

Metabolic syndrome: a psychiatric outlook

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Author contributions

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Competing interests

The authors declare no conflicts of interest.

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Abbreviations

Met-S, metabolic syndrome; HPA, hypothalamic – pituitary – adrenal; GLP-1, glucagon-like peptide-1; GIP, glucose-dependent insulinotropic peptide.

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Abstract

A metabolic syndrome is a cluster of clinical signs that are risk factors for the development of type 2 diabetes mellitus, and cardiovascular disease. This cluster includes obesity, elevated blood sugar, high blood pressure, and high cholesterol. Atypical antipsychotics that are associated with a group of signs and symptoms have resulted in an increased focus on this syndrome.

This review included accessible literature, such as review articles and original research articles. It provides useful guidelines for psychiatrists and gives them psycho-education so that they can identify and monitor patients who may have the syndrome and properly manage it.

Keywords: metabolic syndrome; psychotropic medications; obesity

Introduction

The metabolic syndrome (Met-S) is a group of disorders that increases the risk of heart disease, type 2 diabetes mellitus, and stroke. Excess body fat around the waist, high blood pressure, high blood sugar, and abnormal cholesterol or triglyceride levels are all symptoms of this syndrome [1]. Although psychotropic medicines are one of the risk factors for the development of metabolic syndrome, the specific etiology of antipsychotic-induced metabolic disturbances remains uncertain. When prescribing antipsychotics, doctors do not screen for or treat metabolic syndrome, and the majority of psychiatrists do not believe that they should be the ones to address cardio-metabolic abnormalities. Despite the fact that diagnostic criteria differ, the condition is defined by visceral obesity, and impaired insulin metabolism. A patient has Met-S if they have at least three of the following conditions as part of the adult treatment program (ATT 3): hypertension, abdominal obesity as measured by 102 centimeters (38 inches) for men and 88 centimeters (34 inches) for women. In men, triglyceride levels must be greater than 150 milligrams per deciliter and lower than 59 milligrams per deciliter in women, and fasting glucose levels must exceed 110 milligrams per deciliter.

Psychotropic medications and the metabolic syndrome

The relationship between psychotropic medications and the metabolic syndrome

Antipsychotics of the newer generation, notably the second generation (atypical antipsychotics), are frequently linked to an elevated risk of metabolic syndrome, which is a major risk factor for cardiovascular disease [2, 3]. Premature death is more common in psychiatric patients than in the general population. Psychiatric patients are typically associated with a higher risk of metabolic syndrome (Met-S), a group of symptoms associated with cardiovascular risk factors such as dyslipidemia, abdominal obesity, hypertension, and hyperglycemia. Motivational interviewing can be useful to psychiatrists in lowering the risk of metabolic syndrome in patients. Other non-pharmacologic therapies can help control the deadly symptoms of Met-S. The goals of these interventions are to enhance physical activity, sleep, stress management, and nutritional supplementation. The most effective interventions are increased consumption of fruits, vegetables, and whole grains; increased physical activity; improved sleep; and the use of fish oil. The risk of Met-S is elevated among all types of mental illnesses, including major depressive disorder, bipolar disorder, schizophrenia, anxiety disorder, attention-deficit hyperactivity disorder, and posttraumatic stress disorder [4]. Around 20 to 25 percent of the global population suffers from metabolic syndrome. According to a research meta-analysis, Met-S's prevalence is 58 percent greater in mental patients than the general population [4]. In schizophrenia patients, the prevalence of metabolic syndrome ranges from 22.2 to 60 percent [5]. There are high incidences of type 2 diabetes mellitus seen in schizophrenia patients, ranging from 19 to 30 percent, implying a hereditary link between both illnesses [6]. The study found that people with bipolar mood disorder had a metabolic syndrome frequency of around 30% [7]. Another study found that 36 percent of depression patients had metabolic syndrome, which is associated with major depression [8]. There are specific metabolic syndrome traits associated with individuals suffering from posttraumatic stress disorder [9].

Certain psychotropics, such as atypical antipsychotics, may raise the risk of Met-S by increasing weight gain or causing changes in lipid or glucose metabolism. Despite the fact that several psychiatric medicines cause an increase in serum lipid levels, the researchers were unable to establish a direct link between antipsychotics and dyslipidemia. It states that both dyslipidemia and insulin resistance are predominantly connected with mental illness [10]. Psychiatric patients in these situations require good physical education, proper nutrition, physical activity, and more advanced cognitive-behavioral therapy [11]. The pharmacodynamics of weight gain and insulin resistance in psychotropics are discussed at the receptor level.

According to this process, weight gain occurs when people consume more food while blocking the satiety signal, which causes insulin resistance, hyperlipidemia, and the development of the metabolic syndrome [12].

