ANTIPSYCHOTIC AGENTS – UNDERNEATH THEIR ACTION STRENGHTS AND SHORTCOMINGS

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BACKGROUND AND OBJECTIVES

Schizophrenia (SCZ) is a heterogeneous clinical syndrome comprising a number of psychopathology domains, that vary from patient to patient. It affects around 0.5–0.8% of people worldwide. It is characterized by positive and negative symptoms and often by cognitive impairment ^[1].

Positive psychotic symptoms as required by diagnostic criteria include delusions, hallucinations, and disorganization of thought and behavior. Instead, negative symptoms (NSS) are conceptualized as a deficit or loss of some functions and reflect pathology that Kraepelin described as a weakening of the well-spring of volition resulting in emotional dullness and loss of drive for vocation ^[1,2, 3]. Cognitive impairment, often present, is characterized by dysfunctions in working memory, attention, processing speed, visual and verbal learning, and substantial deficits in reasoning, planning, abstract thinking and problem solving.

This constellation of symptoms, with emphasis on cognitive and negative symptoms, are the major cause of marked functional disability associated with SCZ ^[2, 3, 4, 5, 6].

Fig. 1 – Historical Development of Antipsychotics ^{6,7}.

Literature shows that positive symptoms tend to respond reasonably well to antipsychotics, but negative and cognitive symptoms tend to be more refractory. One third of patients have refractory symptoms and most of them experience a relapse during the course of their illness and up to one third have refractory symptoms ^[7,8].

Antipsychotics revolutionized the treatment of SCZ and helped changing the institutionalization paradigm. Yet many therapeutic needs have to be surpassed ^[7].

Objectives:

- Our aim is to review the literature published to date about positive effects and shortcomings in the treatment of Schizophrenia with antipsychotics.

MATERIALS AND METHODS

Non-systematic review of the literature, in scientific databases Google Scholar and Pubmed, about beneficial effects and insufficiencies of antipsychotic agents as a treatment for Schizophrenia.

RESULTS

Many decades passed since the introduction of the first antipsychotic, Chlorpromazine, which revolutionized the treatment of Schizophrenia. The changes in effectiveness since the first-generation of antipsychotics (FGA) to date wasn't so significant.

What antipsychotics do well:

Second-generation antipsychotics (SGA) are the agents of choice for the first-line treatment of SCZ. All of them offer comparable efficacy, with the exception of clozapine, for initial and maintenance therapy ^[7]. The literature supports the premise that SGA are effective in remission of positive symptoms and in prevention of recurrence (see figure 1.) ^[8].

A recent systematic review reported a weighted mean one-year recurrence rate of 77% without therapy, and by two years the risk of recurrence had increased to over 90%. That changed with antipsychotics. ^[8,9].

What Antipsychotics Do Well

- Suppress positive symptoms;
- Prevent recurrence of symptoms.

Fig. 2. What antipsychotics do well in Schizophrenia.

What Needs Improvement:

In spite of producing some benefits in the subsequent domains, there are five unmet needs identified by researchers and clinicians: drugs that enhance cognition; that treat negative symptoms (such as lethargy, apathy, and social withdrawal); that provide improved options for treatment-resistant patients (approximately 10-30% of patients); that have a better profile regarding side effects and finally that increase compliance ^[7].

What Needs Improvement

- Refractory psychotic symptoms;
- Negative symptoms (such as lethargy, apathy, and social withdrawal);
- Cognitive symptoms;
- Enhanced safety profiles;
- Increased compliance.

Fig. 3 – What needs improvement in antipsychotics effects in Schizophrenia.

What Continues to Be Investigated:

In addition to symptom suppression, longer term studies of patients in their first episode or early stages of illness suggested that antipsychotic drugs, by virtue of their ability to limit the duration and number of psychotic episodes, could impact the clinical deterioration. In other words, antipsychotics might not just be symptom suppressing, but could mitigate the progression of schizophrenia ^[10].

Studies have found that longer periods of active psychotic symptoms prior to first treatment were associated with poorer outcome and after this prevention of relapse. Also, brain studies showed some preventing effects of brain deterioration (e.g. less pronounced cortical thinning) ^[10].

Nevertheless, antipsychotics even if they delay or alter progression of the illness – which are circumstantial conclusion – until now the effect seems to be just mild to moderate. So has yet to come a drug that can really alter the natural course and progression of Schizophrenia ^[10].

What Continues to Be Investigated

- Prevent progression and the natural history of the illness.

Fig. 4 – What continues to be investigated.

CONCLUSIONS

There are many unmet needs in treatment of SCZ. SGA was a remarkable step towards better treatments but the long-term outcome has remained poor. Substantial knowledge barriers have been overcome. With these, hopefully, better treatments will come.

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