“VICTOR BABES" UNIVERSITY OF MEDICINE AND PHARMACY, TIMISOARA
FACULTY OF MEDICINE

5th Department– INTERNAL MEDICINE I

TĂLOI GABRIELA

SUMMARY OF THE PHD THESIS

THE EFFECT OF PSYCHOTROPIC MEDICATION ON HEART FUNCTION

Thesis Advisor:

Prof. Dr. TOMESCU MIRELA CLEOPATRA

T i m i ș o a r a

2 0 2 0

TABLE OF CONTENTS

Keywords: *schizophrenic patients, speckle tracking echocardiography, myocardial dysfunction, sICAM-1, sVCAM-1, schizophrenia, inflammation, atherosclerosis, cardiovascular risk factors*

1.INTRODUCTION: MANAGING THE RISK OF CARDIOVASCULAR DISEASE IN PATIENTS TREATED WITH ANTIPSYCHOTICS: A MULTIDISCIPLINARY APPROACH

The use of antipsychotic drugs around the world has increased greatly in the last fifteen years. The number of people prescribed antipsychotics in the United States increased between 1997 and 2007 from 2.2 million to 3.9 million.

The use of antipsychotics in some pediatric populations has seen an even more dramatic increase and atypical antipsychotic use in pediatrics in the United States population increasing by 60% from 2002 to 2007.

This increase is partly due to the introduction of second-generation antipsychotic drugs that are more attractive to doctors and patients due to decreased pyramidal effects. Traditionally used only for severe mental illness, second-generation antipsychotics are now routinely prescribed as an adjunctive treatment for mood disorders. These drugs are not without significant side effects, many of them related to the cardiovascular health of people with severe mental illness, significantly increasing mortality and resulting in a shorter life expectancy compared to healthy controls.

A recent review estimated that this decline will be as large as a 10-20 year reduction in life expectancy in this population.

Multiple factors are likely to contribute to this increase in mortality but heart problems are identified as a major contributor.

Extensive studies have found that the probability of causal mortality has been almost double in subjects using atypical antipsychotic medication, finding a significantly increased risk of stroke and transient ischemic attacks, as well as an increased risk of coronary heart disease and congestive heart failure.

The World Health Organization has defined an adverse drug reaction as "a response to a drug that is harmful and unintentional and occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease or for altered physiological function."

The increased risk of cardiovascular problems in the mentally ill population is likely due to several factors, including adverse drug reactions, poor access to health care, based on organic comorbidity, and poor adherence to health care. In addition, patients with mental illness often have a higher incidence of cardiovascular risk factors present, including smoking, sedentary lifestyle, lifestyle, etc.

The popularity of second-generation antipsychotics and the complex interaction between the sum of side effects and psychiatric benefits create a growing need for multidisciplinary approaches to deliver optimal results.

As a result, the need for a study on the cardiovascular effects of psychotropic medication was born. This was an observational study, conducted on patients with psychiatric pathology, who were evaluated cardiovascular in the Cardiology Clinic of the Timisoara City Emergency Hospital.

The main objective of the study was to identify potential medical complications due to the administration of antipsychotic drugs.

Antipsychotics can be effective in treating mental illness, but their cardiovascular effects and sometimes overdose toxicity have many disadvantages.

An important topic is related to the diagnosis and treatment of psychiatric disorders in the face of significant comorbidities due to medical conditions, such as cardiovascular diseases. The issue of whether a condition is related to the nature of the underlying disease or the nature of the treatment given must also be addressed.

Drug interaction can lead to cardiovascular complications, so we need to focus on assessing and monitoring heart condition in patients treated with psychotropic drugs. Further studies are needed to explore the cellular and molecular changes in the cardiac profile of psychotropic drugs.

These can lead to new forms of prevention as well as specific treatment. People with mental illness are more likely to have more serious coexisting health problems than the general population.

Although lifestyle and genetics may contribute to independent risks of cardiovascular dysfunction in schizophrenia and other serious mental illnesses, antipsychotic treatment is also an important contributor to the risk of cardiovascular disorders, especially for certain medications and vulnerable patients.

Because patients with psychiatric pathology have limited access to health services and fewer opportunities for cardiovascular screening and prevention, we conducted several studies to recognize the factors involved.

The chapters in the special part of this paper describe the working methodology and the results of the three projects carried out to assess the relationship between mental health and cardiovascular disorders.

