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# Integration of Pharmacological and Psychosocial Treatment for Schizophrenia in Mexico: The Case of a Developing Country Proposal

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## 1. Introduction

For decades, schizophrenia was considered exclusively as a biological disorder. As a result, pharmacotherapy has been considered as the predominant mode of treatment. Antipsychotic medication is indicated for first episode, acute, chronic as well as for refractory patients. So much research has been conducted to evaluate the efficacy of antipsychotics through clinical studies, randomized controlled trials and meta-analyses. Scientific journals are full of research on pharmacotherapy. According to the American Psychiatric Association [APA] (2004), a treatment plan for patients with schizophrenia should include: 1.- The reduction or elimination of symptoms, 2.- Improving quality of life and adaptive functioning, and 3.- Promote and maintain recovery. In the last decades, research in the social sciences and psychiatric rehabilitation has produced a considerable body of knowledge with respect to psychosocial factors that influence the course of this illness. As a result psychosocial treatments have also been designed and implemented. With the beginning of the new century and after more than 60 years of research, there is a consensus that biological, psychological and social factors play a very important role in understanding and treating schizophrenia. Hence, the biopsychosocial model has been considered as the most comprehensive treatment approach for this illness. The treatment of schizophrenia has been the focus of changes since the introduction of neuroleptics in the 1950's which initiated the transition from mental hospitals to the community, with long-stay patients confined in mental institutions going through the deinstitutionalization process, to the new millennium where the majority of them are actually living in the community. A considerable effort has been carried out in recent years to articulate the scientific basis of the treatment for people with schizophrenia. As a result evidence based treatment for schizophrenia has recommended that all persons with schizophrenia should receive the combination of: 1) optimal dose of antipsychotic medication, 2) psychosocial interventions, 3) psychoeducation for patients and carers as well as family therapy, and, 4) assertive home-based management to help prevent and resolve various issues such as: crises, relapse, medication adherence, etc, (Drake et al., 2009; Falloon et al., 2004; Fenton & Schooler, 2000; Lehman & Steinwachs, 2003; Shean, 2009; Thornicroft & Susser, 2001). In summary, scientific

research indicates that the management of schizophrenia should include the following: 1) pharmacotherapy, 2) psychosocial interventions, and 3) the integration of these two approaches. The aim of this chapter is to describe a research area that integrates pharmacological and psychosocial treatment for patients with schizophrenia carried out at the National Institute of Psychiatry, in Mexico City. Based upon scientific research, the second aim consists on presenting a proposal of this integration on a comprehensive treatment approach for schizophrenia patients of a developing country as Mexico.

## 2. Pharmacological treatment

Schizophrenia represents a chronic and debilitating mental disorder that affects about 0.7% of general population all over the world (McGrath, 2008), which means approximately 24 million people worldwide (World Health Organization [WHO], 2011). In the case of Mexico, with a population of 112 million inhabitants, the population at risk between 15-65 years of developing schizophrenia is 63.6 millions, a one percent estimate would indicate that approximately 630,000 individuals suffer schizophrenia as to 2011. Treatment is complex and should always be initiated with pharmacological interventions. Antipsychotics are the drugs of choice (Freedman, 2005; Geddes, 2000; Kane & Marder, 1993; Kane & McGlashan, 1995; Marder, 2002) as they control most of the symptom clusters that characterize this disorder. More than 60 years ago, Jean Delay and colleagues discovered chlorpromazine (López-Muñoz et al., 2002), a then novel sedative compound, and almost at the same time Paul Janssen discovered haloperidol (Granger, 1999), a potent neuroleptic compound. Both drugs were shown to be useful to relieve psychotic symptoms, and so began a new era in the treatment of psychotic disorders, with schizophrenia as the prototype. Emergence of this 2 kind of drugs, phenothiazines and butyrophenones, placed the so called conventional antipsychotics as the first line treatment for schizophrenia for many decades (Geddes, 2000; Kane & Marder, 1993; Kane & McGlashan, 1995; Marder, 2002). Beginning with clozapine some decades ago, but mostly for the last 15 to 20 years, new antipsychotic medications have been developed (Geddes, 2000; Lehman et al., 2004). The now named atypical antipsychotics (more correctly second generation antipsychotics) represent a better said heterogeneous group of drugs (Davis et al., 2003; Geddes, 2000; Haddad & Sharma, 2007). These new agents are quite different in that, at least most of them, do not generate neuroleptization quite so much as some of the conventional medications and in that, most of them are effective antipsychotics with minimal or negligible EPS and hiperprolactinemia (García-Anaya et al., 2001, Geddes, 2000; Rosenheck, 2003). One important issue that distinguishes this group of drugs from conventional antipsychotics is the separation of their clinical efficacy from their neurotoxic effects (Posligua, 1995). Beside this advantages they also appear to have greater effectiveness than conventional antipsychotics in treating the so-called negative symptoms of schizophrenia (García-Anaya et al., 2001; Leucht, 1999; Posligua, 1995), in controlling other symptom clusters like behavioral disturbances, in having an apparent positive impact on neurocognitive functioning (Keefe, 1999, 2003; Rosenheck, 2003) and on psychosocial functioning (Swartz, 2003; Swartz et al., 2007), in lowering relapse and rehospitalisation rates (Csernansky & Schuchart, 2002) and in promoting a better quality of life for patients (Chung, 2004; Jones, 2006). This relative superiority could result from the reduction in side effects, especially EPS, but also maybe from a direct pharmacologic effect, that can explain why this group of drugs are now considered first line treatment choice and, as so, could have a relevant impact in improving social and vocational outcomes of patients with psychotic disorders like schizophrenia.

Antipsychotic	Chemical Group	Usual dose	Available since
Haloperidol*	Butyrophenone	5-20 mg/day	70's
Chlorpromazine	Phenothiazine	25-500 mg/day	70's
Sulpiride	Benzamide	50-600 mg/day	70's
Perphenazine*	Phenothiazine	4-60 mg/day	70's
Trifluoperazine	Phenothiazine	5-50 mg/day	70's
Levomepromazine	Phenothiazine	25-200 mg/day	70's
Clozapine	Thienobenzo-diazepine	25-600 mg/day	80's
Flupenthixol	Thioxanthene	5-20 mg/day	90's
Zuclopenthixol	Thioxanthene	20-60 mg/day	90's
Olanzapine*	Thienobenzo-diazepine	5-20 mg/day	90's
Risperidone*	Benzisoxazole	1-6 mg/day	90's
Quetiapine	Dibenzothiazepine	300-800 mg/day	90's
Ziprasidone*	Benzisothiazol	80-160 mg/day	90's
Amisulpiride	Benzamide	50-400 mg/day	2000's
Aripiprazole	Dichlorophenyl-piperazine	10-30 mg/day	2000's
Sertindole	Phenylindole	12-20 mg/day	2000's
Paliperidone	Benzisoxazole	3-9 mg/day	2000's

