A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia

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Rationale

• Schizophrenia (SZ) is a chronic, severe and disabling mental disorder. The disorder is characterized by a variety of clinical manifestations, including symptoms that are both positive and negative, reduced social function and community participation, and cognitive impairment.

• Medication nonadherence rates are high in schizophrenia, as they are in many chronic medical conditions.

• Currently there is a dearth of long-term data comparing the use and effectiveness of depot and oral antipsychotics after first-episode psychosis.

Aim of the study

• To evaluate the risk of rehospitalization and drug discontinuation in a nationwide cohort of 2,588 patients hospitalised for the first time with schizophrenia during 2000-2007 in Finland.

Study design and outcome measures

• The study was conducted as a register-based case linkage study utilizing data on hospitalization, mortality and antipsychotic prescriptions. The primary outcome measures were
  1) all-cause discontinuation of the initial antipsychotic medication,
  2) reshospitalization due to schizophrenia, and
  3) death from any cause.

Statistical evaluation of the results

• Hazard ratios with 95% confidence intervals (CI) were calculated.
Data sources

- **Hospital Care Register**
  - Diagnosis ICD-10 codes F20-F25
  - Start and discharge date
  - Age, sex
  - Hospital & hospital district

- **Prescription Register**
  - Drug substances ATC code N05A
  - Date of purchase
  - Amount (DDD)
  - VNR-code (package code)

- **Cause of Death Register**
  - Causes of death (ICD10)
  - Date of death

- All patients with at least one hospitalization due to schizophrenia-related illness (ICD-10 codes F20–F25) during 2000-2007 were identified from the Finnish hospital care register.

- Data on medications, hospitalizations and mortality were collected for this study cohort.

- Focus on this article is on naïve patients who had a strictly defined schizophrenia diagnosis (F20) during their first hospitalization.
Description of study population

Hospitalizations in 2000-2007
Diagnosis ICD-10 codes F20-F25
\[ N_{\text{patients}} = 33,318 \]
\[ N_{\text{hospitalizations}} = 122,193 \]

Naïve cohort
Diagnosis ICD-10 codes F20-F25
\[ N_{\text{patients}} = 7,434 (22\%) \]

Longer illness cohort
Diagnosis ICD-10 codes F20-F25
\[ N_{\text{patients}} = 25,884 (78\%) \]

Definition of the naïve cohort
- No prior hospitalization with F20 – F25 diagnoses
- No antipsycotics use within 6 months prior to the first hospitalization

Study population:
- 16-65 years of age, mean age 37.5 years
- 62% male, 38% female

Schizophrenia
ICD-10 F20
\[ N_{\text{patients}} = 25,884 (34.8\%) \]

Schizotypal disorder
ICD-20 F21
\[ N_{\text{patients}} = 331 (4.5\%) \]

Persistent delusional disorder
ICD-10 F22
\[ N_{\text{patients}} = 1,363 (18.3\%) \]

Acute and transient psychotic disorders
ICD-10 F23
\[ N_{\text{patients}} = 2,689 (36.2\%) \]

Induced delusional disorder
ICD-10 F24
\[ N_{\text{patients}} = 11 (0.1\%) \]

Schizoaffective disorder
ICD-10 F25
\[ N_{\text{patients}} = 452 (6.1\%) \]
Risk of all-cause discontinuation of initial medication

- Of 2,588 patients with a first hospitalization
  - 1,507 (58.2%) used antipsychotic medication during the first 30 days after discharge
  - 1,182 (45.7% of total) continued using the initial antipsychotic medication for 30 days and longer

- During a mean follow-up period of 2 years 1,394 patients (53.8%) discontinued their initial antipsychotic
Risk of rehospitalization

- During a mean follow-up period of 2 years, 1,496 patients (57.8%) were rehospitalized because of relapse of schizophrenia symptoms.

- The use of any antipsychotic was associated with a 62% (95% CI 57%-66%) lower risk when compared to no treatment at all.

- Oral clozapine and olanzapine were associated with lowest risk for rehospitalization.
Risk of discontinuation of initial medication

- In pooled analysis the depot antipsychotics were associated with a 59% lower risk of discontinuation (hazard ratio=0.41, 95% CI=0.27–0.61, p<0.0001) and with a 64% lower risk of rehospitalization (HR=0.36, 95% CI=0.17–0.75, p=0.007) than their respective oral formulations.
Conclusions

• The first study of the adherence and comparative effectiveness of specific antipsychotic treatments in a large unselected population of patients in a real-world setting.

• Only a minority of patients are adherent to their initial antipsychotic during the first 60 days after discharge from their first hospitalization for schizophrenia.

• Oral clozapine and olanzapine were associated with more favorable outcomes regarding treatment discontinuation and rehospitalization.

• Use of depot antipsychotics was associated with a significantly lower risk of treatment discontinuation and rehospitalization than use of oral formulations of the same compounds.

• Use of any antipsychotic was associated with a 55% lower mortality (hazard ratio=0.45, 95% CI=0.31–0.67) when compared with no antipsychotic treatment at all.
Acknowledgements

• The study was supported by the Annual EVO Financing (special government subsidies from the Ministry of Health and Welfare, Finland) and by Janssen-Cilag.

• The funders were not involved in the conduct of the study or in the collection, management, analysis, or interpretation of the data.

• The research permission numbers to use the data were obtained from
  ▪ the Social Insurance Institute (Kela 14/522/2009),
  ▪ the National Institute for Health and Welfare (Dnro 206/5.05.00/2009),
  ▪ Statistics Finland (TK-53-739-09)