

Integrated health care, use of psychotropic medications and soy products as alternative in patients who suffer from schizophrenia and metabolic syndrome

Sistema de salud integrado, uso de medicamentos psicotrópicos y productos de soya como alternativa en pacientes que sufren de esquizofrenia y síndrome metabólico

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ABSTRACT

There is a relationship between the increases of metabolic disorders in patients; whom are consuming medication to treat severe mental illnesses. There is also consensus in the relationship between the body fat distribution and cardiovascular disease, diabetes, use of psychotropic drug, among others. On the other hand, psychotropic medications have come to play an increasingly major role in the treatment of psychiatric disorders. However, many patients treated with psychotropic drugs tend to gain corporal weight and are sensitive to the diseases mentioned above. Fortunately, healthy and equilibrated food intake has been associated with the prevention of diseases. This review will address the effects of psychotropic medication intake and how this relates to obesity, risk of cardiovascular diseases in patients who suffer from severe mental illnesses. It will also evaluate the potential use of healthy diets using soy, and exercise to improve the well being of the patient.

Keywords: Severe mental illness, cardiovascular risk, equilibrated nutrition, soy

RESUMEN

Existe una relación entre el aumento de trastornos metabólicos en pacientes; quienes consumen medicamentos para tratar enfermedades mentales graves. También hay consenso en la relación que existe sobre la distribución de la grasa corporal con enfermedades cardiovasculares, diabetes, el uso de drogas psicotrópicas, entre otros. Por otro lado, el uso de sicotrópicos ha llegado a desempeñar un papel cada vez más importante en el tratamiento de trastornos psiquiátricos. Sin embargo, muchos pacientes tratados con estas drogas, tienden al sobrepeso, haciéndose sensible a estos riesgos. Afortunadamente, la ingesta de alimentos saludables y equilibrados se ha asociado con la prevención de enfermedades. Esta revisión dirigirá a los efectos de la ingesta de medicación con sicotrópicos y cómo esto se relaciona con la obesidad, riesgo de enfermedades cardiovasculares en pacientes que sufren de enfermedades mentales graves. También evaluará el uso potencial de las dietas saludables con soya y ejercicios para mejorar el bienestar del paciente.

Palabras clave: Enfermedad mental, riesgo cardiovascular, nutrición equilibrada, soya

INTRODUCCIÓN

It is of consensus that people suffering schizophrenia, depression or bipolar disorder, have worse physical health and reduced life expectancy, compared to the general population. The excess of cardiovascular mortality associated with schizophrenia and bipolar disorder is attributed to an increased risk of the modifiable coronary heart disease risk factors, obesity, smoking, diabetes, hypertension, and dyslipidaemia^{4,5,6}.

By the other hand, second generation antipsychotic (SGAs) or atypical antipsychotics have provided hope for patients and their families struggling with schizophrenia and bipolar disorder. Despite these advances in treatment, metabolic abnormalities, specifically the metabolic syndrome (MetS), are occurring at a greater incidence in persons with severe mental illness (SMI)¹. Indeed, psychotropic medications have come to play an increasingly major role in the treatment² of psychiatric disorders, and many patients that are consuming psychotropic drugs as medication, tend to become obese and are also sensitive to the metabolic abnormalities mentioned³.

Without a doubt, the metabolic disorders, cardiovascular diseases, and Diabetes mellitus have been associated with obesity. In fact, several studies have been reported, and there is an association of body fat distribution with cardiovascular disease, diabetes, blood pressure and serum cholesterol^{2,7}.

Psychotropic drugs that treat schizophrenia and bipolar disorders may increase appetite with a resultant weight gain. Rarely, such agents may be associated with weight loss. Unless circumstances dictate otherwise, clinicians should select psychotropic drugs least likely to induce weight gain when treating schizophrenic patients who suffer from obesity, diabetes mellitus, or metabolic syndrome. Even drugs generally thought to be "weight neutral" may occasionally be associated with weight gain. Thus, alerting patients to this potential and due diligence form the cornerstone of weight management in the depressed patients⁸.

