Original article

Chronic physical illnesses in patients with schizophrenia spectrum disorders are independently associated with higher rates of psychiatric rehospitalization; a cross-sectional study in Croatia

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ABSTRACT

Background: Increased physical morbidity in patients with schizophrenia spectrum disorders (SSDs) is well documented. However, much less is known about the association between somatic comorbidities and psychosis treatment outcomes.

Subjects and methods: This cross-sectional study, nested within the larger frame of a prospective cohort study, was done in 2016 at Psychiatric Hospital Sveti Ivan, Zagreb, Croatia. Data were collected on a consecutive sample of 301 patients diagnosed with schizophrenia spectrum disorders who achieved a stable therapeutic dosage. Key outcome was the number of psychiatric rehospitalizations since diagnosis of the primary psychiatric illness. Predictors were number of physical and psychiatric comorbidities. By robust regression, we controlled different clinical, sociodemographic, and lifestyle confounding factors.

Results: The number of chronic somatic comorbidities was statistically significantly associated with a larger number of psychiatric rehospitalizations, even after the adjustment for number of psychiatric comorbidities and large number of other clinical, sociodemographic, and lifestyle variables.

Conclusions: Chronic somatic comorbidities are associated with higher rates of psychiatric rehospitalization independently of psychiatric comorbidities and other clinical, sociodemographic, and lifestyle factors. Therefore, to treat psychosis effectively, it may be necessary to treat chronic somatic comorbidities promptly and adequately. Chronic somatic comorbidities should be considered equally important as the SSD, and should be brought to the forefront of psychiatric treatment and research with the SSD as one entity. The integrative approach should be the imperative in clinical practice.

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1. Introduction

Schizophrenia spectrum disorders (SSDs) are among the top 10 causes of disability worldwide [1]. In addition to causing disabling psychiatric symptoms, schizophrenia is associated with frequent physical illness [2-3]. People diagnosed with psychosis have a 2.5 times higher risk of dying than the general population [3-4]. Mortality rates in the population with psychiatric disorders and the difference in mortality between patients diagnosed with psychosis and the general population has been increasing [3-5]. Psychiatric patients die earlier of similar causes than do the general population (e.g., heart disease, cancer, and cerebrovascular and respiratory diseases), and these patients account for more than two thirds of this excess mortality [3-9].

The adverse effects of psychiatric pharmacotherapy, high prevalence of unhealthy lifestyle and modifiable risk factors further increase the risks. Schizophrenia is, however, increasingly recognized as a systemic disorder and these patients face an additional burden in terms of somatic comorbidity implying overlapping and interacting disease mechanisms that involve

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neurotransmitter, inflammatory, endothelial and hormonal pathways among others [10–13]. Growing body of evidence has demonstrated that people with psychosis are at greatly increased risk of chronic physical comorbidities (cardiovascular disease, metabolic syndrome, diabetes, and respiratory disease) [10,11]. Furthermore, somatic comorbidities in psychiatric patients may be associated with the poor health related quality of life, independently of different sociodemographic, vital and clinical factors [12]. Also, it has been established that somatic comorbidities, as well as the negative association of somatic comorbidities with patients’ quality of life, are related to pharmacological treatment of psychosis [12–15]. However, access to preventive interventions, the quality of detection, diagnosis, and adequate treatment are still lower in psychotic than in non-psychiatric patients [5,6,10,16–19]. The prevalent current approach still separates physical and mental health care [20,21].

Despite these facts, less is known about the association of somatic comorbidities with the outcome of treatment of psychosis.

Several studies addressed the problem from this “reverse perspective” [22–26], but we have not found conclusive evidence that somatic comorbidities affect symptom exacerbation of schizophrenia spectrum disorders nor the efficacy of their treatment. The objective of this study was to explore whether the number of chronic physical illnesses is associated with a poorer SSD treatment outcome indicated by higher rate of psychiatric rehospitalizations independently of psychiatric comorbidities, and other clinical and sociodemographic parameters.

