Factors Associated with Remission in Schizophrenia: 36-Month Results from the Schizophrenia Outpatient Health Outcomes (SOHO) Study

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ABSTRACT

OBJECTIVES: To analyse the frequency and factors associated with achieving remission during 3 years of treatment.

METHODS: SOHO is a 3-year, prospective, observational study of antipsychotic treatment outcomes. Remission was defined as (i) achieving a level of severity of mild or less (<4 in a scale from 1 to 7) in the CGI positive, negative, cognitive, overall severity score that had been maintained for six months or longer, and (ii) Not having any inpatient admission during that period.

RESULTS: 10,927 patients were enrolled and 10,218 patients were eligible for analyses at baseline; 6516 patients were evaluated in the analysis and 6491 of them (67%) achieved remission. The most important baseline factors associated to achieving remission were: being never treated before baseline (OR 1.76; 95% CI 1.34 – 2.30), and having paid employment (1.49; 1.31 – 1.73). Higher CGI severity at baseline (0.67; 0.70 – 0.92), yrs since schizophrenia onset (0.99; 0.96 – 1.02), and male gender (1.83; 1.54 – 2.19) were associated to lower frequency of remission. Taking Quetiapine (0.86; 0.76 – 0.98), Reiprodine (0.74; 0.66 – 0.83), Oral Typicals (0.84; 0.75 – 0.94), Depot Typicals (0.59; 0.50 – 0.69) and Amsulpride (0.73; 0.64 – 0.94) was associated to a lower frequency of remission compared to patients starting Olanzapine.

CONCLUSIONS: Most of the patients on outpatient treatment achieve remission. Employment status, lower clinical severity, female gender and treatment with Olanzapine were factors associated with remission. The results should be interpreted conservatively due to the observational design study.

OBJECTIVES

To analyse the frequency and factors associated with achieving remission during 3 years of outpatient treatment with clozapine, risperidone, quetiapine, amisulpride, orol and depot typical antipsychotic medications.

SOHO STUDY DESIGN

• Prospective, non-interventional, observational study: All patient care was at the discretion of the participating psychiatrists.

• Patient selection criteria: Outpatients and inpatients were included for correlation among patients.

• Patients followed for 3 years: Assessments at 3, 6, 12, 18, 24, 30 and 36 months post-baseline.

• Ten European countries participated in SOHO: Denmark, Greece, Netherlands, Spain, France, Ireland, Portugal, United Kingdom, Germany, Italy.

METHODS

• Depending on the antipsychotic initiated at baseline, patients were grouped in the following cohorts:
  - Clozapine
  - Olanzapine
  - Risperidone
  - Quetiapine
  - Oral atypical antipsychotics
  - Depot atypical antipsychotics

• 10,927 patients were enrolled at baseline; 6516 patients were evaluated at 36 months and have no more than one missing visit, were included in the analysis. Missing visits were imputed from the previous visit.

• Remission was defined as achieving a level of severity of mild or less (<4 in a scale from 1 to 7) in the CGI positive, negative, overall severity score that had been maintained for six months or longer, and (ii) Not having any inpatient admission during that period.

• A logistic regression model was used to analyse factors associated with remission.

• Since remission was defined as having a low disease severity for a period of at least six months, the follow-up observations were divided into 6-month periods (6–12 months, 12–18 months, 18–24 months, 24–30 months and 30–36 months). Each 6-month period was an observation in the statistical model. A Generalized Estimating Equation (GEE) model with a logit link and an unstructured covariance matrix was used to account for correlation among observations.

• The covariates included in the model were: socio-demographic, patient, country, sex; Clinical: age at first treatment for schizophrenia, time since first treatment, alcohol dependence, substance abuse, suicide attempts, overall CGI, positive CGI, negative CGI, depressive CGI, cognitive CGI, hostility, compliance, body mass index; Social functioning: marital status, living independently, having paid employment, being socially active; Tolerability: extra-pyramidal symptoms, amenorrhea; gynecomastia; weight gain.

