WHITE PAPER

Pharmacotherapy of Schizophrenia

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Schizophrenia is a neurological brain disorder basically a form of psychiatric disease that turns the persons suffering from an overwhelming and happening world of reality to a terrifying world of confusions, danger delusions, and hallucination. Schizophrenia is clinically heterogeneous and is believed to be the common syndrome resulting from a number of different etiopathogenic processes. Symptoms of schizophrenia are often described as “positive”, “Disorganized Symptoms” and “negative”.

**Positive symptoms** or Psychotic symptoms or Overt Symptoms are characterized by the things such as delusions, hallucinations, thought disorders and involuntary movements. Delusions cause the patient to believe that people are reading their minds or plotting against them, that others are secretly monitoring and threatening them, or that they can control other people’s thoughts. Hallucinations cause people to hear or see things that are not there. Approximately three-fourths of individuals with schizophrenia will hear voices (auditory hallucinations) at some time during their illness. These things may come and go in a short span of time. (1)

**Disorganized symptoms** are characterized by thinking, speech and behavior affects. For example, people with schizophrenia sometimes have trouble communicating in coherent sentences or carrying on conversations with others, move more slowly, repeat rhythmic gestures or make movements such as walking in circles or pacing and have difficulty in making sense of everyday sights, sounds and feelings.

**Negative symptoms** are characterized by the things such as reduction in the normal behavior of a person (sign of abnormality), all the facial expressions from the face of a person are gone and there is inability to execute a full-fledged plan which is made by them only. Poor hygiene and infrequent speech are the other symptoms. In some cases schizophrenia occurs continuously while in other cases patients suffer from a disorder named as schizophreniform.

**Steps to manage schizophrenia successfully:**

- **First step** is identifying the signs and symptoms.
- **Second step** is seeking help without delay.
- **Third step** is sticking with treatment.

With the right treatment and support from family, friends, and health professionals, a person with schizophrenia can lead a happy and fulfilling life.

**The most common early warning signs of schizophrenia include:**

- Social withdrawal
- Hostility or suspiciousness
- Deterioration of personal hygiene
- Flat, expressionless gaze
- Inability to cry or express joy
- Inappropriate laughter or crying
- Depression
- Oversleeping or insomnia
- Odd or irrational statements
- Forgetful; unable to concentrate
- Extreme reaction to criticism
- Strange use of words
Types of Schizophrenia:

There are basically five different types of schizophrenia according to various researches and the symptoms of these types vary accordingly.

1) Paranoid schizophrenia: In this type the symptoms are characterized by bizarre delusions and sometimes auditory hallucinations. Patients suffering from this type sometimes believe that someone on the television is talking to them; government has put up a spy for them, etc.

2) Disorganized schizophrenia: This is characterized by strange emotional responses. The various symptoms of this type includes a monotonic voice, inability to laugh, cry and show any type of emotional feeling, emotionless facial display.

3) Catatonic schizophrenia: The symptoms of this type are characterized by making jerky and bizarre movements, in addition to arms and legs flailing without any reason. The person suffering from this type is incapable of caring for himself/herself and suffers from a very severe mental illness.

4) Undifferentiated schizophrenia: In this type we cannot classify the disorder, of which type is it? Some patients show symptoms of different categories and form a new category called as undifferentiated schizophrenia.

5) Residual schizophrenia: This type of schizophrenia is found in persons who may have a past history but they no longer show signs of positive symptoms.

Current Treatment Modalities:

The discovery of antipsychotics in the 1950s revolutionized the treatment of schizophrenia and focused on the positive symptoms. By the 1960s, however, it became obvious that the reduction in positive symptoms did not lead to recovery from schizophrenia and did not improve the functional outcome significantly. The 1990’s first a reintroduction of clozapine with a new understanding of how to prevent agranulocytosis and then, shortly thereafter, some new medications that showed great promise in the treatment of schizophrenia, both in their effectiveness and their side effect profiles.

Neuroleptics or anti-psychotic drugs are highly effective in dealing with the positive symptoms of schizophrenia. Some of these symptoms can normally be brought under control in a matter of days; others in weeks. Usually, a few months may be required to achieve a fully stabilized condition. For people with recurrent schizophrenia, neuroleptics are used to prevent a relapse acute symptoms. Unfortunately, the negative symptoms of chronic schizophrenia, such as depression and apathy do not respond well to medications.

