THE IMPACT OF THERAPEUTIC OPTIONS IN FIRST PSYCHOTIC EPISODE

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AIM OF THE STUDY

The present study is aimed at creating an image of therapeutic options available for the first psychotic episode and the way these options affect the short and medium term evolution of patients with a diagnostic of first psychotic episode.
MATERIAL AND METHODS

The present study is part of a larger pilot study on a number of 80 patients with a diagnostic of first psychotic episode admitted in the Timisoara Psychiatric Clinic and The Day Care Center in the Timisoara Mental Health Center between the years 2003-2005 and prospectively monitored from the moment of their first contact with psychiatric services up to present.

For each patient have been assessed, apart from the clinical parameters:
- Prodrome's duration;
- Duration of Untreated Psychosis (DUP);
- Clinical Global Impression Score (CGI) at onset and after an average course of 3 years.

Also, the attending psychiatrists in charge of ambulatory care have been questioned upon:
- Their first therapeutic option (at onset);
- Patient's adherence to treatment;
- The patient's satisfaction with the administered treatment;
- Side-effects of medication;
- Present treatment administered to patients.

Each patient has completed a questionnaire with three questions pertaining: the utility of administered medication; side-effects of medication, and the patient's subjective satisfaction with the psychotropic medication taken.

Used statistical methods
- Descriptive statistics: average, standard deviation, absolute and relative frequencies.
- Shapiro normality test - data concluded to have a normal distribution, and therefore parametric tests were performed, as follows:
  - T Test (Student) for dependent variables, to determine if differences between Clinical Global Impression (CGI) scores at onset and CGI scores at final evaluation were statistical significant;
  - Pearson correlation test to check for the presence of a statistically significant correlation between patients’ adherence to treatment and other various clinical parameters (Duration of Untreated Psychosis, prodrome duration)
  - T Test for independent groups was used to determine if there are statistically significant differences in regard of patients’ adherence to treatment between the groups formed on: prodrome type; administered neuroleptic medication.

Study design

The study was performed on a number of 80 patients admitted in the Timisoara Psychiatric Clinic and the Day Care Center Unit in the Timisoara Mental Health Center during 2003-2005 with a diagnostic of first psychotic episode.

From these 80 initial patients, 69 could still be found in the registers of the ambulatory care units in Timisoara (33 of these being personally supervised by the author) and the Mental Health Center in Timisoara after a period long enough to allow for a second assessment (average course period – 3 years).

As this is a clinical population, the sample is not statistically representative, and no sampling techniques were used other than inclusion/exclusion criteria.

Inclusion/exclusion criteria used for selection

Inclusion criteria:
1. Age between 18 and 60 years;
2. Patients at first contact with psychiatric services and a hospitalization diagnosis, established according to the ICD-10 criteria, of:
   a. Schizophrenia;
   b. Acute schizophrenia-like psychotic disorder;
   c. Other acute predominantly delusional psychotic disorder;
   d. Acute polymorphic psychotic disorder with symptoms of schizophrenia;
   e. Acute polymorphic psychotic disorder without symptoms of schizophrenia;
   f. Schizoaffective disorder;
   g. Persistent delusional disorders;
   h. Severe depressive episode with mood-incongruent psychotic symptoms;
   i. Mania with mood-incongruent psychotic symptoms;
3. No other psychiatric disorder on Axis I present;
4. Patients gave their informed consent to participate in the study;
5. Residence in Timis county;
6. Currently under care and supervision in the Timisoara Mental Health Center or other ambulatory care units in Timisoara;
7. At least one family member willing and able to participate in the assessment process.

Exclusion criteria:
1. Patients with prior contacts with psychiatric services;
2. Patients following psychotropic drug treatment prior to admission;
3. A diagnosis of organic psychotic disorder;
4. A diagnosis of alcohol and/or drug consumption induced psychosis;
5. Psychotic disorder in the general frame of a present epileptic disorder;
6. Age under 18 years;
7. Patients refusing to participate and/or give their informed consent to participate in the study;
8. Presence of cognitive and/or communication problems that make the obtaining of information difficult, or the obtained information unreliable.

Presentation of socio-demographic traits of the studied sample

The initial sample included a number of 80 patients, of which 37 male (46.2%) and 43 women (53.8%). 68 patients (85%) were from rural areas. Subjects in the initial sample were young people aged between 18 and 55, with an average age of 30.6 years (Std. Dev. = 9.6 years). A large part of the patients (50%) were aged between 20 and 30 years. From the initial sample, at final assessment only 69 subjects could be contacted. The evaluation was made after at least 1 year since the onset of the first psychotic episode; the average period between evaluations was 36 months (Std. Dev. = 11.3 years). The longest course period between assessments was of 5 years.

