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ORIGINAL PAPER

Optimization of Antipsychotic and Benzodiazepine Drugs in Patients with Severe Mental Disorders in an Intensive Case Management Program

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Abstract

The Intensive Case Management (ICM) model is a community-based program for people with severe mental illness that may reduce hospitalization and increase retention in care. The aims of this study were to analyze changes in the antipsychotic and benzodiazepine dosage in 106 patients who participated in an Individualized Service Program based on the ICM model for at least 6 months and to assess the change in the number of patients taking a high or very high dose of an antipsychotic drug and the number receiving antipsychotic polytherapy. Both the average daily dose of antipsychotic and benzodiazepine drugs and the number of patients with high doses of antipsychotic and more than one antipsychotic drug decreased significantly. Implementing the ICM program in patients with severe mental illness could help to decrease adverse drug effects and health care expenditures.

Keywords Severe mental illness · Assertive Community Treatment · Intensive Case Management · Psychosis · Antipsychotics · Benzodiazepines

Introduction

In 1980, when Stein and Santos defined a new intensive treatment model to facilitate the de-institutionalization of patients with severe and persistent mental illness, Assertive Community Treatment (ACT) was born (Stein and Test 1980). From this origin, ACT was implemented successfully in the United States and later replicated in Australia (Hoult 1986) and elsewhere. In an effort to assess the impact of implementing the ACT program in London, a randomized clinical trial (REACT) was designed in 2006. The study found increased adherence to drug treatment and greater patient satisfaction, but no differences were observed in the number of hospitalizations or their clinical and social outcomes (Killaspy et al. 2006). Similar results were later obtained in the Netherlands (Sytema et al. 2007).

The ACT model has three basic characteristics: a team approach, a small caseload (1/10), and shared responsibility for each patient among the entire team of professionals and paraprofessionals providing needed services. Professionals meet with the patient in the appropriate place for each situation, with 24-h crisis care available 7 days a week. Each intervention is individualized for each patient according to

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his or her need, case reports are discussed daily, and decision-making is rapid and flexible (Behavioural Health Planning Council 2003).

The case management (CM) model emerged in the 1960s because of a need to coordinate access to medical and psychiatric care for patients with severe mental illness. Within this model, the health professional puts the patient in contact with the different services needed, including mental health services, without intervening directly. Direct involvement with the patient is more limited than in the ACT model. An exhaustive Cochrane review of the CM model's effectiveness in reducing admissions found instead that admissions nearly doubled [odds ratio (OR) 1.84] and clinical evidence was lacking to recommend CM implementation in public health programs (Marshall et al. 2000).

A more recent model, Intensive Case Management (ICM), is a community-based program for patients with severe mental illness that evolved from these two earlier community models of care, ACT and CM, and emphasizes the importance of a small caseload (< 20 patients) and high-intensity input. Although ICM programs often lack one or more core elements of ACT programs, this new approach is effective in achieving important outcomes in people with severe mental illness. Compared to standard care, ICM may reduce hospitalization and increase retention in care (Dieterich et al. 2017), suggesting that it might not be necessary to apply the full ACT model in order to reduce the need for inpatient care (Burns et al. 2007).

In Catalonia, the care program specifically designed for patients with severe mental illness (Consell Assessor sobre Assistència Psiquiàtrica i Salut Mental 2003) establishes an Individualized Services Program (ISP) based on the CM model for patients who require extensive support to address their difficulties with interpersonal relationships and poor social functioning, and who consume a great many health resources.

