Original Paper

Prescription for psychiatric patients in a Brazilian public hospital: cross-sectional study

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Abstract

Background: The growing use of psychotropic drugs has been attributed to a higher frequency of psychiatric disorders diagnosed, interaction of new drugs on the pharmaceutical market, and new therapeutic indications of existing drugs. Given this scenario, the adequacy of the use of psychotropic drugs needs to be analyzed considering the scientific evidences. **Objectives:** To assess the appropriateness of drug prescriptions used by psychiatric patients in a public hospital in Sorocaba, according to the best available scientific evidence, and to describe the profile of this population. **Methods:** This cross-sectional study collected data from clinical records of patients with psychiatric disorders hospitalized in the psychiatric sector of the Sorocaba Hospital Complex, state of São Paulo, Brazil, between August 2015 and December 2016. The outcomes measured were: inappropriate use, presence of contraindication and serious or contraindicated drug interactions, according to the information available on the Dynamed® and Micromedex® 2.0 databases. **Results:** Patients were predominantly adults, and diagnosed with paranoid schizophrenia or bipolar affective disorder. Antipsychotics, benzodiazepines, and lithium accounted for 84.0% (n=2,938) of the 3,500 drugs prescribed for mental disorders. There were 2,157 (61.6%) inappropriate prescriptions, of which 81.9% corresponded to antipsychotics, benzodiazepines, and lithium. There were 1,712 prescriptions with drug combinations that risked causing drug interactions, predominantly involving antipsychotic use (67.0%). **Conclusion:** The study revealed a high number of inappropriate prescriptions, pointing to a need for greater prescription adequacy to ensure effective safe treatment for psychiatric patients.

Keywords: Psychotropic, drug prescriptions, mental disorders.

Prescrição para pacientes psiquiátricos em hospital público brasileiro: estudo transversal

Resumo

Introdução: O aumento no consumo de psicotrópicos pode ser atribuído a maior frequência de diagnósticos de transtornos mentais, introdução de novos medicamentos no mercado farmacêutico e novas indicações terapêuticas de fármacos já existentes. Diante disso, se torna necessária analisar a adequação do uso de medicamentos psiquiátricos, considerando as evidências científicas disponíveis. **Objetivos:** Analisar a adequação das prescrições medicamentosas utilizadas por pacientes psiquiátricos em um hospital público de Sorocaba, de acordo com as melhores evidências científicas disponíveis e descrever o perfil dessa população. **Métodos:** Este estudo transversal de coleta de dados de prontuários clínicos dos pacientes com transtornos mentais, internados no setor de psiquiatria do Conjunto Hospitalar de Sorocaba, estado de São Paulo, Brasil, foi realizado entre agosto de 2015 e dezembro de 2016. Os desfechos medidos foram o uso inadequado e/ou presença de contraindicação e de interações medicamentosas graves ou contraindicadas, seguindo as informações disponíveis nas bases de dados Dynamed® e Micromedex® 2.0. **Resultados:** Predominou indivíduos adultos, diagnosticados com esquizofrenia paranóica e transtorno afetivo bipolar. Antipsicóticos, benzodiazepínicos e lítio representaram 84,0% (n=2.938) dos 3.500 medicamentos prescritos para os transtornos mentais. Observou-se 2.157 (61,6%) medicamentos prescritos inadequadamente dos quais 81,9% corresponderam aos antipsicóticos, benzodiazepínicos e lítio. Houve 1.712 precrições com associações de fármacos com risco de causar interações medicamentosas, a maioria ocorreu devido uso de antipsicóticos (67,0%). **Conclusão:** O estudo revelou um alto número de prescrições inadequadas, apontando para a necessidade de uma maior adequação da prescrição para garantir tratamento seguro eficaz aos pacientes psiquiátricos.

Palavras-chaves: Psicotrópicos, prescrições de medicamentos, transtornos mentais.

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Introduction

The introduction of psychotropic drugs in the 1950s promoted a change of paradigm for treating psychiatric patients in becoming more centered on medication.[1] There is a high prevalence of use of psychotropic drugs by the world population, explained by the increase in diagnoses of mental disorders, registration of new drugs and introduction of new therapeutic indications for existing drugs.[2]

One in ten people have mental health disorders, which affect approximately 12% of the world population.[3,4] In Brazil, an estimated 23 million people have a mental disorder, 5 million of whom suffer from persistent, severe disorders.[5]

Over the past five years, Brazil has invested about 2.5% of the Federal health budget on the Mental Health Policy, promoting community health care as an alternative to hospital care. This policy is supported by Federal law 10.216/01, which prioritizes care in community-based services.[6]

