Principles of treatment in psychoses with onset in childhood or adolescence

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ABSTRACT:
In the treatment of psychosis with onset in childhood or adolescence, multimodal therapy has been proven to be the most effective; that is combining antipsychotic treatment with behavioral therapy and social rehabilitation programs. Among antipsychotics drugs, atypical ones are preferred because the safety profile reported better efficacy on target symptoms comparable with typical antipsychotics and an improvement of cognitive deficit. Compliance to treatment has a great importance in therapeutic success.

Key words: multimodal therapy, atypical antipsychotics, typical antipsychotics, compliance.

REZUMAT:
În tratamentul psihozelor cu debut în copilărie sau adolescență, cea mai eficientă a fost dovedită terapia multimodală, care combină tratamentul antipsihotice cu terapia comportamentală și programele de reabilitare socială. Dintr-un punct de vedere psihofarmacologic, medicamentele antipsihotice sunt preferate cele atipice, întrucât au fost raportate profile de siguranță mai bune, eficacitate pe simptomele șintă comparabilă cu a antipsihoticelor tipice și o îmbunătățire a deficitului cognitiv. O importanță deosebită în reușita terapeutică o are complianța la tratament.

Cuvinte cheie: terapie multimodală, antipsihotice atipice, antipsihotice tipice, complianță.

Since appearing in the process of neurodevelopmental treatment onset psychosis in childhood or adolescence requires special care in choosing a particular psychopharmacological treatment. For both schizophrenia and affective psychoses, the goals of treatment are (after McClellan et al 2005, 2009; Kowatch, 2005; Penn et al, 2004, 2005, Kapur, 2001; Baroni, 2009):

- removal or improvement of symptoms
- relapse prevention and reduced long-term morbidity
- promote normal growth and development
- emotional control skills and impulse control, emotional and social skills
- social and educational reintegration
- achieve an optimal level of quality of life
- preventing stigma.

The treatment plan is aimed at both children and families, with social, psychological and educational implications. It is also focused on the treatment of comorbidity disorders such as substance abuse, reactive depressive episodes and the development of adaptive mechanisms in response to bio-psycho-social stressors and on improving psychological and social effects of these inevitable disorders. (McClellan et al, 2005; Birmaher et al, 2009; Baroni et al, 2009).

In the case of schizophrenia in children or adolescent, drug treatment consists mainly in antipsychotics, which are used in both acute episodes and for long-term treatment. Therefore, in addition to clinical efficacy, we are interested in the safety and tolerability profile, reducing the side effects to minimum.

Current recommendations for treatment of early-onset affective disorders derive from studies in adults. Provisions of traditional stabilizers (such as lithium and valproate) and/or atypical antipsychotics are first-line treatment in acute mania and as a maintenance therapy in bipolar disorder, while typical antipsychotics are considered adyvants, designed for special situations, comorbidity disorders or cases resistant to treatment (McClellan et al, 2007; Pavuluri et al, 2009).

In the case of bipolar disorder a mood stabilizer is considered, either an atypical antipsychotic or an atypical antidepressant. In the case of major depressions, considered unipolar, the first-line drugs that are indicated are SSRI antidepressants (specific serotonin reuptake inhibitors) but these are used with caution especially in the first episode, because they may precipitate a manic episode. It is useful to assign an atypical antipsychotic.

In major depressions due to bipolar disorder a mood stabilizer is considered.
stabilizer drug such as valproate associated with an atypical antipsychotic is recommended. Even if we are very interested in the patient’s physical comfort, use of antidepressants is exceptional, carefully monitored, the risk of turning into a manic episode being high (Pataki, 2000, McClellan et al., 2007).

These recommendations should be seen as broad, based on the experience of experts but most drugs, with few exceptions, are used „off label“ in bipolar disorder and major depression in children and adolescents; that is the responsibility of prescribers (McClellan et al., 2005, Milea, 2010).

As shown, drug therapy should have a beneficial effect on both the disease symptoms and the most important aspects of each patient’s life. The focus is mainly on the patient’s functioning deficits, while trying to facilitate the patient’s rehabilitation.

So far, there are no standard or „golden“ protocols for the treatment of very early or early onset psychosis. It has been shown that multimodal therapy that combines behavioral therapy with antipsychotic treatment and social rehabilitation programs has been the most effective method (McClellan, 2004, 2009).

Among the antipsychotics, there is a preference of the atypical ones, as better safety profile, efficacy on target symptoms comparable to typical antipsychotics and improvement of the cognitive deficit have been reported. We should not neglect the side effects of atypical antipsychotics, particularly metabolic weight gain (more severe in children and adolescents compared with adults), tardive dyskinesia (of the so-called „nonclozapine“) respectively agranulocytosis for clozapine, which requires close monitoring and regular clinical and therapeutic reassessment.

