Assessment and treatment of schizophrenia in children and adolescents: a current review

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**SUMMARY**

Schizophrenia is a severe and chronic disorder affecting children, adolescents, and adults. The international recommendations for the treatment of pediatric patients with this disorder point to a comprehensive management, which includes early detection programs, and pharmacological and psychosocial treatments. This work presents a review of current information regarding the efficacy and safety of antipsychotics in children and adolescents, as well as the effect of psychosocial interventions on the academic and social functioning of patients with early onset schizophrenia.

The goal of pharmacological treatment is to achieve optimal outcome with the lowest effective dose and the fewest side effects. Treatment should be started with an antipsychotic that has been assessed for its efficacy and safety in this age group. Risperidone, olanzapine and aripiprazole have been approved by the FDA for the treatment of schizophrenia in adolescents; clozapine has shown greater efficacy with the treatment-resistant psychosis, while its adverse side effects must be monitored during use.

The objectives of psychosocial treatment are to provide information, to promote the patient’s adaptation, to reduce comorbidity and to prevent relapses through psychoeducation, psychotherapy, and rehabilitation programs. Psychoeducation programs include information about the characteristics and causes of the illness, the available treatment choices and the factors associated with recovery or relapse. Psychotherapy in schizophrenia has been examined in individual, group, and family modalities; cognitive behavioral therapy has demonstrated efficacy on cognition, social adjustment, and quality of life. Rehabilitation programs include training on social skills, cognitive remediation therapy, and exercise programs, which would increase the wellbeing of patients and reduce metabolic alterations associated with the use of antipsychotics.

In conclusion, the treatment of patients with early onset schizophrenia must be multimodal with the aim of improving their long-term outcome.

**Key words:** Schizophrenia, treatment, children, adolescents, antipsychotics.

**RESUMEN**

La esquizofrenia es un trastorno prevalente, crónico e incapacitante en niños, adolescentes y adultos. Las recomendaciones internacionales para su tratamiento en edad pediátrica incluyen programas de detección temprana y tratamiento farmacológico y psicosocial. El presente trabajo muestra una revisión actualizada de la eficacia y la seguridad de los antipsicóticos en niños y adolescentes, así como el efecto de las intervenciones psicosociales en el funcionamiento académico y social en pacientes con esquizofrenia de inicio temprano.

La meta del tratamiento farmacológico es lograr un resultado óptimo a dosis mínimas efectivas del antipsicótico y tener el menor número de efectos secundarios. Deben de considerarse los antipsicóticos evaluados en estudios controlados en edad pediátrica. La risperidona, la olanzapina y el aripiprazol han sido aprobados por la FDA para el tratamiento de la esquizofrenia en adolescentes; la clozapina ha mostrado mayor eficacia en el tratamiento de la psicosis resistente, sus efectos adversos deben de ser monitorizados durante su uso.

El tratamiento psicosocial brinda información al paciente y su familia, promueve la adaptación y disminuye la comorbilidad para prevenir recaídas, por medio de programas de psicoeducación, psicoterapia y rehabilitación. Los programas de psicoeducación incluyen la información acerca de la enfermedad y sus causas, los tratamientos disponibles y los factores asociados a las recaídas. La psicoterapia puede darse en el contexto individual, familiar o grupal, de acuerdo a las necesidades del paciente. La terapia cognitivo conductual ha mostrado eficacia en la adaptación social, cognitiva y en la calidad de vida. Los programas de rehabilitación incluyen entrenamiento en habilidades sociales, rehabilitación cognitiva y un programa de acondicionamiento físico para promover el bienestar general del paciente y evitar la aparición de los efectos secundarios sobre el metabolismo.

En conclusión, la esquizofrenia en niños y adolescentes requiere de tratamiento multidisciplinario a fin de mejorar el pronóstico de los pacientes.

**Palabras clave:** Esquizofrenia, tratamiento, niños, adolescentes, antipsicóticos.
INTRODUCTION

Schizophrenia is among the ten most common disabilities in the world1,2 and is defined as a psychotic disorder that affects the perception, thought, emotions, and behavior of patients, breaking down their family, academic, and social functioning.

