Characterization of depressive syndrome in schizophrenic outpatients*
Caracterização de uma síndrome depressiva em pacientes esquizofrênicos ambulatoriais

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Abstract
Objective: The authors carried out a cross-sectional study with the aim of characterizing and describing depressive pictures in schizophrenic patients seen at the Psychiatry Outpatient Clinic of the Federal University of Pernambuco (HC-UFPE). The patients had the diagnosis of schizophrenia confirmed on the basis of the operating criteria of the DSM-IV.

Methods: Those who were in the period of stabilization of the clinical picture were selected for the study defined according the following criteria: the last psychotic episode must be happened two months before at least, and during this period the alterations of the antipsychotics doses had been lower than 5 mg of haloperidol or equivalent doses of others neuroleptics. A total of one hundred and four patients took part. Following the identification of the depressive symptoms using the Calgary Depression Scale for Schizophrenia (CDSS), thirty-one patients (29.8%) fulfilled the diagnostic criteria described in the DSM-IV. Of these, 22.1% had the diagnosis of major depression and 7.7% of minor depression according the DSM-IV. Two groups were constituted: Group A, schizophrenics with a depressive syndrome, and Group B, schizophrenics without such a syndrome. An assessment was made of the distribution of the symptoms of the CDSS scores in both groups, the sociodemographic, clinical and therapeutic variables in relation to the frequency of the depressive syndrome, and the patients clinical course. For the investigation of certain clinical features, the following tools were used: problem list (psychosocial stressors) contained in axis IV of the DSM-IV intended to detect the presence of factors triggering the initial episode of schizophrenia and the Global Assessment of Functioning (GAF – Axis V – DSM-IV) to characterize the current functioning of the patients.

Conclusions: The results obtained allowed the authors to draw the following conclusions: all the items that comprise the Brazilian version of the CDSS were statistically significant in characterizing the depressive syndrome; a comparison of the sociodemographic and therapeutic variables revealed no statistically significant differences between the two groups, and this was also the case with the majority of the clinical features. Statistically significant differences, however, were found in relation to the greater frequency of life events (psychosocial stressors) in triggering the first episode of schizophrenia and the higher incidence of affective disorders antecedents in family members (first and second degree) among the depressed patients. The mean duration of the depressive syndrome during follow-up of the patients was 5.30 months. The patients in whom there was a recurrence of the psychotic episode presented a delusional-hallucinatory clinical picture. This study seeks to contribute to the inclusion of the Postpsychotic Depressive Disorder (PSD) of Schizophrenia (DSM-IV), in the group of Schizophrenic Disorders.

Keywords
Schizophrenia. Depression. Depressive symptoms.

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Métodos: Foram selecionados pacientes que se encontravam no período de estabilidade do quadro clínico, definido de acordo com os seguintes critérios: o último episódio psicótico ter ocorrido há no mínimo dois meses e durante esse período as alterações nas doses dos antipsicóticos tenham sido inferiores a 5 mg de haloperidol ou doses equivalentes de outros neurolépticos. Participaram do estudo 104 pacientes. Após a identificação dos sintomas depressivos pela utilização da versão em português da Escala Calgary de Depressão para Esquizofrenia, 31 doentes (29,8%) preencheram os critérios diagnósticos para quadros depressivos. Desses, 22,1% preencheram os critérios para episódio depressivo maior pelo DSM-IV e 7,7% para episódio depressivo menor. Foram constituídos dois grupos: A (pacientes esquizofrênicos com depressão – DSM-IV) e B (sem síndrome depressiva). Avaliaram-se as distribuições dos sintomas e dos escores da ECDE em ambos os grupos, as variáveis sociodemográficas, clínicas e terapêuticas em relação à frequência da síndrome depressiva e a evolução clínica dos pacientes. Foram empregados os seguintes instrumentos: estressores psicossociais contido no eixo IV do DSM-IV e a Escala de Avaliação Global do Funcionamento (AGF - Eixo V- DSM-IV).