Risk factors for metabolic syndrome in psychiatric disorder

In psychiatric patients, metabolic syndrome has a variety of causes and risk factors. Psychotropic medicines, including second-generation or atypical antipsychotics, as well as mood stabilizers, are known risk factors. Excessive smoking, excessive alcohol intake, a lack of physical activity, poor sleep hygiene, and unhealthy food habits may all lead to Met-S [13]. Met-S also gives out biological variables, including hypothalamic-pituitary-adrenal (HPA) axis dysfunction and insulin resistance. Another genetic risk factor is the presence of specific genes linked to a metabolic propensity, as well as polymorphisms in the leptin and melanocortin pathways, which contribute to heterogeneity in antipsychotic-induced weight gain. There are also hormonal abnormalities related to cortisol and leptin levels that contribute to the condition.

Psychiatric disorders are associated with metabolic syndrome not only because of psychotropic drugs, but also because of genetic polymorphisms, inflammation, endocrinopathies, and unhealthy lifestyles. A number of risk factors contribute to metabolic syndrome in chronic psychiatric illness, such as genetics, excessive alcohol consumption, food imbalance and poor eating habits, sedentary lifestyles, hormonal imbalances affecting cortisol and leptin, sedentary lifestyles, and second-generation antipsychotics that may have side effects [14].

Antipsychotics

Weight gain, insulin resistance, dyslipidemia, impaired glucose tolerance, or type 2 diabetes, and hypertension are all common side effects of second-generation antipsychotics. Ultimately, metabolic syndrome results from metabolic dysfunction. As antipsychotics may cause weight gain, they are not recommended as substitutes for placebos. No antipsychotic can be considered fully weight-neutral when compared to a placebo [15-17]. Second-generation antipsychotics like clozapine and olanzapine have metabolic side effects like diabetes and dyslipidemia, which, if not treated properly, can lead to dangerous consequences [18]. According to the researchers, second-generation antipsychotics like clozapine, and olanzapine, have the greatest potential to cause weight gain. Among other antipsychotics such as quetiapine, risperidone, paliperidone, and iloperidone, there is a moderate risk of weight gain. Weight gain is decreased or nonexistent with aripiprazole, amisulpride, ziprasidone, asenapine, and lurasidone. Antipsychotics can cause weight gain through a variety of mechanisms. A number of receptors, including 5-HT_{2C}, H₁, and D₂, are involved in the selective antagonistic action of antipsychotics. The antagonism of serotonin 5-HT_{2C} receptors increases insulin resistance and decreases glucose absorption by skeletal muscles, increasing the risk of diabetes mellitus, whereas histamine agonists prevent weight gain [19]. Antipsychotics also have an anti-histaminergic effect, which means they compete with histamine for binding sites on H₁ receptors, resulting in sedation and a decrease in metabolism. Weight gain can be caused by a blockage of adrenergic 1, serotonergic 5HT₂ and 5-HT_{2C} transmission, as well as histaminergic H₁ transmission of neuropeptides such as leptin and ghrelin [20].

Researchers have interpreted that olanzapine, and clozapine enhance the risk of diabetes mellitus through both direct and indirect mechanisms, such as increasing peripheral insulin resistance and promoting weight gain. Different antipsychotics are likely to produce hyperglycemia in a variety of ways. As an example, olanzapine is linked to a 37 percent higher risk of diabetes mellitus than risperidone [21]. An additional antipsychotic, clozapine, causes insulin resistance due to increased levels of TNF-cytokines produced by adipocytes. In fact, it can be used to predict obesity when certain antipsychotics are taken. If we focus on a single drug, olanzapine has a high propensity to derange metabolic parameters in patients with schizophrenia. It is

recommended that olanzapine be monitored closely and that lifestyle modifications are made in order to prevent adverse metabolic effects. According to NCEP ATP III criteria, the prevalence of Met-S before initiation of olanzapine was 15.4%, and it increased to 56.9% after one year [22]. A study on drug-naïve individuals found that 3.8% of participants had Met-S before initiation of Olanzapine [23]. Researchers also compared the increase to CATIE's phase 1 trial, in which the metabolic prevalence grew from 34.8% to 43.9% after three months in patients taking olanzapine [24].

Antidepressants

According to researchers, antidepressants rarely cause metabolic syndrome. The metabolic syndrome is more common with older antidepressants like tricyclics, and it is uncommon with newer classes of antidepressants. Insulin resistance and hypertriglyceridemia are side effects of tricyclic antidepressants. The weight gain associated with tricyclics, such as amitriptyline and doxepin, has been documented [25]. Paykel coined the phrase "carbohydrate hunger" to characterize the increased appetite seen in individuals taking tricyclic antidepressants. Distinct effects of tricyclic to noradrenergic, histaminergic, it is also discovered that amitriptyline has a powerful anti-histaminergic action, and that doxepin is to blame for the weight gain. Serotonin-specific reuptake inhibitors, on the other hand, due to their selective action on the rise in serotonin transportation, do not induce a large gain in body weight. However, it can be reduced by decreasing hunger. The use of antidepressants that increase body weight, such as amitriptyline, paroxetine, and mirtazapine, is not associated with a hormone like leptin. In contrast, amitriptyline and mirtazapine raise TNF- levels, which are absent with TNF-friendly fluoxetine, paroxetine, and venlafaxine [25]. In patients with type 2 diabetes, antidepressants like fluoxetine increase insulin action. The risk of metabolic syndrome with serotonin-selective reuptake inhibitors is very low.

