

**UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA
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**CLINICAL AND EVOLUTIVE RISK FACTORS IN
DEPRESSIVE DISORDER**

ABSTRACT

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Keywords: therapeutical association, psychiatric comorbidities, side effects, differentiated therapy

INTRODUCTION

Depression, one of the most common mental disorders, has always been a subject of debate for psychiatrists. Nowadays depressive disorder is a public health problem because of the high prevalence, the high degree of recurrence and chronicity, disability involved, and socio-economic costs. Depression substantially alter the lifestyle of the individual, reduce quality of life and, as a result of suicidal risk involved, is associated with increased mortality. Depression is a condition that can take a dramatic turn, with serious psycho-outputs, personality impairment and chronic evolution and may manifest as chronic or temporary disturbance in adapting to everyday life.

It is estimated that at least 10% of subjects presenting to the general practitioner are depressed [1]. In this regard, it is useful to distinguish between the usual sense of depression (sadness or negative emotion) and psychopathology, where suffering is itself abnormal, perverted, distorted, with the subject becoming "subject to its own suffering" [2].

Depressive syndrome is the chapter of psychopathology which was marked by a significant progress in the last decades, especially in deciphering the etiopathogenic mechanisms which generated the appearance and proliferation of antidepressants. However, the overall management of individuals with depression is often far from ideal. Even in modern times, stigma and discrimination cause reticence to potential depressive patients to visit the specialist for diagnosis and treatment [3].

Major sociocultural changes of the contemporary world have determined the subject of depression to transgress boundaries of psychopathology, to be discussed in various scientific and cultural situations, often beyond the medical field. Specialists' efforts to identify the optimal solutions in the diagnosis and management of the most common pathological situations in daily activities [4]. Clinical and epidemiological analyses unanimously recognize that in the field of major mental disorders, depression is at least 10 times more common than schizophrenia [5]. The discrepancy between the evolution of epidemiological data for schizophrenia and depression could be related to biological and social differentiated vulnerability [6].

Biological Psychiatry tries to produce objective data on neurobiochemical or cerebral indicators that could confirm the diagnosis of depressive disorder based on biological evidence.

METHODS

Hypothesis: Study of depressive disorder is motivated by a multidisciplinary interest aroused by this illness, following the correlation of a number of individual variables. We have proposed the establishment of multidimensional criteria, which could contribute to better predictability of depressive disorder evolution in the medium and long term. Choice of the

population for study is an important subject by its representativeness. Clinical criteria for inclusion and exclusion groups met the terms of the psychopathological study.

Objectives

1. Highlighting of clinical and evolutive peculiarities of depressive disorder in patients hospitalized in the Department of Psychiatry from Emergency Military Hospital Focsani and quality assessment of response to antidepressant medication.
2. Identification of risk factors for unfavorable outcome of the therapy of inpatients, and under medium and long term for outpatients from ambulatory.

Study groups

N group - Based on the inclusion and exclusion criteria was constituted a lot of patients, N=333, diagnosed with major depressive disorder or recurrent depressive disorder, admitted to the Military Emergency Military Hospital Focsani within 5 years (January 1, 2007 - December 31st 2011), performed the initial assessment at first hospitalization recorded in the studied period.

N1 group - N1 group of patients was selected from the initial patients of group N which, after discharge, were actively monitored by ambulatory clinic of MND Focsani until 30 June 2013. The clinical retrospective-prospective catamnestic assessment was performed, between 1 July 2012 and 30 June 2013. A number of 282 patients were found active and for 3 patients death based on medical records was confirmed. The remaining 48 patients were not submitted to the evaluation and treatment during this period.

Data sources: observation sheets of patients admitted to psychiatric ward, psychological examinations and laboratory results for N; existing medical documentation in the ambulatory clinic of MND Focsani (sheets and dispensary books) for N1.

Items registered

Demographic items: age, area of residence, educational level, employment status, marital status, socio-economic status;

Clinical items: presence / absence of psychotrauma in childhood (3-12 years), family history, previous somatic comorbidity, diagnosis, premorbid personality type, nature of onset, onset precipitating conditions, onset symptomatology, range between real and apparently onset, number of hospitalizations for depressive disorder;

Treatment, therapeutic response and evolution of depressive disorder items: antidepressant class used during hospitalization, medication associated, therapeutic compliance, quality of response after first hospitalization, side effects of treatment, psychiatric comorbidity, adherence to maintenance treatment, psychiatric and somatic comorbidities occurred after the first evaluation.

Working tools: Hamilton Depression Rating Scale (HAM-D17), Global Assessment of Functioning Scale (GAFS).