The lifetime prevalence of this illness has been reported at between 0.3% and 1.6%3 and its incidence is between 0.002% and 0.011%. In one third of patients with schizophrenia the onset of the condition occurs before the age of 18,4 and in 6% before the age of 16.5 Within this population a higher proportion of cases have been described among males, with a ratio of 2:1.6

CLINICAL CHARACTERISTICS

Clinical manifestation of schizophrenia includes diverse symptoms that are classified as positive (deliriums and hallucinations), negative (apathy, anhedonia, a reduction in the lucidity and content of speech), affective (depression or anxiety that can accompany both the positive and the negative symptoms), cognitive (loss of memory, impaired judgment, disorganization), and excitability/hostility (agitation, aggression). In the case of pediatric patients the manifestation of these symptoms is frequently preceded by developmental disorders, and a higher frequency of low IQ, cognitive deficits and acute negative symptoms has been noted. There is also a high prevalence of undifferentiated and disorganized subtypes of the illness in children and adolescents.7,8

In the same way as adults, psychotic symptoms can often be preceded by prodromal symptoms.5 These include a decrease in attention, concentration and motivation, energy, mood disorders, abnormalities in the sleep-wake cycle, isolation, suspicion, and a decrease in functioning.

The course of schizophrenia includes remissions and exacerbations, although in some patients a serious psychotic state will persist. Factors associated with a poor prognosis include poor premorbid functioning,9,10 greater duration of untreated psychosis,11 greater severity of the illness and a greater number of relapses.5

This work presents a current review of all aspects of treatment for this condition, offering recommendations regarding the handling of schizophrenia in our field. For this review articles were identified that covered the efficacy and safety of antipsychotic medications in children and adolescents, as well as the effects of psychoeducation and other psychosocial interventions on the symptoms as well as the academic and social functioning of patients. The search for materials focused on articles published in medicine and psychology databases (PsychINFO, Medline, 1966–2011, Cochrane); also examined were the works referred to in the tracking studies.

EVALUATION OF PATIENTS WITH SCHIZOPHRENIA

The process of clinically assessing a pediatric patient with schizophrenia includes a clinical history supported by diagnostic interviews such as the K-SADS-PL12 or the MINIKid,13 and once the diagnosis is confirmed, through specific severity scales such as the Brief Psychiatric Rating Scale (BPRS)14, or the Positive and Negative Symptoms of Schizophrenia (PANSS) scale.15 It is important to assess the risk of auto- or hetero-aggression and the patient’s capacity for self-care.

Laboratory and clinical studies should also be considered, as they provide information about the patient’s state of health prior to commencing pharmacological treatment and help to rule out any physical pathology that influences psychotic symptoms.

TREATMENT

In Mexico there are few mental healthcare centers for children and adolescents. The few there are handle the majority of cases of schizophrenia. In such centers the comprehensive management of schizophrenia should include programs for early detection, and pharmacological and psychosocial treatment.16

Early detection

In early detection it is important to take into account risk factors for the manifestation of psychotic symptoms, such as a family history of psychosis, perinatal and neurodevelopmental disorders, substance abuse, adolescence, and stress. Different healthcare workers can participate in the early detection programs designed to examine these risk factors. The principal components of such programs are information about the illness, referral of patients to care centers that specialize in their assessment and treatment, and the follow-up of cases in a way that can determine the effect of the staff’s intervention on the symptoms and functioning of patients over the medium- and long-term.17

Pharmacological treatment

Trifluoperazine was the first antipsychotic medication assessed in a controlled clinical study.18 One of the first efficiency studies compared chlorpromazine and haloperidol,19 which was subsequently compared with the atypical antipsychotics.20

Risperidone has been studied in various open clinical21 and placebo-controlled22,23 trials, and with other atypical antipsychotics like quetiapine.24 Olanzapine25 and aripiprazole26 are the antipsychotics most recently approved for use in adolescents with schizophrenia. Clozapine was assessed in controlled studies with haloperidol27 and olanzapine.28
Recent reviews recommend it for patients who have not responded to other antipsychotics;29,30 it has been recommended for patients who have not responded to other treatments and has been assessed in a clinical study. Recently the study for Treatment of Early Onset Schizophrenia Spectrum Disorders (abbreviated to TEOSS) compared the efficacy of typical and atypical antipsychotics, showing no significant differences between molindone, olanzapine and risperidone when monitored at eight weeks and at one year, emphasizing that the affects of atypical antipsychotics on metabolism must be monitored.31,32

Treatment should be started with an antipsychotic medication that has been assessed for efficacy and safety for the pediatric group. Such medication should be prescribed in adequate doses for a minimum of six weeks. At the end of this period the patient should be assessed regarding reduction of symptoms as well as functional improvement. If a good response is observed (a 30% score reduction on the scales and a functional improvement), treatment should be maintained for at least two years. If a good response is not observed (after adherence to the treatment has been confirmed), a change in antipsychotics should be considered. If there is a predominance of positive symptoms a typical antipsychotic should be considered, and if there is a predominance of negative symptoms, an atypical. If after six weeks on a second antipsychotic there is no response, an assessment of the use of clozapine is recommended.33

In establishing and monitoring treatment with antipsychotics it is advisable to use the minimum effective dose of the medication, as the use of a high dose won’t accelerate the recovery of the patient, but would in fact increase the risk of side effects and the need for polypharmacy to control them. Furthermore, it is important to take note of side effects such as tardive dyskinesia, neuroleptic malignant syndrome, extra-pyramidal symptoms, hyperprolactinemia, metabolic syndrome and agranulocytosis; although these side effects have been associated with specific antipsychotics, they could occur with the use of any atypical antipsychotic.4,34-36 It is therefore recommended that laboratory tests be conducted every six months, as well as the recording of vital signs and weight of the patient at every appointment.