(\*) Available in the Mexican public health system

Table 1. Oral antipsychotic drugs available in Mexico

2.1 Introduction and use of antipsychotic drugs in Mexico

History of Latin American countries use of antipsychotics parallels some socio-cultural and economic issues; Some cases like Cuba and some central American countries are characterized by having only available some conventional antipsychotics like haloperidol and chlorpromazine (González et al., 2004), and, in most Latin American countries, even though having second generation antipsychotics available, economic issues have limited their use. In Mexico we have had available conventional antipsychotics from the 70's, initiating with the prototypes of the first two classes of this group of drugs: the butyrophenone haloperidol and the phenothiazine chlorpromazine, and then some other phenothiazine compounds and first generation atypical drugs (Table 1). Some first generation antipsychotic drugs like fluphenazine, thioridazine and penfluridol were available in Mexico in the past but now they are not available anymore. Some of this conventional antipsychotic drugs are frequently used in most public psychiatric hospitals and institutions and even some of them are still included in the “Cuadro básico” (Basic Table of Medications) of the Mexican public health system (Secretaría de Salud, 1999). Second generation antipsychotics were introduced in Mexico in the 80's with their first representative drug, clozapine and then in the 90's, drugs like olanzapine, risperidone, quetiapine and ziprasidone were available. Finally, in the 21th century, four more second generation antipsychotic drugs are now available: amisulpiride, aripiprazole, sertindole and paliperidone. Some of this second generation antipsychotic drugs, like risperidone and olanzapine, are being introduced in the Mexican public health system, so they now are at hand for more patients.

## 2.2 Clinical considerations for prescribing antipsychotics

Once a diagnosis of schizophrenia is established, patient should be started on antipsychotic treatment as soon as possible, meanwhile other therapeutic measures are initiated. Election of antipsychotic drug by a physician must take into account some issues like illness related characteristics, drug efficacy, side effects and cost (Kane & McGlashan, 1995; Leuch, Corves et al., 2009), patient characteristics including age, gender, health status, other drugs being taken by the patient, history of previous use of any antipsychotic drug and some other socio-cultural aspects. In a prospective naturalistic study (Edlinger, 2009), the factors influencing physicians' choice of antipsychotic drug therapy in the treatment of patients with schizophrenia were investigated; it was concluded that antipsychotic drug side effects have a larger influence on the choice of antipsychotic than other factors like demographic or illness-related variables, with the exception of the severity of positive symptoms, which did influenced decision. As it was mentioned above, in developing countries like most Latin American countries, including Mexico, aspects like antipsychotic drug availability and drug cost should always be considered when making a choice for any antipsychotic. Some general important issues concerning the adequate use of antipsychotic drugs that should always be considered every time pharmacological treatment is started on a patient with schizophrenia include:

1. **Type of antipsychotic drug:** At this time, second generation drugs are usually considered as first line treatment for individuals with newly diagnosed schizophrenia (Leucht, 1999; Leucht, 2003; Leuch, Corves et al., 2009), even though their heterogeneity has brought some concerns about their superiority over conventional drugs (Geddes, 2000; Leucht, 1999; Leuch, Corves et al., 2009; Marder, 2002), and in between them (Leuch, Kommosa et al., 2009). In Mexico and some other developing countries, is not rare that some patients could still be started on conventional antipsychotics mostly regarding availability and cost-effectiveness issues. The choice for oral, parenteral or depot formulations will be considered later.
2. **Recommended dosage of antipsychotic drug:** Any antipsychotic drug given to treat a schizophrenic patient should be started at the lowest effective level of the recommended therapeutic range (Davis & Chen, 2004). Dosage outside of this range should be justified and documented always; "rapid neuroleptisation" is not recommended, and in case of using rapid loading doses, this manoeuvre should be made with extreme caution. Subsequent titration of antipsychotic drug on follow up should be made according to clinical response and tolerability, sometimes using blood levels as a useful manoeuvre (Citrome & Volavka, 2002).
3. **Antipsychotic drug treatment duration:** Treatment should be continued for at least 12 months, then, just in the eventual situation of the disease remitting fully, drug treatment may be ceased gradually over at least 1-2 months. In most cases, however, antipsychotic drug treatment should be continued indefinitely, as this stance represents the best option for the long standing control of symptoms.
4. **Definition and management of antipsychotic treatment resistance:** If a patient with schizophrenia has been unresponsive to at least two adequate trials (that is using therapeutic doses of the drugs, for enough time to get a response) of two different antipsychotic medications, then it can be established the diagnosis of antipsychotic treatment resistance. If so, a trial of clozapine should be offered to patients, as this second generation antipsychotic has been recognized as the drug of choice for treatment

resistant schizophrenic patients (Chakos, 2001; Lehman et al., 2004; Marder, 2002; Wahlbeck, 1999).

5. **Switching of antipsychotic drug treatment:** Reasons for switching antipsychotic drug treatment include lack of clinical response and important side effects (Essock, 2002; Lehman et al., 2004; Stroup, 2011). Treatment trial with a first prescribed antipsychotic drug should be kept for at least 4-8 weeks before considering the use of another antipsychotic medication, and only after optimizing first drug dosage, which could mean dose titrating until the maximum recommended (Essock, 2002). Two antipsychotic medications at a time, whatever second generation or conventional, should not be prescribed together, although this aspect is still controverted (Barnes & Paton, 2011; Lehman et al., 2004; Miller & Craig, 2002), with the exception of short periods to cover changeover when switching to another antipsychotic. Switching strategies of antipsychotic medications include 3 options (Weiden, 2006):
  - Discontinuation: This option consists in abruptly discontinuing the first drug before starting the second medication. This method of switching minimizes risk of dosing errors and allows closer monitoring for signs of relapse and can be an appropriate choice when switching from a conventional antipsychotic to a second generation one or from a depot medication to any oral formulation. This method has the inconvenience of potentially favoring symptom exacerbation and withdrawal reactions derived from discontinuation of the previous antipsychotic.
  - Cross-tapering: This option consists in gradual tapering of the first medication while starting and titrating the second antipsychotic drug, with temporal simultaneous administration of both the original and the new drug. This method of switching is suitable when stable patients are experiencing significant side effects from their previous medication. The time elapsed for the cross-titration usually goes between 1 and 4 weeks (De Nayer et al., 2003) although a slower withdrawal period is convenient when switching particular antipsychotics. This option has the inconvenience of exposing patients to subtherapeutic dosages of both medications, with risk of relapse.
  - Delayed withdrawal: This option consists in starting a second antipsychotic drug, which is titrated to a therapeutic dose, before tapering of the first drug. Keeping the patient on a therapeutic dose of the new medication before reducing previous medication avoids exposure to subtherapeutic dosages, and may represent the safest switching method. This method may be suitable for patients who have not accomplished a complete stabilization following a recent relapse and for patients who are not having a good adherence to treatment. Using this method should require physicians to ensure the crossover is complete, without allowing patients to continue with both medications indefinitely. This method has the inconvenience of having patients exposed to the side effects of two antipsychotic drugs (Lehman et al., 2004).
6. **Follow-up of patients receiving antipsychotic medication:** Routine laboratory and clinical monitoring should occur before starting an antipsychotic drug and during treatment follow up as well (Marder, 2002; Lehman et al., 2004). According to toxicology and potential side effects of the drug of choice, laboratory parameters to evaluate may include Complete Blood Count (CBC), Liver Function Tests (LFT), Blood Glucose (BG), Cholesterol (Total, HDL and LDL), Triglycerides, Prolactin Blood Level (PBL) and Electrocardiogram (EKG). Clinical parameters to evaluate include Blood Pressure (BP), Weight, Body Mass Index (BMI) and Waist Circumference (WC).