In Brazil, studies evaluating individuals in use of drugs for mental disorders reveal a profile that differs from one location to another. Studies of individuals with psychotic disorders living in the city of São Paulo, for example, found that around 90% of patients used antipsychotics regularly, and 38% practiced polypharmacy.[7] A Brazilian study conducted within basic health units in Ribeirão Preto, State of São Paulo, found that the use of psychotropic drugs was a factor associated with inappropriate use.[8]

In the context of polypharmacy, considered use of five or more drugs concomitantly,[9] 93% Brazilian elderly who use at least one drug chronically and 18% then used polypharmacy. This scenario is associated with a higher occurrence of drug interactions, adverse drug events and potentially inappropriate prescribing from use psychotropic and/or others drugs.[10]

The inappropriate choice of pharmacological treatment may predispose patients to a greater risk of adverse effects, while dependence and prolonged use can cause health problems, compromising the effectiveness and safety of treatment. Therefore, ensuring the appropriateness of prescriptions of these drugs can contribute to rational use.[4]

The objective of this study was to assess the drug prescriptions used by psychiatric patients in a public hospital in Sorocaba, state of São Paulo, Brazil, according to the best available scientific evidence, and to describe the profile of this population.

Methods

Study design

A cross-sectional study was carried out based on data collection from clinical records of Psychiatric Unit of Sorocaba Hospital Complex (Conjunto Hospitalar de Sorocaba - CHS) in Sorocaba, state of São Paulo, Brazil.

Study site and data collection period

The CHS Psychiatric Unit serves 48 cities in the state of São Paulo. The public service attends patients with psychiatric disorders of all age groups from Sorocaba and the region covered by the Regional Directorate of Health 16 (Diretoria Regional da Saúde - DRS-16), and currently has 14 beds for clinical observation. About 400 patients are attended per month by this service. Patients are provided with routine care in the In-patient sector by a nursing professional and later by the medical team (psychiatrists and resident physicians).

The data collection period of the study was from August 2015 to December 2016.

Study population

Patients with mental disorders hospitalized at the CHS Psychiatric Unit in use of drugs to treat the diseases.

Eligibility criteria

Adults (18 years of age or older) with illness of psychiatric nature (schizophrenia, dementia, and psychosis due to alcohol use or illicit drugs, among others) were included. Clinical records with incomplete information such as age and ICD - International Classification of Diseases, should be excluded.

Data collection

All clinical records of patients admitted to the CHS Psychiatric Sector in the study period were evaluated. The date collected were: characterization of patient (gender, age and clinical diagnoses (according to the ICD - International Classification of Diseases);[11] characterization of drugs used by the patient (generic name, classification according to the ATC (Anatomical Therapeutical Chemical),[12] dosage and route of administration); characterization of appropriateness of drug prescriptions according to the best evidence available.

The ATC system has fourteen main anatomical/pharmacological groups or 1st levels. Each ATC main group is divided into 2nd levels which could be either pharmacological or therapeutic groups. The 3rd and 4th levels are chemical, pharmacological or therapeutic subgroups and the 5th level is the chemical substance. All levels were used in the present study. Polypharmacy was considered as the use of five or more drugs.[9]

The data from Dynamed® (EBSCO, MA, USA)[13] and Micromedex® 2.0[14] were used as a theoretical reference to classify the indication according to the best clinical evidence of efficacy.

Measured outcomes

The inappropriate use was classified according to the indication, recommendation of use (use not recommended/use with caution), contraindicated use (absolutely prohibited) and presence of drug interactions.

The interactions were characterized according to the Micromedex® 2.0 regarding to the severity of interaction and quality of information, defined as: *contraindicated* (which absolutely precludes the continuation of concomitant use of the drugs), *important* (that threaten the life of the patient who may or may not require the drug), *moderate* (resulting in exacerbation of the patient's health problem and/or requiring treatment change) and *secondary* (resulting in limited clinical effects, increased frequency or severity of side effects of treatment). The quality of the information described was classified as excellent, good, fair or not available.[14]

Data analysis

Categorical variables were expressed as percentage and continuous variables data were expressed as mean ± standard deviation. Continuous variables were assessed by the *t*-test and Chi-square and Fisher's exact proportions comparison tests. The level of significance adopted in all analyses was of 5% ($p \leq 0.05$). The statistical program used was Bioestat® (version 5.3, Instituto Mamirauá).

