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Journal of Neuroscience and Neurological Surgery
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Short Communication

The Place of Antipsychotics in the Treatment of Anxiety Disorders

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Received date: April 29, 2024; Accepted date: May 16, 2024; Published date: May 23, 2024

Citation: Elizaveta I Bon, (2024), The Place of Antipsychotics in the Treatment of Anxiety Disorders, *J. Neuroscience and Neurological Surgery*, 14(4); DOI:**10.31579/2578-8868/316**

Abstract

Antipsychotic drugs, also known as antipsychotic drugs, are used to treat a variety of mental disorders and symptoms. They are divided into two classes: first-generation, or "typical", antipsychotics, and second-generation, or "atypical" antipsychotics. These drugs are used for a variety of neuropsychiatric conditions such as ADHD (attention deficit hyperactivity disorder), depression, insomnia, anxiety disorders, PTSD (post-traumatic stress disorder), eating disorders, personality disorders and others.

Keywords: as antipsychotic drugs; anxiety disorder

Introduction

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First generation antipsychotics may cause extrapyramidal side effects, namely dystonia, bradykinesia, rigidity, tremor, neuroleptic malignant syndrome and tardive dyskinesia due to dopamine receptor hypersensitivity and hyperprolactinemia. [1]

Antipsychotics are believed to have anxiolytic properties, which makes them useful in the treatment of anxiety disorders.

Anxiety disorders are one of the most common groups of mental disorders. More often, their first manifestations begin in early adulthood. [2] Characteristics of anxiety disorders have a number of signs such as excessive fear, anxiety, avoidance of possible threats, which are constant and have a harmful effect on health. Factors influencing the likelihood of developing anxiety disorders include environmental factors, genetic, and epigenetic connections.

Anxiety disorders are very often comorbid with each other and with other mental disorders, primarily with depression, and somatic disorders are also possible. This comorbidity often leads to more severe symptoms and a greater clinical burden, which leads to difficulties in treatment. To reduce the severity of illnesses associated with anxiety disorders, it is necessary to prescribe appropriate treatment in a timely and accurate manner. [2]

Most likely, the pathophysiology of anxiety disorders is based on a disruption of significant anxiety mediators in the central nervous system. These include norepinephrine, serotonin, dopamine and gamma-aminobutyric acid (GABA), and the autonomic nervous system, particularly the sympathetic nervous system, contributes to most symptoms.[3]

Serotonin receptors, which serve as targets for serotonin and are also implicated in the pathogenesis of depressive disorders, come in different 5-HT receptor subtypes, including 5-HT1A, 5-HT2A, 5-HT1B, 5-HT2C, 5-HT4, and 5-HT7. In addition, there is heterodimerization between different 5-HT receptor subtypes 5-HT1B-5-HT1D, 5-HT1A-5-HT7, 5-HT1A-5-HT2A, 5-HT2A-5-HT2B or with HT2A-5- HT2C and 5-HT2B-5-HT2C.[13] DA receptors play an important role in connecting different neural circuits that may be involved in depression. Because of their ability to recognize ligands and act on cAMP, DA receptors were originally classified as D1-like and D2-like. D1-like receptors are associated with proteins that, when activated, stimulate adenylate cyclase (AC). This

process increases cAMP/PKA activation and intracellular events, leading to changes in corticostriatal glutamatergic synapses.[14]

Also, the amygdala plays an equally important role in inhibiting fear and anxiety. It turns out that patients with anxiety disorders have an increased response of the amygdala to alarm signals. The amygdala and limbic system structures are connected to areas of the prefrontal cortex, and disturbances in prefrontal-limbic system activation can be reversed through pharmacotherapy. [3]

Neuroleptics include

1. Aripiprazole (Aripiprazole, Aripegis, Abizol, Arip MT, Aristada, Abilify Maintena)
2. Risperidone (Risperidone, Rilept, Rispolept, Torendo, Torendo - Q-Tab, Sizodon)
3. Quetiapine (Quetiapine, Ketilept, Outipin, Kvetiamed, Qupinex, Seroquel)
4. Asenapine (Asenapine, Saphris)

Aripiprazole affects dopamine and serotonin activity in various brain regions such as the nucleus accumbens, ventral tegmental area and frontal cortex, which helps manage the positive, negative and cognitive symptoms of schizophrenia. The drug is generally regarded as a partial agonist of the 5-HT1A and dopamine D2 receptors, as well as a 5-HT2A receptor antagonist.[4]

Aripiprazole has a long half-life of approximately 75 hours. It is extensively metabolized in the liver by cytochrome P450 isoenzymes (CYP) 2D6 and 3A4.