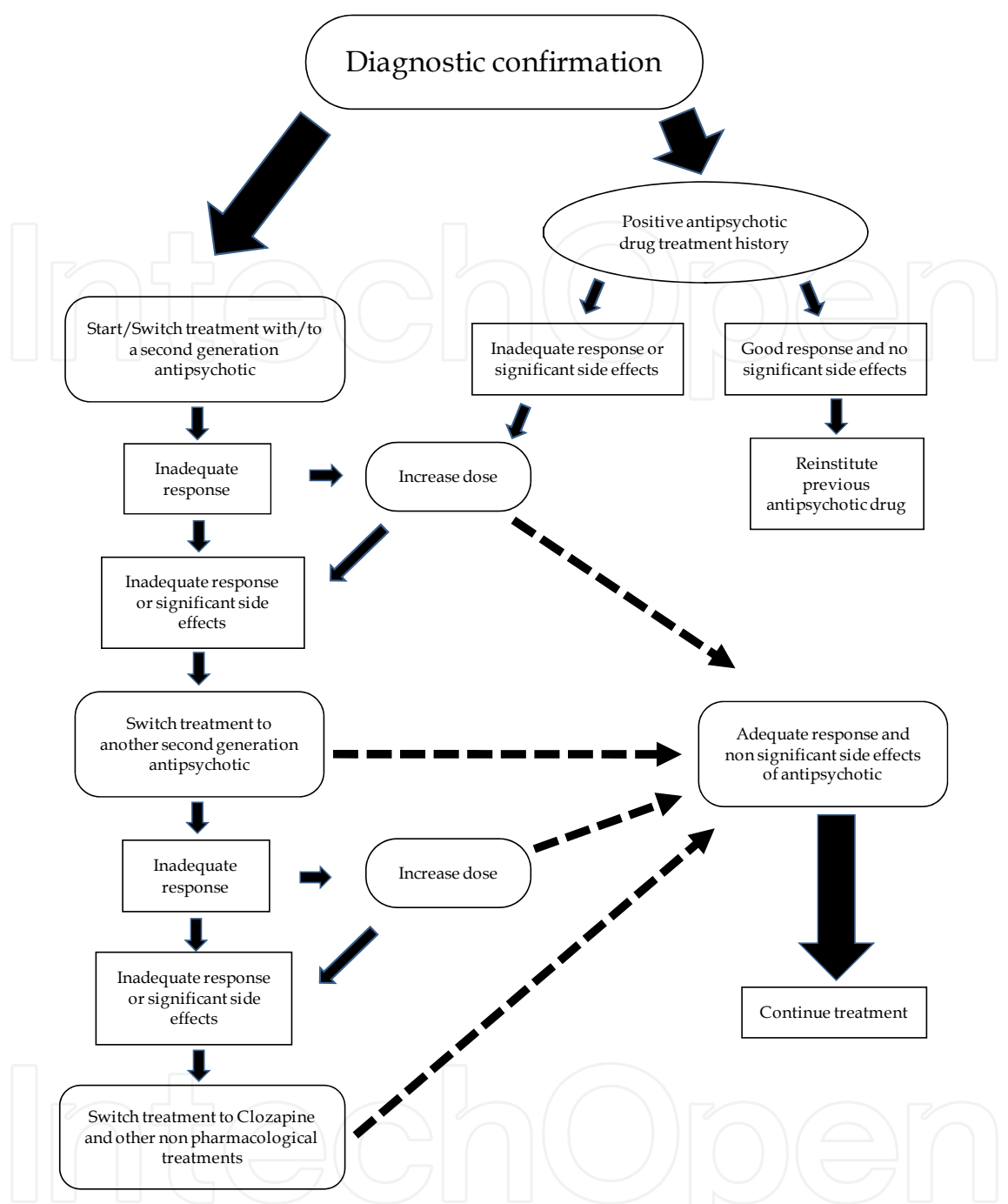


Fig. 1. Therapeutic algorithm for the use of antipsychotic drugs in the treatment of schizophrenia

7. **Tolerability and toxicologic aspects of antipsychotics:** Beyond the clear differences in side effects and toxicologic risks between antipsychotics, either conventional drugs or second generation drugs, there are common potential consequences that should be kept in mind every time an antipsychotic is prescribed to a schizophrenic patient (Haddad & Sharma, 2007; Lehman et al., 2004; Marder, 2002). Parkinsonism and other extrapyramidal side effects are common with potent conventional drugs like haloperidol and fluphenazine (Ortega-Soto et al., 1998; Ortega-Soto & Valencia, 2001), but also with some second generation antipsychotics like risperidone (Haddad &

Sharma, 2007). Hyperprolactinemia is associated again with potent conventional drugs and some second generation drugs like risperidone and amysulpiride (García-Anaya et al., 2001; Haddad & Sharma, 2007). Metabolic side effects were originally described with some low potency conventional drugs but they were later evidently associated with some of the second generation drugs: Weight gain (Allison, 1999; Haddad & Sharma, 2007; Newcomer, 2005; Rosenheck, 2003); Hyperlipidemia (Haddad & Sharma, 2007; Koro, 2002; Newcomer, 2005); Glucose metabolism disturbances (Haddad & Sharma, 2007; Henderson, 2005; Newcomer, 2005), and even Diabetes Mellitus (Leslie & Rosenheck, 2004; Newcomer, 2005) have been highly associated with clozapine and olanzapine, fairly associated with quetiapine and risperidone and lightly associated with haloperidol, ziprasidone, aripiprazole, amysulpiride and paliperidone. Sedation is usually expected with Chloropromazine, Thioridazine, Clozapine, Olanzapine and Quetiapine (Haddad & Sharma, 2007; Lehman et al., 2004; Ortega-Soto & Valencia, 2001). Prolongation of QT interval (QTc) is at highest risk with thioridazine, ziprasidone and sertindole (Haddad & Sharma, 2007; Lehman et al., 2004). Other side effects reported in patients receiving antipsychotic drugs include sexual dysfunction, anticholinergic symptoms, postural hypotension, agranulocytosis, seizures and neuroleptic malignant syndrome (Haddad & Sharma, 2007; Lehman et al., 2004; Marder, 2002). Finally, cerebrovascular events have recently been associated with second generation antipsychotics (Haddad & Sharma., 2007).