During the following section the terms SMI, metabolic disorder and some of its consequences, such as; Diabetes Mellitus, heart diseases, and obesity will be defined. Finally, the relationship between food intake and health, and the use of soy milk will be discussed.

Severe Mental Illnesses

For the purpose of this review, SMI is defined as all mental disorders characterized by having a psychotic feature such as: schizophrenia, psychotic disorders and mood disorders. Schizophrenia and psychotic disorders are all characterized by having psychotic symptoms as their defining feature. According to the Diagnostic and Statistical Manual of Mental Disorders⁹ psychotic is a term restricted to delusions or prominent hallucinations, with the hallucinations occurring in the absence of insight into their pathological nature. In other words, a conceptual definition

could be a loss of ego boundaries or a gross impairment in reality testing. Mood disorders include disorders that have a disturbance in mood as their predominant feature. These disorders are divided into depressive disorders, the bipolar disorders, and two disorders based on etiology (mood disorders due to a general medical condition and substance induced mood disorder).

Metabolic Disorders

Metabolism is the process your body uses to get or make energy from the food you eat. Food is made up of proteins, carbohydrates and fats. Chemicals in your digestive system break the food parts down into sugars and acids, your body's fuel. Your body can use this fuel right away, or it can store the energy in your body tissues, such as the liver, muscles and body fat. A metabolic disorder occurs when abnormal chemical reactions in the body disrupt this process. When this happens, you might have too much of some substances or too little of other ones that you need to stay healthy. A person can develop a metabolic disorder when some organs, such as your liver or pancreas, become diseased or do not function normally¹⁰ (diabetes is an example).

Diabetes Mellitus

Diabetes Mellitus represents a group of diseases of heterogeneous etiology, characterized by chronic hyperglycemia and other metabolic abnormalities, which are due to deficiency of insulin effect. After a long duration of metabolic derangement, specific complications of diabetes (retinopathy, nephropathy, and neuropathy) may occur¹¹. Other studies have indicated the increase on diabetes that SMI population suffers¹. Diabetes is a disease in which your blood glucose, or sugar, levels are too high. Glucose comes from the foods you eat, and insulin is a hormone that helps to regulate the levels of glucose. With Type 1 diabetes, your body does not make insulin. With Type 2 diabetes, the more common type, the body does not make or uses insulin well. Without enough insulin, the glucose stays in your blood and over time, having too much glucose in your blood can cause serious problems. It can damage your eyes, kidneys, and nerves¹¹. Symptoms of Type 2 diabetes may include fatigue, thirst, weight loss, blurred vision and frequent urination. However, some other people have no symptoms. A blood test can show blurred vision and frequent urination. However, some other people have no symptoms. A blood test can show if an individual has diabetes. Exercise, weight control and sticking to your meal plan can help control diabetes. People should also monitor their glucose level and take medicine if prescribed. Diabetes can also cause stroke, even the need to remove a limb and very commonly heart diseases¹².

Heart Diseases

The most common cause of heart diseases is the coronary arteries disease: The narrowing or blockage of the coronary artery, the blood vessel that supply blood to the heart itself. It is the major reason people have heart at-

tacks. Other kinds of heart problems may happen to the valves in the heart, or the heart may not pump well and cause heart failure. People can help reduce risk of heart diseases by taking steps to control factors that put them at greater risk: Controlling blood pressure, lowering cholesterol, avoiding smoke and getting moderate exercise and controlling nutrition habits¹³⁻¹⁷.

Obesity

Excessive weight may raise levels of total cholesterol, cause high blood pressure, and increase the risk of coronary artery disease. Obesity increases the probability of acquiring other cardiovascular risk factors such as; resistance to insulin, metabolic syndrome, and diabetes¹⁸.