2.A NEW APPROACH TO CARDIOVASCULAR DISORDERS IN PATIENTS WITH SCHIZOPHRENIA TREATED WITH LONG-ACTING INJECTABLE DRUGS

This study evaluates the long-term cardiovascular impact of injectable antipsychotic therapy in patients diagnosed with schizophrenia. In our study, we tried to quantify the potential causes of cardiovascular damage, to evaluate cardiovascular parameters and to correlate them with the time elapsed from the onset of psychosis to the initiation of injectable antipsychotic therapy, and the duration of long-acting injectable antipsychotic drug therapy. , to compare two of the most widely used long-acting injectable drugs (LAIs) (olanzapine vs. risperidone). In this cross-sectional study were enrolled 64 outpatients followed in 2 centers, under treatment with antipsychotics LAI (long acting injectable) for schizophrenic disorder. The study is performed using outpatient clinical data, laboratory blood test results, routine echocardiography, and speckle tracking echocardiography. With the introduction of long-acting injectable formulas (LAIs), antipsychotics can be given monthly or every 3 months, promising more stable blood levels and remarkable results for the treatment of psychosis. Observational studies that reflect real-life conditions emphasize the superiority of LAI medication in preventing psychotic recurrences. However, for long-term treatments, it is important to evaluate the side effects of the medication. Antipsychotics can have an unfavorable impact on patient mortality through their influence on metabolic and cardiovascular parameters. The increase in cardiovascular disease mortality and morbidity in psychotic patients may be due to the underlying complications of the disease that cause anxiety and depression, but also to the accumulation of risk factors such as sedentary lifestyle, increased smoking, obesity and poor cardiology.

Prospective and retrospective studies have identified metabolic dysfunction in patients with psychosis, both before and after the introduction of antipsychotic medication. It seems that both the disease itself and the psychotropic medication are involved in the cardiovascular pathology of these patients.

In our study, we tried to quantify the two potential causes of cardiovascular injury by assessing patients' cardiovascular parameters such as blood pressure, electrocardiography and echocardiography and their correlation with the time from the onset of psychosis to the start of injectable antipsychotic therapy (before LAI) and the duration of LAI therapy.

In order to develop a cardiovascular risk profile for these patients, it is necessary to give priority to changes that may lead to the development of severe cardiovascular pathology. Risk factors such as hyperlipidemia, smoking, hypertension and a diagnosis must be considered. early to myocardial injury.

The results of our study corresponded to the results of other international studies. Among patients with longer durations of antipsychotic treatment, body mass index, mitral velocity values (E and A waves) and global longitudinal strain (GLS) are significantly correlated with patients' myocardial contractility.

The study also found that GLS was significantly lower in the group in which it was pre-LAI and was not influenced by the duration of LAI treatment. Furthermore, patients receiving olanzapine showed a significant improvement in myocardial contractility, as measured by the above parameters, compared to patients treated with risperidone.

According to our results, a delay in initiating LAI treatment of patients with schizophrenia is a statistically relevant risk factor for cardiovascular disease, evidenced by LV relaxation dysfunction and also a modified GLS. The first stages of impaired myocardial relaxation were detected echocardiographically by changes in E and A velocity, E / A ratio, prolonged IVRT, and decreased GLS, and are correlated with pre-LAI duration. It is known that patients with schizophrenia have a more altered cardiovascular profile than the general population.

The results of our study indicate that patients suffering from schizophrenia and which are left untreated or poorly treated for a longer period of time can develop myocardial dysfunction. The changes can be both secondary to a high prevalence of cardiovascular risk factors and can also be generated by the disease itself. The group receiving olanzapine showed improved results over a longer period of time without adequate medication. . The changes are probably related to the high prevalence of metabolic syndrome, but are also caused by the disease itself. This may help monitor patients with comorbidities for early initiation of cardiovascular medical therapy.

3. THE PREDICTIVE VALUE OF MARKERS OF ENDOTHELIAL INFLAMMATION AT THE ONSET OF SCHIZOPHRENIA

This study aimed to evaluate the serum levels of the intracellular adhesion molecule (sICAM-1) and vascular cell adhesion molecule (sVCAM-1) in the first psychotic episode of patients with schizophrenia (SZ), before and after six months of treatment. antipsychotic. The study included 50 patients with a first hospitalization for SZ and 50 control subjects who were matched by age, sex, body mass index and smoking status.

The assessment included the presence of cardiovascular risk factors, measurement of systolic and diastolic blood pressure, body mass index, smoker status, ankle-arm index, intimate-

average carotid thickness and echocardiography. It was calculated for these patients Short Scale Psychiatric Assessment (BPRS), the total score. Plasma glucose levels at rest, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, sICAM-1 and sVCAM-1 were determined initially in all subjects and after six months of antipsychotic treatment. Thirty patients (60%) were treated with olanzapine and 20 (40%) with risperidone.
Inflammation and endothelial dysfunction appear to be common pathways of atherosclerosis and schizophrenia (SZ) and a possible explanation for the increased cardiovascular risk in patients with schizophrenia. It is known that early medical intervention improves the results of schizophrenia.

Patients in the first episode of psychosis (EFF), usually in late adolescence or early adulthood, are preferable to assessing the prognostic factors of the disease, because in this case the stage, the number of variables related to chronic diseases and the associated medication is smaller. The effects of antipsychotic drugs appear to be more pronounced in the first months of treatment. But, it is important to note that inflammatory stress, oxidative and metabolic disorders may precede VET and initiate antipsychotic treatment.

