

REVIEW ARTICLE

Antipsychotic Induced Weight Gain: Review

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ABSTRACT

Antipsychotic drugs, Second-generation or atypical anti psychotics are commonly used in the treatment of patients with schizophrenia, second-generation cause lesser extra pyramidal (motor) problems, but they pose new challenges, as they often contribute to metabolic disturbances such as weight gain, hyperlipidemia, insulin resistance, and type 2 diabetes mellitus.

Schizophrenia is a debilitating disorder of the central nervous system. Its symptoms have been divided into two classes: positive symptoms, including hallucinations, delusions and conceptual disorganization; and negative symptoms, including social withdrawal, blunted affect, and poverty of speech (Donaldson *et al.*, 1983). This disorder reduces the ability of the individual to interact with the society. The typical neuroleptics used to treat schizophrenia are highly effective, but are associated with severe extra pyramidal side effects (EPS). Second-Generation (“Atypical”) antipsychotic drugs are much less likely than typical anti psychotics to cause movement disorders. But the newer drugs come with a new variety of side effects like metabolic complications. This presents a treatment challenge, since schizophrenic patients have been found to be predisposed to diabetes. In this article we will offer brief profiles of the atypical anti psychotics commonly used, with particular emphasis on the metabolic disturbances that have been attributed to their use.

Key words: Antipsychotic drugs, Atypical psychotic drugs, Schizophrenia.

INTRODUCTION

Use of atypical antipsychotics may also place patients at risk for a complicated disorder known as metabolic syndrome. Gain in weight may be an indication of metabolic side effects in patients treated with antipsychotics. Physicians treating patients with psychiatric disorders need to be familiar to physical changes that may be a sign of serious medical conditions such as diabetes or metabolic syndrome. Metabolic syndrome often encompasses medical conditions such as weight gain, hypertriglyceridemia, and increased insulin, glucose, and low-density lipoprotein cholesterol levels.

The Typical Anti psychotics:

First-generation anti psychotics, although effective, have been gradually falling out of favor because of their side effects, especially their extra pyramidal effects, including Parkinsonism, acute dystonic reactions, akathisia, and tardive dyskinesia.

The typical antipsychotics are broadly classified into two categories.

Phenothiazines: chlorpromazine, thioridazine, fluphenazine, trifluoperazine.

Butyrophenones: haloperidol, bromperidol, and others.

The Atypical Anti psychotics:

The high rates of extra pyramidal side effects with first-generation anti psychotics, their suboptimal effectiveness against schizophrenia's cognitive symptoms (disorganized thoughts, poor memory, and difficulty concentrating, following instructions, and completing tasks) and its “negative” symptoms (lack of motivation and drive, lack of pleasure from activities, restricted affect), and experience with the first atypical antipsychotic, clozapine (Clozaril), all contributed to the development of newer antipsychotic drugs, broadly classified as atypical. Some atypicals, such as clozapine, risperidone (Risperdal), olanzapine (Zyprexa), and amisulpiride, may be

superior to first-generation anti psychotics in alleviating negative symptoms [3-5] and cognitive symptoms.[6-8] Second-generation anti psychotics are a heterogeneous group. Because they act on many different receptors (dopamine, serotonin [5-hydroxy-tryptamine], alpha adrenergic, histamine H1, and muscarinic M1), their exact mechanism of action is not known.

Side effects associated with receptor blockade:

Alpha1 adrenergic: Orthostatic hypotension, sexual side effects, nasal congestion

Muscarinic M1: Anticholinergic: constipation, blurring of vision, urinary retention

Histamine H1: Sedation and weight gain

Serotonin 5-HT2: Weight gain, increased appetite

Dopamine D2: Extra pyramidal effects (Parkinsonism, dystonia, akathisia, tardive dyskinesia), elevated prolactin.

Possible Mechanisms of Weight Gain:

The specific mechanisms by which atypical anti psychotics cause weight gain are not fully understood [8]. However numerous central nervous system, hormonal and metabolic mechanisms have been proposed [1]. Effects on serotonergic, dopaminergic, adrenergic, histaminergic, glutaminergic and anticholinergic receptors are all thought to promote weight gain [9,10]. The balance between oestrogen and testosterone is also implicated [9]. Insulin sensitivity can lead to insulin resistance is associated with physiological changes maintaining obesity [1,9]. Leptin and neuropeptides are also involved in weight gain [9]. Weight gain depends on an interaction between biological, psychological and environmental factors [1]. The factors inducing or reducing weight are finely balanced and weight gain can occur if this equilibrium is upset [1].

Relative Effect of Second Generation Antipsychotics on Weight Gain

Generic (Trade Name)	Weight Gain
Olanzapine (Zyprexa)	High
Clozapine (Clozaril)	High
Risperidone (Risperdal)	Moderate
Quetiapine (Seroquel)	Moderate
Asenapine (Saphris)	Low to Moderate
Iloperidone (Fanapt)	Low to Moderate
Ziprasidone (Geodon)	Low
Aripiprazole (Abilify)	Low
Paliperidone (Invega)	Low

Adapted from Church TJ, et al. U.S. Pharmacist; 35(11): 41-48.

Management of weight gain will be an important part of the management of psychosis, and behavioral interventions will have a major role. However, the characteristics of this population mean that this will be even more difficult to achieve than in populations without mental health

difficulties. In consequence, further better-conducted research is needed to establish the effectiveness of behavioral methods on weight control in patients prescribed anti-psychotics

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