Food, Diet and Health

Currently the consensus is the relationship between the prevention of diseases and type of food ingested. Some type of food are currently been developed with modifications in its composition (by decreased, removal or addition of nutrients) in order to avoid and to prevent health diseases¹⁹⁻²¹. Moreover, dietary habits are implicated in the occurrence of cardiovascular diseases (CVD). To deal with the unhealthy diets, there is an urgent need to develop targeted strategies and measures, that match will the levels of economic development and local customs. A fast food dietary pattern, high in saturated fat dietary and low fiber intake is prevalent among most of the social groups, and a quite less population practice a healthy eating associated with lower CVD risk markers.

The traditional Mediterranean diet is a high unsaturated fat diet due to customary use of olive oil and it contains abundant vegetable products (cereals, legumes, fresh vegetables, fruits, and nuts). In addition, fish is a common staple and meals are usually accompanied by wine. On the contrary, the Mediterranean diet includes little consumption of meat, dairy products and commercial sweets rich in refined sugar. Several controlled clinical studies, usually short-term and with small sample sizes, have shown that intervention with the Mediterranean diet or its main components has a clear beneficial effect on intermediate risk markers, such as blood pressure, the lipid profile glucose tolerance, the oxidative status, inflammation, and endothelial function^{3,7,22-25}. The use of diets such as; the traditional Mediterranean diet, on the SMI population could be a possible help to prevent the (MetS) and then the CVD risk.

Risk of the patient with SMI

The increase of mortality rates associated with severe mental illnesses (SMI) due to preventable medical conditions: Metabolic disorders, cardiovascular diseases, diabetes mellitus and high prevalence of obesity are concerning⁶.

Prior studies have found that patients with SMI were less likely to receive coronary revascularization and have higher risk of death following Acute Myocardial Infarction (AMI)²⁶. The cited reasons for this inequality include in-

creased medical co-morbidity, reduced access to medical technology, social isolation, low income, interference with informed consent because of the cognitive symptoms and provider hesitation to aggressively treat SMI patients²⁷.

Different disorders of the metabolism have been associates to the intake of psychotropic medications. Moreover, today, there is quite little information in regard to the effects of the psychotropic medications on the health of individuals, specially who suffer from severe mental illnesses (SMI), and who have being treated by these medications. Besides, there are not specific diets to improve the physical health of those patients. Additionally, despite the continuous increasingly use of psychotropic medications to treat mental illnesses, data regarding their efficacy and safety are limited. Correll and Carlson 2006²⁸ pointed out, that because youth are still physically developing at the time of psychotropic drug exposure, most reference values need to be adjusted for gender and age; as in adults, and youngsters receiving lithium require monitoring for thyroid dysfunction. Psychostimulants appear to cause mild reversible growth retardation in some patients, most likely because of decreased weight or slowing of expected weight gain; some patients may experience clinically significant reductions in adult height. Although still controversial, valproate use has been associated with an increased risk for polycystic ovary syndrome, in addition to causing weight gain. Endocrine and metabolic adverse effects are among the most concerning adverse effects of commonly used psychotropic medications²⁸.

Many psychoactive medications have prominent cardiovascular side effects, toxicities, and undesirable drug interactions with cardiovascular medicines^{29,30}. Kovac and Arora, 2008³¹, have pointed out that in a psychiatric population, the prevalence of cardiovascular disease is higher than in the general population, because of a different lifestyle and greater frequency of risks factors such as smoking, obesity, and increased stress. In addition, in the Journal of Current Problems in Cardiology had been pointed out some discoveries that have shown that some psychiatric illnesses: eg, depression³² and phobic anxiety³³ may have direct effects as independent cardiovascular risk factors. Moreover, in this review pointed out that clinical cardiologist are increasingly asked to consult about these effects³⁴. In addition, Alexander and Niño, 1969³⁵ had published a preliminary report over the cardiovascular complications in young patients taking psychotropic drugs. Additionally, Correl and Carlson, 2006²⁸, have pointed out, that although more data are required, children and adolescents appear to be at higher risk than adults for antipsychotic-induced hyperprolactinemia, weight gain, and possibly, associated metabolic abnormalities, which is of particular concern. The authors have concluded that the clinicians and caregivers need to be aware of potential endocrine and metabolic adverse effects of psychiatric medications. A careful selection of patients, choice of agents with potentially lesser risk for these adverse events, healthy lifestyle counseling, as well as close health monitoring are warranted to maximize effectiveness and safety.

