CONTRIBUTIONS TO THE STUDY OF THERAPEUTIC ADEQUACY IN DEPRESSIVE DISORDER

ABSTRACT

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INTRODUCTION

Although it has been described as a distinct clinical entity more than 2000 years before, depression remains one of the great challenges for the modern medicine. Its etiopathogeny, clinical manifestations, treatment outcome and social effects have such variability that the recognition and treatment of this disorder demand both the science and art of the clinician.

Despite the knowledge brought by the scientific research during the last 3 decades concerning the neurobiological origin of depression, thus clarifying many unknown mechanisms, we have to acknowledge the fact that depression remains each time a step forward. No matter what progress has been made in the therapeutic area or in the improvement of social programs, this disorder managed to reach the second place regarding prevalence, before the cardio-vascular or neurological diseases. The World Health Organization estimates that one person out of three will suffer at least one depressive episode during lifetime. The impact of profound social changes on the individual life is not negligible, but the increase in prevalence and incidence of depression as a result of the higher vulnerability is a serious reason for concern. The effects of disability caused by depression generate costs that are hard to be evaluated. Hospitalizations, medical leaves and early retirements mean millions of lost work-hours that value billions of Euros each year. The quality of life is dramatically altered, the risk for suicide rises, while the majority of cases have concomitant comorbidities, substance abuse disorders and residual symptoms. Recent clinical studies reported that the rate of relapse, recurrence and chronicity of depression increased 4-fold in the last 100 years.

While the problems caused by depression are well known, it becomes very clear that dealing with these issues is not such an easy task as considered in the middle of the last century, when the first antidepressants have been developed. As a result, the target is to reduce the costs through prevention programs, early diagnosis and adequate treatment that may recover completely a patient with depression and give back the full social, professional and family role. If this objective is logical and coherent in theory, practice demonstrates almost the
opposite. The individual expression of symptoms in terms of intensity, theme, cultural influences and way of perception raises many nosological issues. More that one study groups and task forces are trying to create a new classification of the depressive disorder that should allow the recognition of all its types. The attempts of prevention by identifying the risk groups and elaborating programs for life quality have encountered another problem that is stigma. There is still a large withdrawal in addressing the psychiatric disorders. Denying and minimizing the sadness and slow, but progressive alteration of global functioning have become the worst enemies of professionals in their attempt of early diagnosing and treating a depressive episode. Mistaking depression with madness is probably the worst attitude of a person with depression. From another point of view, it has been considered that the development of therapeutic arsenal will allow successful treatment in most of the cases. Paradoxically, the large variety of biological and non-biological therapies have only increase the difficulty of choosing the right treatment strategy.

The biological types of depression, the compliance of the patient, the ethical and social pressure are common challenges in the management of the case. Under these conditions, the therapeutic adequacy becomes a progressively discussed concept in the literature, based on the progresses of Biological Psychiatry.

Acknowledging this issues of the usual practice and trying the systematize this difficulties are the premises of the present study that will attempt to identify and quantify, at least in part, the way in which the clinical and biological characteristics of depression are correlating with the socio-demographical particularities of the patient in the course of depression.

**Keywords**

Depression, epidemiology, treatment outcome
**METHODOLOGY**

**Hypothesis**

Despite the large amount of data regarding the biology of depression and the development of antidepressant medications, the treatment of this debilitating disorder is still targeting mainly the symptoms. Deciphering the relationships between the patient characteristics, depression type and neuro-biochemical background may lead to the elaboration of individual therapeutic strategies with benefits that range from the quality of remission, smaller number of relapses and better quality of life to the reduction of direct and indirect costs of the disorder.

**Primary objective**

To establish the correlations between the individual characteristics course of depression and type of treatment in patients hospitalized for unipolar depression.

**Secondary objectives**

- Quantifying the impact of depression in a clinical setting.
- Quantifying the evolution of hospitalization indicators in patients with unipolar depression during the analyzed period.