On the other hand, more and more authors believe that atypical antipsychotic medication can help improve social and school / vocational skills, both indirectly by reducing / removing psychotic symptoms, shortening acute episodes and preventing relapse and directly by having a benefic effect on cognition (slowing or stopping cognitive impairment) compared with typical antipsychotics. Also, taking control of psychotic symptoms, with a better side effects profile which affects more than the welfare of the patient provides a better framework for psychosocial interventions (Mueser et al., 1991, 2006, McClellan, 2005, 2009, Kahn et al., 2008).

The biological and psychiatric advances, which made possible the discovery of new classes of antipsychotic drugs, the understanding the mechanisms of psychosismodifying and receptor mechanisms of action of antipsychotics, have enabled remarkable improvement in therapeutic strategies in order to ensure optimal treatment, appropriate in each case.

Although there is still no protocol for treating psychosis with onset in childhood or adolescence and only two antipsychotic drugs have been approved so far for this age group, the general line of treatment recommended by experts combines behavioural therapy with antipsychotic treatment and social rehabilitation programs. With regards to antipsychotic treatment, atypical antipsychotics are preferred because of their efficacy compared to that of positive symptoms of atypical antipsychotics, high effectiveness on negative symptoms and cognition, a better side effect profile and a favorable effect on the quality of life (Mueser et al., 1991, 2006, Jibson & Tandon, 1998; Chakos et al., 2001; Namjoshi et al., 2002; Jerell, 2002, McClellan, 2005, 2009, Rosenheck et al., 2006, Hugenholtz et al., 2006; Weiden, 2007, Johnsen & Jorgensen, 2008, Kahn et al., 2008).

Knowing the action of the receptor mechanisms of antipsychotic drugs is extremely important, as is understanding the biological layer of psychotic symptoms for choosing the most appropriate drug in each case.

Discerning the links between the clinical overview, genetic substratum, neurobiological models, etiopathogenesis mechanisms, natural course of mental disorders, the development, prognostic factors and action mechanisms of psychotropic drugs, although not yet at an optimal level, provides more and more opportunities to develop effective and targeted therapeutic strategies, adapted to symptoms, thus creating a clearer outline for the therapeutic adequacy principle. Biological psychiatry has undergone a remarkable development in recent decades, due to evidence provided by basic research and progress of neuroimaging in conjunction with psychopharmacology studies.

Antipsychotics are probably the most complex pattern of receptor binding (over 10 types of receptors), but actions with the most important effect are on the dopamine D2 receptors, 5HT-A2 receptors and 5HT-A1.

a) Action on receptors of typical antipsychotics

As noted earlier, typical antipsychotics are dopamine D2 receptor antagonists, but they also block the muscarinic receptors, histamine and noradrenergic α1NA. This profile of action on receptors explains the therapeutic effect and side effects.

High-potency typical antipsychotics have strong antipsychotic effects, extrapyramidal effects but important cardiovascular effects respectively; reduced anticholinergics, while medium or low potency neuroleptics have medium antipsychotic effects, respectively; low and strong sedative effect, low extrapyramidal effects and strong cardiovascular and anticholinergic effects.

We mention that sedation is not always an undesirable effect; in some cases, it is even the expected therapeutic effect (eg in acute episodes, when there is psychomotor
agitation, insomnia, aggressive manifestations, extreme anxiety or other symptoms requiring sedating / tranquilizing the patient).

Due to the efficient effects of antipsychotics on positive symptoms of aggressive behavior or psychomotor agitation and due to a rapid and effective sedation they have been called „chemical power shirt“. Typical antipsychotics are still very useful drugs in psychosis with onset in childhood or adolescence, especially in acute episodes, being used „off label“ in this age group.

Typical antipsychotics are generally given in the most difficult periods of acute episodes, when the symptoms described above have a high degree of severity and can be administered either as a single medication at that time, later being replaced with atypical antipsychotic or as an adjunct, with the first one atypical antipsychotic.

Long-term administration of typical antipsychotics does not seem to be a good solution especially in children and adolescents, because, although efficacy on positive symptoms appears to be similar to atypical ones, non-selective binding of D2 receptors and muscarinic receptor blockade, histamine and noradrenergic causes worsening of cognitive deficits, negative symptoms and quite important extrapyramidal, endocrine and anticholinergic side effects. These effects can have a negative impact on the quality of life, can affect school reintegration and also negatively influence compliance.

Emphasis of dopaminergic hypoactivity from the level of mesocortical tracts (dorsolateral cortex and ventromedial prefrontal) by blocking D2 receptors contribute to the persistence or worsening of the cognitive deficits and negative symptoms and can lead to irreversible changes over time by promoting apoptosis and synaptic depletion (Stahl, 2008).

\[ \text{b) The action of atypical antipsychotics receptors} \]

Atypical antipsychotics have selective action on D2 receptors to mesolimbic and tonsillar level in contrast to the striatal dopaminergic tract, which explains the low rate of side effects. They also have an antagonist effect on serotonin receptors and may have a partial agonist effect on D2 receptors or on 5HT1A receptors or the antagonist effect on D2 receptors may be characterized by rapid dissociation of these receptors.

