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Review Article

A Review on Current Effective Medications in the Treatment of Schizophrenia

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ABSTRACT

Being a devastating, chronic and often disabling mental health condition that impacts the lives of schizophrenia patients, their families and caregivers, Schizophrenia is a non curable disease but different treatments are available to reduce its effects and symptoms. Many second generation antipsychotics such as Risperidone, Secuado, Abilify Lauroxil, Abilify Mycite, Aristada, etc. are very effective and having lower risk of serious effects than the first generation antipsychotics. However these antipsychotics may cause some serious side effects. They may lead to a variety of extrapyramidal symptoms such as Akasthisia and dystonia, tremors, slurred speech, etc. The disabling adverse effects such as Akasthisia and Dystonia (movement disorders) are treated with anti-tremor medications. The study of various effective medications over Schizophrenia and related problems can help the patients to recover effectively and faster.

1. Introduction

Schizophrenia is a non curable hazardous mental disorder that disrupts broad areas of mental function, including thought, cognition, affect and motor performance. This disease mainly affects a person's ability to think, feel and behave clearly. Effective management of schizophrenia requires continuous long-term treatment in order to keep symptoms under control and to prevent relapse; among the different treatments of schizophrenia, medications such as antipsychotics, neurotransmitter inhibitors, anti-tremor drugs are more likely to reduce the symptoms of the disorder. Antipsychotics effectively ease symptoms such as delusions and hallucinations. There is an enormous unmet need for new types of schizophrenia treatments to give the people living with this illness and their family members new options that may help them effectively manage their symptoms. Many new medications are invented which are approved by the U. S. Food and Drug Administration (FDA) for the treatment of schizophrenia, these medications include antipsychotics such as Caplyta, Secuado, Perseris (Resperidone), etc. and also anti-tremors for the treatment of adverse effects of antipsychotics such as Akathisia and Dystonia. These new drugs provide additional treatment options for physicians to help them improve their patients' health.

2. MEDICATIONS

Antipsychotics:

The goal of treatment with antipsychotic medications is to effectively manage signs and symptoms at the lowest possible dose. The newer medications also called as second-generation medications are generally preferred because they pose a lower risk of serious effects than the first-generation antipsychotics.

Caplyta capsules are intended for oral administration. It contains lumateperone, an atypical antipsychotic, present as lumateperone tosylate salt with chemical name 4-(3-methyl-2,3,6b,9,10,10a-hexahydro-1H,7H-pyrido(3',4',:4,5)pyrrolo[1,2,3de]quinoxalin-8-yl)-1-(4-fluoro-phenyl)-butan-1-one 4-methylbenzenesulfonate. The recommended oral dose is 42mg of lumateperone (equivalent to 60 mg of lumateperone tosylate) which shows significant benefit over placebo. The most common adverse reactions (⩾ 5% and twice the rate of placebo) for the recommended dose of caplyta vs placebo were somnolence/sedation (24% vs 10%) and dry mouth (6% vs 2%). The drug demonstrated clinical efficacy on the positive

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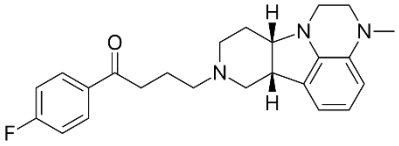
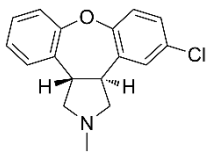
and negative syndrome scale (PANSS), a tool used to measure symptom severity in schizophrenia. The positive symptoms include thought disorder, movement disorder, hallucinations and delusiuons, while the negative symptoms are connected to emotions and behaviors and also include reduced feelings of pleasure, limited speaking, and flat effect. Caplyta mainly targets serotonin, dopamine and glutamate neurotransmitters in the brain. The molecular formula of lumateperone is $C_{31}H_{36}FN_3O_4S$, and its molecular weight is 565.71 g/mol.