Antipsychotic	Chemical Group	Usual dose	Available since
Haloperidol*	Butyrophenone	5-60 mg a day	70´s
Zuclopenthixol Acetate	Thioxanthene	50-100 mg q/2-3 d.	90´s
Olanzapine*	Thienobenzo-diazepine	10-30 mg a day	90´s
Ziprasidone*	Benzisothiazol	10-40 mg a day	90´s

(\*) Available in Mexican Public Health System

Table 2. Parenteral antipsychotic drugs for acute states available in Mexico

**Management of acute episodes:** Acute states of patients with schizophrenia require initiating or adjusting antipsychotic treatment to control new and/or exacerbated symptoms (Kane & McGlashan, 1995). This episodes are sometimes managed in the psychiatric hospital setting (Lehman et al., 2004) A frequent problem found in these acute descompensated patients is the lack of conciousness about the need for an acute treatment intervention and a lack of disposition for receiving pharmacological treatment as well. So patient relatives are often confronted with difficult decisions like taking the patient into a closed institution where pharmacologic and other treatment strategies could be initiated even without patient cooperation. Under these circumstances, parenteral antipsychotic drugs -usually trough intramuscular administration- are very frequently used, as they are easier to administrate to patients not accepting treatment, with lower harm risks for them. Most of these drugs should be administrated once or more times during a day, as they usually have half lives no longer than 24 hours, with the exception of Zuclopenthixol (Clopixol Aquaphase), which can be administrated every 48 to 72 hrs. These drugs are useful for getting a faster control of symptoms and for facilitating treatment continuation. Table 2 shows parenteral antipsychotic drugs available in Mexico, used in acute episodes of schizophrenic patients.

**Issues regarding treatment adherence:** As we all know now, schizophrenic patients should keep pharmacologic treatment in the long term, as far as it has been repeatedly demonstrated that a good treatment adherence means a more complete and a more rapid control of their symptoms, a low chance for future decompensations, and, in general, a more frequent reintegration to society and a better quality of life for them. CATIE and other international studies (Lieberman et al., 2005) have shown that about 75% of schizophrenic patients stop treatment because of different reasons, including lack of clinical response and presence of side effects like sedation, EPS, weight gain, and other metabolic disturbances. This so high non-adherence rate to pharmacologic treatment means for schizophrenic patients more numerous acute decompensation states, more hospitalizations and some other negative consequences. Having said this, one important issue on pharmacologic treatment of schizophrenic patients is promoting treatment adherence. To reach the goal of keeping schizophrenic patients on treatment, depot formulations of antipsychotic drugs are becoming a very useful alternative that favors this purpose. This long acting group of antipsychotic drugs allow patients, their families and other people taking care of them, to administrate drugs at intervals of 2 to 4 weeks, instead of taking them once or even more times a day, thus facilitating and assuring adherence to treatment, First depot antipsychotic drug available in Mexico were Pipothiazine and Haloperidol Decanoate, then other depot formulations have been introduced like the two thioxanthenes Zuclopenthixol Decanoate and Flupenthixol Decanoate and more recently Risperidone and Paliperidone Palmitate.

Antipsychotic	Chemical Group	Usual dose	Available since
Pipothiazine	Phenothiazine	25-200 mg/ every 2-4 weeks	70's
Haloperidol* Decanoate	Butyrophenone	50-150 mg/ every 30 days	80's
Zuclopenthixol Decanoate	Thioxanthene	200 mg/ every 30 days	90's
Flupenthixol Decanoate	Thioxanthene	20-100 mg/ every 2-4 weeks	90's
Risperidone*	Benzisoxazole	25-50 mg/ every 2 weeks	2000's
Paliperidone* palmitate	Benzisoxazole	39-234 mg/ every 30 days	2000's

Table 3. Shows depot antipsychotics now available in Mexico

**Psychothropic drugs other than antipsychotic drugs used in the pharmacologic treatment of schizophrenia in Mexico:** Beside any antipsychotic drug, and mostly used as adjuvant treatment, correcting and complementary pharmacologic treatments for patients with schizophrenia, some other classes of drugs are used in the Mexican psychiatric scenarium. Lithium and some anticonvulsive drugs like carbamazepine and valproate are frequently added to antipsychotic treatment as potentiators of response, especially in patients with partial response to antipsychotic drugs alone. Anticholinergic drugs like biperiden and trihexifenidile are usually prescribed to correct EPS like parkinsonism as well as beta blockers like propranolol, mostly in the presence of acathisia. Sedative-ansiolitic drugs like clonazepam, alprazolam and bromazepam are sometimes indicated in cases of anxious states accompanying classic symptoms of schizophrenia. Finally, antidepressant drugs are used when comorbidity with depressive symptoms is detected.

### 3. Psychosocial treatment

#### 3.1 Historical perspective of psychosocial treatment

The introduction of psychosocial treatment for schizophrenia is very much related to the fact that psychotic disorders produce dysfunctions, disabilities, and deficits in various domains of everyday functioning. Poor psychosocial functioning is a defining characteristic of schizophrenia. Social dysfunction is one of the most relevant factors associated with the disability of the illness (APA, 1995). Disabilities include difficulties in social and independent living skills that act as an impediment for a more normal functioning, (Kopelowicz & Liberman, 2003). From all illnesses of mankind, schizophrenia is ranked as the seventh illness that causes disability (WHO, 2001). Since schizophrenia patients are often functionally impaired, impairments in social functioning could be understood as the inability to take care for his/her self, to maintain interpersonal relationships, or the inability to work. These are important reasons for considering psychosocial functioning as an important dimension of schizophrenia. Deficits in social functioning are a core feature of schizophrenia (Burns & Patrick, 2007). Lauriello, Lenroot & Bustillo (2003), state that: "Patients with schizophrenia have limitations in their social competence and vocational functioning for a significant period. To some extent, these limitations are a consequence of the multiple symptoms and cognitive impairments of the disorder". Role functioning indicates the individual's abilities to demonstrate role performance according to his/hers demands at work, school, social, and family situations. Even when psychotic symptoms are in remission with antipsychotic medication, approximately two-thirds of schizophrenia patients are unable to accomplish basic social roles, such as parenthood, friendship, worker, or being a spouse (Bellack et al., 2007). Schizophrenia is characterized by a deterioration, or failure to achieve adequate levels of social functioning. Because of the early illness onset many individuals with schizophrenia never learned the necessary skills required for adult functioning. The psychosocial environment that comprises family factors is another relevant component as demonstrated with a great amount of research in the area of Family Expressed Emotion (Leff et al., 1987), and family care of schizophrenia (Falloon et al., 1984; Kuipers et al., 2002). One of the most complicated challenges in schizophrenia treatment has been to restore impaired psychosocial functioning (Swartz et al., 2007), considering that current management has a strong emphasis on living in the community (Leucht & Van Os, 2009). The integration of pharmacological and psychosocial approaches has been recommended as a means of improving the outcome of patients with schizophrenia (Marder, 2000). In addition schizophrenia patients face several problems: relapse rates have been reported as high as 70% (McCann et al., 2008; Muller, 2004); even with the use of second generation antipsychotics, negative symptoms still persist (Leucht, Corves et al., 2009; Stahl & Buckley, 2007;); approximately 50% meet criteria for substance or drug dependence (Bellack et al., 2007); cognitive deficits (Sharma & Harvey, 2000) and poor quality of life (Lehman, 1983) should also be considered. Some of these issues remain unresolved.

