, from zero to five, moderate and in the negative ranges are considered as non-adherent.⁴³ This instrument has a Spanish version carried out by Ramírez et al.⁴⁴ in the year 2004. According to the psychometric properties, this instrument shows an inter-rater reliability index of 0.61 ($p < 0.001$) and an internal consistency coefficient of 0.57. The Spanish version of the DAI shows convergent validity as well as moderate reliability.⁴⁴ The scores analyzed in this study were obtained from the patients.

Barnes Akathisia Scale (BAS):³² Four-item scale that assess the presence or level of the akathisia induced by the medicines. It must be managed by the clinic and includes objective and subjective items, along with an all-embracing clinical evaluation of akathisia. The scores, for each of the first items range from 0 (out-off) to 3 (serious akathisia). The fourth item is to grade the all-embracing level. For each score there are understandable definitions. It assesses the stress inflicted to the patient by a specific symptom, which is rated using the all-embracing clinical evaluation. The scores that are analyzed in this study were obtained from the assessment of the psychiatrist or medical personnel in charge of the patient. This instrument has a coefficient of reliability of 0.74 for the objective item, 0.73 for the subjective restlessness, 0.90 for subjective discomfort and 0.96 for the all-embracing assessment.

(Positive and Negative Syndrome Scale, PANSS):³³ Consists of 30 items that assess the schizophrenic syndrome. Each item is scored according to a seven point Likert scale. In this scale the 1 always is equivalent to the absence of the symptom and the seven to presence in an extreme level. This instrument consists of three subscales of different symptoms: positive, negative and general psychopathology. The PANSS Scale has been translated and validated in Spain by Peralta and Cuesta (1994)⁴⁵ and also Fresán et al. (2005)⁴⁶ examined the psychometric properties of this instrument in Mexico. This instrument has good inter-observer and construct validity, high internal consistency (Cronbach's alpha of 0.73 for the positive scale, 0.83 for the negative and 0.87 for the general psychopathology) and adequate test-retest stability. The intraclass correlation coefficient is about 0.80 for the three subscales.

Demographic and clinical characteristics: Demographic characteristics of the patient included gender, age, ethnicity (Aymara and Non-Aymara), educational stage (low or high), marital status (with or without partner), occupation and family income (total monthly salary of all family members average, expressed in dollars). Clinical characteristics included severity of the disorder as measured by the PANSS

Scale, number of hospitalizations in the last three years, and measurement of medication side effects by the Barnes Akathisia Scale (range of 0 to 5). The rank for the diagnosis of akathisia was a total score of two or more.

Statistical analysis

First, a *t-test* was used to assess differences in DAI-10 score among Aymara and Non-Aymara patients. Subsequently, to investigate other socio-demographic variables that could explain the differences in medication adherence between the two groups, a linear regression model was used, controlling the socio-demographic and clinical characteristics of the patients. When possible, the outcome variables were used as continuous scales. Data were analyzed with SPSS version 17.0.

Results

Two hundred fifty-three patients with schizophrenia participated in the current study. The average age was 35.6

years, 66.4% were men and 46.2% of the patients were Aymara. The severity of the symptoms was moderate, with a total PANSS score of 71.3 (DT = 28.2). The mean in the Barnes Scale was 0.87 (DT = 1.97) below the diagnostic rank for akathisia. Aymara patients present a significantly higher score in the Concern of restlessness subscale ($t = -2.09$; $p = 0.03$).

The scores obtained in the DAI-10 show a moderate adherence to the medication in the total sample and a lack of adherence in 19.8% of the subjects. Aymara patients presented lower adherence than Non-Aymara patients, however, these differences were not significant ($t = 1.29$; $p = 0.19$). This is reflected in the high percentage of the sample with one or more hospital incomes in the last three years (59% overall, 69% for Aymara).

Additional characteristics of Aymara and Non-Aymara patients are presented in table 1.