There is also growing evidence of metabolic changes induced by antipsychotic drugs that increase patients' cardiovascular risk. Circulating cell vascular adhesion molecule-1 (sVCAM-1) and intracellular adhesion molecule-1 (sICAM-1) are known biomarkers of inflammation and endothelial dysfunction that are associated with an increased risk of atherosclerosis. Many studies have shown exaggerated levels of inflammatory markers in patients with SZ.

Decreased levels of sICAM-1 in SZ may represent a decrease in type 1 immune activity, but the role of activating inflammation and immunity in severe mental disorders is still poorly understood. Echocardiography, carotid ultrasonography, the intima-media ratio and the ankle-arm index (ABI) are known as accurate methods for detecting and stratifying the risk of subclinical atherosclerosis.

This study aimed to determine the best method to detect the presence and progression of endothelial inflammation and subclinical atherosclerosis in patients with naïve antipsychotic SZ at the first psychotic event and to determine the differences from healthy individuals at the beginning and after 6 months. antipsychotic treatment.
The results of the study showed that in patients with the first episode of SZ, sICAM-1 levels were lower, while sVCAM-1 levels were higher than in healthy control subjects. Antipsychotics

used to treat schizophrenia increased sICAM-1 and decreased sVCAM. The sVCAM-1 level was an independent predictor of the BPRS score> 120.

4. COMPARATIVE STUDY OF CARDIOVASCULAR RISK FACTORS FOR DIFFERENT TYPES OF PSYCHIATRIC DISORDERS

Cardiovascular disease (CVD) and severe psychiatric illness (PSI) are the leading causes of morbidity and mortality worldwide. The link between BCV and PSI has been studied for decades and different types of connections between the two major diseases have been suggested. A higher prevalence of CVD in patients with PSI has been demonstrated in several studies. The aim of this study is to assess the impact of classic cardiovascular risk factors (age, sex, smoking, alcohol, hypertension and lipid profile) and the Framingham Score for the risk of death at 10 years due to cardiovascular disease in various types of severe mental illness. Based on the premise that patients with psychiatric illness have a life expectancy 10-17.5 years lower than the general population, mainly due to cardiovascular disease, we conducted a retrospective study of 165 patients admitted to the psychiatric clinic for a period of 1 year. In all 165 patients, cardiovascular risk factors, age, sex, smoking status, lipid profile, BP values, as well as other risk factors for cardiovascular disease (presence of associated drugs, renal function, alcohol co Most similar studies were selected for health subjects in the control group, which makes it difficult to interpret the differences between the groups. In our study, the control group was deliberately selected from inpatients for various diseases, to reveal whether psychiatric patients have similar cardiovascular parameters to these control subjects. Patients with schizophrenia had a higher percentage of smokers (50%) and alcohol consumption (25%) than in the control group (smoking 13.5% and alcohol consumption 4.7%). Regarding the presence of lifestyle factors of patients who would interfere with cardiovascular disease72-75, patients with severe depression (smoking 39% and alcohol consumption 45.1%) and patients with other severe mental illnesses (smoking 35% and consumption alcohol (37.5%) also had higher percentages than in the control group. All psychiatric patients had a higher risk of cardiovascular death than in the control group. An extremely high level is in patients with Alzheimer's disease, but also in patients with severe depression and patients with schizophrenia. Efforts to improve the clinical condition and reduce the mortality of patients with severe mental illness must address the cardiovascular risk factors, which contribute greatly to the negative evolution, in all psychiatric patients. The different risk between these patients is not only life factors, but also biological

factors, which seem to be common in both psychiatric and cardiovascular diseases. According to our results, patients with severe mental illness clearly have an increased risk of cardiovascular death compared to the control group.

5.CONCLUSIONS

The aim of the paper was to establish the cardiovascular effects of psychotropic medication among the population with mental illness and to analyze the pharmacological mechanisms and clinical profiles associated with changes in metabolic regulation. The conclusion of the first study is that among patients with longer durations of antipsychotic treatment, body mass index, mitral velocity values (E and A waves) and global longitudinal strain (GLS) are significantly correlated with myocardial contractility of patients. The study also found that GLS was significantly lower in the group in which it was pre-LAI and was not influenced by the duration of LAI treatment. The second study shows that in patients with the first episode of SZ, sICAM-1 levels were lower, while sVCAM-1 levels were higher than in healthy control subjects. Antipsychotics used to treat schizophrenia increased sICAM-1 and decreased sVCAM. The sVCAM-1 level was an independent predictor of the BPRS score> 120. The third study showed that all psychiatric patients had a higher risk of cardiovascular death than in the control group, patients with severe mental illness had a higher percentage of smokers and higher alcohol consumption than in the control group, and the cardiovascular risk parameters, with the exception of systolic blood pressure, are modified in the sense of increasing the cardiovascular risk compared to the control group.