On the other hand, the prevalence of Diabetes Mellitus (DM) is becoming a serious public health problem. The use of atypical antipsychotics has been associated with disruption of the glucose metabolism and therefore with causing DM. The underlying mechanisms are unknown, but knowledge of the differences between the pharmacological features of various antipsychotics combined with their diabetogenic profile might help us understand those mechanisms³⁶. This author describes how the binding of various essential receptors or transporters in essential body tissues, adipose tissue, pancreatic tissue and liver and skeletal muscle tissue can cause disruption of the glucose metabolism. With such knowledge in mind one can try to explain the differences between the diabetogenic propensities of various antipsychotics. It is well known that clozapine and olanzapine cause weight gain and DM, whereas aripiprazole and ziprasidone have much less disruptive clinical profiles. The most significant risk factor for adiposity seems to be strong blocking of histaminergic receptors. An agonistic activity on serotonergic-1a receptors, with a very low affinity for muscarinergic-3 receptors, might protect against the development of DM. More data will become available which may help to solve the puzzle³⁶.

Body weight gain frequently occurs during drug treatment of psychiatric disorders and is often accompanied by increased appetite. The consequence of weight gain in most patients is overweight or obesity. Weight classification is based on the body mass index (BMI, weight (kg)/height (m)). Normal subjects have a BMI between 18.5 and 24.9 kg/m². Subjects with a BMI from 25 to 29.9 kg/m² are classified as overweight, and from 30 to 39.9 kg/m² as obese. Patients with a BMI above 40 kg/m² are designated extremely obese^{18,37}. Some studies investigated health effects of obesity in the context of psychotropic drug treatment. Fontaine et al., (2001)³⁸ estimated the consequences of antipsychotic treatment-induced weight gain on health and mortality rate, based on data from the Framingham Heart Study. Assuming a weight gain of e.g. 12.5 kg, they predict the occurrence of 2335 additional cases of diabetes mellitus, 9456 cases of hypertension, and 662 additional deaths among 100,000 schizophrenic patients within 10 years. This virtual²⁴ model corresponds to epidemiological data on the causes of excess mortality in schizophrenic patients reviewed by Harris and Barraclough (1998)³⁹.

Therefore, if of consensus that the use of psychotropic drugs that treats depression may increase appetite with resultant weight gain^{37,40,43} and understanding that the overweight and obesity not only induce aesthetic problems affecting well-being, but profoundly increase morbidity and mortality³⁷. Clinicians and caregivers need to be aware of potential endocrine and metabolic adverse effects of psychiatric medications, performing statistically correlations with the cardiovascular risk and provide those healthy factors that can reduce it

The mortality rate for individuals who suffer from severe mental illness is on average at least 25 years earlier than

the general population^{44,45}. While suicide and injury account for 30% of excess mortality, the other 60% is caused by natural causes such as cardiovascular diseases, diabetes, respiratory diseases and infectious diseases^{46,47}.

In a study conducted in Maine in which the authors compared health problems between SMI and Non-SMI group's results concluded that twice as many people who suffer from SMI developed health problems in contrast to the Non-SMI groups. A total of 9224 SMI and 7352 non-SMI individuals were studied and compared and results indicated that 33.9% developed gastro intestinal problems versus 20% of the non-SMI group. 30% develop obesity/dyslipid versus 20% of the non-SMI group. 22.8% develop hypertension versus 18% of the Non-SMI, diabetes (16.5% vs. 10%), cancer (11.5% Vs. 10%), heart diseases (11.5% vs. 8%), and liver diseases (5.9% vs. 1%)⁴⁸.