Regression analysis is presented in table 2. Once the socio-demographic and clinical factors of the patients have been controlled, it is observed that the ethnicity does not present a significant relation with the adherence to the

Table 1. Socio-demographic and clinical characteristics of patients Aymara, Non-Aymara and of the total sample

Socio-demographic variables	Category (%)		
	Total sample	Aymara	Non-Aymara
Gender			
Male	66.0	66.0	67.0
Female	34.0	34.0	33.0
Ethnicity		46.2	53.8
Marital status			
Married	6.3	6.8	5.9
Non married	93.7	93.2	94.1
Occupation outside the home			
With occupation	30.4	31.0	31.3
Without occupation	69.6	69.0	68.7
Educational level			
Low (< 12 years)	84.2	86.3	82.4
High (≥ 12 years)	15.8	13.7	17.6
		Mean (SD)	
	Total sample	Aymara	Non-Aymara
Age	35.6 (12.4)	33.9 (11.5)	36.9 (13.1)
Monthly family income in US dollars	417.6 (429.4)	295.1 (218.9)	536.7 (538.3)
Severity – Total PANSS*	71.3 (28.2)	73.0 (29.2)	69.9 (27.3)
Number of hospitalizations in the last three years	1.2 (1.5)	1.3 (1.4)	1.1 (1.5)
BARS Total	0.8 (1.9)	1.0 (2.1)	0.7 (1.8)
Objective criteria	0.2 (0.5)	0.2 (0.5)	0.1 (0.5)
Concern of restlessness	0.2 (0.4)	0.2 (0.5)	0.1 (0.3)
Discomfort for restlessness	0.2 (0.5)	0.2 (0.5)	0.1 (0.5)
Global clinical assessment	0.2 (0.6)	0.2 (0.7)	0.1 (0.5)
DAI-10	3.0 (4.8)	2.6 (4.9)	3.4 (4.6)

Note: SD = Standard Deviation; PANSS = Positive and Negative Syndrome Scale; *PANSS final score (PANSS 58 = Mild; PANSS 75 = Moderate; PANSS 95 = Moderate-Severe; PANSS 116 = Severe); DAI-10 = Drug Attitude Inventory-10; BARS = Barnes Akathisia Rating Scale.

pharmacological treatment. A significant association between DAI-10 and the severity of the disorder by PANSS is declared, showing that the most seriously ill have a lower adherence to antipsychotic treatment, $\beta = -1.56$ (-2.34, -0.77). Similarly, the age variable showed a significant association with DAI-10, younger patients showed less adherence to pharmacological treatment $\beta = 1.41$ (0.67, 2.14).

DISCUSSION AND CONCLUSION

The results show that, in general, both indigenous and non-indigenous patients present a positive attitude toward medication, which implies a moderate adherence to antipsychotics.

Data allows to partially confirm the hypothesis of the study. Although indigenous patients have less adherence than non-indigenous patients, the differences are not significant. These results could be related to the fact that the indigenous patients of this sample are integrated to the Mental Health Services that offer a biomedical approach. Although there is the will to develop a biopsychosocial treatment, in practice, this is mostly limited to a more medical approach, with a strong emphasis on pharmacological treatment, brief hospitalization in case of psychotic crisis and outpatient follow-up. Psychosocial interventions are still scarce in these contexts.⁴⁷

Table 2. Linear regression model of the Drug Attitude Inventory-10 (DAI-10)

Regression coefficient (CI 95)	DAI-10
Ethny*	-0.09 (-1.47, 1.29)
Aymara	
Non-aymara (Ref)	
Gender*	-1.45 (-2.97, 0.07)
Female	
Male (Ref)	
Age [#]	1.41 (0.67, 2.14)**
Marital status*	1.67 (-1.35, 4.70)
Without partner	
With partner (Ref)	
Occupation*	-0.83 (-2.30, 0.63)
No	
Yes (Ref)	
Educational level*	0.40 (-1.53, 2.35)
≥12 years	
<12 years (Ref)	
Monthly family income [#] (US Dollars)	0.22 (-0.45, 0.91)
Number of hospitalizations in the last three years	0.00 (-0.71, 0.72)
PANSS Total [#]	-1.56 (-2.34, -0.77)**
BARS Total [#]	0.00 (-0.79, 0.81)

Note: CI = Confidence Interval; * = Not standardized coefficient beta; [#] = Standardized coefficient beta; Ref = Group of reference. ** $p \leq 0.01$. PANSS = Positive and Negative Syndrome Scale; DAI-10 = Drug Attitude Inventory-10; BARS = Barnes Akathisia Rating Scale.