Though the mechanism of action of caplyta in the treatment of schizophrenia is unknown, its efficacy could be medicated through a combination of antagonist activity at central serotonin 5-HT2A receptors and postsynaptic agonist activity at central dopamine D2 receptors. Caplyta cannot be used for the treatment of patients with dementia-related psychosis. According to latest studies it is revealed that caplyta caused some tiredness (24% in the drug group vs 10% in the placebo group) and dry mouth (6% vs 2%), the medication had promising results when it came to metabolic changes. Both caplyta and placebo showed weight gain, fasting glucose, triglycerides, and total cholesterol level. Caplyta don't cause akasthisia, a feeling of jitteriness among patients which is very uncomfortable.

Secuado (asenapine) is an FDA approved transdermal atypical antipsychotic formulation indicated for the treatment of adults with schizophrenia. Secuado is the first schizophrenia treatment approved as a transdermal patch formulation. Asenapine belongs to the class Dibenzo-oxepino pyrroles (chemical name: trans-5-chloro-2-methyl-2,3,3a,12b-tetrahydro-1H-dibenz[2,3:6,7]oxepino [4,5-c] pyrrole).



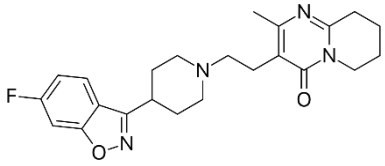
Secuado transdermal system is a translucent rounded square product available in three dosage strengths: 3.8 mg/24 hours, 5.7 mg/ 24 hours, and 7.6 mg/ 24 hours. The patch is applied to clean, dry, and intact skin at one of the sites such as upper arm, abdomen or hip. Patient should apply the patch at different sites each day to minimize the problem of skin reaction.

In the international, phase 3, double blind, placebo-controlled study, Secuado achieved the primary endpoint of statistically significant improvement from baseline in the change of total positive and negative syndrome scale (PANSS) compared to placebo at sixth week.

Dosage strength (Asenapine)	Total Asenapine content per transdermal system	Transdermal system size
3.8 mg/day	6.4 mg	20 cm^2
5.7 mg/day	9.6 mg	30 cm^2
7.6 mg/day	12.8 mg	40 cm^2

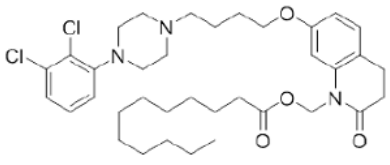
Secuado may also cause major side effects such as increased risk of death in elderly person with dementia related psychosis, neuroleptic malignant syndrome (NMS), orthostatic hypotension, lowering of WBCs count, cerebrovascular problems in elderly people, tardive diskinesia, irregukar heart beats, hyperprolactinemia, seizures, impaired thinking, and various allergic reactions.

Perseris (Injection), an antipsychotic medication which acts by changing the effects of chemicals in the brain. Perseris is sold under generic name, 'Risperidon' (Injection) and Brand name 'Risperdal Consta'. 'Risperidone' is the main content in perseris which belongs to the chemical class 'benzisoxazole' derivative with molecular formula C23H27FN4O2 and molecular weight 410.5 g/mol.



Perseris is used to treat 'Schizophrenia' and symptoms of bipolar disorder. Perseris uses extended delivery system to form a subcutaneous depot that provides sustained levels of risperidone over 1 month. Risperidone causes some major side-effects such as Aggressive behavior, agitation, anxiety, blurred vision, difficulty in concentration or in speaking or swallowing, inability to move the eyes, loss of balance, problem with urination, restlessness, skin rash or itching, muscle spasm etc. Healthcare professionals advice to administer Perseris by the route- abdominal subcutaneous injection only. The injection must be administered under the guidance of healthcare professionals aseptically with maintaining proper care and in hygienic conditions. 'Perseris' is a new advanced method which is nothing but, a New and Long Acting, atypical antipsychotic drug - delivery system. In this method Long-Acting Injectable (LAI) antipsychotics are used for the improvement of the patient's healthcare and adherence. Some examples of LAI are Risperidone, Paliperidone, haloperidol, Aripiprazole, Fluphenazine etc. FDA approved 'risperidone' as the first atypical LAI in 2004. Risperidone LAI (Risperdal Consta) is most effective in nature and improves patient's health and quality of life. The study of period of treatment of LAIs Vs OAPs (Oral antipsychotics) reveals that, in the same patient LAIs has better impact than OAPs. There are so many advantages of LAIs- 1) Used in treatment of Schizophrenic patients. 2) It is important alternative to oral medication. 3) It has fewer relapse rate. 4) Reduces hospitalization. 5) It is cost effective.