**Design**

The present research is a five-year (2004-2009) prospective epidemiological study of the cases with depressive disorders hospitalized in the University Clinic of Psychiatry Craiova. All admissions between January, 1st, 2004 and December 31st, 2004 for unipolar depression (ICD.10 Code 321, categories F32-F33) have been registered. After 5 year of monitoring the subsequent admissions, between January 1st, 2009 and December 31st, 2009, patients with current severe episode and at least one admission in 2004 have been selected and included in the study sample (N=109). After obtaining the informed consent, the course of the patients in sample N during the corresponding 5 years has been thoroughly analyzed regarding demographic, pathological and therapeutic characteristics. The sources used have been the individual file of the patient and further take of history that
was absolutely essential in completing the data. The information has been input into the computer in a file protected with a password. Personal identification data has been erased and a unique number for each patient has been allocated. Furthermore, for each year of the studied period, all admissions for unipolar depression and for any psychiatric disorder were registered and several statistical parameters were extracted.

The analysis encompassed several directions:

- The descriptive analysis by gender, age group, educational level, residence, marital status, employment status year of onset, presence of comorbidities, presence of somatic illness, psychotic symptoms and suicidal behavior.
- The study of correlations searched for the direction and intensity of the relation, as well as the probability for the correlation between the duration of stay and the complexity of the treatment in each year of the studied period. Dynamically, several other correlations were studied.
- The prediction study has been oriented to the type antidepressant used, calculating and comparing the indicators that predict a higher probability for success after selecting a certain medication. The prediction indicators by gender for different categories of medication were calculated.
- The impact of depression in a clinical setting among all psychiatric disorders has been described by comparative analysis of data by gender, age group, number of admission and mean duration of stay.
- The study of depression per se has been conducted dynamically, by gender age group, number of admissions and mean duration of stay.

**Variables**

Gender, age, educational level, residence, year of onset, comorbidities, marital status, employment status, number of days for each stay, somatic illness, suicidal behavior and treatment type entered in the analysis.

**Sample characteristics**

RESULTS

Sample descriptive characteristics

Gender and age groups

By gender, there is a predominance of women - 53.21%. The distribution of the age groups has a Gaussian aspect, with a maximum point in the 45–54 group, where almost two thirds of the cases are included. Men are dominant after age 55 (Figure 1).

The correlation study

Duration of stay – antidepressants (by gender)

The intensity and trend of the correlation between the duration of stay and the antidepressive treatment varies quite largely. If during the first two years, the correlation factor \( r \) employed small values, toward the end of the period, there is a trend for the strengthening the correlation (Figure 2).
**Severity – Somatic illness**

There is a negative correlation during the whole period, with medium or high intensity and statistically significant. The high p values in 2006 and 2008 indicate a strong relationship between the two parameters. The probability of the correlation decreases in 2009, but still significant (Figure 3).
The impact of depression in the clinical setting

Total number of admissions
Out of the total number of admissions for any psychiatric disorder, between 2004 and 2009 more than 40% were for unipolar depression.

Number of admissions by gender
By gender, women are dominant. While men with depression represent almost one third of the total number of admission, in women, more than half of the admission were depressions.

Mean duration of stay
Regarding the mean duration of stay, depression is associated with a longer duration in comparison with the mean value calculated for any psychiatric disorder – 17.24 days and 16.04 days, respectively.

Number of admissions by age group
Analyzing the age groups, the results have showed that more than 70% of the cases fall into the age group 45-54 years. There is a slow, but constant increase of the cases in the group 55-64 years, while the extreme groups remain relatively unchanged.
DISCUSSIONS

Descriptive elements

The sample was highly homogenous, the distribution of the variables is relatively similar with other report, but several differences were found regarding the residence, education, comorbidities and suicidal behavior. The absence of published national studies prevented a comparison of the results that may better explain these particularities. Such epidemiological studies should be design and conducted in the near future.