Another approach to the results obtained opens the possibility that these indigenous patients are changing their conception of disease. Previous studies in this population have shown that, opposing to what might be expected, Aymara patients did not present greater magical-religious beliefs about schizophrenia, rather, these patients attributed causality to psychosocial factors. These last factors are related to difficulties in economic aspects, lack of employment, low education level, among others. Thus, these Aymara patients would be incorporating a different causality model from the one presented by previous generations.⁴⁸

A third reason that could explain the results of this study points to the migratory dynamics that have been generated during the last decades. A major number of families have migrated to urban areas. These intercultural dynamics have led to an identity crisis in this group of people, who for various reasons no longer identify themselves as belonging to this ethnic group.³⁷ One study states that the Aymara population in the Chilean Andean context has passed from the monolingual Aymara inhabitants to Spanish-speaking monolingual speakers.⁴⁹ These culture and society changes have promoted the loss of ethnic traditions and customs, gradually adopting new and increasingly intercultural lifestyles.⁵⁰

From our perspective as researchers and clinicians, the results of this study are positive. To the extent that adequate pharmacological adherence is maintained, relapses are reduced, a better symptomatological course is obtained and even promotes a better social interaction.^{51,52}

It is noteworthy that in the same course of previous studies,⁵³⁻⁵⁷ the severity of the disorder presents an important association in adherence to medication. Although it is not possible to establish causality, it is possible that the most severely affected patients present a lower adherence, however, it is also possible that, with less adherence, the treatment is discontinued and, consequently, the patient relapses (more severe).

The age variable, as in previous investigations,^{8,58} is positioned as an important factor, thus, younger patients show less adherence, thus these patients constitute a risk group.⁵⁹ Other socio-demographic variables were not related to adherence, as Lacro et al. obtained in 2002.⁵ Plus it was not found that side effects to medication had an impact on DAI-10 rates. This result is similar to those found by Perkins et al., 2006;⁶⁰ 2008⁶¹ and Vassileva & Milanova in 2012.⁶²

The study presents an amount of limitations. First, the cross-sectional design used in this research does not allow causal relationships to be established, so it is necessary to carry out longitudinal studies. Second, the absence of differences among Aymara and Non-Aymara patients may be related to sample selection. In fact, we have compared attitudes towards medication in patients receiving treatment in the same Mental Health Services, however, we cannot extrapolate our results to all Aymara patients and especially to

those who have problems accessing services, many of these patients still reside in the Altiplano. Third, measurement of attitudes towards medication was based on a subjective assessment of the same and did not have more objective measurements. Fourth, the study did not have an antipsychotic classification used by patients, future investigations should consider differently between the effects of classic and atypical antipsychotics, in addition to incorporate other elements related to adherence, such as therapeutic alliance, the time-evolution of untreated psychosis, family and social support. Thus, it could also be assessed whether the use of atypical long-acting injectable antipsychotics could be better tolerated by ethnicity patients. On the other hand, the information obtained did not allow the consideration of the psychosocial components or the psychoeducational needs of the subjects, which are factors associated to the therapeutic adherence.

Despite the limitations mentioned, the results indicate a lower pharmacological adherence in indigenous patients and an overall positive attitude toward medication, which, while not statistically significant, should be demonstrated in another study. Professionals in charge should be aware of not applying stereotypes regarding the relation between ethnicity and psychoactive drugs, as it is essential to incorporate psychotherapeutic and psychoeducational interventions that discourse this issue in the mental health centers of these countries. Likewise, it is expected that the professionals will incorporate key elements from cross-cultural psychiatry, along with that these elements be talked from the beginning.

Both patients, family members and professionals must give the importance that settles in the establishment of an adequate adherence to the treatment to finally achieve a better life quality.

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Conflict of interests

Does not exist.