Conclusões: Os resultados obtidos permitiram aos autores elaborarem as seguintes conclusões: todos os itens que compõem a versão brasileira da ECDE foram estatisticamente significantes na caracterização da síndrome depressiva; as variáveis sociodemográficas e terapêuticas não obtiveram diferenças estatisticamente significantes quando comparadas entre os dois grupos, assim como a maioria das características clínicas; entre os doentes deprimidos, diferenças, com significância estatística, foram assinaladas em relação a maior frequência de eventos vitais (estressores psicossociais) no desencadeamento do primeiro surto esquizofrênico e a maior incidência de antecedentes familiares de portadores de transtornos do humor (primeiro e segundo graus). O tempo médio de duração da síndrome depressiva durante o período de acompanhamento dos pacientes foi de cinco meses e dez dias; os doentes que tiveram recidivas do episódio psicótico apresentaram quadros clínicos delirante-alucinatórios. Esse estudo busca contribuir para a inclusão do transtorno depressivo pós-psicótico da esquizofrenia no grupo dos transtornos esquizofrênicos.

disease’s course. Thus, this research aimed to characterize and describe the clinical evolution of depressive pictures that occurred in the stable phase of schizophrenia. We took into account three aspects to choose specifically this phase of the disease:

1. Current nosographic systems contain operating criteria to diagnose the depressive syndrome in the stable phase of schizophrenia, and there are no criteria to make a characterization in other phases of the disease;
2. Reliability tests of the Brazilian version of the Calgary Depression Scale for Schizophrenia (ECDE) had demonstrated good results between examinators. After we started our field research the validation study of the scale was concluded and considered as reliable, valid and specific to check depression in stable schizophrenic patients; 3. The definition of a secondary depressive syndrome in schizophrenia allows the development of somatic and psychosocial interventions to improve the assistance and to decrease the patient’s suffering.

We used the operative criteria of the DSM-IV, as they are better outlined. According to this classification, the essential characteristic of this clinical picture is the occurrence of a major overlapped depressive episode that occurs only in the disease’s residual phase. However, the current literature refers to the possible presence of depressive symptomatology that does not fulfill criteria for a major depressive episode. In these cases, we used DSM-IV’s operating criteria for Minor Depressive Disorder.

After the identification of the depressive symptoms by the ECDE, the schizophrenic patients that fulfilled the diagnostic criteria for depressive pictures in the DSM-IV were gathered in a group and the patients who had not been characterized as depressive in another one. We studied, in both groups the distribution of symptoms and total scores of ECDE, the sociodemographic, clinical and therapeutic variables, and the clinical evolution.

Methods

Sample

We assessed 104 patients diagnosed as schizophrenic according to the DSM-IV criteria, seen only by one investigator (the first author) in the psychiatric outpatient clinic of the HC-UPE, from May/1997 to May/1999.

Inclusion criteria: outpatients of both sexes, aging from 15 to 50 years, diagnosed as schizophrenic according to the DSM-IV, having the disorder lasted for at least one year and having their psychopathological picture stabilized at least for the last two months.

The criterion used to characterize stability was that the last acute psychotic episode had occurred at least two months before and during this period the alterations in the doses of antipsychotics were less than 5mg of haloperidol or equivalent doses of other neuroleptics.

Exclusion criteria: presence of clinical diseases that might be associated with depression, organic mental disorders, alcohol dependence or abuse and severe mental retardation.

Study design

In the first phase, we did a cross-sectional inquire. The first author who collected the anamnesis data (sociodemographic characteristics, clinical history, background, life curve and mental examination) examined patients. We also assessed the occurrence of triggering factors using the list of psychosocial and environmental problems of the axis IV - DSM-IV; we also performed the global assessment of the functioning using the Global Assessment of Functioning (GAF Scale of the axis V - DSM-IV) and the presence of depressive symptoms using the Brazilian version of the Calgary Depression Scale for Schizophrenia (ECDE).

After the depressive symptoms were identified two groups were formed: group A for patients who fulfilled the DSM-IV diagnostic criteria for major depressive episode or minor depressive disorder and group B for those who presented one or none depressive symptom.