Psychosocial treatment aims to improve the management of schizophrenia with the use of various techniques such as coping with symptoms, medication adherence, relapse prevention, and acquisition of psychosocial skills to improve functioning in certain areas such as social relations, work, school, home, recreation, use of mental health facilities, or independent living in the community. In the last fifty years a great array of psychosocial interventions have been designed such as: social skills training (Bellack et al., 2004; Glynn et al., 2002; Liberman, 2007), supported employment (McGurk et al., 2009; Mueser et al., 2001;

Tsang, 2001), teaching illness management skills (Atkinson et al., 1996; Birchwood et al., 1989; Mueser et al., 2002), integrated psychological therapy (Briand et al., 2006; Roder et al., 2006), assertive community treatment (Bond et al., 2001; Burns et al., 1999; Thornicroft et al., 1998), cognitive rehabilitation (Bell et al., 2009; Velligan et al., 2006; Vesterager et al., 2011), integrated treatment for comorbid substance abuse (Bellack et al., 2006; Ridgely et al., 1990; Shaner et al., 2003), family psycho-education (Bauml et al., 2006; Murray & Dixon, 2004; Xia et al., 2011), and housing (McCrone & Strathdee, 1994; Harvard Medical School, 2001; Trainor et al., 1993). A large body of research supports the efficacy of psychosocial treatments, with Reviews (Bellack & Mueser, 1993; Benton & Schroeder, 1990; Heinssen et al., 2000; Huxley et al., 2000; Kopelowicz et al., 2006; Penn et al., 2005); Randomized control trials (Glyn et al., 2002; Granholm et al., 2005; Guo et al., 2010; Hogarty et al., 2004; Liberman, 1998); Meta-analysis (Kurtz & Mueser, 2008; Mojtabai et al., 1998; Pilling et al., 2002; Roder et al., 2006) and Treatment recommendations (APA, 2004; Dixon et al., 2010; Kreyenbuhl et al., 2009; Lehman & Steinwaschs, 1998, 2003).

### **3.2 Introduction of psychosocial treatment in Mexico**

The introduction, application and research in Mexico of psychosocial treatment can be divided in two stages: 1) Interventions with acute psychotic hospitalized patients, and 2) Interventions with chronic out-patients with schizophrenia.

#### **3.2.1 Psychosocial treatment for acute psychotic hospitalized patients**

In 1980, a study was conducted to assess the delivery of services of a Psychiatric Hospital for acute mentally ill patients, in Mexico City. It was found that the only treatment that patients were receiving was antipsychotic medication. As a result a proposal was made that considered the convenience to integrate pharmacological and psychosocial rehabilitation approaches, as a consequence a pilot study that was carried out between 1980 and 1984. Psychosocial treatment was included as a new component, in addition to pharmacological treatment, in a clinical trial that integrated a treatment and rehabilitation program for acute hospitalized psychotic patients. After patients were clinically stabilized with antipsychotic medication, (allowing a two week stabilization period), they participated in daily sessions during 4 weeks of the hospitalization period. Patients learned a variety of skills in various domains: 1.-Taking care of personal hygiene, appearance and clothing, 2.-Management of symptoms and medication, 3.-Occupational skills, 4.-Social skills, 5.-Communication and problem solving skills with the family, and 6.-Leisure and sports activities. Verification of the skills learned was recorded with the use of a check list. Using a quasi- experimental design, an experimental group (n=35) treated with pharmacological and psychosocial treatment was compared with a control group (n=35) that was treated with pharmacological treatment alone. Psychopathology and global functioning were assessed before and after treatment, using the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) and the Global Assessment Scale (GAF) (Spitzer et al., 1976). Patients from the experimental group demonstrated significant improvements in symptoms such as: anxiety, tension, depression, unusual thought content and blunted affect. No improvements were found in psychopathology in the control group. These patients experienced more anxiety and tension than that reported when they started treatment. Similar results were found in global functioning since experimental patients improved their functioning: mean =52 before

treatment to a mean=72 at the end of treatment. Control patients showed no improvements since they remained at the same level of functioning (51-60) with a mean=59 and a mean=58, before and after treatment. It was concluded that an integrated program that combined pharmacological and psychosocial treatment was more effective for acute hospitalized psychotic patients than pharmacological treatment alone (Valencia, 1988; Valencia, 1991). Considering the outcome of this treatment program, it was recommended that the combination of pharmacological and psychosocial treatments should be used as the best delivery approach for treating these patients. Unfortunately, the rehabilitation work could not continue due to the fact of the lack of financial funds and changes in health politics that were oriented to alcohol and drugs research at that time.

### 3.2.2 Psychosocial treatment for chronic outpatients

Prior to the initiation of the intervention, we consider a necessity to take into account all persons that should be involved in a treatment process. Therefore, we included patients, relatives and mental health professionals as relevant participants of this process. Patients and relatives were considered as healthy allies and collaborators of the treatment team. Relative's participation was considered as a key element since approximately 90% of our patients live with family members (Valencia et al., 2003). Their opinions and ideas served as the background for considering the content of a psychosocial treatment program that would be offered as an add-on to pharmacotherapy. Hence, we developed a methodology for the design of integrated psychosocial and pharmacological interventions, for a developing country, as Mexico. The information came from three important sources: a) clinically stabilized chronic patients with schizophrenia, b) caregivers living with their ill relatives and aware of the patient's, daily activities, and c) mental health professionals with experience in the treatment of schizophrenia patients and their relatives. Information was collected considering the clinical needs and psychosocial problems of our patients, as well as the caregiver's needs and demands. The design process included seven stages: 1) Identifying clinical and psychosocial problems through two sources: a) an exploratory study including patients as participants, so, they would give their opinions about their clinical and psychosocial needs, and, b) Using focus groups with patients, relatives and mental health professionals (psychiatrists, clinical psychologists, psychiatric social workers, and psychiatric nurses), to collect information from these three sources; 2) Establishing a consensus about clinical and psychosocial problems from all sources; 3) Designing the content of the intervention, and, in addition, with the advice of clinical and social science researchers, consider the corresponding methodological issues (experimental design, study groups, instruments); 4) Implementation of the treatment program; 5) Determining its effectiveness; 6) Follow-up, and 7) Dissemination. All patients were receiving exclusively pharmacological treatment. Psychosocial and clinical problems were identified as when patients: do not have friends (60-70%); do not have a loving relationship (90-96%); unemployed (50-80%); lack of financial sources (80-90%); economically dependent upon his/her family (80-90%); do not have good family relations (70-80%); do not know the characteristics of the illness (90-95%); do not know his/her diagnosis (55-65%); consider that they do not need medication (70-80%); and, consider that they do not need psychotherapy (80-90%). In addition, the consensus indicated the presence and persistence of deficits in various skills areas that were interfering in the patient's community functioning. It was recommended the importance of developing the following skills: the importance of effective

Treatment			
Pharmacological	Psychosocial	Psychoeducation	Family intervention
<ul style="list-style-type: none"><li>• Antipsychotic medication</li><li>• First generation</li><li>• Second generation</li><li>• Other classes of medications: Antidepressants</li><li>• Mood stabilizers</li><li>• Antianxiety medications</li></ul>	<ul style="list-style-type: none"><li>• Symptom management</li><li>• Medication management</li><li>• Occupation</li><li>• Social relations</li><li>• Couple relations</li><li>• Family relations</li><li>• Money management</li></ul>	<ul style="list-style-type: none"><li>• Illness management</li><li>• Medication management</li><li>• Medication compliance</li><li>• Recognition and management of warning signs of relapse</li></ul>	<ul style="list-style-type: none"><li>• The importance of medication</li><li>• Medication compliance</li><li>• Keeping appointments with treating psychiatrist</li><li>• Management of warning signs of relapse</li><li>• Improve communication skills</li><li>• Problem solving as needed</li></ul>
Participants			
Patient	Patient	Relatives	Patient and relatives
Frequency			
Monthly appointments	Weekly sessions, or twice a week	Weekly sessions	After psychoeducation
Duration of sessions			
20 minutes	90 minutes	90 minutes	90 minutes
Therapeutic modality			
Individual consultation	Group sessions	Group sessions for all relatives	Family therapy for the patient and his/her relatives
Duration of treatment			
6 months or 1 year	6 months or 1 year	8 sessions or 12 sessions	4 sessions or 5 sessions

