

Psychopharmacology for the Clinician

Psychopharmacologie pratique

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.

Metabolic syndrome: relevance to antidepressant treatment

Antidepressant medications are often associated with weight gain and metabolic abnormalities in vulnerable patients. It is well known that obesity, insulin resistance and diabetes are associated with a large number of deaths all over the world. Patients with such psychiatric disorders as depression, anxiety and psychosis are at higher risk for cardiac mortality compared with the general population. This is compounded by the fact that many psychiatric drugs, such as antidepressants and antipsychotics, are associated with weight gain. Some drugs, such as tricyclic antidepressants, can cause insulin resistance and can increase serum lipids independent of their effect on weight.

The original description of metabolic syndrome (MBS) comprised obesity, insulin resistance, hypertension, impaired glucose tolerance or diabetes, hyperinsulinemia and dyslipidemia, characterized by elevated triglycerides and low high-density lipoprotein (HDL) concentrations. All of the above are risk factors for atherosclerosis and thus pose a significant risk for coronary heart disease. Obesity/overweight and insulin resistance also present a significant risk for developing type-II diabetes. The risks for coronary heart disease and diabetes with metabolic syndrome are greater than those for simple obesity alone; thus an understanding of the pathogenesis of heart disease and diabetes and a rational approach to their therapy are of prime importance. There is a substantial amount of literature linking weight gain to the

subsequent development of MBS related to psychotropic medication.

Treatment with tricyclic antidepressants (TCAs), amitriptyline and doxepin can cause a substantial increase in weight—one of the main factors leading to treatment noncompliance, as shown in several previous studies. The newer antidepressant drugs, such as serotonin reuptake inhibitors, can lead to a small decrease in weight in the short-term and an increase during long-term treatment in some of these patients. Several factors need to be considered in this context. In some patients, depression itself is associated with weight gain. This is compounded by treatment side effects, which may include a decrease in basal metabolic rate in addition to an increase in appetite and carbohydrate craving. An increase in weight is associated with type-II diabetes and possible insulin resistance. Depression is reportedly associated with hypertension and atherosclerotic changes in some patients.

Depression can also be associated with other comorbid disorders, such as anxiety, which may make these patients even more vulnerable to cardiac mortality. Recent literature has shown that some of the noninvasive measures, such as beat-beat heart rate and QT-interval variability on the surface electrocardiogram (ECG) provide valuable noninvasive measures to assess cardiac autonomic function. These measures are also useful in assessing prognosis in patients with cardiac illness and concomitant affective disorders. A decrease in vagal function and a relative increase in sympathetic function can be associated with the development of atherosclerosis and hypertension. In this regard, it is important to note that TCAs can be more cardiotoxic, and

some of the serotonin reuptake inhibitors can have a neutral or a positive effect. For example, sertraline and paroxetine appear to be less toxic than TCAs. In addition to choosing an appropriate antidepressant, the clinician has to check the lipid profiles and blood glucose of these patients on a regular basis and, most importantly, use an appropriate antihypertensive medication in patients who need such treatment. This includes careful consideration of angiotensin converting enzyme (ACE) inhibitors, such as enalapril and lisinopril and their protective effect on type-II diabetes in some patients. Most importantly, regular physical exercise, which has several positive effects on weight gain, serum cholesterol levels, blood pressure and type-II diabetes, needs to be emphasized as a component of treatment. It will also be valuable to study the effects of the newer antidepressant drugs on cardiac autonomic function and also to understand the pharmacology of the antihypertensive drugs, which improve cardiovascular function in general.

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Psychopharmacology for the Clinician columns are usually based on a case report that illustrates a point of interest in clinical psychopharmacology. They are about 500 words long, and references are not necessary.

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