Lost subjects were due to:
- Change of residence in another county (2 subjects);
- Lack of contact with mental health services in the interim period (9 subjects).

A series of prospective studies realized in the last years also show the loss of 10 to 15% of the subjects in the initial samples, even for study duration of 2 years. The most recent study of the EPPIC (Early Psychosis Prevention and Intervention Center) in Melbourne, published in 2007, revealed the loss of 10% of the subjects from the initial sample.9

RESULTS

Characteristics of first psychotic episode (FPE)

The average calculated duration of prodrome period was 28.31 weeks (approximately 7 months); some patients have no identifiable prodrome. The longest prodrome was of 200 weeks (50 months–over 4 years).

The largest part of the subjects (41%) have a prodrome under 3 months long: 18% of the subject had no identifiable prodrome and 23% of the subjects had a prodrome over 1 year long.

Studies in the last 20 years regarding first psychotic episode have identified an average duration of prodromal symptoms of 48 weeks up to 455 weeks.

Most studies have established an average duration similar to the one found in the present study – between 150 and 230 weeks.10-13

The average DUP (“Duration of Untreated Psychosis”) was of 15.3 weeks (approximately 4 months); for some patients no DUP could be established with some reliability. The longest identified DUP was of 144 weeks (36 months – 3 years).

Surprising for this study is that, despite the lack of early detection strategies, the results are similar with those identified in countries recognized for their community services and active strategies for detection in severe psychiatric illnesses.

Table 1. Studied sample’s distribution according to the ICD-10 diagnostic criteria.

<table>
<thead>
<tr>
<th>ICD-10 diagnostic</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>F20.0 – Paranoid schizophrenia</td>
<td>15</td>
<td>18.7</td>
</tr>
<tr>
<td>F20.1 – Schizophrenia, hebephrenia-like</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>F20.2 – Schizophrenia, catatonic</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>F22.0 – Persistent delusional disorder</td>
<td>7</td>
<td>8.8</td>
</tr>
<tr>
<td>F23.0 – Acute polymorphic psychosis, without schizophrenia symptoms</td>
<td>4</td>
<td>5.0</td>
</tr>
<tr>
<td>F23.1 – Acute polymorphic psychosis, with schizophrenia symptoms</td>
<td>4</td>
<td>5.0</td>
</tr>
<tr>
<td>F23.2 – Acute psychotic disorder, schizophrenia-like</td>
<td>10</td>
<td>12.5</td>
</tr>
<tr>
<td>F23.3 – Acute psychotic disorder, delusional</td>
<td>20</td>
<td>25.0</td>
</tr>
<tr>
<td>F25.0 – Schizo-affective disorder, manic type</td>
<td>3</td>
<td>3.7</td>
</tr>
<tr>
<td>F25.1 – Schizo-affective disorder, depressive type</td>
<td>3</td>
<td>3.7</td>
</tr>
<tr>
<td>F30.2 – Mania with non-congruent psychotic symptoms</td>
<td>6</td>
<td>7.5</td>
</tr>
<tr>
<td>F32.3 – Major depressive episode with non-congruent psychotic symptoms</td>
<td>6</td>
<td>7.5</td>
</tr>
</tbody>
</table>

Sample’s distribution on ICD-10 diagnosis

Table 1 presents the distribution of the studied sample according to the ICD-10 criteria. The most frequent diagnostic established for patients on their first admission in a psychiatric service was “Acute psychotic disorder, delusional” (F23.3). Most prospective studies on the first psychotic episode carried on until today have focused on subjects with a first episode of schizophrenia and, eventually, with a schizophrenia-like disorder. Prospective studies that included in the studied sample patients from other diagnostic groups were started only in the last 3-4 years, and still had samples formed mainly by subjects with a first diagnostic of schizophrenia and schizophrenia-like disorder. The general interest seems to be still centered around the first episode of schizophrenia.14-16 In this pilot study, the intention was to have a larger view on the area of first psychotic episode, including first affective episodes with incongruent psychotic symptoms. It is a naturalistic survey, and this diagnostics of the first episode will be changed in time, as our studies showed in the last 10 years.
The Pearson correlation test shows the existence of a significant correlation between the duration of prodrome and the CGI (Clinical Global Impression) for illness course \( (R=0.36, p<0.05) \). The longer the prodrome, the worse the improvement of illness during course. (Fig 1)

The prodrome duration is directly correlated with the number of the patient’s relapses \( (R=0.25, p<0.05) \); a longer prodrome is correlated with a higher number of relapses during the patient’s illness course.