The Mental Health Network of Osona, a county in central Catalonia, has adopted the ISP, adapting it to their population and their needs and moving from a CM to an ICM model that incorporates the main elements of the ACT program. This ICM initiative began with an integrated model, in which the same mental health professionals visit both hospitalized patients and outpatients. The monitoring program for drug dependency is also incorporated into this mental health network, as well as a program for people with severe mental illness that includes interdisciplinary meetings and promotes assertive attitudes. For these reasons, the program was able to implement key ACT characteristics, such as assigning a lower caseload of patients, working with the patient in the community, making home visits, and actively helping patients gain access to resources in health care, rehabilitation, employment, and recreation. The program relies on a multidisciplinary team approach, always including a psychiatrist and a psychologist as well as a nurse, social worker, and nursing assistants, and the same team of professional's shares responsibility for patient follow-up and care for all the patients assigned to the team. The Osona ISP program lacks some elements of the original ACT model because the team is available to patients Monday to Friday from 8 am to 7 pm, with patients referred to conventional emergency department services overnight and on weekends.

Drug Therapy

Antipsychotic drugs provide the basis for symptomatic treatment of psychotic disorders, and for schizophrenia in particular. The main guidelines on using antipsychotics for the treatment of the schizophrenia spectrum disorders recommend the use of a single drug (monotherapy) and adding a second antipsychotic before trying clozapine monotherapy (Lehman et al. 2004; National Collaborating Centre for Mental Health 2009). However, several published studies around the world show the high prevalence (up to 50%) of treatment with more than one antipsychotic drug (polytherapy) (Kroken et al. 2009; Barnes and Paton 2011). In recent decades, the average daily doses of antipsychotic (Clark et al. 2002) and antipsychotic polytherapy (Clark et al. 2002; Nielsen et al. 2010) have increased. Two randomized studies of changing from polytherapy to monotherapy in stabilized patients show contradictory results; one observed no complications and the other reported an increase in clinical psychosis (Yamanouchi et al. 2015; Constantine et al. 2015).

The available evidence on the risks and benefits of using high doses of antipsychotic drugs is mixed, and generally not considered adequate to justify a recommendation for routine use. A systematic review of 30 randomized clinical trials on the use of antipsychotics in patients with schizophrenia or schizoaffective disorder, carried out by the Canadian Health Agency in 2012, found marginal improvements in efficiency with high doses or combinations of antipsychotics, compared with standard doses or monotherapy; they did not find evidence of adverse effects, except for the combination of clozapine with a second antipsychotic drug (Canadian Agency for Drugs and Technologies in Health 2012).

Treatment with high doses of antipsychotics (both typical and atypical drugs) may encourage the emergence of serious adverse effects such as cardiac arrest and sudden death (Ray et al. 2009; Torniainen et al. 2015). To raise awareness among mental health professionals about the safe use of high doses of antipsychotics, the English national health system (National Health Service Foundation Trust 2012) published a document that recommends, among other things, individual recording and regular monitoring of physical health as well as possible drug interactions.

Although the use of benzodiazepines to enhance antipsychotic medication is common in clinical practice, a recent

meta-analysis found no evidence of any positive effect, and recommended that their use should be restricted to very specific situations (e.g., agitation) and of short duration (Dold et al. 2013).

Finally, apart from antipsychotic therapy, which has a key role in the treatment of severe mental disorders, cognitive-behavioural therapy has been effective in improving chronic psychotic symptoms that are resistant to antipsychotic treatment. This psychological therapy is based on the stress–vulnerability model of psychiatric disorders and on the cognitive mechanisms that underlie psychotic symptoms (Garety et al. 2000; Rathod et al. 2008).

We only found a study that measures the variation in the dose of antipsychotic drugs in a model of community treatment. After a year of monitoring in an ACT program, outpatients in Japan who were diagnosed with schizophrenia and other related disorders showed a significant decrease in the average daily dose of antipsychotics they received, but not in the number of patients with antipsychotic polytherapy (Satake et al. 2011).

Objectives

1. To analyze changes in dosage of antipsychotics and benzodiazepines when patients are discharged from the ICM program compared to dosage at ICM admission.
2. To evaluate, in the majority group of patients on the schizophrenia spectrum, whether ICM participation decreased (a) the dosage of antipsychotic medication and (b) the number of patients receiving antipsychotic polytherapy.