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REFERENCES

1. Gilmer TP, Ojeda VD, Barrio C, Fuentes D et al. Adherence to antipsychotics among Latinos and Asians with schizophrenia and limited english proficiency. *Psych Serv* 2009;60(2):175-182.
2. Nitzan U, Bukobza G, Aviram, S, Lev-Ran S et al. Rebelliousness in patients suffering from schizophrenia-spectrum disorders - a possible predictor of adherence. *Psychiatr Res* 2013;209:297-301.
3. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophr Bull* 1997;23:637-651.
4. Jeste SD, Patterson, TL, Palmer BW, Dolder CR et al. Cognitive predictors of medication adherence among middle-aged and older outpatients with schizophrenia. *Schizophr Res* 2003;63:49-58.
5. Lacro JP, Dunn LB, Dolder CR, Leckband SG et al. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *J Clin Psychiatry* 2002;63(10):892-909.
6. Razali MS, Yahya H. Compliance with treatment in schizophrenia: a drug intervention program in a developing country. *Acta Psychiatr Scand* 1995;91:331-335.
7. Sun SX, Liu GG, Christensen DB, Fu AZ. Review and analysis of hospitalization costs associated with antipsychotic nonadherence in the treatment of schizophrenia in the United States. *Curr Med Res Opin* 2007; 23:2305-2312.
8. Velligan DI, Weiden PJ, Sajatovic M, Scott J et al. The expert consensus guideline series: adherence problems in patients with serious and persistent mental illness. *J Clin Psychiatry* 2009;70(4):S1-S46.
9. Young JL, Zonana HV, Shepler L. Medication noncompliance in schizophrenia: codification and update. *Bull Am Acad Psychiatry Law* 1986;14:105-122.
10. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS et al. Clinical antipsychotic trials of intervention effectiveness (CATIE) investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005;353(12):1209-1223.
11. World Health Organization. Adherence to long-term therapies evidence for action. World Health Organization. 2003;107-114. <http://www.who.int/bookorders/anglais/detart1.jsp?sesslan=1&codlan=1&codcol=15&codcch=526>. Accessed October 19, 2010.
12. Dilla T, Valladares A, Lizán L, Sacristán JA. Adherencia y persistencia terapéutica: causas, consecuencias y estrategias de mejora. *Aten Primaria* 2009;41:342-348.
13. López San Román A. Treatment adhesion, treatment adherence or treatment compliance? *Rev Clin Esp* 2006;206:414.
14. Medina E, Salvà J, Ampudia R, Maurino J et al. Short-term clinical stability and lack of insight are associated with a negative attitude towards antipsychotic treatment at discharge in patients with schizophrenia and bipolar disorder. *Patient Prefer Adherence* 2012;6:623-629.
15. Fleischhacker WW, Oehl MA, Hummer M. Factors influencing compliance in schizophrenia patients. *J Clin Psychiatry* 2003;64(16):10-13.
16. Morken G, Widen JH, Grawe RW. Non-adherence to antipsychotic medication, relapse and rehospitalisation in recent-onset schizophrenia. *BMC Psychiatry* 2008;8:32-34.
17. Borrás L, Mohr S, Brandt PY, Gilliéron C et al. Religious beliefs in schizophrenia: Their relevance for adherence to treatment. *Schizophr Bull* 2007;33(5):1238-1246.
18. Eaddy M, Grogg A, Locklear J. Assessment of compliance with an-