Statistical tools

Data processing was performed with Microsoft Excel with XLSTAT suite for MS Excel and secondary processing data was performed using Pivot Tables, Statistical Functions, Chart and Analysis of Data commands of Excel. Complex statistical tests (Chi square, Fisher exact, Student and ANOVA) were performed by XLSTAT module commands or using SPSS.

RESULTS

Between 2007-2011, the Emergency Military Hospital Focsani hospitalized 3107 patients with a diagnosis of depressive disorder, representing 48.73% of all cases, representing FOR both genders, the most common diagnosis.

The predominance of women (61.86%) was notable for N=333, well above their weight in the general population and the highest rate in the age group 50-59 years, with a slight superiority of women in the second and third decade. Urban patients are also prevalent (61.56%), men outnumber women (72.44%), vocational school graduates (51.95%), pensioners (48.95%), married people (81.68%), with average income (51.4%).

Psychotrauma factors have been highlighted since the onset (12.31%), and family history risk factors (depressive disorder, bipolar disorder) were present in 32.1% of subjects. Somatic comorbidity (31.53%) were represented by cardiovascular disease (14.71%), chronic hepatitis (2.40%), digestive disorders (14.41%) and the psychiatric comorbidities (personality disorders and anxiety) were present in 74.86%.

In the N group, the major depressive disorder single episode (55.4%) was predominant more frequently in men with an insidious onset type (89.2%) precipitated by psychotrauma (48.5%), manifested by pure depressive symptoms (33.6%), with at least one relapse during the study (83.8%). Antidepressant therapy was performed with tri- and tetracyclic antidepressants (16.22%), SSRIs being the most used medication, and the most frequent drug combination was with the benzodiazepine (51.05%) and mood stabilizers (32.43 %).

In the N1group was noticed the predominance of women (57.80%), age groups 40-49 and 50-59 years (79.79%), urban residence (65.25%), average educational level (77 66%), employed (45.39%), and married (84.40%). Outpatients treatment consisted of 35.46% SSRIs, followed at considerable distance, by the NSRI, tianeptine, TCA, NaSSA, and NDRI. At the end of the study SSRIs were found on the first place (36.52%). Initial adjuvant treatment of outpatients consisted on benzodiazepines (51.42%) and mood stabilizers (32.27%). Psychiatric comorbidities identified were

personality disorders (37.23%) and anxiety (28.01%), and somatic were digestive (14.89%) and cardiovascular disorders (12.41%).

The global evolution for the N1 group was assessed in accordance with following criteria: clinical improvement, quantified by psychiatric examination and HAM-D scores, functional improvement, as judged by GAF scores using both the patient's story and that of his entourage, therapeutic compliance : respect for the periodicity of visits, absence of side effects, patient satisfaction to treatment; absence of somatic and psychiatric comorbidities during ambulatory monitoring; assessing and monitoring the risk of relapse and suicide. According to these criteria, N1 had a favorable outcome rate of 78.4%.

DISCUSSIONS

There were significant differences between gender distribution of N and the general population ($p < 0.001$), age distribution ($p < 0.05$) and area of residence ($p < 0.05$), percentage of patients in urban area being significantly higher than their share in the general population. The difference in distribution by residence of the N1 group and the general population is also highly significant statistically ($p < 0.001$). For N were found highly significant differences of distribution between the two genders in terms of education ($p < 0.001$), difference which is maintained in the N1 ($p < 0.001$). Regarding the marital status of patients, in N we found a highly significant difference between men and women, the latter being mostly divorced or widowed, while men were more often married ($p < 0.001$), a difference also found in N1 ($p < 0.05$).

For the N group, differences were found between main psychiatric treatments recommended and gender of patients, which are highly significant statistically ($p < 0.001$), similar to N1, both in the treatment at baseline ($p < 0.001$), and maintenance therapy ($p < 0.001$). In both study groups we found a significant difference between the genders regarding adjuvant therapy associated ($p < 0.05$), with high statistically significant differences ($p \sim 0$) between adjuvant treatment prescribed at baseline and at the end of the study.

Some highly significant differences in the association of other psychiatric illnesses were observed in the group N ($p < 0.001$), men suffering mainly from personality disorder, while women were more often associated with depression with anxiety disorders; the situation is similar both in terms of statistical signifier and the specific nosological psychiatric comorbidities in N1 group ($p < 0.001$).

In the group N, HAMD score in women (17.44 ± 2.55) is significantly higher than in males (16.03 ± 2.37) ($p < 0.001$) and for N1 group differences between mean values of HAMD score at the baseline and at the end of the study are highly statistically significant ($p \sim 0$) confirming the remittent development of depressive disorder properly monitored. Final average scores reflect a marked

improvement, which is below the lower limit of mild depression without declines within the domain of complete remission (<7).