Correlation elements

The study of correlations between several variables of the sample has demonstrated strong and significant connections between the duration of stay and the treatment used, the presence of somatic illness and age, but also the absence of correlation between certain parameters considered to be mutually determined, such as the suicidal behavior and severity on one hand, and the gender, age, education and residence on the other. These results urge for large-scale studies that could confirm or deny the outcome based on a representative sample and an exhaustive collection of the variables.

Prediction elements

Over the time, there were several attempts to identify factors for prediction of treatment outcome, such as early clinical improvement or the absence, comorbid anxiety, melancholic or atypical features, concomitant substance abuse, gender or certain biological parameters like the genetic polymorphism induced by treatment. All these potential factors are still in a preliminary research, waiting for operational models that could be tested on a significant sample.

The prediction study for the choice of the antidepressant in men and women during the 5 years did not offer clear evidence in order to calculate accurately the probability. On the other hand, it supports the need for therapeutic adequacy based on the recognition of symptoms, the choice of the ideal type of medication and the best prediction of the outcome.
Elements of impact and course of depression

Taken as a whole, the results of the study of depression course in comparison with all psychiatric disorders and per se are not surprising. With all methodological limitations, they offer a clear image of the status-quo of this disorder and may help in elaborating more flexible, but complete programs of clinical and administrative management.

Strengths and limitations

This study has several strong points, but also limitations.

Firstly, to the best of my knowledge, is one of the few epidemiological studies, while most of the current research is based on randomized controlled trials. The advantage of this approach is given by the fact that the sample is more close to the real situation as opposite to the controlled studies where the population subjects must meet several strict criteria and the results may not be applicable in current practice. Considering the objective of this study, I have selected a group of patients that are representative for a small geographical area and have monitored them for 5 years in non-interventional frames.

Secondly, the statistical analysis revealed several contradictions compared to the reports from other research with similar target population. Considering that these discrepancies remained after statistical correction, it becomes imperative to conduct a study on a large sample of subjects to be included as naturalistically as possible, in order to have a clear-cut distinction of the data. Moreover, the own results raise again the question which kind of study may offer the best combination between the “ideal” patient form the randomized controlled studies and the “real” patient from the epidemiological research, while keeping a high and accurate level of methodological design and statistic.
CONCLUSIONS

1. Out of the total number of admissions in the clinic, unipolar depression had a global proportion of 42.07% with the highest percent for the age group 45-54 years– 72.24%.

2. At the inclusion, only 15.59% of the patients were still working, which demonstrates the high potential for disability of depression, but affects other results of the research.

3. The studied cases of unipolar depression have showed no significant differences regarding the gender – 46.79% men and 53.21% women.

4. The majority of the patients in the sample were between 45 and 54 years of age – 62.39%, medium to high educational level – 86.24% and had somatic comorbidities – 62.38%.

5. The duration of stay correlates directly with the level of treatment complexity (p<0.01) and reversely with the age of the patient (p<0.01).

6. The level of severity correlates reversely and very significantly with the somatic illness (p<0.01), in contradiction with the literature.

7. The correlation between the level of severity and the duration of stay decreases progressively to become non-significant (p>0.05).

8. The severity of depression does not correlate with age (p=0.19), education (p=0.17) or residence (p=0.99).

9. The probability of receiving an adequate treatment varied around 50% for all types of antidepressants.

10. More than half of the patients has not received treatment or has received inadequate treatment by type or duration (Negative Predictive Value >90%).

11. The evolution of prediction indicators (Classification Error and Accuracy) showed that the therapeutic associations or frequent change in therapy are based on administrative criteria rather than therapeutic adequacy.

12. The concept of therapeutic adequacy could be implemented in usual practice only by choosing that treatment that will consider the particularities of the patient within flexible and clear administrative frames that will place the patient in the center of the system.