- tipsychotic treatment and resource utilization in a Medicaid population. *Clin Ther* 2005;27:263-272.
19. Robinson D, Woerner MG, Alvir JM et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Arch Gen Psychiatry* 1999;56:241-247.
 20. Weiden PJ, Olfson M. Cost of relapse in schizophrenia. *Schizophr Bull* 1995;21:419-429.
 21. Czobor P, Van Dorn RA, Citrome L, Kahn RS et al. Treatment adherence in schizophrenia: a patient-level meta-analysis of combined CATIE and EUFEST studies. *Eur Neuropsychopharmacol* 2015; 25(8):1158-1166.
 22. Opolka JL, Rascati KL, Brown CM, Gibson PJ. Role of ethnicity in predicting antipsychotic medication adherence. *Ann Pharmacother* 2003a;37(5):625-630.
 23. Opolka JL, Rascati KL, Brown, CM, Barner JC et al. Ethnic differences in use of antipsychotic medication among Texas medicaid clients with schizophrenia. *J Clin Psychiatry* 2003b;64(6):635-639.
 24. Diaz E, Woods SW, Rosenheck R. Effects of Ethnicity on Psychotropic Medications Adherence. *Community Ment Health J* 2005;41:521-537.
 25. Gilmer TP, Dolder CR, Lacro JP et al. Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *Am J Psychiatry* 2004;161:692-699.
 26. Valencia M, Rascon ML, Juarez F, Murow E. A psychosocial skills training approach in Mexican out-patients with schizophrenia. *Psychol Med* 2007;37(10):1393-1402.
 27. Valencia M, Rascon ML, Juarez F, Escamilla R et al. Application in Mexico of psychosocial rehabilitation with schizophrenia patients. *Psychiatry* 2010;73(3):248-263.
 28. Valencia M, Juarez F, Ortega H. Integrated treatment to achieve functional recovery for first-episode psychosis. *Schizophr Res Treatment* 2012; doi:10.1155/2012/962371
 29. Valencia M, Fresan A, Juárez F, Escamilla R et al. The beneficial effects of combining pharmacological and psychosocial treatment on remission and functional outcome in outpatients with schizophrenia. *J Psychiatric Research* 2013;47(12):1886-1892.
 30. Valencia M, Moriana JA, Kopelowicz A, Lopez SR et al. Social-Skills training for Spanish-speaking persons with schizophrenia: Experiences from Latin America, Spain, and the United States. *Am J Psychiatr Rehabil* 2015;18(3):209-246.
 31. Hogan TP, Awad AG, Eastwood R. A self-report scale predictive of drug compliance in schizophrenics: reliability and discriminative validity. *J Psychol Med* 1983;13:177-183.
 32. Barnes TR. A rating scale for drug-induced akathisia. *Br J Psychiatry* 1989;154:672-676.
 33. Kay SR, Fiszbein A, Opler L. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 1987;13:261-276.
 34. Köster G. Los Aymaras: Características demográficas de un grupo étnico indígena antiguo en los Andes centrales. En: Van den Berg H, Schiffers N (eds.). *La cosmovisión Aymara* La Paz, Bolivia: UCB/ Hisbol; 1992; pp. 81-111.
 35. Van Kessel J. La cosmovisión Aymara. En: Hidalgo J, Schiappacasse F, Niemeyer F, Aldunate C, Mege P. (eds.). *Etnografía: Sociedades indígenas contemporáneas y su ideología*. Santiago, Chile: Editorial Andrés Bello; 1996; pp:169-187.
 36. Gundermann H. Las organizaciones étnicas y el discurso de la identidad en el norte de Chile, 1980-2000. *Estudios Atacameños* 2000;19:75-91.
 37. Zapata C. Memoria e historia: El proyecto de una identidad colectiva entre los aymaras de Chile. *Chungara* 2007;39:171-183.
 38. De Munter K. Tejiendo reciprocidades: John Murra y el contextualizar entre los aymara contemporáneos en Chungara. *Chungara* 2010;4:243-251.
 39. Juntuma de Chapiquiña. *Medicina indígena y alimentación tradicional del pueblo de Chapiquiña*. Trabajo fundando por el Programa de Salud y Pueblos Indígenas (PEPSI); 2002.
 40. Laks, Jordana. Reflexiones sobre la tristeza y la preocupación en las personas Aymara de Putre, Chile. Independent Study Project (ISP) Collection. Paper 1054; 2011. http://digitalcollections.sit.edu/isp_collection/1054. Accessed March 19, 2013.
 41. World Health Organization. *ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines*. Ginebra, Suiza: World Health Organization; 1992.
 42. Nielsen RE, Lindström E, Nielsen J, Levander S. DAI-10 is as good as DAI-30 in schizophrenia. *Eur Neuropsychopharmacol* 2012;22(10):747-750.