In randomized trials, aripripazole was found to be effective in increasing response rates in depressed and manic patients). Scores on the YMRS (Young Mania Rating Scale) were also improved by 3 points. However, evidence of improved remission rates is lacking.[5]

A randomized, double-blind, placebo-controlled study examined the effectiveness of aripiprazole in patients with MDD with somatic symptoms. The aripiprazole group showed significant improvement in scores compared with the placebo group.[6]

Thus, aripiprazole is effective in both depressed and manic patients, but has associated side effects.[7] [8]

Risperidone has M-anticholinergic, sedative, α-adrenergic blocking effects and a low risk of dyslipidemia. It can also cause a mild increase in appetite and hyperglycemia. Risperidone and its active metabolite paliperidone can increase prolactin levels in the blood even at low doses. Risperidone has been shown to be highly effective in a variety of psychoses, including acute psychosis, adolescent schizophrenia, autism and bipolar disorders. A long-acting injectable form of risperidone is also available and is given every 2 weeks.

Paliperidone is an active metabolite of risperidone with similar properties. Unlike risperidone, it is characterized by a less pronounced sedative effect and the presence of a prolonged injection form, which is prescribed once a month.

Second-generation antipsychotics, in particular risperidone, achieve their therapeutic effect by blocking not only D2 receptors, but to a greater extent by blocking serotonin receptors, in particular 5HT2A. These drugs have low affinity for D2 receptors and are able to quickly unbind from them, which may explain less extrapyramidal symptoms. [9]

In a double-blind, randomized study in which patients were randomized to receive risperidone or lithium or haloperidol for 28 days.

The primary outcome measure in the study was the Young Mania Rating Scale (YMRS), while the Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression (CGI), and Global Assessment of Function (GAF) were secondary measures. The Simpson-Angus Score (SAS) for extrapyramidal symptoms (EPS) was used for safety measures. All three groups of patients in the study showed improvement on all rating scales. A double-blind, placebo-controlled study assessed the efficacy and safety of risperidone in acute bipolar mania. Inclusion criteria for the study included patients over 18 years of age with a high YMRS score and a low MADRS score. The risperidone group showed a statistically significant improvement in the YMRS compared with the placebo group as early as 3 days after the start of treatment. [10]

Quetiapine has high affinity for the 5-HT2 receptor. Its pharmacological effects are mainly mediated by its antagonistic effects on 5-HT2. In addition, quetiapine acts on dopaminergic D1 and D2 receptors, acting as an antagonist at D2 and 5-HT2 receptors. Both quetiapine itself and its active metabolite norquetiapine are thought to have anxiolytic and antidepressant properties through inhibition of the norepinephrine transporter (NET) and partial agonist activity at the 5-HT1A receptor, respectively. Blocking the D2 receptor in the mesocortical and mesolimbic pathways is indicated in the treatment of schizophrenia to improve negative and positive symptoms, respectively, as increased dopamine levels in these pathways are associated with the development of schizophrenia.

Studies also indicate the antidepressant effects of quetiapine due to its antagonistic effects on the 5HT2A and 5-HT7 receptors. In addition, norquetiapine has affinity for other receptors, including histamine H1 receptors, serotonergic receptors 5-HT1E, 5-HT2A, 5-HT2B, 5-HT7, muscarinic receptors M1, M3 and M5, and α1-adrenergic receptors.[11]]

In moderate doses (300 mg/d), quetiapine is prescribed as an antidepressant, while in high doses (800 mg/d) it is used as an antipsychotic. In small doses (50 mg/d), quetiapine has a strong hypnotic effect.

In a multicenter study, 76 adults with a primary diagnosis of unipolar depression with at least one anxiety disorder were assigned to a flexible dose of extended-release quetiapine or placebo. Levels of depression, anxiety, life satisfaction and possible adverse effects were assessed. Improvements in depression, anxiety, and overall functioning were significant in both groups. On primary outcome measures, quetiapine was superior to placebo in improving depression (17-point reduction on the Hamilton Depression Rating Scale).[12]

In the study, 187,563 young people were prescribed antipsychotics within a year of a new ADHD diagnosis. Youth with ADHD treated with antipsychotics were more likely than their peers not treated with antipsychotics to be recently diagnosed with self-harm and/or suicidal ideation, oppositional defiant disorder, and substance use disorder. Youth who received antipsychotics were also more likely to receive inpatient treatment. Thus, approximately half of youth newly diagnosed with ADHD may have a reasonable indication for antipsychotic medication. [15]

Conclusion

Thus, based on the mechanism of action, pathophysiology of anxiety disorders and clinical effectiveness of antipsychotics, it can be concluded that antipsychotics can be considered as the drugs of choice in the treatment of anxiety disorders.

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DOI: 10.31579/2578-8868/316