2. Methods

2.1. Study design

This cross-sectional study enrolled patients during 2016 at Psychiatric Hospital Sveti Ivan, Zagreb, Croatia. The study was nested within the larger frame of a prospective cohort study named, “Somatic comorbidities in psychiatric patients (SCPP)”, which has an expected end date of June 2017. The main study protocol was registered at ClinicalTrials.gov (NCT02773108), and it was approved by the Ethics Committee of Psychiatric Hospital Sveti Ivan. Informed consent was obtained from all patients. The study complied with World Medical Association Declaration of Helsinki 2013 [27].

2.2. Study population

The targeted population was patients diagnosed with SSDs (ICD-10; DSM-V) who were treated in a psychiatric hospital and achieved a stable therapeutic dosage. Inclusion criteria were ICD–10 (F20–F29); DSM-V: schizophrenia spectrum disorders, both genders, age ≥18 years, treated in a psychiatric hospital as inpatients or outpatients, and ability to answer the questionnaire. Exclusion criteria were acute suicidality; dementia, mental retardation, acute psychosis, and intoxication. We chose a consecutive sample of outpatients by the order of their arrival at the exam, and all patients who were hospitalized during the enrollment period.

2.3. Needed sample size

Power analysis was performed before the start of the enrolment as the component of power analysis performed for the main prospective cohort study. A sample size of 231 achieves 90% power to detect an $R^2 ≥ 0.05$ attributed to two independent variables: number of physical illnesses and number of psychiatric comorbidities, using a F-test with a significance level ($α$) of 0.05. The independent variables tested will be adjusted for an additional 10 possible confounding variables with an $R^2 ≥ 0.05$. Expecting up to 15% of respondents would have missing data on dependent (number of hospitalizations) and independent variables, the initially needed sample size was determined to be $n = 272$. Power analysis was done in PASS 14 Power Analysis and Sample Size Software (2015) (NCSS, LLC, Kaysville, Utah, USA).

2.4. Outcomes

Our outcome was the number of psychiatric hospitalizations since diagnosis of the primary psychiatric illness. This is not a direct measure of clinical success, however, it has been used in many observational studies as an outcome measure to evaluate antipsychotic effectiveness (e.g. [28–31]) and, as Burns concluded, it showed as a good proxy outcome measure in schizophrenia [32]. The number of rehospitalizations was assessed objectively from hospital records archived in Psychiatric Hospital Sveti Ivan. We used the row number and not the standardized one (e.g., average number of hospitalizations annually) because we planned to control duration of illness since diagnosis and patients’ age by multivariate analysis.

2.5. Independent variables (predictors)

Our independent variables were number of chronic somatic comorbidities and the number of psychiatric comorbidities. Chronic somatic illness was defined as the non-mental illness that requires medical treatment and lasted for at least six months. Trained psychiatrists recorded all comorbidities after consultation of medical records and clinical interview.

2.6. Possible confounders

Possible confounders whose effect we tried to control by multivariate analysis were sex, age, education, marital status, number of household members, work status, diet, smoking, excessive alcohol consumption, physical activity, duration of primary psychiatric illness, severity at diagnosis measured by the Clinical Global Impression-Severity (CGI-S) scale, antidepressants and benzodiazepines. Alcohol consumption was measured by self-completion of 7-item Alcohol Use Disorders Identification Test (AUDIT) and 2nd wave European Health Interview Survey (EHIS) questions on frequency and number of standard alcoholic drinks [33]. We calculated the average number of standard alcoholic drinks daily based on questions AL2. “Thinking of Monday to Thursday, on how many of these 4 days do you usually drink alcohol?” and AL3. “Number of alcoholic (standard) drinks on average on one of the days (Monday to Thursday)”, and the same two questions for the period Friday to Sunday (AL4 and AL5). Excessive alcohol consumption was defined as more than 20 g/day (2 standard units) for men and 10 g/day (1 standard unit) for women [34]. Duration and intensity of average PA was measured by EHSIS-PAQ [35]. The instrument was developed for the second wave of European Health Interview Survey (EHIS). According to recent validation, it has good validity and reliability [36]. EHSIS-PAQ referent time is “average week”. Total PA defined as proportion of individuals being sufficiently physically active in total, that is who are performing ≥150 minutes of aerobic PA or ≥2 muscle-strengthening PA weekly [35].

2.7. Statistical analysis

The level of statistical significance was set at $P < 0.05$, and we gave all confidence intervals at 95% level. In all instances, we used two-tailed tests. According to the protocol, it was planned that in
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