CONCLUSIONS

1. Depressive disorder is on the first place of hospitalizations from EMH Focsani, representing 48.73% of all cases. However, due to the stringency of the selection criteria, only 10.72% of the subjects were eligible for our study.
2. Females predominated both in group NI (61.86%) and in group N1 (57.80%), much higher than in the general population ($p<0.001$), representing a risk factor for development of depressive disorder, and in accordance with the specialized literature data.
3. Other demographic factors identified risk for depressive disorder in both groups were: age groups over 40 years – 82,28% in group N and 80.85% in group N1 ($p<0.05$), urban residence (N - 61.56%, respectively N1 - 65.25%) ($p<0.001$) average educational level (N - 75.67%, respectively N1 - 77.66%) ($p<0.001$) unemployed persons, in particular pensioners (48.95% in group N and 44.68% in group N1), medium income (95.6%).
4. major depressive disorder single episode ranks first in frequency in group N - 55.4% at the expense of recurrent disorder, with insidious onset (89.2%), mainly precipitated by psychotrauma (48.5%).
5. Most common psychiatric comorbidities were represented by anxiety disorder more common in women - 28.3% in group N and 28.01% in group N1 ($p<0.001$) and personality disorders in men - 36.64%, respectively 37.23%, ($p<0.001$).
6. Comorbid somatic disorders identified in group N had a share of 31.53% of the cases, the main diagnoses were cardiovascular disease (chronic ischemic heart disease, hypertension, circulatory failure vertebral basilar, angina) (14.71%) and digestive disorders (ulcer, gastritis, esophagitis) (14.41%). Although statistical analysis revealed no significance for the evolution of depressive disorder, in group N1 somatic comorbidities share decreased from baseline, being present in 29.43% of patients (gastrointestinal disorders - 14.89%, cardiovascular diseases - 12.41%).
7. In group N, 72.8% of inpatients became inpatients within a year of the depressive symptoms, representing a risk factor for poor prognosis correlated with demographic risk factors. ($p<0.001$)
8. Statistical analysis of therapeutic approach revealed that in the two study groups, the new antidepressants were imposed as the first therapeutic option (83.78% in N group and 92.20% in N1 group); were identified highly significant differences ($p<0.001$) in the management

differentiated by gender: SSRIs and tianeptine are prescribed mainly in women, while men have been prescribed predominantly NDRI and SNRI.

9. Differences between the treatment used in N and N1 groups were not statistically significant, arguing good compliance and adherence to medication and lack of side effects and somatic comorbidities during monitoring evolution that required therapeutic switch.
10. Associated treatments were identified at baseline in 90.69% of cases (benzodiazepines - 51.05%, mood stabilizers - 32.43%, antipsychotics - 7.21%), while in N1 group they diminished, being identified only in 55.32% of the patients ($p \sim 0$); the classes of drugs used are identical, with a weight similar to benzodiazepines (51.42%) and mood stabilizers (32.27%) and an important reduction in the use of antipsychotics (0.71%). Statistically significant differences were found by gender and type of adjuvant therapy associated ($p < 0.05$), especially in the case of antipsychotics (7.28% in women, 3.94% in men); for N1 group the ratio between the two genders and antipsychotics used was maintained (1.23% in women, 0.00% in men) ($p < 0.05$).
11. HAM-D initial assessment for N group revealed that a highly statistically significant difference of score in women than men ($p < 0.001$), difference that remained significant at the final assessment ($p < 0.05$), confirming the woman's vulnerability for depression and intense symptoms.
12. Remission assessed by the Hamilton scale (average score 7.72 ± 2.08) showed an improvement of symptoms in N1 group, which is below the lower limit of mild depression without falls within the domain of complete remission (< 7) ($p < 0.05$) confirmed by the GAF S scores on overall functionality.
13. Global evolution of depressive disorder as evidenced by clinical assessments established in methodology was favorable in 78.4% of N1 group.
14. The factors of favorable evolution of depressive disorder highlighted by our study are:
 - Use of only novel type antidepressant and avoiding the use of tri- or tetracyclic antidepressants ($p < 0.001$);
 - Therapeutic approach differentiated by gender ($p < 0.001$);
 - Use of antipsychotics only under strict instructions, mainly during hospitalization ($p < 0.05$);
 - Close monitoring, adherence and compliance to treatment;
 - Absence of side effects induced by medication and somatic comorbidities under maintenance therapy for at least 24 months.

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