The link between depressive disorder and metabolic syndrome is complicated, and numerous factors play a role. To begin with, people with depression are less likely to adhere to dietary restrictions and are more likely to be physically inactive. As a result, these patients are more likely to engage in unhealthy behaviors such as smoking and alcohol consumption. Obesity and insulin resistance are the results of this sort of patient behavior [26, 27]. Secondly, stimulation of the HPA axis raises plasma cortisol levels, resulting in pseudo-Cushing's syndrome and other metabolic syndrome symptoms [28]. Finally, insulin and leptin levels have increased. This can lead to an increase in circulating catecholamines poor glucose metabolism, blood pressure regulation, and belly fat buildup, all of which can activate the sympathetic nervous system. [29]. Fourth, elevated levels of pro-inflammatory cytokines [30] and leptin [31] have been linked to depressive disorder in patients with metabolic syndrome. In addition, dysfunction of the vascular endothelium can contribute to depression [32].

Mood stabilizer

The metabolic syndrome has been linked to mood stabilizers, particularly lithium and sodium valproate. Others, such as sodium valproate, can cause weight gain by increasing the level of circulating leptin. The impact is comparable to valproate when combined with carbamazepine, although gabapentin and lamotrigine have no effect on body weight while topiramate does. According to researchers, the effects of lithium on glucose metabolism are inconsistent, if not contradictory. They claim that it improves glucose metabolism in certain cases and reduces tolerance to glucose in others [33].

Management

Non-pharmacological intervention

In patients with metabolic syndrome, psychiatrists must support good lifestyle behaviors and suitable dieting habits. The patient must be informed about their psychiatric disease, and medications, which is a

critical factor. It improves drug adherence as well as relapse prevention. Some advice for preventing clusters of Met S symptoms includes the correct selection of an atypical antipsychotic, counseling for behavioral or lifestyle management, early initialization, and preventive pharmaceutical control of risk factors. If psychiatric patients suffer metabolic side effects when taking an atypical antipsychotic, they can switch to a low-risk atypical antipsychotic. Pharmacological management of the various components of metabolic syndrome, such as weight gain, diabetes mellitus or hyperglycemia, hypertension, and dyslipidemia, is followed by an evaluation of all other drugs and substance use histories that may contribute to metabolic syndrome. The psychiatrist should assess all metabolic parameters before beginning any intervention in order to prevent or correct metabolic side effects from atypical antipsychotics. It is best to use weight loss medications as a last resort after attempting to change one's lifestyle through behavioral programs. Dieticians and weight management specialists can provide further details about diet and exercise. Patients should also have access to holistic well-being programs; enrolling patients in weight-loss support groups may encourage them to stay healthy. The use of cognitive behavioral therapy can help people eliminate negative health-related thoughts and behaviors. The most successful technique was determined to be a cognitive behavioral approach combined with psychoeducation [34]. These psychotherapeutic approaches are more effective than weight-loss drugs in psychiatric patients for weight loss and diabetes prevention, especially when used consistently throughout the treatment program [35].

Pharmacological intervention

The main goal of pharmacological management of the metabolic syndrome is to treat the specific components of the syndrome, such as hypertension, dyslipidemia, and increased blood sugar. Antihypertensive and cholesterol-lowering medications, as well as anti-diabetic medications, can reduce the risk of cardiovascular disease with a potentially fatal outcome. A variety of medications have been effective in reducing excessive weight gain caused by second generation antipsychotics, sodium valproate, ephedrine, a beta adrenergic agonist combined with caffeine; orlistat, a lipase inhibitor that reduces fat reabsorption in the bowels; naloxone, an opioid antagonist that inhibits hunger; and metformin, an oral anti-diabetic drug that reduces excess weight gain caused by atypical antipsychotics. An analysis of 32 randomized controlled trials on pharmacological interventions for weight loss in antipsychotic-induced weight included metformin, d-fenfluramine, sibutramine, topiramate, reboxetine, amantadine, nizatidine, orlistat, metformin plus sibutramine, famotidine, dextroamphetamine, fluoxetine, and rosiglitazone. Endogenous incretins such as glucagon-like peptide-1 (GLP-1), and glucose-dependent insulinotropic peptide (GIP) influence insulin secretion and have been employed in the treatment of metabolic syndrome [36]. Bariatric surgery is one of the surgical interventions that is indicated for significantly obese people [37].

Conclusion

In psychiatric patients, metabolic syndrome is a serious yet under-recognized illness. Before beginning treatment with these atypical antipsychotics, doctors should consider the possibility of potential therapeutic benefits against the metabolic side effects. We also urge that practitioners give psychoeducation about the metabolic hazards of second-generation antipsychotics to the patients and their families. Researchers must develop psychotropic drugs that are less likely to cause metabolic syndrome and assess the efficacy and safety of pharmacological agents such as metformin and GLP-1 agonists on the syndrome.

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