The conventional neuroleptics chlorpromazine, haloperidol, and related compounds are the general first line of schizophrenia treatment. It is clearly understood that they do fairly well against positive symptoms of schizophrenia (delusions, hallucinations, etc.), but they do little for the negative symptoms and have a side effect profile that is of major concern and frequently leads to noncompliance and relapse. The main issue with conventional neuroleptics is that they cause extrapyramidal side effects (pseudoparkinsonism and tardive dyskinesia, and an elevation of mood and mental clarity) due to their antagonism and depletion of dopamine.

The newer atypical neuroleptics are appearing to change some of these medications. Clozapine and its descendants risperidone (Risperdal) and olanzapine (Zyprexa) work through targeting specific dopamine (D2) and serotonin (5HT2A and 5HT2C) receptors rather than simply blocking the effects of all dopamine. The result is that both the positive and negative symptoms are handled effectively, with far fewer side effects in general, and a much lower incidence specifically of extrapyramidal symptoms like pseudoparkinsonism and tardive dyskinesia, and an elevation of mood and mental clarity. Risperidone, in particular, has been shown to be effective in treatment of both acute and chronic...
conditions, and has some possible effectiveness against tardive dyskinesia. Some patients that show no improvement with conventional neuroleptics have done very well with risperidone or olanzapine, and those who fail to respond to those medications do well with clozapine.

Compliance issues have led to the development of "depot" medications, that is, extended release forms of neuroleptics that must be taken by injection every week or two. There has been some concern that the newer atypical neuroleptics, with their shorter half-lives, are not available in depot form, but in fact, in most cases they do not need to be. The primary reason for noncompliance is side effect problems, and they exist far less than conventional neuroleptic side effects. In practice, compliance is much better with the atypical neuroleptics. To ensure compliance in inpatient settings, an orally disintegrating form of olanzapine is being developed, which will begin dissolving in the mouth immediately and will be fully dissolved within a minute, eliminating the problem of "cheeking" medications holding them between the cheek and gum, pretending to swallow them, then spitting them out at a later time. (2)

**Insulin Shock Therapy:** It's not widely known that large doses of insulin were commonly used in psychiatric institutions in the 1940s and 1950s to treat schizophrenia and other mental illness. Insulin shock therapy was regarded as the treatment of choice for schizophrenia for about twenty years, enjoying uncritical acceptance in Europe and America.

The “treatment” was considered a type of shock therapy. Patients were given regular insulin injections to produce five or six diabetic comas a week for weeks at a time. Insulin therapy continued until the patient improved, or until 50 to 60 comas had been induced.

The originator of insulin shock therapy, also known as insulin coma therapy, was Dr. Manfred Sakel. The Polish doctor stumbled upon the therapy accidentally while working in Vienna, when a patient in whom he’d provoked an insulin coma showed a remarkable improvement in her mental functioning. Sakel believed that the seizures and unconsciousness experienced by psychiatric patients undergoing an insulin-induced hypoglycemic episode resulted in dramatic change in their mental state. (3)

**Conclusion:**
Throughout history, there has been incidence of schizophrenia, roughly one percent of the population, consistently, in every culture. One thing that has happened in recent years is that, for better or worse, the schizophrenic has been able to rejoin society. Previous treatment modalities were carried out inside the walls of a mental institution, and families regularly shuttled off their schizophrenic brood to live and die in secrecy. As treatments have improved and media began focusing on abuses within the mental institutions, there was a call to close the institutions and allow treatment to happen at home. The reality is, however, that society and medicine may not have been ready for such a change, though to be honest, the change forced medicine and society to catch up. Still, there is good reason to question whether that promise is being fulfilled and if schizophrenics are receiving the best treatments that can be provided. If nothing else, there is now new research going into the treatment of schizophrenia, which was not the case twenty years ago. The inevitable result of that is that, whether with the current class of atypical neuroleptics, newer medications, or other treatment modalities, there will eventually be a safe and effective way of dealing with schizophrenia.

**References:**

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