Another authors completed a study on n=608 participants in the Ohio area and they found that the major factor for deaths for SMIs included diseases of the heart (n=126), diabetes mellitus (n=18), malignant cancers (n=44), pneumonia and influenza (n=16) and chronic respiratory diseases (n=31)⁴⁷.

According to Prior et al., (1996)⁴⁹ the longevity of SMI individuals is lower than their non-SMI counterparts and they are at a greater risk of dying from all causes.

In order to effectively treat people who are suffering from psychotic features prescribers utilize psychotropic such as: Haldol (haloperidol), Loxitane (Loxapine), Mellaril (Thioridazine), Anafranil (clomipramine), Asendin (amoxapine), Elavil (Amitriptyline), Luvox (fluvoxamine), Paxil, (Paroxetine), etc. Most of these psychotropic medications have a positive effect on the psychotic symptom but a negative effect on the health of the person's body organs⁴⁹.

Psychiatric patients have limited access to general healthcare, with less opportunity for cardiovascular risk screening and prevention, than would be expected in a non-psychiatric population. The European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC) published this statement aiming to improve the care of patients suffering from severe mental illness within the context of integrated health care. The intention is to initiate co-operation and shared care between the different health care professionals and to increase the awareness of psychiatrists caring for patients suffering from severe mental illness to screen and treat increased cardiovascular risk factors and diabetes⁶. Moreover, psychosocial factors could be important determinants of cardiovascular disease. Exposure to such factors may influence health directly through neuroendocrine mechanisms or indirectly, through their association with unhealthy behaviors. Anger, hostility, depression, anxiety and other personality factors have been related to an increased risk of cardiovascular disease⁵⁰.

Nutrition exerts a life-long impact on human health, and the interaction between nutrition and health has been known

for centuries. There is increasing evidence that consumption of soy protein in place of animal protein lowers blood cholesterol levels and may provide other cardiovascular benefits. Epidemiologists have long noted that Asian populations who consume soy foods as a dietary staple have a lower incidence of cardiovascular disease than those who consume a typical Western diet⁵¹.

The soybeans are very rich in nutritive components; have high protein content, lot of fiber and are rich in calcium, magnesium. They are also rich in unsaturated fatty acids and low in saturated fatty acids, which need to be avoided. The soy protein has a high biological value and contains all the essential amino acids. In addition, there is growing interest in the physiological functions of soy isoflavones, especially in whether they affect cognitive function and have beneficial effects on neurodegenerative diseases. There is evidence that estrogen might benefit memory and other cognitive abilities in younger postmenopausal the recent evidence from clinical and experimental studies supporting a role for soy isoflavones in cognitive function. Soy isoflavones may mimic the actions and functions of estrogens on brain, and they have been shown to have positive effects on the cognitive function in females; however, studies on their effects on spatial memory have not provided consistent results in males. Although data from humans, cultures, and animal models are currently insufficient for elucidating the metabolism of soy isoflavone actions on cognitive function and the nervous system, we suggest two putative pathways; (1) an estrogen receptor-mediated pathway and (2) via the inhibition of tyrosine kinase, in particular by genistein, which is one of the soy isoflavones. Although soy isoflavones appear to have a positive effect on brain function, further research is needed to determine not only the efficacy but also the safety of soy isoflavones on the nervous system and cognitive function⁵².

Given in that consensus that a healthy and equilibrated food intake could help to prevent diseases⁴, the effect of a treatment with a special diet and patients engagement on a healthy lifestyle habits must be studied, in order to control the prevalence of metabolic disorder and for hence the diseases risks.

