UNIVERSITY OF MECINE AND PHARMACY

OF CRAIOVA

DOCTORAL SCHOOL

CLINICAL AND EVOLUTIONARY PECULARITIES OF DEPRESSIVE DISORDER IN PSYCHIATRIC OUTPATIENTS

DOCTORAL THESIS

-ABSTRACT-

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GENERAL CONSIDERATIONS

CHAPTER I

1.1 INTRODUCTION. IMPORTANCE.

Currently, depression has become more than a psychiatric diagnosis due to its high frequency and important individual, family and social consequences, representing a challenge for public health policies. The effects of depressive disorder are determined not only by the symptoms of the disease per se, but also its frequent association with other medical or psychiatric conditions, both acute and chronic. This leads to complications in its evolution and management, as well as a significant increase in the burden of disease experienced by people with this diagnosis and their families or carers.

In this regard, the World Health Organization forecasts on trends in this matter are even more worrying: it is estimated that by 2030 depression will become the leading cause of disability worldwide.

In this context, this study attempts to evaluate and highlight the clinical, evolutionary and therapeutic peculiarities of depressive disorder in psychiatric outpatients, in direct correlation with their socio-demographic characteristics.

CHAPTER II

2.1 DEPRESSIVE DISORDER. EPIDEMIOLOGY.

New research conducted according to the DSM-IV and DSM IV TR criteria revealed prevalence rates throughout life ranging from 2.9% in Korea, 5.2% (Epidemiological Catchment Area - ECA), 9.2% in Germany, 12.4% in Italy, to 19% in Lebanon. Other epidemiological studies based on the ICD-10 and Clinical Interview Schedule (CIS-R) reveled 1 year prevalence rates for depression of 5.1% in Australia and 9.3% in Finland, as well as 1 week prevalence rates between 2.3% and 2.6% in the UK.

2.2 DEPRESSIVE DISORDER. ETIOPATHOGENESIS.

2.2.1 Genetic vulnerability

Gentic predisposition is currently recognized as being involved in approximately 40% of cases with affective disorders. One of the most important predictors is represented by a positive family history for depression.

2.2.2 Neuroanatomical vulnerability

The supporting evidence for the involvement of neuroanatomical vulnerability in the etiopathogenesis of depressive disorder is represented by the role played in major depressive disorder by brain areas that control the mood (the prefrontal cortex, cingulate cortex, thalamus, amygdala, hippocampus, ventral striatum, temporal and parietal cortex), and the anatomical connections between these areas which modulate emotions (frontostriatal and cortical-thalamic-pallido-striatal-limbic circuits), the central position being occupied by the amygdala which controls the the mood and modulates the activity of these circuits.

2.2.3 Neurobiochemical vulnerability

Monoamine hypothesis in depressive disorder postulates the existance of a functional cerebral deficiency of serotonine and/or noradrenaline and, in the same time, constituted the theoretical foundation for the development of selective inhibitors for the release of these neurotrnsmitters as antidepressants. Positive therapeutic results obtined with these antidepressants confirmed the validity of this hypothesis.

2.2.4 Neuroendocrine vulnerability

The role played by the neuroendocrine system through the hyperactivity of the hypothalamic–pituitary–adrenal axis in the etiopathogenesis of depressive disorder was indicated more than half a century ago by high levels of plasma corticosteroids during the episodes as a response to psychic stress, and by dexamethasone suppression tests.

2.2.5 Psychosocial vulnerability

Psychosocial vulnerability for the emergence and development of depressive disorder is based on several models generated by different psychological and psychoanalysis schools.

CHAPTER III

3.1 DEPRESSIVE DISORDER. SYMPTOMS. DIAGNOSIS. THERAPY.

3.1.1 Symptoms

The psychological picture of depression, dominated by feelings of sadness, despair, loneliness, self-reproach and self-punishment, decreased self-esteem, may be completed by inhibition or psychomotor agitation, vegetative symptoms such as insomnia and anorexia, and social isolation.

3.1.2 Diagnosis

Currently, the diagnosis of psychiatric disorders is carried out on the basis of valid statistical diagnostic manuals, ICD-10 (1992), the DSM-IV-TR (1994) and DSM-5, which include both specific criteria for all mental health disorders (all three manuals listed), and a multiaxial diagnostic and registration system (DSM IV TR).