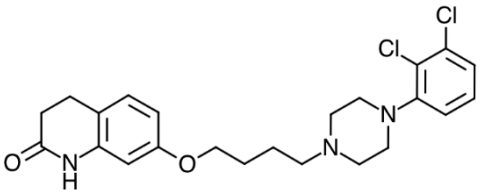
Aristada (Aripiprazole Lauroxil) is an atypical type of long-acting injectible antipsychotic medication used for the treatment of Schizophrenia in adults which works by changing the actions of chemicals in the brain. Aristada contains aripiprazole lauroxil, which is not only an atypical antipsychotic class of drug but also a pro-drug of aripiprazole. It is sold under the Generic name 'Aripiprazole' and Brand name 'Abilify Maintena', 'Abilify', and 'Aristada'. The Chemical name of Aripiprazole lauroxil is 7-{4-[4-(2, 3-dichlorophenyl)-piperazin-1yl] butoxy}-2-oxo-3, 4-dihydro-2H-quinolin-1-yl) methyl dodecanoate, having molecular formula C36H51C12N3O4 with molecular weight 660.7 g/mol.



FDA has approved Abilify in 2002 for the treatment of schizophrenia. Generally, Aristada is given in the form of aqueous extended-release suspension via intramuscular injection. Aristada injection is given once in

every 4-8 weeks, depending on patients condition. Different volumes of aristada in the single dose pre-filled syringe are: 441 mg, 662 mg, 882 mg etc. Aripiprazole lauroxil is contradicted in the patients with known hypersensitivity to aripiprazole.

Abilify Mycite (Aripiprazole) is a combination of Aripiprazole tablet and a patch in which each tablet has an embedded sensor, and that patch detects the signal from tablet sensor. Abilify with Generic name 'Aripiprazole', is an atypical type of antipsychotic drug which works by maintaining the balance between certain natural chemicals (neurotransmitters) in the brain. Chemical name of Aripiprazole is, 7-[4-[4-(2, 3-dichlorophenyl)-1-piperazinyl]butoxy]-3,4-dihydrocarbostyril. And its molecular formula is C23H27Cl2N3O2 with molecular weight 448.38 g/mol.



Abilify Mycite is orally administered drug which is taken once daily without regard to meals. The tablet is not to be chewed or crushed, one should directly swallow the complete tablet. The tablets given with Ingestible Event Marker (IEM) sensor are in the strengths: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg. These dosage strength should increases gradually but not before 2 weeks.

Dosage strength (Abilify Mycite)	Initial dose	Recommended dose	Maximum dose
Schizophrenia (adult)	10-15 mg/day	10-15 mg/day	30 mg/day

