Universitatea *Transilvania* din Braşov

HABILITATION THESIS

SUMMARY

Antipsychotics in clinical practice: receptorial properties that set differences

Domain: Medicine

Author: prof. dr. Victoria BURTEA

„Transilvania" University of Braşov

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After obtaining my medical degree at the Carol Davila University of Medicine and Pharmacy in Bucharest, in 1976, I trained in general medicine until 1979. I began my career in psychiatry at Gheorghe Obregia Hospital in Bucharest, as resident in 1979, and after that at the Psychiatry and Neurology Hospital in Brasov, specializing in the clinical field of emergency psychiatry. I became senior psychiatrist from 1991 and I worked extensively in the field of acute psychosis and affective disorder.

My clinical responsibilities grew in 1994 then I became Head of the Clinical Psychiatric Department in the same hospital, with 65 beds for acute psychiatric patients. Between 2003-2008 I was Coordinator of the Mental Health Funds in the National Psychiatric Programs 2.5 and 2.1.

My doctorate thesis was focused on the nosografic status of schizoaffective disorder (Carol Davila University of Medicine and Pharmacy in Bucharest, 1998).

Since 1998 I have been Assistant Proffesor of the Psychiatric Department at the Faculty of Medicine of Transilvania University, in Brasov, and since 2014 I am currently Proffesor in the same University.

I started my research activity as a member of The Danubian Psychiatric Association in 1996, when we initiated joint research including census studies. Two census studies were performed, one in 1996 and one in 1999 in five European countries (Austria, Hungary, Romania, Slovakia, Slovenia), concerning legal status of inpatients, type of ward (open or locked), length of stay till census day, employment, numbers of doctors and nurses. The results were published in European Psychiatry. This was for the first time ever that psychiatric inpatient treatment centers in five different countries provided data on all inpatients on a fixed day, on two occasions three years apart, using the same method.

As a validation of my work I was between the first psychiatrists selected in Romania as principal investigator in several multicenter clinical trials (phase IIa, IIb, III and IV).

An important treatment goal in recently exacerbated patients with schizophrenia is the rapid symptom control and discharge from the hospital.

One of the most important clinical trials where I participated (RIS-SCP-402) had as principal objective the comparison of the efficacy of two most widely used atypical antipsychotics (Risperidone and Quetiapine) in patients with schizophrenia experiencing a recent exacerbation of symptoms. The results of the study suggested that treatement with Risperidone was associated with a consistently greater clinical response than treatment with Quetiapine across all measures (including less need for added psychotropic medications and faster readiness for discharge), according with their pharmacological profile and D2 receptor antagonism. Janssen LLC expressed their appreciation for my participation in RIS-SCP-402 study and named me as coauthor of the article published in Schizophrenia Research.

The conflicting views about the second and the first generation of antipsychotic prompted members of the European Group of Research in Schizophrenia to design a pragmatic

randomised controlled clinical trial. This study was called EUFEST and its aim was to compare treatment with atypical antipsychotics (Amisulpride, Quetiapine, Olanzapine and Zyprasidone) to low dose of Haloperidol in first episode schizophrenia patients with minimal prior exposure to antipsychotics.

The results were finalized by publishing two referential articles in Schizophrenia Research and Lancet, where I was mentioned as contributor.

The assessment of a new chemical entity (BL-1020) developed by BIOLINE RX – Israel in two phase IIa and IIb studies, allowed me to participate with Transilvania University as manager of the project.

The control of belligerent, agitated schizophrenic patients is very important in short term treatment. In order to reduce physical restraints and increase the patient security and confort, we developed and evaluated the effectivenes and safety of a new method: rapid Clozapine titration in schizophrenia. Our naturalistic cohort study about rapid Clozapine titration appeared safe and effective for the treatment of schizophrenia, suggesting that the traditional slow dosing regimen may be abandoned in patients where rapid symptom control is warranted. The results were published in Acta Psychiatrica Scandinavica.

Knowing the mood-stabilizing properties of Clozapine and its use to reduce symptom severity in patients with manic epsiode, concomitant with our finding in schizophrenia patients, we hypothesized that the methods of rapid titration of Clozapine are equally effective and safe in the patients with bipolar disorder. Our research, which was a retrospective study, pseudorandomized, from Januray 1, 2005 through December 31, 2013, is the first demonstration of the safety and effectivenes of rapid Clozapine titration in treatment-refractary bipolar disorder. The results were published in Journal of Affective Disorder.

Sudden unexpected death in psychiatric inpatients with schizophrenia was analyzed in a consecutive cohort of patients treated for schizophrenia from January 1, 1989 through December 31, 2013, in Brasov. The autopsy findings support the hypothesis that the causes of sudden death in schizophrenia are not different than the community population: coronary artery disease that has produced a myocardial infarction. This was the first study in which all sudden deaths in patients with schizophrenia have been witnessed and an autopsy was carried out without delay in a near-totality (89.5%) of cases. The results were published in Schizophrenia Research.

The Projects for the near future perspective include metabolic syndrome prevalence, concomitent with the number and prevalence of individual criteria of metabolic syndrome in patients with schizophrenia versus patients with bipolar disorder and normal control. Metabolic syndrome is a common finding in both psychiatric conditions. However, because most patients (both conditions) are drug-treated, it is difficult to separe abnormalities associated with the disease from those that may be drug-induced. This will be for the first time in Romania when significant cohort of schizophrenic patients will be compared with bipolar ones and control group.

There is currently a need for data in Romania on metabolic syndrome prevalence from a large sample of patients with schizophrenaia and bipolar disorder to accurately assess the prevalence of this phenomenon cross-sectionally, and examine the features of metabolic syndrome in those patient cohorts, especially when compared with the general population. Specifically, I intend to test the hypothesis that metabolic syndrome is more prevalent among patients with schizophrenia and bipolar disorder than dermographically matched counterparts in general population, with no significant differences between the two diseases.

I am also interested in studying a new psychiatric condition: gaming disorder / internet gaming disorder – that has significant public health importance. Adolescent males seem to be at greater risk of developing this condition. The literature suffers from lack of a standard definition from which to derive prevalence data, lack of associated diagnoses or natural histories of cases. Gaming disorder can be mild, moderate or severe depending on the degree of impact which it has on normal activity.