3.1.3 Therapy for depressive disorder

3.1.3.1 Pharmacological therapy

It is based on treatment guidelines validated on the basis of evidence provided by research which propose a number of psychopharmacologic opportunities considering the whole spectrum of elements characteristic for the disorder, but also the needs of the patient.

3.1.3.2 Other therpeutic means

The therapeutic arsenal also includes a series of antidepressant and non-pharmacological means used both as adjuvants, as well as independently or as supportive therapeutic methods for psychotropic substances.

CHAPTER IV

4.1 DEPRESSIVE DISORDER AND SOMATIC COMORBIDITIES

The evolution, clinical behavior and prognosis of depressive disorder are largely influenced by somatic comorbidities present in 10-40% of individuals diagnosed with depression. These comoridities complicate the mental illness, produce significant interferences and alter the quality of the therapeutic response.

PERSONAL CONTRIBUTION

CHAPTER V

5.1 HYPOTHESIS. OBJECTIVES. MATERIALS AND METHODS.

5.1.1 Hypothesis. Aim

The description of the clinical and therapeutic peculiarities of depression in outpatients during monitoring and treatment, demonstration of possible clinical and evolutionary correlations as well as socio-demographic elements which may influence the onset, evolution, and the results of treatment, may all constitute factors contributing to the improvement of the therapeutic management strategies for inpatients, outpatiens, but also for general practitioners who play an important long-term role in the monitoring of individuals affected by the disease. Thus, a number of premises can be generated which would provide the basis for therapeutic strategies in the long run, but also primary and secondary psiychoprophylaxis, through demonstration of predictive factors. The present study aims at evaluating the therapeutic, clinical, and socio-demographic factors involved in the evolution of depression in psychiatric outpatients, as well as the demonstration of the importance of quality therapeutic intervention on the evolution and prognosis of the disease.

5.1.2 Objectives

• Evaluation of clinical and socio-demografic characteristics of psychiatric outpatients monitored for depressive disorder.

• Study of the effectiveness of psychopharmacologic strategies in depressive disorder.

• Demonstration of relations between socio-demographic characteristics, somatic comorbidities, and risk factors in the development of depressive disorder.

5.1.3 Methodological coordinates

A retrospective clinical study of patients monitored for diagnosis of depressive disorder in the Mental Health Centre in Craiova, Bunavestire Outpatients Clinic, and the praxis of Dr. Bogdan Stania Dr. Bogdan Stănia, between January 1, 2013 and June 30, 2015. Based on the

inclusion and exclusion criteria referred to above, N = 338 patients with diagnosis of depressive disorder were included in the study.

Psychometric instruments

•The Hamilton Depression Rating Scale (HAMD17).

• Global Assesment of Functioning scale – GAF.

Statistical analysis

For the statistical analysis of the data we used the Microsoft Excel software, along with the XLSTAT 2014 add-on, and IBM SPSS Statistics 20.0. The information obtained had been registered in Microsoft Excel files, then being processed statistically to highlight correlations between clinical and paraclinical data.

CHAPTER VI

6.1 RESULTS

6.1.1 Socio-demographic characteristics of the patients (N = 338)

The descriptive analysis of the study batch (N = 338) was performed based on data collected according to the indicators referred to in the research methodology, data which intended to show the full picture for the studied outpatient population with a diagnosis of depressive disorder.

6.1.2 Clinical characteristics of the patients (N = 338)

The population (N = 338) was analysed based on the clinical indicators mentioned to the methodology, data obtained completing the general picture of the patients included in the study.

6.1.3 Somatic comorbidities

In the case of outpatients with depressive disorder the presence of one or more somatic comorbidități, and the nature and degree of severity of them constitutes a challenge for both the psychiatrist and general practitioner or other specialists that have treated these patients, a translational therapeutic process, based on an excellent multidisciplinary communication leading to an efficient solution for this complex disease is required.

6.1.4 Psychopharnacologic treatment

Antidepressants were administered to 273 patients (80.77%), with a higher proportion in women (82.11%) then in men (77.17%).

CHAPTER VII

7.1 DISCUSSION

7.1.1 Socio-demographic indicators

Analysis of the results obtained on the basis of socio-demographic indicators demonstrate the importance of these elements in establishing the vulnerability profile of the population affected, both in terms of conditions that favour the onset of depressive disorder, and future evolution. They influence the efficiency of the therapeutic management, the evolution and severity of somatic comorbidities and also a possible prevention program.