Group A patients were followed since the first interview up to the end of the observation period predetermined for the study (18 months). The reassessments were fortnightly made and we used the ECDE, the PANSS scale to check positive and negative symptoms, the extrapiramidal symptom scale (ESS), and a follow-up psychiatric interview. We assessed the mean time of observation of patients, the mean duration of the depressive syndrome, the recidivism of psychotic episodes, the rehospitalization and the compliance.

Instruments

1. Semi-structured anamnesis: was elaborated to collect the main sociodemographic, clinical and therapeutic data. In the anamnesis we investigated the presence of schizophrenic and mood disorders among 1st and 2nd-degree relatives, the basis for this differentiation being the diagnostic criteria of the DSM-IV.
2. Diagnostic criteria of the DSM-IV: Schizophrenia, Major Depressive Disorder, Minor Depressive Disorder and Post-psychotic Depressive Disorder of Schizophrenia.
3. Brazilian version of the Calgary Depression Scale for Schizophrenia (ECDE).
4. Global Assessment of Functioning scale (GAF – Axis V – DSM-IV)
5. List of psychosocial and environmental problems of axis IV - DSM-IV
6. Positive and Negative Syndrome Scale for Schizophrenia (PANSS)
7. Extrapiramidal Symptoms Scale (ESS)

Statistical analysis

For statistical analysis we used the software (SAS-Statistical Analysis Systems), version 6.12. We studied the associations between categorical variables with independent Chi-Square (X²) or Fisher’s Exact test, provided the conditions to use the first test were not fulfilled. The associations between
numeric variables were verified with Mann-Whitney test for the two independent samples, and we choose this test due to the lack of data normality per group. The verification of the hypothesis of normality was performed through the specific Shapiro Wilks test. The level of significance considered for the statistical tests was 5%.

**Results**

Depressive symptoms identified by the brazilian version of the CCDS and characterization of the depressive syndrome by the DSM-IV

| Table 1 - Distribution of patients according to the diagnosis of depression by DSM-IV per group. |
|-------------------------------------------------|-----------------|-----------------|
| Group                                           | Number of patients | %               |
| Group A                                         |                  |                 |
| Major depressive episode                        | 23              | 22.1            |
| Minor depressive disorder                       | 08              | 7.7             |
| Group B                                         |                  |                 |
| Absence of depressive symptoms                  | 62              | 59.6            |
| At least one depressive symptom                 | 11              | 10.6            |
| Total                                           | 104             | 100%            |

As shown in Table 1, of the total sample of 104 patients diagnosed with schizophrenia, 42 (40.4%) presented at least one depressive symptom identified by the ECDE and 62 (59.6%) did not present any symptom. Of the 42 patients who had at least one depressive symptom, 23 (22.1%) fulfilled the diagnostic criteria for major depressive episode and were characterized as having Post-Psychotic Depressive Disorder of Schizophrenia. Eight (7.7%) presented depressive symptoms although they did not fulfill the criteria for a major depressive episode and were characterized as having minor depressive disorder. Seventy-three patients (70.2%) did not present depressive disorders.

As shown in Table 2, the association between the presence of depressive symptoms and the characterization of Depression (DSM-IV) is statistically significant for all ECDE items, according to the results of p (Independence Chi-square test).

Total ECDE scores obtained in Group A had a mean of 10.22 and median of 10 whereas in Group B they were quite inferior, with a mean of 0.18. When we analyzed differences of total ECDE scores for patients with major depressive episodes compared to minor depressive episode and without depressive episode, with the Mann-Whitney test, we confirmed that there is a statistically significant difference, that is, the better the depressive conditions are characterized according to DSM-IV criteria, the greater are the ECDE scores obtained with patients.