 43. Saleem F, Hassali MA, Shafie AA, Awad AG et al. Association between knowledge and drug adherence in patients with hypertension in Quetta, Pakistan. *Trop J Pharm Res* 2011;10:125-132.
 44. Ramírez Barreto F, Robles García R, Salazar Alvarado V, Páez Agraz F. Evaluación de actitudes al medicamento en pacientes con esquizofrenia: propiedades psicométricas de la versión en español del DAI. *Actas Esp Psiquiatr* 2004;32(3):138-142.
 45. Peralta V, Cuesta MJ. Validación de la Escala de los Síndromes Positivo y Negativo (PANSS) en una muestra de esquizofrénicos españoles. *Actas Luso Esp Neurol Psiquiatr Cienc Afines* 1994;22(4):171-177.
 46. Fresán A, De la Fuente-Sandoval C, Loyzaga C, García-Anaya, M et al. A forced five-dimensional factor analysis and concurrent validity of the Positive and Negative Syndrome Scale in Mexican schizophrenic patients. *Schizophr Res* 2005;72:123-129.
 47. Markkula N, Alvarado R, Minoletti A. Adherence to guidelines and treatment compliance in the Chilean national program for first-episode schizophrenia. *Psychiatr Serv* 2011;62(12):1463-1469.
 48. Caqueo-Úrizar A, Breslau J, Gilman S. Beliefs about the causes of schizophrenia among Aymara and non-Aymara patients and their primary caregivers in the Central-Southern Andes. *Int J Soc Psychiatry* 2015;61(1):82-91.
 49. Gundermann H. Acerca de cómo los aymaras aprendieron el castellano (terminando por olvidar el aymara). *Estudios Atacameños* 1997;12:89-104.
 50. Gavilán V, Viguera P, Carrasco A, Cabezas R et al. Pautas de crianza Aymara. Significaciones, actitudes y prácticas de familias Aymara en relación a la crianza y cuidado infantil de los niños y niñas desde la gestación hasta los diez. Chile: Centro de Investigaciones para el Desarrollo del Hombre en el Desierto, Universidad Arturo Prat, Chile; 2006.
 51. Tsai JK, Lin WK, Lung FW. Social interaction and drug attitude effectiveness in patients with schizophrenia. *Psychiatr Q* 2011;82(4):343-51.
 52. Yang J, Ko Y-H, Paik J-W et al. Symptom severity and attitudes toward medication: Impacts on adherence in outpatients with schizophrenia. *Schizophrenia Res* 2012;134(2-3):226-231.
 53. Gaebel W, Riesbeck M, von WM, Burns T et al. Drug attitude as Predictor for effectiveness in first-episode schizophrenia: results of an open randomized trial (EUFEST). *Eur Neuropsychopharmacol* 2010;20:310-316.
 54. Mohamed S, Rosenheck R, McEvoy J et al. Cross-sectional and longitudinal relationships between insight and attitudes toward medication and clinical outcomes in chronic schizophrenia. *Schizophr Bull* 2009;35(2):336-346.
 55. Nakonezny PA, Byerly MJ, Rush AJ. Electronic monitoring of antipsychotic medication adherence in outpatients with schizophrenia or schizoaffective disorder: an empirical evaluation of its reliability and predictive validity. *Psychiatry* 2008;157:259-263.
 56. Sellwood W, Tarrier N, Quinn J et al. The family and compliance in schizophrenia: the influence of clinical variables, relatives' knowledge and expressed emotion. *Psychol Med* 2003;33:91-96.
 57. Freudenreich O, Cather C, Evins A, Henderson D et al. Attitudes of schizophrenia outpatients toward psychiatric medications: relationship to clinical variables and insight. *J Clin Psychiatry* 2004;65:1372-6.
 58. Nosé M, Barbui C, Tansella M. How often do patients with psychosis fail to adhere to treatment programmes? A systematic review. *Psychol Med* 2003;33:1149-1160.
 59. Sajatovic M, Valenstein M, Blow F, Ganoczy D et al. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. *Psychiatr Serv* 2007;58(6):855-863.

60. Perkins DO, Johnson JL, Hamer RM, Zipursky RB et al. Predictors of antipsychotic medication adherence in patients recovering from a first psychotic episode. *Schizophr Res* 2006;83(1):53-63.
61. Perkins DO, Gu H, Weiden PJ, McEvoy JP et al. Predictors of treatment discontinuation and medication nonadherence in patients recovering from a first episode of schizophrenia, schizophreniform disorder, or schizoaffective disorder: a randomized, double-blind, flexible-dose, multicenter study. *J Clin Psychiatry* 2008;69(1):106-113.
62. Vassileva IV, Milanova VK. Attitudes toward antipsychotic medication, insight and psychopathology in outpatients with schizophrenia. *Folia Med* 2012;54(4):62-68.