Table 4. Proposal of the integration of pharmacological and psychosocial treatment for Mexican out-patients with schizophrenia

communication with the treating psychiatrists, the need to be informed about medication benefits, learning medication side effects, learning skills to cope with persistent symptoms, planning a long term pharmacological treatment, be willing to collaborate in making decision concerning medication, learning skills for avoiding alcohol and drug abuse, learning skills to improve adherence to antipsychotic medication, identifying warning signs of relapse and developing a relapse preventive plan, developing skills to improve social relations, and learning problem-solving skills for improving family relations (Valencia et al., 2010). The consensus also recommended the inclusion of various therapeutic modalities integrated in a comprehensive biopsychosocial service delivery system including: pharmacotherapy, psychosocial therapy, psychoeducation, and family therapy. The content of these modalities are shown on table 4. After the study protocol was approved by the Scientific Research Committee, and for the Ethics Committee of the National Institute of

Psychiatry, stages 4) Implementation, and 5) Determining treatment effectiveness were tested. A research area was developed where various experimental trials were conducted comparing experimental and control groups, or four treatment groups: psychosocial treatment, musictherapy, multimodal therapies, and a control group, including 4, 5 or 7 psychosocial treatment areas, either during a one year or during six months of treatment. In all trials pharmacological treatment was delivered once a month, psychosocial treatment included one or two sessions per week, 8 or 12 sessions were conducted for psychoeducation, 4 or 5 sessions for family therapy, in the last trials, the assessment of the level of expressed emotion was also included as an important variable to determine the emotional environment in the home as expressed by relatives. (Valencia et al., 2004a, 2004b, 2006, 2007, 2010)

In this chapter we describe the results of a research program that integrated pharmacological and psychosocial treatments that was carried out at the National Institute of Psychiatry in Mexico City. Out-patients diagnosed with schizophrenia according to the DSM-IV (APA, 1995) that was corroborated with the CIDI (Robins et al., 1988) participated in the study according to the following inclusion criteria: women or men, between 16 to 50 years, with at least six years of education, living with their relatives in Mexico City or the metropolitan area. Patients had to be under pharmacological treatment and therefore demonstrate to be clinically stable as regards to their psychotic symptoms according to the PANSS within a range of 60-90 before the initiation of treatment. One hundred and fifty six out-patients attending the Schizophrenia Clinic were randomly assigned, in an alternate order, to two treatment conditions: a study group (n=78), or to a comparison group (n=78). Of the 156 patients initially included in the study, 10 from the study group (12.8%) and 17 from the comparison group (21.7%) corresponding to a total of 27 patients (17.3%) of the sample, failed to complete the study, leaving a final sample of 129 patients: n=68, in the study group and n=61, in the comparison group. Patients of the study group received psychosocial treatment, specifically, psychosocial skills training and psychoeducation for their relatives, while the comparison group received the standard pharmacological treatment alone. Both groups completed one year of treatments. Pharmacological treatment for the two groups under study was provided at the Schizophrenia Clinic of the Institute, once a month, during twenty minutes, by two psychiatrists, who prescribed antipsychotics, verified medication compliance, keep a record of the attendance to appointments, and registered relapse and rehospitalizations. The treating psychiatrists were blind to the two treatment conditions. Psychosocial treatment included seven treatment areas as specified in Table 4. The aims of the intervention were: 1) facilitate patients' acquisition of psychosocial skills; 2) improve psychosocial and global functioning, 3) prevent relapse and rehospitalizations, 4) promote compliance with medication and treatment adherence. A team of two therapists trained in psychosocial skills training held weekly group sessions during 90 minutes. To carry out the therapeutic work with the patients, therapists had to follow the therapist's manual that describes the training strategies for all sessions (Valencia et al., 2001). For acquisition of the skills, a technique known as the "learning activities" was utilized and modified for our patients (Valencia et al., 2007). This technique was developed and empirically validated for schizophrenia patients (Lieberman, 2007; Wallace et al., 1992), as well as for Latinos with schizophrenia in the United States (Kopelowicz et al., 2003). A check list was also available to verify that patients learned the corresponding skills for each treatment area. A research assistant utilized a therapist fidelity evaluation check list to

assure that each learning activity included in the training manual was taught competently during treatment. Psychoeducation provided information for relatives about the management of schizophrenia, coping with the illness, antipsychotic medications and its side effects, compliance with medication, and with psychiatric consultations, and understanding and management of signs of relapse. This intervention was held during ten sessions in a group format. The two groups under study were evaluated before and after treatment. The Positive and Negative Syndrome Scale [PANSS], Spanish adaptation, (Kay et al., 1990), and the Global Assessment of Functioning Scale [GAF] (APA, 1995), were used to assess psychopathology and psychosocial functioning. Relapse, and rehospitalization rates, compliance with antipsychotic medication and adherence to treatment were also assessed.

	Study Group n = 68	Comparison Group n = 61
Gender, <i>n</i> (%)		
Male	50 (73.5)	47 (77.0)
Female	18 (26.5)	14 (23.0)
Marital status, <i>n</i> (%)		
Single	65 (95.6)	55 (90.2)
Married	2 (2.9)	3 (4.9)
Speratated/divorced	1 (1.5)	3 (4.9)
Occupation, <i>n</i> (%)		
Employed	9 (13.2)	16 (26.2)
Housewife	2 (2.9)	4 (6.6)
Student	2 (2.9)	8 (13.1)
Unemployed	55 (80.9)	33 (54.1)
Age, years, $\bar{X}$ (s)	29.6 (6.9)	29.5 (7.1)
Education, years, $\bar{X}$ (s)	11.2 (2.1)	11.1 (2.1)
Age at onset $\bar{X}$ (s)	21.6 (6.5)	21.2 (4.6)

Table 5. Participants demographic and clinical data at baseline

All participants expressed in a written informed consent their desire to participate in the research project. Data analysis included the following: Descriptive and Chi square analysis to compare percentages, Student *t* tests to verify that there were no significant differences between the two groups under study in their initial levels of psychopatology, and psychosocial functioning, Analysis of variance for repeated measures (ANOVA) to detect pre-post differences within and between the two study groups. For the assessment of effect size, three levels were considered: small= .25, medium= .50 and large= 1.00 irrespective of the sign (+ or -) of the number (Kazdin & Bass, 1999). Standardized estimate of effect sizes were calculated using Cohen's (1977) *d* formula defined as:  $d = \bar{x}_1 - \bar{x}_2 / s$ . Where  $\bar{x}_1$  and  $\bar{x}_2$  are the means at baseline and at the end of treatment of the two groups under study, and *s* is the pooled within-group standard deviation (*SD*). At baseline, no statistically significant differences were found between the two groups under study in psychopathology, (PANSS) or psychosocial functioning (GAF), or in their doses of antipsychotic medication as determined by calculation of chlorpromazine equivalents. Participant's demographic and

clinical data at baseline is shown in table 5. Patients in both treatment conditions were similar with no differences on any of these variables, except for the occupational status with a minor percentage of unemployed patients in the comparison group.