Also, Duration of Untreated Psychosis (DUP) is directly correlated with the Clinical Global Impression severity score at second assessment \( (R=0.30, p<0.05) \), indicating that a longer DUP is likely to lead to an increased severity of illness, and thus to a negative illness course. (Fig 2)

These results are similar to the results of other studies showing that a shorter DUP can have a favorable influence on the first psychotic episode’s remission, on the further course of the illness.\(^7^-^9\)

In addition, in this study, the Duration of Untreated Psychosis was found as a good predictor for the patient’s adherence to treatment. A shorter DUP is correlated with a better adherence.

This results are integrated in a very controversial area of discussions in all similar international studies. Despite the voices which denial the prodrome’s or DUP importance for the clinical status at the first episode, or for the long term evolution, the evaluation of this two parameters could have a major impact for the therapeutic strategies and for the prognostic. The results presented from this study and those from the past years, are very important factors which influenced this statement.

**Drug treatment during the first and the second assessment and its influence on the clinical state of patients**

Presently, the palette of drugs available for the treatment of first psychotic episode is large. In Figure 3 are presented the options of attending physicians for treatment at the onset of disorder, and in Figure 4 their options at the final assessment of patients. The heterogeneity of antipsychotic agents could influence the doctor’s decision, but also the evolution of the illness.

Between the first psychotic episode and the final assessment, patients have undergone several changes in treatment. Figure 5 shows the changes in drug therapy for patients in the studied sample. It can be noticed that physicians tend to give up the use of typical antipsychotic drugs (Haloperidol) and favor the atypical ones, especially the newest (aripiprazolum, quetiapinum).

Figure 6 presents the switch between typical and atypical antipsychotics for patients in the studied sample from onset to final assessment. The frequency of therapeutic switches and their underlying motives shows that:

- For most patients (61%) was not necessary to change the drug therapy during illness course, but for some patients (29%) a switch was needed, and for a few patients (10%) even two or three such changes of therapy;
The most frequent causes for initiating a therapy change were drug therapy's side effects (35%), patients non-respondence to treatment (19%) and relapses (9%).

The influence of administered treatment on the illness course

The type of administered drug influences the improvement of illness, as shown by the results of the Student T test for independent groups applied on two groups: patients with typical antipsychotic drug treatment versus patients with atypical antipsychotic drug treatment. The group of patients who was administered atypical antipsychotic medication have shown a significantly better improvement of symptoms, indicated by the CGI scores for illness improvement ($T = -3.83$, $p = 0.32$). Differences are graphically presented in Figure 7.

No other statistically significant differences could be identified in relation with the type of administered medication and the resulting clinical state. Nevertheless, the type of drug therapy (typical versus atypical antipsychotics) has great importance in regard of resulting side-effects and the benefits of therapy (as they are perceived by the patient and as they are assessed by the attending psychiatrist). Significant differences have been found between the patients' self-assessment and the assessment of the physicians in regard of the perceived satisfaction with the administered treatment and the side effects of the psychotropic drug treatment.
Figure 7. The influence of administered drug treatment, as shown by the differences in the Clinical Global Index Scale.

Side-effects of medication, according to the assessment of current physician, are significantly stronger for typical antipsychotics than for typical ones, as shown by the results of the Student test for independent groups \( T = -2.39, p = 0.019 \); also subjective satisfaction of the patient, is higher for typical antipsychotics than for the typical ones \( T = 2.31, p = 0.02 \).

Figure 8. Presents patients’ appreciation of administered treatment.

- 20% of the patients appreciate the utility of administered treatment as very low; only 13.7% consider that the administered treatment was extremely useful.

Patients’ adherence to treatment.

From the studied sample, most subjects (43.5%) presented a good adherence to treatment. A vast proportion of First Psychotic Episode patients (57%) tend to give up treatment in the first year of course, especially non-adherent patients and patients with a low adherence to treatment. These data are graphically presented in Figure 9.

Figure 9. Studied sample’s distribution according to the patients’ adherence to treatment.

Patients’ adherence to treatment seems to be influenced by some clinical parameters specific to the first psychotic episode, rather than the type of administered medication. This result is a new perspective for the evaluation of therapeutic adherence. All similar studies consider that the adherence is most of all influenced by the type of medication.

- The duration of the prodrome influences the therapeutic adherence of patients: the longer the prodrome, the lower the patient’s adherence to treatment, as indicated by the Pearson correlation test results. \( R = -0.29, p < 0.05 \); also, for the subjects in this study, it seems that the type of prodromal phase is relevant, more patients with type C are less adherent to medication or to other therapeutic interventions;

- Patients’ adherence to treatment is influenced also by the patient’s age at onset: the older the patient, the better the patient’s adherence to treatment is (Pearson correlations test result: \( R = 0.24, p < 0.05 \)).

