Psychiatria Danubina, 2010; Vol. 22, No. 1, pp 75–78 *Conference paper*

BIPOLAR DISORDER AND METABOLIC SYNDROME: COMORBIDITY OR SIDE EFFECTS OF TREATMENT OF BIPOLAR DISORDER

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SUMMARY

Objective: *There is evidence that people with mental disorders are more likely to suffer from metabolic syndrome. In the last decades there has been an increase in interest for researching metabolic syndrome in psychiatric patients and plenty of evidence about their association. However, investigations on the prevalence of metabolic syndrome in patients with bipolar disorder are still surprisingly rare. The aim of this paper is to analyze comorbidity of bipolar disorder and metabolic syndrome, and the association of treatment with antipsychotics and mood stabilizers with metabolic syndrome, as well as to point out the necessity of appropriate preventive measures and treatment of metabolic syndrome in patient with bipolar disorder.*

Content analysis of literature: *Literature research included structured searches of Medline and other publications on the subject of comorbidity of bipolar disorder and metabolic syndrome, and the association of treatment with antipsychotics and mood stabilizers with metabolic syndrome, as well as preventive measures and treatment of metabolic syndrome in patient with bipolar disorder.*

Conclusion: *Metabolic syndrome is present in 8-56% of patients suffering from bipolar disorder. Metabolic syndrome in patients with bipolar disorder can significantly contribute to morbidity and mortality, and it is certainly necessary to think of it, to take adequate preventive and therapeutic measures in treating its individual components. Further investigation on association between bipolar disorder and metabolic disorder, and the association of treatment with antipsychotics and mood stabilizers with metabolic syndrome are necessary.*

Key words: *metabolic syndrome - bipolar disorders – prevalence-side effects- comorbidity*

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INTRODUCTION

In the last decades there has been an increase in the interest for studying the metabolic syndrome in psychiatric patients and plenty of evidence about the relationship exists. There are still many uncertainties, doubts, and controversies related to metabolic syndrome and bipolar disorder. Some researches have very critical opinions who are trying to challenge metabolic syndrome as an independent diagnostic entity (Bakker et al. 2007, Reaven, 2005). On the other hand, it is known that the timely detection of metabolic syndrome or its individual components can be of great clinical significance, especially in some patients with mental disorders including a bipolar disorder (Jakovljević 2007, Bakker et al. 2007). In many psychiatric patients the risk factors, which are an integral part of metabolic syndrome, are rarely controlled. They are often underestimated and insufficiently treated. There is evidence that people with mental disorders are more likely to suffer from metabolic syndrome. On the other side, people who are diagnosed with metabolic syndrome often suffer from mental disorders. However, research on the prevalence of metabolic syndrome in patients with bipolar disorder is still surprisingly rare.

The aim of this paper is to analyze comorbidity of bipolar disorder and metabolic syndrome, and the association of treatment with antipsychotics and mood stabilizers with metabolic syndrome, as well as to point out the necessity of appropriate preventive measures and treatment of metabolic syndrome in patient with bipolar disorder.

CONTENT ANALYSIS OF LITERATURE

Literature research included structured searches of Medline and other publications on the subject of comorbidity of bipolar disorder and metabolic syndrome, and the association of treatment with antipsychotics and mood stabilizers with metabolic syndrome, as well as preventive measures and treatment of metabolic syndrome in patient with bipolar disorder.

Bipolar disorder and metabolic syndrome

Research linking mental disorders and metabolic syndrome is in its early stages, especially when it comes to bipolar disorder. It is evident that it should be continued because present work in this field indicates the existence of a probable cause and effect relationship between these two types of a disorder (Jakovljević et al. 2006, Babić et al. 2007, Maslov et al. 2007, Martinac et al. 2007). In 2002, a group of authors from the University of Washington in Seattle (USA) published the results on research linking chronic stress, metabolic syndrome and coronary heart disease. Dr. Raikkonen and his colleagues investigated the two-way type relationship and concluded that people with metabolic syndrome often suffer from depression, uncontrolled anger, and tension. On the other hand, people with mental disorders in a form of depression, uncontrolled anger, and tension often end up with metabolic syndrome (Anderson et al. 2000, Deykin et al. 2001). Insight into the complexity of the issues on bipolar disorder and metabolic syndrome includes different factors through a variety of variables: constitutional factors, development conditions, premorbid state, and degree of maturity, emotional stability, intelligence and interaction in etiopathogenesis.

38% of people with metabolic syndrome are diagnosed with one or two psychiatric illnesses; most commonly depressive anxious states and bipolar affective disorder and other disorders. The number of obese people in the world and those with metabolic syndrome is increasing daily. The situation is declared as a global pandemic of the metabolic syndrome. In parallel with the increasing number of people with metabolic syndrome in the world, there is a growing number of the patients with metabolic syndrome complications making this the most important epidemiological problem in modern preventive and therapeutic medicine (Perlmutter et al. 2000). Trief et al. (2006) found the prevalence of metabolic syndrome to be 20-30% in the general population of middle and older age. Violani et al. (2006) and Babić et al. (2007) report a significant increase in the prevalence of metabolic syndrome in policemen and war veterans with symptoms of severe PTSD. Whether these disorders are part of the pathological processes of mental illnesses of increased stress and inflammatory process, genetic vulnerability or environmental factors or whether they are the effects of treating the disease, it is still not completely clear. Only recently, the research in the field of psychiatry has begun to observe these states in the context of metabolic syndrome. People with metabolic syndrome generally have increased mortality, particularly mortality from cardiovascular disease (Takeshita et al., Perlmutter et al. 2000, Anderson et al. 2000, Deykin et al. 2001).