Patients with schizophrenia could develop comorbidity with other psychopathologies throughout their lives. Those most frequently reported are attention deficit hyperactivity disorder (84%), oppositional defiant disorder (43%), and depression (30%).37,38 Comorbidity with disorders due to substance abuse should particularly be examined in adolescents. The treatment of comorbidity should be multimodal.33

**Psychosocial treatment**

The objectives of psychosocial treatment are to increase knowledge about the illness, promote adjustment, improve psychosocial function, reduce comorbidity, and prevent relapses. The strategies for this treatment include psychoeducation, psychotherapy, and rehabilitation, which are applied in comprehensive treatment programs. An example of this is the «Trialog» Project in Germany, which includes psychoeducation and provides tools for social competence and self-care, as well as a process of cognitive rehabilitation for adolescents with schizophrenia. Results at two years showed that patients experienced a lower intensity of symptoms, and an improvement in cognition and social functioning.39 Here in Mexico, a randomized study of adult patients with schizophrenia showed that the combination of pharmacotherapy with a program of psychosocial treatment increased adherence to treatment, reduced the severity of symptoms, and improved the overall functioning of the patients, while also reducing relapses.40

The process of psychoeducation includes familiarization with the characteristics and causes of the illness, the available treatment options, and the factors that help or hinder the patient’s recovery. Furthermore, it provides tools for managing stress and for the timely detection of symptoms in case of relapse. Although information is scarce regarding psychoeducation programs for adolescents, studies in adults have proven the efficacy of psychoeducation,41 even in comparison with cognitive behavioral therapy.42,43

Psychotherapy for schizophrenic patients can be given in several contexts, according to their personal needs and state of health, as shown in Table 1.44

Cognitive behavioral therapy has proven effective in decreasing symptoms and the number of rehospitalizations, and in improving the quality of life; various studies have assessed its efficacy in comparison with psychoeducation programs.45-47

The rehabilitation of patients with schizophrenia should include training in social skills,48 personal care tasks, an exercise program to increase patient’s general wellbeing and prevent metabolic alterations,49,50 and cognitive rehabilitation, particularly in processes of attention, memory, and information processing, with the aim of facilitating the academic reentry of the patient.33,51

**Table 1. Key objectives of psychotherapy in its various contexts**

<table>
<thead>
<tr>
<th>Context</th>
<th>Key Objectives</th>
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<tr>
<td>Individual</td>
<td>Reduce vulnerability and stress, optimize adjustment capability and functioning of the patient, and prevent deterioration.</td>
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<tr>
<td>Group</td>
<td>Improve adherence to treatment, promote problem solving, encourage social interactions and prevent relapses.</td>
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<tr>
<td>Family</td>
<td>Build partnerships with families, foster families’ potential to anticipate and resolve problems, reduce outbursts of distress and guilt, along with maintaining realistic expectations about the functioning of the patient.</td>
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CONCLUSIONS

This review presents the current outlook of the clinical characteristics, assessment, early detection, and treatment of schizophrenia in children and adolescents with evidence-based information. Schizophrenia is one of the costliest health conditions both to health services and to society in general; the earlier the age of onset, the more complicated the treatment becomes and the poorer the prognosis. The handling of pediatric patients with schizophrenia is based on the use of antipsychotic medications, which have not been assessed in controlled studies of child and adolescent populations in their entirety. This is important due to the fact that development plays a fundamental part in the response to antipsychotics and in susceptibility to the side effects of such medications. In our field, the lack of information regarding the chronic nature of the illness and the need to take medication during prolonged periods causes patients to abandon treatment a few weeks after starting. This necessitates further investigation into the efficacy of a comprehensive treatment model that combines the use of antipsychotics with psychoeducation, psychotherapy and rehabilitation, considering the cost-benefit relationship of these interventions over the long term.

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Schizophrenia in children and adolescents; diagnosis and treatment


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Conflict of interest declaration

Dr. Rogelio Apiquian Guitart has served as part of the Advisory Board of Astra Zeneca and has been paid as a lecturer from Janssen Cilag and Astra Zeneca. He has participated in and/or received payment for Janssen Cilag, Astra Zeneca, and Roche randomized, controlled studies. The other authors have no relationship with the pharmaceutical industry or other institutions that could result in a conflict of interest.