Working Hypothesis

1. Incorporating ICM will lead to a reduction in the daily dose of antipsychotics and benzodiazepines.
2. In the group of patients on the schizophrenic spectrum, the ICM will lead to a reduction in the number of patients taking high doses of antipsychotic drugs and the number of patients treated with more than one antipsychotic.

Methodology

Study Design

A retrospective analysis assessed patterns of drug therapy in patients with severe mental disorders before and after participation in an individualized program of psychiatric services based on the ICM model.

Participants

All current and discharged patients who received care from the ISP of the Mental Health Network of Osona between November 2006, when it was implemented, and November 2015 were eligible for inclusion, regardless of comorbidity with mental retardation or drug addiction.

Study Population: Sample Size and Selection

The Mental Health Network of Osona has treated 106 patients in the ACT-based program for at least 6 months. The researchers did not calculate a sample size or select a study population because anonymized data for all patients meeting the inclusion criteria were analyzed.

Information Sources

All study data were obtained from the electronic medical records system of the Consorci Hospitalari de Vic. The local Ethics Committee approved the study, which followed established protocols for anonymization of data.

Main Outcome Variable

The change observed in the mean daily dose of antipsychotics and benzodiazepines between the date of inclusion in the program and date of discharge (or data collection date if not yet discharged) was recorded. The mean daily dose of antipsychotics was calculated by converting the dosage to olanzapine equivalents, in accordance with expert consensus (Gardner et al. 2010). In the case of antipsychotic polytherapy, each dose was converted to its olanzapine equivalent and the two values were added together. Benzodiazepine dosage was converted to diazepam equivalents (Villa Alcázar and Esteban Calvo 2011). The number of patients taking high and very high daily doses of antipsychotics was also recorded (>20 mg and >30 mg olanzapine equivalent, respectively), along with the number of patients taking antipsychotic polytherapy (>2 and >3 antipsychotics).

Independent Variables

The following independent variables were recorded: age, sex, main clinical diagnosis and comorbidities of interest (drug abuse or dependency and mental retardation).

Statistical Analysis

Quantitative variables were summarized and distributions were described using means and standard deviations (SD). Qualitative variables were described using frequency distributions, percentages, and median values. Bivariate analysis

was done using parametric and nonparametric tests. Differences before and after program participation (or date of data of collection) were compared using paired *t* tests.

Results

Age and Sex

Of the 106 patients, 59.4% were men and 40.6% were women. The mean age was 40.5 (SD 12.5). There was no age difference between men and women. (T test > 0.05).

Diagnoses

Most of the patients (81 [76.4%]) had a schizophrenia spectrum disorder: schizophrenia, delusional disorder, schizoaffective disorder or schizotypal personality disorder; 19 patients (17.9%) had affective disorder (bipolar disorder and recurrent major depression); and 6 patients (6.6%) had other diagnoses (Table 1).

Comorbidities: Abuse, Drug Dependency, Mental Retardation, Personality Disorder

Forty nine patients (48.2%) met the criteria for drug abuse or dependence, including alcohol, cannabis, cocaine and/or heroin. Eleven patients were dependent on one drug and five patients on two or three drugs. Seventeen patients (16.0%) had mild to moderate mental retardation and seven patients (6.6%) had a borderline personality disorder, but not as a primary diagnosis.

Table 1 Distribution by primary diagnosis (N = 106)

Schizophrenia spectrum disorders	
Schizophrenia	56
Schizoaffective disorder	17
Delusional disorder	1
Schizotypal personality disorder	7
Subtotal	81
Mood disorders	
Bipolar disorder	13
Major depressive disorder	6
Subtotal	19
Other disorders	
Obsessive/compulsive disorder	2
Borderline personality disorder	4
Subtotal	6
Total	106

Decrease in Average Daily Dose of Antipsychotics and Benzodiazepines

Between program admission and discharge (or the date when data were recorded), the average daily olanzapine-equivalent dose of antipsychotic drugs decreased significantly: 4 mg in the overall group and 5 mg in the group with a diagnosis on the schizophrenia spectrum (Table 2).