**Sociodemographic, clinical and therapeutic variables in relation to depression frequency according to the DSM-IV criteria (Table 3)**

Clinical evolution of depressive syndrome during the period of study

All schizophrenic patients with depressive pictures (group A) at the initial interview were regularly followed for an eigh...
The 22.1% frequency found for patients which had a major depressive episode, necessarily including depressed mood, is therefore the Post Psychotic Depressive Disorder of Schizophrenia rate of the current research. The DSM-IV reported that up to 25% of schizophrenic patients could present this clinical condition.

Regarding the distribution of total scores of ECDE and of depressive symptoms in the groups, we observed that symptoms such as depressed mood, hopelessness, self-depreciation and morning depression were prominent, as they were present in all group A patients. The importance of these symptoms was also emphasized in other authors’ researches. On the other hand, the symptom that reached the highest percentage among group B patients was early awakening. Becker reported that, among other symptoms, insomnia may occur in schizophrenic patients with or without depression. Researchers such as Bastos and Addington et al emphasized that, among insomnia types, the terminal one (early awakening) would be more common among depressed schizophrenic patients.

After performing statistical tests, we observed that total ECDE scores were significantly higher in group A. The score interval in our research was 0 to 16 points. Addington et al found a greater spectrum of depressive symptoms (score interval of 0 to 23) and Bressan reported a 0-12-interval. The ECDE, in the current study, was able to discriminate, in a statistically significant way, the minor depressive conditions from the severe ones (patients with Post Psychotic Depressive Disorder of Schizophrenia), as described by other author in their studies.

Sociodemographic characteristics

The proportion of male patients was greater than the female ones, although this difference was not statistically significant. Studies with schizophrenic patients generally show this trend. The mean age of the total sample was between 16 and 47 and this is a remarkable characteristic of the schizophrenic patients seen at the psychiatric ambulatory of the HC-UFPE as they are mostly young patients. Mcglishan & Carpenter reported that for most patients the depressive symptoms start in their youths.

Regarding the marital status, there are more singles in both sexes and in the groups but there are no significant differences regarding this variable. The fact that most patients are single points out the difficulty of these patients to establish affective links. These patients generally depend on their parents and on siblings. Among singles there is a lack of ability and loss of confidence to establish relationships with the other sex. Most patients of this study have had their depressive symptoms started 45 days after the remission of the productive symptoms. This patient was still depressed at the end of the research.

Discussion

Studies that assess the frequency of depression in schizophrenic patients present quite distinct rates, due to the great variation in their methodology. Other aspects also favor the disparity in results, such as the utilization of several definitions for depressive conditions, the use of different diagnostic criteria for schizophrenia and the assessment of patients in distinct phases of the schizophrenic disease, i.e., in its prodroms, the acute psychotic phase, the post psychotic period and the residual phase.

The 22.1% frequency found for patients which had a

<table>
<thead>
<tr>
<th>Depressive syndrome duration (in months)</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=31</td>
<td></td>
</tr>
<tr>
<td>Minimum value</td>
<td>4</td>
</tr>
<tr>
<td>Maximum value</td>
<td>7</td>
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<tr>
<td>Mean</td>
<td>5.30</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.82</td>
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<tr>
<td>Median</td>
<td>5.00</td>
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<tr>
<td>IQO (amplitude interquartílica)</td>
<td>1.00</td>
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</table>
Clinical features

Differences in the age of onset of schizophrenia were not statistically significant between sexes and groups. Men had earlier onset, before 20, than women. These data confirm reports that schizophrenia is a disease that affects young adults with a slight trend to have an earlier onset among male patients.\textsuperscript{32,34,35}

When we compared the age of the first hospitalization and the age of onset, we observed that in both groups there was a trend to a first hospitalization just after the psychosis’ onset. After the beginning of psychiatric assistance this fact changed, that is, when we analyzed the number of subsequent acute phases and hospitalizations, we verified that the latter decreased. Patients, even while in acute phases, were kept in ambulatory treatment, assisted by a multidisciplinary team that aimed to treat them in their own social environment. There were no significant differences in the number of relapses and hospitalizations between groups. These results agree with several authors\textsuperscript{14,15,25} and disagree with others.\textsuperscript{9}

As mainly young patients composed the sample, this was directly reflected in the mean duration of schizophrenia and there were no significant differences between sexes and groups.