In the last decade it has been focused the researching attention on the use of soybean and soy milk in the prevention of diseases. For example; Bricacello⁵³, have associated the soy milk diet with low-density lipoprotein cholesterol reduction (baseline = 157 ± 5 mg/dL; soy milk = 148 ± 4 mg/dL; non-fat cow milk = 158 ± 4 mg/dL; P < 0.05, soy milk versus other treatments) and with high-density lipoprotein cholesterol increase (baseline = 58 ± 2 mg/dL; soy milk = 62 ± 2 mg/dL; non-fat cow milk = 57 ± 2 mg/dL; P < 0.05, soy milk versus other treatments). In addition, the author pointed out that the plasma thiobarbituric reactive substances were reduced by the soy milk diet (baseline = 1.82 ± 0.12 nM/L; soy milk = 1.49 ± 0.09 nM/L; non-fat cow milk = 1.91 ± 0.11 nM/mL; P < 0.05, soy milk versus non-fat cow milk). Changes in lipid profile were not influenced by APOE genotypes. These results

indicate that soy milk as part of a lipid-lowering diet has beneficial effects in improving lipid profile and reducing lipid peroxidation.

A crossover study performed by Welty et al., 2007⁵⁴, on 60 women with hypertension (high blood pressure), pre-hypertension (moderate elevated blood pressure) and normotension (normal blood pressure) was carried out. This was a whereby all women followed both diets, a standard diet and a soy nuts diet containing half a cup of unsalted soy nuts, during 8 weeks. The total protein content of both groups was identical. This quantity of soy nuts contained 25 g soy protein and 101 mg of aglycones isoflavones. It was found that the intake of soy nuts resulted in a significant reduction of the systolic (peak pressure) and diastolic (lowest pressure) blood pressure in all three group of women. In hypertensive women the intake of soy nuts also reduced low-density lipoprotein cholesterol (= bad cholesterol) and apolipoprotein B (indicator for plaques formation and atherosclerosis) levels by 11% and 8% respectively. They concluded that the intake of soy nuts have a cardioprotective effect. Fradrad in 2009 et al., are also reporting similar data⁵⁵. A randomized crossover clinical trial (Azadbakht et al., 2007) was undertaken in 42 postmenopausal women with the metabolic syndrome. Participants were randomly assigned to consume a control diet (Dietary Approaches to Stop Hypertension, DASH), a soy-protein diet, or a soy-nut diet, each for 8 week. Red meat in the DASH period was replaced by soy-protein in the soy-protein period and by soy-nut in the soy-nut period. The authors pointed out that the soy-nut regimen decreased the homeostasis model of assessment-insulin, fasting plasma glucose, LDL cholesterol, serum C-peptide concentrations significantly compared with the soy-protein and control. Concluding that short-term soy-nut consumption improved glycemic control and lipid profiles in postmenopausal women with the metabolic syndrome⁵⁶.

In a study performed by Hermansen in 2005, 100 subjects (58 women and 42 men) were randomly assigned to 24 weeks of daily intake of either a soy supplement, Abalon® (30 g soy protein, 9 g cotyledon fibre and 100 mg isoflavones) or placebo (30 g of casein). In the study, no difference in fasting plasma lipid levels or insulin sensitivity was found between soy-based supplement and placebo. A significant postprandial increase in GIP to the meal test was observed in the soy group (P<0.05). In a sub study, no difference between the groups in changes in flow-mediated vasodilatation (P=0.84) was detected, while the soy supplementation caused a reduction in LDL and total cholesterol. No significant effects on blood lipids were observed in the main study to a soy supplementation in hypercholesterolaemic subjects after 24 weeks. In the sub study, the soy supplementation, however, reduced LDL and total cholesterol but did not influence markers of arterial function⁵⁷.

By all research summarized before, it could be postulated that parallel to the treatments with psychotropic in pa-

tients whom are suffering SMI, it must be recommended the inclusion of integrated health care and a special diet (including soy products) and patients engagement on healthy lifestyle habits.

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