In the overall group, and in the groups of the schizophrenia and affective spectrum, there were significant differences in the mean daily dose of benzodiazepines (converted to diazepam equivalents). The average decrease was 9 mg of diazepam in the group of the schizophrenia spectrum and 19 mg in the group on the affective disorders (Table 3).

There were significant differences in the average daily doses of both antipsychotics and benzodiazepines (chi square, $p < 0.05$).

Number of Patients Taking High Doses of Antipsychotic Drugs

Doses of antipsychotics are considered high when the average daily olanzapine-equivalent dose exceeds 20 mg (maximum dose recommended on the technical chart) and very high when the dose exceeds 30 mg.

The number of patients with high doses of antipsychotics decreased from 54 to 48 and very high doses from 38 to 28. The group of patients on the schizophrenia spectrum had a higher percentage of high and very high doses of

Table 2 Mean daily dose of antipsychotic drugs, converted to mg olanzapine, before and after ISP program participation (all patients)

	ISP admission[a] Mean (SD)	ISP discharge[a] Mean (SD)
Schizophrenia spectrum disorders	30.56 (2.11)	25.45 (1.73)
Mood disorders	15.38 (3.63)	14.48 (3.57)
Other disorders	7.91 (3.66)	9.26 (3.24)

[a]Total daily dosage of antipsychotic drug (in mg olanzapine equivalents)

Table 3 Mean daily dose of benzodiazepines, converted to mg diazepam, before and after ISP program participation (all patients)

	ISP admission[a] Mean (SD)	ISP discharge[a] Mean (SD)
Schizophrenia spectrum disorders	17.26 (3.41)	8.00 (1.36)
Mood disorders	41.09 (14.5)	22.23 (12.3)
Other disorders	25.83 (15.02)	10.71 (2.47)

[a]Total daily dosage of benzodiazepines (in mg diazepam equivalents)

antipsychotics. In this group, the number of patients with high doses of antipsychotics decreased from 49 to 45 and very high doses from 34 to 26. The results showed significant differences (chi square, $p < 0.05$).

Number of Patients Taking More Than One Antipsychotic Drug

The number of patients diagnosed on the schizophrenia spectrum who were taking two or more antipsychotic drugs decreased from 43 to 40 and the number taking three or more antipsychotics was halved from 10 to 5 (Chi square $p < 0.05$).

Discussion

The mean daily doses of antipsychotic drugs were decreased in patients with severe mental illness who were included in an ISP plan based on the ICM approach, as was also observed in a Japanese study evaluating an ACT program (Satake et al. 2011). This decrease occurred both in general and in the subgroup of patients with a diagnosis on the schizophrenia spectrum. In contrast to the Japanese study cited, our study also showed a decline in the number of patients with more than one antipsychotic drug, the number of those with high and very high doses of antipsychotics. This finding was also observed for the group overall and in the subgroup of psychotic patients.

We also studied the impact ICM program on the concomitant use of benzodiazepines, not recommended in the clinical guidelines on chronic treatment of patients with severe mental disorders. We achieved a reduction in the daily average in the overall group of patients with schizophrenic spectrum, in the group with a diagnosis of schizophrenia spectrum and in the group of patients with mood disorders.

One of the study limitations is the lack of an analysis of changes in treatment in a control group of patients, such as a group of outpatients, for example, who were not included in the ICM program. Another limitation is the lack of analysis of psychiatric stability, patient income level, or emergency room visits by patients included in this study. In the coming days, the study authors plan to study the differences in the number of patients admitted to hospital during their participation in this program, compared to the number of previous admissions.

The present study showed the importance and repercussions of implementing the ACT program in patients with severe mental illness in an effort to achieve more integrated care and reduce psychopharmacological treatment, which can also decrease adverse drug effects and health care expenditures.

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