As for the mean time elapsed since the last psychotic episode, it is important to remember that at the time of the cross-sectional study, patients that entered group A were already depressed. Probably, the depressive condition began earlier after the last acute phase. All patients had not any productive symptoms.

In this research we used a list of psychosocial and environmental problems to assess the presence of triggering factors of the schizophrenic disease, described by axis IV - DSM-IV. A psychosocial or environmental problem could be a negative life event, an environmental difficulty or deficit, a family or interpersonal stressor, inadequate social support or personal resources or any another problem related to the context in which the person’s difficulties have developed. The so-called “positive stressors”, such as a job promotion, should be listed only if they constitute or lead to a problem, as when it is difficult for someone to adapt to a new situation.

The psychosocial problems have a role in the onset or in the exacerbation of a mental disorder and may also interfere in the chronicity of the disease that compromises their whole psychical life. There were no significant differences in the number of relapses and hospitalizations between groups. These results agree with several authors\textsuperscript{14,15,25} and disagree with others.\textsuperscript{9}

Therapeutical characteristics

One of the most important aspects of this research was the evidence that, although all patients have already been medicated at the first interview, most of them had never taken antidepressants, even when there was reference to previous depressive pictures. Siris\textsuperscript{44} reported that long-term maintenance treatments with antidepressants would be beneficial for patients who responded favorably to the initial treatment. He stated that besides the fact that some patients were resistant and even refractory to pharmacological treatment, it would be also probable that therapists found it difficult to administer high doses of anti-depressants to these patients. The fear of recidivation of psychotic symptoms would lead either to the regular use of subtherapeutical doses of antidepressants making it difficult to cure this syndrome and to a subsequent chronicification of patients or to not much efficient and very long treatments.

Group A patients underwent treatments more regularly than those of group B, although this difference was not significant. What made treatments irregular was the poverty in which patients lived, added to non-compliance. There was no significant statistic difference in the average daily dose of the antipsychotic used by patients of both groups. Several studies in the area\textsuperscript{10,12,21,25} presented similar results.

Clinical evolution of the depressive syndrome

After the cross-sectional study patients who had depressive syndrome started to be regularly followed-up. The follow-up average time was 22,61 months. In this second phase of the...
study there was not a comparison group, the data analysis has a much more descriptive characteristic. Besides the follow-up psychiatric interviews we used the Brazilian version of the ECDE to reassess the depressive symptoms.

An important finding was that the duration of the depressive syndrome was very similar between men and women and between patients with major and minor depressive episodes. We had previously revised several works that presented various results about the depression evolution time.\(^4,13\) The comparisons of these studies with our own is limited for several reasons: utilization of distinct methodologies; observation of the depressive syndrome at different moments; utilization of different instruments to assess mood alterations and employment of distinct therapeutics.

We did not perform clinical trials. All group A patients used imipramine as antidepressant (in doses from 100 mg/day to 150 mg/day) associated with a neuroleptic (most of them used haloperidol, for its availability at the hospital’s pharmacy). Recommendations contained in Siris’ works\(^44\) were respected.

The four patients who withdrew from the research had their depressive symptoms remitted and were, therefore, included in the statistic analysis of the average duration of depression. For two of these patients we had doubts about the diagnosis of schizophrenia because they had greater social and occupational autonomy; one of them had finished Law school (although being retired, with a schizophrenic pathology. Some of them had predominantly negative symptoms and others, extrapiramidal symptoms, caused by typical antipsychotics. Through ECDE reassessments, there were mild depressive symptoms that, however, did not characterize a full syndrome.

The authors consider, as Mcglashan & Carpenter,\(^13\) that the duration of this study would not allow greater contributions concerning these patients’ prognosis. Besides, we did not have a comparison group in the research’s second phase, what might be done later on. Furthermore, there are several characteristics, related or not to the prognosis, to be better studied in this population.

Referências