In recent years there has been a growing interest in the research of somatic diseases and mental disorders relationship as well as the relationship between traumatic experiences and metabolic syndrome (Weisberg et al. 2002). Numerous studies have shown that traumatic stress can have a negative impact on somatic health (Goodwin et al. 2005) and some research suggests that people with chronic PTSD in comparison with the general population have increased cardiovascular disease and diabetes (Grundy et al. 2000, Weber-Hamann et al. 2002). Until now, available data have linked cognitive impairment, abdominal obesity, bone density reduction, type 2 diabetes, and hypertension in patients with depression and hypercortisolemia, and currently there is no clear evidence of a relationship between depression and hyperlipidemia (Schweiger et al. 2000, Eaton et al. 1996, Davidson et al. 2000, Karlović et al. 2004). Jakovljević et al. (2006) found that metabolic syndrome was present 31.9% in patients suffering from PTSD, while for patients suffering from PTSD of stronger intensity, metabolic syndrome was present 66.7%. Although the research between PTSD and metabolic syndrome relationship is still in its infancy, previous research supports the theory that PTSD is a multisystemic disorder that is only a developmental stage in the pathogenesis of many mental disorders (Jakovljević et al. 1998, 2006).

Research dealing with the relationship of metabolic syndrome and bipolar disorder is very rare. Literature research found that metabolic syndrome occurs in 8-56% of patients suffering from bipolar disorder. D Mello et al. (2007) reported an increased frequency of cardiovascular disease compared with the general population and diagnosed metabolic syndrome in 56% of those suffering from bipolar disorder. In a study from the United States, Fagiolini et al. (2005) diagnosed metabolic syndrome in 30% of the respondents in Spain Bobes (2007) 24.6%, and in Croatia Vuksan et al., 35.29% of those suffering from bipolar disorder. In comparison with bipolar disorder and other psychiatric disorders in relation to the presence of metabolic syndrome, literature research shows that metabolic syndrome was diagnosed as a significant percentage. Schizophrenia: 19% to 63% (Jakovljević et al. 2007), schizoaffective disorder: 42.4%, depressive disor-

der: 32-36%, and chronic PTSD: 31.9% to 35% (Jakovljević et al. 2006, Babić et al. 2007).

The obtained data on current research are insufficient and refer to the relatively small sample including some doubts and controversies. It is certain that the soul and the body are one unit and it is accurate only if they are observed in such way and that significant number of people suffering from bipolar disorder also has somatic disorders in the form of metabolic syndrome or its individual components. This combination further burdens health, reduces quality and shortens the length of life, and contributes to the increase in suicides. It is necessary to continue the research on the presence and the relationship of metabolic syndrome in patients with bipolar disorder and other psychiatric disorders. Only this approach can contribute towards the prevention of long-term somatic illnesses, successful treatment, increased quality of life and prolong the life of patients with bipolar disorder.

A number of investigations focused on association of treatment with mood stabilizers or/and antipsychotics and metabolic syndrome in patients with bipolar disorder. The question is in what extent is metabolic syndrome a result of side effects of medications applied in the treatment of bipolar disorder. The results of a cross-sectional study that included patients with diagnose of bipolar disorder and treated with lithium, valproate or both showed that 13.7%, 36.8%, 53.0%, 18.6%, and 61.0% of the patients met the criteria for hyperglycemia, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), hypertension and large waist circumference, respectively. 33.9% of the patients met the IDF 2005 criterion for metabolic syndrome. The prevalence of metabolic abnormalities was significantly higher in patients who have been cotreated with second-generation antipsychotics (Chang et al. 2009). The results of an earlier analysis of previously published articles focusing on the prevalence of overweight and obesity in bipolar disorder, the risk and magnitude of weight gain associated with medications used to treat bipolar disorder, and the prevention and treatment of overweight and obesity in patients with bipolar disorder showed that comorbid binge-eating disorder, the number of depressive episodes, treatment with medications associated with weight gain, alone or in combination, excessive carbohydrate consumption and low rates of exercise appeared to be risk factors for weight gain and obesity in patients with bipolar disorder (Keck & McElroy 2003). The results of an investigation that aimed to review the association of most commonly used psychopharmacological drugs with weight gain in bipolar disorder showed that obesity and overweight in bipolar disorder are partly related to prescribed drugs with a strong effect of clozapine and olanzapine. Lesser but still relevant weight gain is caused by quetiapine, risperidone, lithium, valproate, gabapentin and by some antidepressants. According to results, ziprasidone, aripiprazole, carbamazepine and lamotrigine do not seem to cause significant overweight. The authors concluded that careful monitoring of weight changes in patients before and after drug prescription should be implemented in the clinical routine and drugs which potentially cause weight gain should be avoided in overweight patients with bipolar disorder (Torrent et al. 2008). Many studies report the combination of mood-stabilizing agents with conventional antipsychotics and atypical antipsychotics. Combination therapies produce a number of adverse side effects. Atypical antipsychotics (other than clozapine) are now rated as first-line agents for adjunctive treatment of mania because they produce less adverse side effects (Vacheron-Trystram et al. 2004).

CONCLUSION

Metabolic syndrome is present in 8-56% of patients suffering from bipolar disorder. There is a significantly greater percentage of presence of its individual components. Metabolic syndrome in patients with bipolar disorder can significantly contribute to morbidity and mortality, and it is certainly necessary to think of it, to take adequate preventive and therapeutic measures in treating its individual components. Further investigation on association between bipolar disorder and metabolic disorder, and the association of treatment with antipsychotics and mood stabilizers with metabolic syndrome are necessary.

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