Medication Started at Study Entry for the Patients Included in the Analysis

- clozapine
- olanzapine
- quetiapine
- risperidone
- amrisulpride
- depot atypical antipsychotics
- oral atypical antipsychotics

Medication started at study entry for the patients included in the analysis.

<table>
<thead>
<tr>
<th>Medication Initiated</th>
<th>N=6,516</th>
</tr>
</thead>
<tbody>
<tr>
<td>clozapine</td>
<td>52.3%</td>
</tr>
<tr>
<td>olanzapine</td>
<td>25.8%</td>
</tr>
<tr>
<td>quetiapine</td>
<td>1.4%</td>
</tr>
<tr>
<td>risperidone</td>
<td>0.4%</td>
</tr>
<tr>
<td>amriusulpride</td>
<td>0.4%</td>
</tr>
<tr>
<td>depot atypical</td>
<td>2.9%</td>
</tr>
<tr>
<td>oral atypical</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

Proportion of Patients Who Achieved Remission During Three Years of Treatment

<table>
<thead>
<tr>
<th>Remission (N=4206)</th>
<th>No Remission (N=2310)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>10.6 (10.2)</td>
<td>14.0 (11.7)</td>
</tr>
<tr>
<td>28.7 (10.2)</td>
<td>28.1 (10.2)</td>
</tr>
<tr>
<td>4.2 (1.0)</td>
<td>4.8 (0.8)</td>
</tr>
<tr>
<td>3.8 (1.3)</td>
<td>4.8 (1.1)</td>
</tr>
<tr>
<td>3.5 (1.3)</td>
<td>4.2 (1.3)</td>
</tr>
<tr>
<td>26.0 (4.6)</td>
<td>26.7 (5.1)</td>
</tr>
<tr>
<td>55.2%</td>
<td>62.1%</td>
</tr>
<tr>
<td>11.7%</td>
<td>0.75%</td>
</tr>
<tr>
<td>24.4%</td>
<td>10.7%</td>
</tr>
<tr>
<td>2.1%</td>
<td>2.3%</td>
</tr>
<tr>
<td>33.7%</td>
<td>41.9%</td>
</tr>
<tr>
<td>8.6%</td>
<td>10.7%</td>
</tr>
<tr>
<td>18.1%</td>
<td>17.6%</td>
</tr>
<tr>
<td>36.1%</td>
<td>43.1%</td>
</tr>
</tbody>
</table>

Odds Ratios of the Baseline Factors Found to be Associated with Lower Frequency of Achieving Remission

- Clozapine
- Olanzapine
- Risperidone
- Quetiapine
- Oral atypical antipsychotics
- Depot atypical antipsychotics
- CGI Positive score at baseline
- CGI Overall severity score at baseline
- Age at first treatment for schizophrenia
- Years since first treatment for schizophrenia
- Use of antidepressants
- Use of mood stabilizers
- Substance abuse at baseline
- Achievement of remission
- Extra-pyramidal symptoms

FINDINGS

- Approximately 65% of the sample achieved remission over the 36-month follow-up period.
- Being female, having good social functioning, and a shorter duration of illness were factors significantly associated with achieving remission.
- A higher clinical severity and the use of concomitant medication were associated with a lower frequency of remission.
- Treatment with olanzapine was associated with a higher likelihood of remission compared to treatment with typical antipsychotics, amisulpride, chlopizephine, quetiapine, 2+ antipsychotics and risperidone.

LIMITATIONS

- Our measure of remission was based on the CGI scale, which is not specifically a measure of clinical severity in schizophrenia but rather a measure of overall severity.
- The results should be interpreted conservatively due to the observational study design.

CONCLUSIONS

- A high proportion of patients achieving remission at some point during follow-up in the SOHO study.
- As it was expected, social integration and participation predicted a favourable clinical course.
- We have found that duration of illness influenced the probability of achieving remission. Thus, the probability of remission tends to decrease over the longitudinal course of the disease.
- Clozapine was the medication associated to a higher frequency of remission.
- Olanzapine, which was associated with a lower frequency of remission than clozapine, was used for severe treatment-resistant patients, who may improve with treatment but not enough to achieve remission.