Patients’ adherence to treatment also depends on the following factors:
- The utility of administered medication, as perceived by the patient (Pearson correlations test results: $R = 0.56, p < 0.05$);
- Patient’s subjective satisfaction with the administered medication (Pearson correlations test results: $R = 0.56, p < 0.05$);

The influence exercised by the type of administered medication is presented in Figure 10.

Even if the statistical differences indicated by the $\chi^2$ test are not significant ($\chi^2 = 3.5, p = 0.17$), it can be seen in Figure 10 that non-adherent patients are more frequently found among patients with typical antipsychotic medication.

There are statistically significant differences between the way the attending physician regards the side effects of medication and the way the patients perceive these side effects. Patients tend to give higher importance to the side effects than physicians do (Student Test for independent groups results: $T= -5.61, p = 0.00$)

As a conclusion, patients’ adherence to treatment is influenced both by the traits of the first psychotic episode and the way the patients perceive the side effects and the general utility of the administered medication, which can be different from the way the attending physician consider these effects. The differences between the way patients and physicians perceive the side-effects of administered medication is presented in Figure 11.

The influence of psychotherapy on the patients’ clinical evolution.

From the 69 patients in the final sample, 40 patients have benefited, apart from the psychopharmacological treatment, also from a type of psychotherapy. 20 patients (28.9% of the total sample) have followed a type of systemic family therapy and psychopedagogy therapy, and the other 20 patients (28.9%) have only benefited of psychopedagogy type therapy. The sample distribution on type of treatment is presented in Figure 12.

The Student test for independent groups results are presented in Table 2. These results indicate that
psychotherapy had a positive effect on the global functioning of the patients, but no significant effect on the clinical course of the illness or its severity. The significant difference in the scores assessing the level of global functioning of patients at final evaluation is confirmed by the interpretation of the average scores: patients that benefited of psychotherapy had an average Global Assessment of Functioning (GAF) score showing a level of “mild deterioration in social, professional and/or scholar functioning” and tending towards a “good functioning in all areas”, while patients treated with medication only had an average GAF score showing “mild symptoms or difficulties in social, professional and/or scholar functioning”.

In order to check for differences induced by the types of applied psychotherapy, the T (Student) test was used for independent groups formed by the patients benefited by the two different types of psychotherapy. Statistical differences between average scores on the used scales were not significant. Differences are graphically represented in Figure 13.

**DISCUSSIONS AND CONCLUSIONS**

- Some results of the present study are similar with results of other studies.¹⁰⁻¹³
- The inclusion of first affective episode with psychotic symptoms in the studied sample gives a larger vision on the area of first psychotic episode which is met in daily practice.
- This study gives a greater importance to the parameters of First Psychotic Episode, even for the adherence at the treatment, but also for the response and evolution after specific interventions.
- For future studies it is important to determine if the presence of affective symptoms in the first psychotic episode has any influence in the choice of antipsychotic medication.
- The heterogeneity of antipsychotic agents could influence the physician’s decision.

### Table 2. Scale scores for patients at final evaluation according to the type of administered treatment and the statistic significance of scores’ differences.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Average scores at final evaluation</th>
<th>Statistical difference of average scores (t)</th>
<th>Statistical significance of differences (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with combined treatment: medication and psychotherapy</td>
<td>Patients with medication only</td>
<td></td>
</tr>
<tr>
<td>GAF score</td>
<td>79.75</td>
<td>69.07</td>
<td>2.12</td>
</tr>
<tr>
<td>CGI – severity of illness score</td>
<td>2.85</td>
<td>3.13</td>
<td>-1.12</td>
</tr>
<tr>
<td>CGI – improvement score</td>
<td>1.92</td>
<td>2.27</td>
<td>-1.36</td>
</tr>
</tbody>
</table>

Figure 13.

- The evolution of first psychotic episode could be influenced by the therapeutic strategy.
- Also, the therapeutic response and the clinical and functional evolution in first psychotic episode is influenced by the heterogeneity of antipsychotic agents.
- Patients’ adherence to treatment seems to be influenced by some clinical parameters specific to the first psychotic episode, rather than the type of administered medication. This result is a new perspective for the evaluation of therapeutic adherence.
- Clinical psychiatrists would have to dedicate more time and interest to establishing a therapeutic alliance with their patients with first psychotic episode.
- An individualized strategy is required in order to establish for each patient the adequate means and ways of intervention before initiating any type of therapy.
- The patient’s subjective satisfaction and the
way patients appreciate the utility of administered treatment are important factors to influence the patient's adherence to therapy.

- Ensuring adequate opportunities for the diagnostic and early intervention in cases of first psychotic episode can play a determinant role in the short and long term course of first psychotic episode.

- Combined therapeutic strategies that include medication and psycho-social interventions are most beneficial for inducing a good quality remission in both clinical and functional evolution of FPE patients.

REFERENCES