Its overdose shows some symptoms like trouble in breathing, fast heartbeats, loss of consciousness etc. It is contraindicated in the patients with known hypersensitivity to aripiprazole tablets. Abilify Mycite should be stored at room temperature and keep away from sunlight and also moisture. The ability of Abilify Mycite to improve patient observance is not yet set up. Also, Abilify Mycite is not recommended during an emergency due to retardation in detection of drug action. Abilify Mycite is not approved for the treatment of patients with dementia-related psychosis because they are already treated with antipsychotic drugs and so there is mostly chances of drug interactions which may cause increased risk of death. The safety and effectiveness of this medication have not been showed in pediatric patients. There are some common side effects of both Aristada and Abilify Mycite such as Dizziness , Drowsiness , Nausea, Vomiting, Constipation, Triedness, Execss saliva (Drooling), Blurred vision, Headache, Trouble to sleep, depression, suicidal thoughts, anxiety, risk of falling down. Older patients may be more sensitive to the side-effects of these drugs. Aristada in addition shows some major side effects such as increased CPK value (Creatinine Phosphokinase) in the blood, loss of balance, insomnia, shuffling to walk, stiffness of limbs and increased triglycerides level in the brain. Aripiprazole is rarely used during pregnancy because there are many chances of passing this medication in breast milk. So, after delivery and before breast feeding, the patient must consult the physician.

Anti-tremor:

The movement disorders associated with antipsychotics are disabling which include some abnormal muscle movements like tremors (Akasthisia) and stiffness (Dystonia) can be managed using anti-tremor medication.

Akasthisia is an acute neurological adverse effect of antipsychotics which includes motor restlessness followed by subjective feelings of discomfort and inner tension. Also, it may coexist with parkinsonian symptoms. Studies show that rapidly increasing doses of high potency antipsychotic medication increases the development of Akasthisia. Aksthisia is commonly seen to be occurred with First Generation Agents (FGAs), but studies have also found that it can also occur with neuro-drugs such as Quetiapine and Aripiprazole. One of the major challenges faced by the clinicians is the distinction between Akasthisia and agitation. The increase in the dose of antipsychotics to treat agitation may worsen the Akasthisia. Generally Akasthisia has its onset frequently after 5 days of the antipsychotic treatment, but in some patients it may appear after 2nd or 3rd day of the treatment. Management of Akasthisia can be done either by reduction of antipsychotic dose or by changing the antipsychotic medication. In the case of antipsychotic medication cannot be changed, beta-blockers such as Propanolol has shown effective results. Also, high potency benzodiazepines such as Clonazipam can also be used.

Dystonia, an acute neurological adverse effect of antipsychotic medications is a condition that causes muscular spasms or abnormal contraction of muscles and leads to twisting of the body posture. In Dystonia, muscle spasm may occur in any group of muscles, but most commonly intermittent and sustained muscle contractions are seen in the tongue, face, neck and back region. These Dystonia symptoms typically occur during the first 5 days of the antipsychotic treatment, but in 10% of the cases this may occur in the 1st hour of antipsychotic therapy. Young patients are on the high risk Dystonia especially those who are treated with high potency agents such as Haloperidol and Perphenazine. Studies have found that Dystonia respond rapidly to antiparkinsonian medications. Dystonia is treated with injectible anticholinergics such as Benztropine (2 mg IM q 15-30 min; upto 8 mg) and Trihexyphenidyl (5 mg IM q 15-30 min; upto 20 mg), and antihistamines such as Diphenhydramine (most commonly used) (50 mg IM q 15-30 min; upto 200 mg). after the condition is controlled, the treatment is maintained at lower doses of Benztropine (1-2 mgp. o. q 6 hours; upto 8 mg/day), Trihexyphenidyl (2-5 mg p. o. q 6 hours ; upto 20 mg/day), and Diphenhydramine (25-50 mg p. o. q 6 hours ; upto 200 mg/day) in addition with Dopaminergics such as Amantadine (100 mg p. o. q 6-8 hours; upto 300 mg /day).

3. Conclusion

Schizophrenia requires a life-long treatment which involves combination of several medications like antipsychotics, anti-tremor medications along with psychotherapy and professional care unit for the schizophrenia patients. The treatment adherence is a major challenge in schizophrenia due to the complexity of the disease. Nowadays it is important to have additional options available for physicians to improve their patient's health. So, there is a need to study various treatments in the schizophrenia.

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Conflict of Interest

The author(s) confirm that this article content has no conflict of interest.

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