THE CHOICE OF ANTIPSYCHOTIC MEDICATION

By analyzing the profile of atypical antipsychotic receptors it can be seen, at least theoretically, that it correlates with a similar profile of efficiency on positive symptoms and with a better efficiency profile on negative symp-

toms and cognitive deficits. Numerous double-blind placebo controlled multicenter studies performed in adults without evidence support this theory. In children and adolescents there are more consistent evidence for risperidone and aripiprazole, the only approved antipsychotic drugs for schizophrenia and bipolar disorder with onset in childhood or adolescence, but almost all existing antipsychotics are used „off label“ if required by the clinical picture and are recommended by an experienced clinician (McClellan, 2005, 2007, 2009, Stahl, 2008).

There is, however, one question whose answer is not at all easy: what antipsychotic to use for a particular patient?

The choice of treatment according to the moment when the child or adolescent’s psychosis occurred is more difficult than for other disorders; psychoses are among the most severe disorders. In addition, at this age, at the onset of psychosis, is often almost impossible to accurately frame it in a particular group (the group of schizophrenia or affective disorders), this difficulty is maintained even after the time required for diagnostic formulation, respectively (eg 6 months for schizophrenia).

Many psychotic episodes which have at onset a characteristic appearance for schizophrenia spectrum evolves to a bipolar disorder in time and vice versa; there is schizophrenia which at onset seems to be an affective disorder. Therefore, it is important to make a rigorous analysis of symptoms: positive, negative, affective, cognitive, aggressive manifestations, catatonic syndrome. For this purpose, there are some very useful issues that need to be taken into account: knowing the receptor action of antipsychotic drugs, being aware of biological mechanisms behind the psychiatric symptoms, and clinician’s experience. Also, when choosing a particular drug, it must be weighed against efficacy and tolerability, risks and benefits, costs and resources.

Although monotherapy is desirable, there are situations when it is not possible, especially when the events are aggressive, when there are positive or negative symptoms with a high degree of severity, affective symptoms, side effects that need to be dealt with, other aspects of the clinical picture or unresponsive to a single medicine. In those situations it is necessary to choose drugs whose actions contribute to achieving an optimal therapeutic effect, whose mechanisms of action act synergistically or at least do not hinder mutual lead of the action or do not augment the adverse effects.

ADHERENCE TO TREATMENT

Adherence to treatment means the degree to which each patient respects the treatment requirements, both psy-
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chopharmacology and psychotherapy, and other recommendations on lifestyle, hygiene, presentation to control, the daily or other recommendations of the doctor or other professionals in the therapeutic team.

In the treatment of psychosis, treatment compliance is extremely important because its conditions are severe, with fatal chronic evolution, conditions that require long term treatment.

Manner and degree to which the child or adolescent respond, compliance / adherence to treatment are largely conditioned by family factors (in children and adolescents, parents or legal guardians are those who consider submitting to the doctor and following the instructions and its recommendations). Among family factors we remind the following:

Personality / mental health of parents / legal guardians
- The parents level of education
- Relationships between family members
- Stability and family cohesion
- Socio-economic status

Physician – family relationship and parental counseling are key elements of any therapies that address to the child and adolescent with mental disorders. Patient’s family plays a key role in therapy, being able to decide the application to a psychiatrist consultation, acceptance of treatment and its proper administration, and implementation of a favorable climate.

Parental counseling, doubled in some cases by family therapy, contributes fundamentally to a better compliance to treatment. Advice includes: information on the disease, training of parents on techniques to be applied to relieve symptoms and child development skills to cope with the psychopathogene effects of child / adolescent disorders and ensure adequate care.

Parental counseling aimed at developing coping skills to the disease is indicated in all evolving chronic mental illness. It has the following purposes:
- Reducing the negative influences of disease on the family’s mental health as a system
- Informing parents to understand that it is a mental disorder and that none „is not to blame“ to increase adherence to treatment and to observe early signs of possible relapse / worsening
- Training for the role of co-therapist/ parental care person
- Preventing or amelioration of family dysfunction that can arise from this context (divorce, family violence, alcohol and drugs) that interfere with disease progression and therapeutic management.

The ways to increase adherence to treatment overlap partially on ways how to increase the competence of the patient and his family (Dehelean P, 2009):
- Provide information on diagnosis, disease, treatment and evolution in clear language understandable to the patient and his family, in a gentle but honest way
- Request feedback from the patient and family
- Information about and combating adverse effects
- Active involvement of family in the therapeutic process (counseling about appropriate attitudes and care needs in the acute episode and during periods of remission)
- Encourage the whole family to speak openly about the disease and feelings related
- Encourage patient and family to participate in support groups.

REFERENCES


