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REVIEW ARTICLE

Non-adherence to pharmacological treatment in schizophrenia and schizophrenia spectrum disorders – An updated systematic literature review

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Abstract
Background and objectives: The primary treatment for schizophrenia and schizophrenia-spectrum disorders is antipsychotic medication. One of the many public health challenges in mental illness, is to identify contributing factors to non-adherence to pharmacological treatment. The objective of this study was to perform an updated systematic review of risk factors for non-adherence to pharmacological treatment in schizophrenia in a European and American context.

Methods: The study was a systematic literature review of studies that included at least two measurements of pharmacological adherence in adult schizophrenic patients. This was done to validate the measures of adherence adequately which is rarely done in previous adherence research. It was conducted using PRISMA guidelines surveying Pubmed and PsycINFO.

Results: The definition of non-adherence varies greatly in eligible studies and the methodological approach to investigation of non-adherence is inconsistent. Thirteen studies fit the inclusion criteria and demonstrated several risk factors statistically influencing non-adherence rates. The most frequent risk factors identified for non-adherence were poor insight into or lack of awareness of illness, alcohol or drug abuse and unspecified younger age.

Conclusions: The findings in this systematic literature review are consistent with previous reviews on non-adherence and schizophrenia. It stresses the methodological challenges in psychiatric adherence research and establishes the need for more systematic and rigorous study design and methods within this field.

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Introduction

Mental illness affects all ages, ethnic, racial, socioeconomic and cultural groups.[1] No part of the world is exempted from these diseases and the burden of mental illness can therefore be considered a global public health problem.[2]

Schizophrenia is a major group of mental disorders characterized by psychosis. The causes are multifactorial and still largely unknown. The primary treatment for schizophrenia and schizophrenia-spectrum disorders is pharmacological and the most widely applied medications are second generation antipsychotics (SGA).[3] SGA are administered orally or as long acting injection therapy (LAI), that were developed especially to improve adherence.[4] Maintenance therapy with LAI has been shown to reduce relapse with relative and absolute risk reductions of 30% and 10% respectively[5] and have been associated with 50–65% reduction in re-hospitalization.[6]

Side-effects of pharmacological treatment are common and can significantly influence patient's quality of life. The older first generation antipsychotics (FGA) can cause extrapyramidal symptoms, dry mouth and sedation as well as rare, but serious, side effects such as neuroleptic malignant syndrome and tardive dyskinesia. SGA have a different side effect profile linked to metabolic and cardiovascular complications often resulting in sexual dysfunction and reproductive complications, disruption in normal hormone production, weight gain, diabetes as well as cognitive deficits.[7–9] The specific substance Clozapine, which is widely considered the golden standard of treatment of schizophrenia, also have an increased risk of possibly fatal agranulocytosis compared to other SGA.[5,10,11]

One of the many challenges in treatment of mental illness is to identify contributing factors to non-adherence to pharmacological treatment as non-adherence is a known predictor for relapse and re-hospitalization.[12,13] Patients who are non-adherent are 70% more likely to be hospitalized compared to patients with partial adherence, who are 30% more likely to be hospitalized than adherent patients.[12] The economic cost of patients who have relapse of illness are three times higher than stabile patients and relapse leads to increased morbidity, mortality and decreased quality of life.[12–14]

Within adherence research, both subjective and objective measures of adherence are applied. Objective measures are derived from clinical measurements such as blood and urine samples and are generally considered to be reliable but also expensive and intrusive for patients. Subjective measures are the most frequently applied measurement in adherence research with approximately 75% of current literature using information derived from patient, family or clinician.[15] Both types of measurement have limitations when applied in clinical studies and methodology of current adherence research is heterogeneous.

This systematic literature review provides an updated assessment on factors associated with non-adherence. Furthermore it aims to evaluate the rate of non-adherence as well as expose and address potential methodological limitations within adherence-research.

Material and methods

Search strategy

This study was a systematic review conducted according to the PRISMA Statement for transparent reporting of systematic reviews.[16] PubMed/Medline and PsycINFO was searched for a combination of the following terms: antipsychotic, neuroleptic, adherence, non-adherence, nonadherence, non adherence, compliance, non-compliance, noncompliance, non compliance, schizophrenia, risk factor, risk factors predictor, predictors. The search was restricted to articles published from 1 January 1990–31 December 2014.

Study selection

English language articles that were randomized clinical trials or observational studies were included if they assessed quantitative risk factors for non-adherence to psychopharmacological treatment in adults (age 18–65) with validated schizophrenia or schizophrenia-spectrum disorders (defined by ICD9/10 or DMS-IV/V). Adherence must be assessed by a minimum of two measurements and the study-population must represent the working age general population in the developed world, thereby excluding subpopulations such as veterans, adolescents and the elderly as well as studies from the developing world.

Titles and abstracts were screened and full-text articles were retrieved if they appeared relevant or if there was some ambiguity as to whether the article was relevant. References in all included articles were reviewed and included in the systematic review if they meet the inclusion criteria.

Data extraction and quality assessment

From each of the included studies the following characteristics were extracted:

Study-specific: Country of origin, study design, study period, population size as well as age, sex and ethnicity of included patients.

Treatment-specific: Type of antipsychotic treatment (FGA/SGA), medication administration regime (Oral/LAI) and setting (Inpatient/Outpatient) were extracted if available.

Adherence-specific: Rate of adherence and type of measure (subjective/objective and dichotomous/categorical) as well as reported risk factors for non-adherence, divided into patient-related, mental illness-related, medication-related and environmental-related risk factors for non-adherence.

The quality of each included study was critically appraised using The STROBE Statement checklist for cross-sectional, cohort and case/control studies,[17] and The Quality Assessment Tool for Observational Cohort and cross-sectional studies developed by the National Institute of Health (NIH).[18]