	Study Group n = 68	Comparison Group n = 61	Statistics <sup>b</sup>		
			Main effect for time	Main effect for group	Interaction of group and time
PANSS <sup>a</sup> overall score, $\bar{X}$ (s)					
Baseline	92.6 (41.6)	83.5 (33.9)	p < .001	--	p < .001
Post	43.4 (13.0)	55.7 (16.4)			
Effect size	-1.2	-.80			
PANSS positive <sup>a</sup> , $\bar{X}$ (s)					
Baseline	21.1 (11.5)	18.3 (9.8)	p < .001	--	p < .01
Post	9.1 (2.8)	11.6 (4.5)			
Effect size	-1.0	-.70			
PANSS negative <sup>a</sup> , $\bar{X}$ (s)					
Baseline	24.4 (11.2)	22.4 (9.4)	p < .001	--	p < .001
Post	11.6 (5.2)	15.0 (6.3)			
Effect size	-1.1	-.80			
PANSS GPS <sup>a, c</sup> , $\bar{X}$ (s)					
Baseline	47.1 (20.5)	42.8 (16.4)	p < .001	--	p < .001
Post	22.7 (6.0)	29.1 (8.3)			
Effect size	-1.2	-.80			
Level of global functioning <sup>d</sup> (GAF) , $\bar{X}$ (s)					
Baseline	43.1 (6.4)	43.1 (6.8)	p < .001	p < .001	p < .001
Post	67.0 (9.2)	43.7 (9.2)			
Effect size	3.8	.10			

<sup>a</sup> Higher scores indicate more severe symptoms. <sup>b</sup> Analysis of variance for repeated measures. <sup>c</sup> GPS, General Psychopathology Scale. <sup>d</sup> Higher scores indicate better global functioning. Effect size levels: small=0.25; medium=0.50; large=1.00

Table 6. Psychopathology and Psychosocial Functioning of the Study and Comparison Group

When considering the mean change scores, over one year of treatment, the results indicated that statistically significant improvements in psychopathology, as rated by the PANSS, were observed in positive and negative symptoms, general psychopathology and in total PANSS score for both groups under study. Group-by-time analysis demonstrated significantly greater improvement in psychopathology in patients of the study group when compared with patients receiving standard pharmacological treatment. Comparison of the effect sizes were large for the study group on the total PANSS score, positive scale, negative scale, and in the general psychopathology scale. Effect sizes were medium for all score scales of the comparison group. Significant improvement in psychosocial functioning was also found for patients of the study group but not for patients under standard pharmacological care since they remained at the same level of functioning (41-50) from baseline to post treatment

assessment. Patients of the study group improved two levels of functioning from 41-50 at baseline to 61-70 at the end of treatment. Effect size was large for the study group and small for the comparison group (Table 6).

	Study group n = 68	Comparison group n = 61	Statistics <sup>b</sup>		
			Main effect for time	Main effect for group	Interaction of group and time
Antipsychotic medication dose, <sup>a</sup> $\bar{X}$ (s)					
Baseline	300.8 (286.4)	328.1 (265.4)	p < .05		
Post	367.0 (167.5)	408.8 (336.6)			
Dose Range, lower – higher					
Baseline	14 - 1600	25 - 1200			
Post	29 - 1000	50 - 2400			

<sup>a</sup> Chlorpromazine equivalents in mg per day. <sup>b</sup> Analysis of variance for repeated measures.

Table 7. Antipsychotic dosage of the Study and comparison Group <sup>a</sup>

Table 7, illustrates that patients in the two treatment conditions had significant increases in the dosage of antipsychotic medication from baseline to post-treatment. At the end of treatment, the variability on medication dosage was much higher in patients who received standard care. Of the total sample, 65.8% were taking first-generation and 34.2% second-generation antipsychotics. The three most prescribed medications were: First generation: Haloperidol (21.4%), Trifluoperazine (18.8%), and Sulpiride (9.4%). Second generation: Risperidone (21.4%), Clozapine (14.3%), and Olanzapine (3.6%).

Variable	Study Group n=68		Comparison Group N=61		X <sup>2</sup>
	n	%	n	%	
Relapse	8	11.8	17	33.3	p < .01
Rehospitalizations	3	4.4	7	13.7	--
Compliance with medication	62	91.2	40	78.4	--

Table 8. Relapse, rehospitalizations and adherence

Lower relapse (11.8%) and rehospitalization rates (4.4%) were found in the study group compared to 33.3% and 13.7% respectively for the group that received medication alone. Compliance with antipsychotic medication was higher in the study group (91.2% versus 78.4%) of the comparison group, (Table 8)

3.2.3 Integrating pharmacological and psychosocial treatment

We conclude that a therapeutic approach that included the integration of pharmacological and psychosocial treatments for schizophrenia patients can be effective in a developing country as Mexico. Patients that received this integrated approach demonstrated significant improvements in psychopathology, psychosocial functioning, lower relapse and

rehospitalisation rates, and higher compliance with antipsychotic medication, as compared with their counterparts that received pharmacotherapy alone. The proposal of integrating pharmacological and psychosocial approaches has been described throughout this chapter and illustrated in table 4. Of the seven stages developed for designing the interventions, five stages were accomplished that ended up with their implementation. We had certain limitations with stage 6 since we could not carry out the patient's "follow-up" due to the lack of financial funds. We still have a long way to go since stage 7 "dissemination" is also a pendant task for all schizophrenia patients of our Institute as well for all schizophrenia patients in Mexico that would be willing to participate in integrated treatment approaches. To accomplish "dissemination", we could face some complications", if we consider that only 0.36% of the Gross Internal Product (GIP) in Mexico is allocated to scientific research, compared to 0.49 % in Argentina, 1.11% in Brazil, 2.61% in the United States, 3.22% in Japan, and 3.32% in South Korea. It seems that scientific research is not considered a priority in Mexico, as a result schizophrenia research neither. However, we have high hopes as being optimistic. We expect the necessary support to continue our efforts. When connecting clinical practice with scientific research through research protocols, we were able to carry out this type of research at the National Institute of Psychiatry whose main goals are to conduct research, provide treatment for mental disorders, and training for mental health professionals. The Institute belongs to the Coordination of National Research Institutes of Mexico that includes 13 Institutes dedicated to treatment and scientific research. Financial support for this project was possible with funds from the Institute and a grant from the National Council on Science and Technology of Mexico. It was interesting to find out that the areas where Mexican patients had psychosocial problem skills were similar to those utilized in psychosocial treatment programs in first world countries (Lieberman, 2007, Roder et al., 2006; Thornicroft & Susser, 2001). It seems that schizophrenia patients share similar problems all over the world. Above all, evidence indicates that psychosocial approaches when combined with pharmacotherapy results in better outcomes, than either antipsychotic medication alone or psychosocial treatment alone. For example, when these two approaches are integrated, relapse rates can be reduces as less than 20% (Hogarty, 1993). Understanding what bio psychosocial approaches can do for persons with schizophrenia could help us to face a new reality that indicates that although there is not a "total cure" for this disease research indicates that substantial advances have been made for improving the life of people with schizophrenia in the community with the integration of pharmacological and psychosocial approaches.