7.1.2 Clinical indicators

One of the most important indicators of prognosis and evolution in depressive disorder is suicidal behavior (9.76 in our population).

7.1.3 Somatic comorbidities

Results of epidemiological studies have demonstrated that cardiovascular disease ranks first in terms of prevalence in association with depressive disorder, with estimated values of over 25%, the data obtained for our study group (N = 338) being close to the upper limit of these estimates, 31.95% percent of subjects having an associated cardio-vascular disease diagnosis.

CHAPTER VIII

8.1 CONCLUSIONS

1. Between January 1, 2013 and June 30, 2015, at the Craiova Mental Health Centre, Bunavestire Outpatients Clinic and the praxis of Dr. Bogdan Stania, a total of 338 individuals with the diagnosis of depressive disorder were monitored and met the inclusion criteria.

2. In the study group the prevalence in women was far superior to that in the general population (72.78%, $p < 0.0001$), representing a first risk factor for the onset and evolution of depression, according to data from international epidemiological studies.

3. Other socio-demographic risk factors for depressive disorder in psychiatric outpatients were: age groups 50-54 years (52.45 + 3.17 years) in females, respectively 55-59 years of age (54.75 + 3.77 years) in males ($p < 0.001$); urban residence (92.31%, $p < 0.0001$); the average educational level (profesional studies in men – 34.78%, and high school in women – 43.50%, $p < 0.05$), cessation of professional activity (89.94%, $p < 0.05$); divorce or widowhood in women ($p < 0,05$).

4. Increased severity of depressive symptomatology was influenced by rural area of residence ($p < 0,05$), inactivity ($p < 0.05$), alcohol consumption ($p < 0.05$) and smoking ($p < 0,05$), mostly in men ($p < 0,01$).

5. The severity of depressive symptoms was correlated with clinical indicators as well as the large number of admissions (more than 5) ($p < 0,05$), and the presence of suicidal thoughts and behaviour ($p < 0.01$), while an insidious onset of the disease was significantly more frequent in men from (78.26%, $p < 0.05$).

6. The most common somatic comorbidities were osteoarticular disorders (32.54%), cardiovascular diseases (31.95%), surgical interventions (23.96%), diabetes (18.64%) and diseases of the liver (16.86%); endocrine disorders (13.91%) were significantly more frequent in women with depression (16.26%, $p < 0.05$).

7. The evolution of depressive disorder was significantly influenced by the presence of cardio-vascular comorbidities ($p < 0,05$), diabetes ($p < 0.05$), disorders of the gastro-intestinal tract ($p < 0.05$), and the increased number of comorbidities in the same individual ($p < 0,05$).

8. The association of two or more somatic comorbidities lead to a poor outcome, characterized by a high number of episodes which resulted in hospitalization ($p < 0,05$).

9. The statistical analysis of therapeutic options used showed that antidepressant substances (80.77%) positively influenced the evolution ($p < 0.01$), as well as adjuvant treatments with antipsychotic substances (43.79%, $p < 0.01$), benzodiazepines (37.28%, $p < 0.01$) and thymostabilisers (18.05%, $p < 0.05$).

10. The use of different classes of antidepressant drugs was not significantly influenced by gender, but was directly correlated ($p < 0.05$) with the number of somatic comorbidities; SNRIs (42.01%, $p < 0.05$) and serotonin modulators (10.06%, $p < 0.01$) led to a significant reduction of symptom severity during monitoring.

11. Adjuvant treatment with antipsychotic substances has led to significant results for both neuroleptics (8.28%, $p < 0.01$) and atypical antipsychotics of the second generation (36.98%, $p < 0.01$), their administration being also influenced bythe number of associated comorbidities ($p < 0,05$).

12. The clinical and therapeutic peculiarities of depressive disorder in psychiatric outpatients revealed in our study are as follows:

☐ prevalence of single women from urban areas, medium education and aged between 50 and 54;

☐ increased number of recurrences and the presence of autolytic ideation;

☐ increased frequency of somatic comorbidities with direct influence on the therapeutic process;

☐ administration of novel antidepressants;

☐ augmentation of antidepressant therapy with antipsychotics, thymostabilisers and benzodiazepines;

☐ In this context, in order to achieve a favorable evolution, strict multidisciplinary monitoring is required.

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