#### **4. Pharmacological and psychosocial treatment in Latin America**

Research on integrated pharmacological and psychosocial treatment for schizophrenia has been carried out mostly in developed countries. We wondered what would be the situation in Latin America as to find out what treatments are actually available in this region of the world. In order to get a complete picture we searched the following electronic bibliographic databases: Medline, Psychiatry, EBM Reviews, PsychINFO-APA, Psychology & Behavioral Sciences, Base Salud en Español, CC Clinical Medicine, CC Social and Behavioral Sciences, Medic Latina, Elsevier Science Direct, LILACS, SciELO, MEDCaribe, ISI Current Contents, PAHO Catalog, The Cochrane Library, Biblioteca Cochrane Plus, Ciencias de la Salud-BIREME, Organización Mundial de la Salud, WHOLIS, and Science Electronic Library On

Line. We used the following key words: schizophrenia, pharmacological treatment, antipsychotic medication, psychosocial treatment, psychological therapy, psychosocial intervention, psychosocial rehabilitation, psychoeducation, and family therapy. We searched the literature with publications in Spanish, Portuguese and English from January 1970 to July 2011. We found that in addition to Mexico, integrated approaches have been carried out in two countries: Brazil (Zimmer et al., 2003, 2006, 2007), and Peru (Sotillo, et al., 1998). It is worth mentioning that since the early 1950's, the first generation "conventional" antipsychotic medication, and later on, the second generation, or "atypical", have been considered as the only traditional treatment in Latin America for persons suffering from schizophrenia. For the year 2011, this approach continues as the customary treatment in most Latin American countries. Twenty five years ago, rehabilitation and psychosocial treatments were nonexistent in this region of the world; however, in the last twenty years some changes have occurred at least in three countries: Brazil (2003-2007); Mexico (1982-2011) and Peru (1998). The most reasonable explanation why psychosocial treatments have not been carried out is because of the lack of economic or financial funds. If clinical services still face serious deficits: old and huge hospitals, too many patients and a reduced staff, it is not difficult to understand why research on behavioural or psychosocial treatments is practically nonexistent. With this scenario there is no doubt that the situation in Latin America is quite different than first world countries. We have a long way to go.

## 5. Conclusion

Based upon international evidenced-based practices, treatment recommendations and practice guidelines for schizophrenia, an area of research that integrated pharmacotherapy and psychosocial therapies was implemented for Mexican patients with schizophrenia. Valuable contributions from patients, relatives, mental health professionals, as well as cultural considerations were taken into account for the design of the interventions. What is good to consider was to find out the effectiveness of these therapeutic modalities as described in this chapter as a comprehensive care system for people with schizophrenia in Mexico. What is new to consider is that these interventions are available for a developing Latin American country. However, reality indicates that the great majority of schizophrenia patients in Mexico and Latin America do not receive integrated approaches. We recommend the implementation of these therapeutic modalities for all schizophrenia patients in Mexico and in Latin America, because patients deserve to receive the best quality of service that goes beyond the traditional and exclusively approach of pharmacotherapy. Limitations in the implementation in clinical settings as well as problems in translating research into everyday practice should be considered (Margison, 2003). Although, antipsychotic medication can usually help to stabilize symptoms, impairments and disabilities still persist. Wouldn't it be nice if medication could help to restore the individual suffering from schizophrenia, to "normal" life, and regain his/her ability to function in society, to make up for lost time. However, patients could never learn new skills for their survival in the "real world" by taking medication. They need medication as well as psychosocial services. Living in the community independently and successfully should be a goal to pursue. The purpose is the re-integration of persons with schizophrenia in the community. Future research should focus on an independent living-beyond medication- in the community. To reach this goal, patients should go through various conditions that include new and resent proposals: 1) the achievement of "symptomatic remission" (Andreasen et al., 2005), with the use if

antipsychotic medication. 2) psychosocial improvements, such as “psychosocial remission”, (Barak et al., 2010), with psychosocial approaches, and, 3) the combination of these two variables that would lead to “recovery” (Leucht & Lasser, 2006; Liberman, et al., 2002; Liberman & Kopelowicz, 2005; Liberman, 2008; Torgalsboen & Rund 2010). Understanding “functional recovery” as the ultimate goal for an independent living in the community. To complete the puzzle, the family must be considered as an important component. Patients and relatives can become active participants in the “recovery process” since it has been demonstrated that with the use of psychoeducation and family approaches, expressed emotion can be reduced, so patients and their carers could live in a less stressful psychosocial environment. Enhanced monitoring practices could also help for patients, relatives and the treatment team, to be in close contact, as demonstrating “good therapeutic alliance” to intervene when necessary, and also verifying that patients are not only “getting well”, but also “staying well” in the community (Yeomans et al., 2010). This general picture indicates that some patients with schizophrenia are still unable to cope with tasks such as having friends, holding a job or living independently. Others have demonstrated that they could experience periods of symptomatic relief and enhanced functioning as being “in recovery”, considering the notion that recovering from schizophrenia is possible. Recovery should be a goal to pursue for the future.

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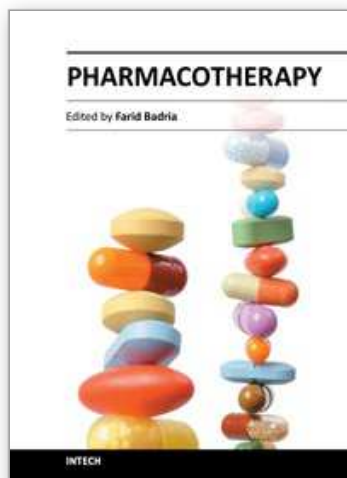
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## **Pharmacotherapy**

Edited by Dr. Farid Badria

ISBN 978-953-51-0532-9

Hard cover, 194 pages

**Publisher** InTech

**Published online** 29, June, 2012

**Published in print edition** June, 2012

The intent of this book is to provide an overview of current conceptualizations of Pharmacotherapy. The book focuses on three major areas; diagnosis, treatment, and prevention for a wide array of diseases; Cognitive and Psychological disorders (Schizophrenia and Nicotine addiction), Inflammatory disorders (New Chemical anti-inflammatory and Immunotherapy), updated antihypertensive therapy and healing of ulcers with venous origin. A separate chapter is dedicated to the rationality of drug use in earthquake injuries. The last chapter deals with Imaging of potential therapeutic or diagnostic agents in animal models in the early stage of research. We hope this book is useful to a wide range of people, from students first learning about Pharmacotherapy, to advanced clinicians and researchers.

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Marcelo Valencia, Alejandro Diaz and Francisco Juarez (2012). Integration of Pharmacological and Psychosocial Treatment for Schizophrenia in Mexico: The Case of a Developing Country Proposal, Pharmacotherapy, Dr. Farid Badria (Ed.), ISBN: 978-953-51-0532-9, InTech, Available from: <http://www.intechopen.com/books/pharmacotherapy/integration-of-pharmacological-and-psychosocial-treatment-for-schizophrenia-the-case-of-a-develo>

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