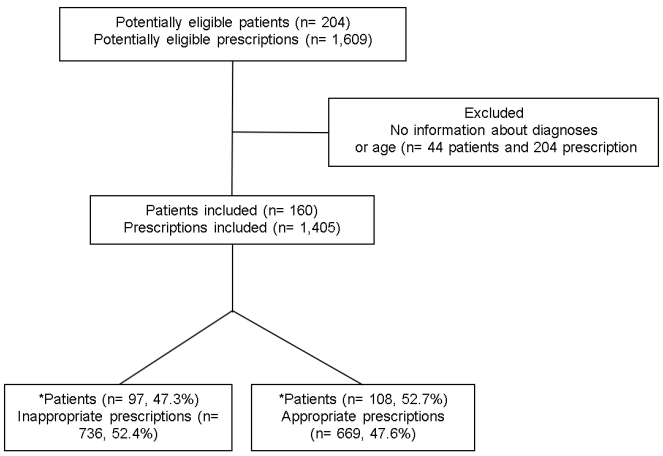
Ethical aspects

The project was approved by the Research Ethics Committee (CAAE: 19403813.4.0000.5500) of the University of Sorocaba (UNISO).

Results

Data on 204 patients (1,609 prescriptions) were obtained, of which 44 were subsequently excluded for lacking key information. This gave a final study sample of 160 patients and 1,405 prescriptions (Figure 1).

Figure 1. Patient Selection Flowchart



*The same patient had appropriate and inappropriate prescription.

The sample comprised predominantly adults (mean age 39 years), not in use of polypharmacy, diagnosed with paranoid schizophrenia or bipolar affective disorder (current manic episode with psychotic symptoms or hypomanic episode), that were psychiatric patients hospitalized with inappropriate and/or inappropriate prescriptions (p<0.001) (Table 1).

The sample comprised predominantly adults (mean age 39 years), not in use of polypharmacy, diagnosed with paranoid schizophrenia or bipolar affective disorder (current manic episode with psychotic symptoms or hypomanic episode), that were psychiatric patients hospitalized with inappropriate and/or inappropriate prescriptions (p<0.001) (Table 1).

Table 1. Characteristics of psychiatric patients hospitalized with appropriate and/or inappropriate prescriptions in the CHS Psychiatric Unit, between August 2015 and December 2016 (N= 205)

Variables	Total	Appropriate (N= 108) n (%)	Inappropriate (N= 97) (%)	p-value
Gender				
Male	95 (46.3)	59 (54.6)	36 (37.1)	0.7596
Female	110 (53.7)	49 (45.4)	61 (62.9)	
*Age Group (years)				
18-59	194 (94.6)	102 (94.4)	92 (94.8)	0.8546
≥ 60	11 (5.4)	6 (5.6)	5 (5.2)	
Mean age ± SD (39.0 ± 11.9) (years)				
#Polypharmacy				
Yes	0 (0.0)	0 (0.0)	0 (0.0)	1.000
No	205 (100.0)	108 (100.0)	97 (100.0)	
Most frequent diagnoses				
Paranoid Schizophrenia (F20)	44 (18.9)	29 (22.0)	15 (14.8)	*0.0010
Bipolar affective disorder, current episode manic with psychotic symptoms (F31.2)	35 (15.0)	12 (9.1)	23 (22.8)	-
Bipolar affective disorder (F31)	34 (14.6)	14 (10.6)	20 (19.8)	-
Unspecified non-organic psychosis (F29)	26 (11.1)	16 (12.1)	10 (9.9)	-
Organic hallucinosis (F06) and delusional organic disorder (F06.2, F06.3)	17 (7.3)	10 (7.6)	7 (6.9)	-
Mental and behavioral disorders due to multiple drug use and use of other psychoactive substances and acute intoxication (F19)	13 (5.6)	9 (6.8)	4 (4.0)	-
Mental and behavioural disorders due to cocaine use, multiple drugs or other psychoactive substances (F14.2, F19.1, F19.2, F19.5)	13 (5.6)	8 (6.1)	5 (4.9)	-
Catatonic residual and unspecified schizophrenia (F20.2, F20.5, F20.9)	9 (3.9)	7 (5.3)	2 (2.0)	-
Paranoid, dissocial and emotionally unstable personality (F60, F60.2, F60.3)	8 (3.4)	7 (5.3)	1 (1.0)	-
Recurrent depressive disorder; current mild, moderate and severe episode with psychotic symptoms (F33, F33.1, F33.3)	7 (3.0)	3 (2.3)	4 (3.9)	-
Mental and behavioral disorders due to alcohol use (F10, F10.3, F10.5)	5 (2.1)	5 (3.8)	0 (0.0)	-
Other specified mental disorders due to brain injury and dysfunction or physical disease (F06.8)	4 (1.7)	3 (2.3)	1 (1.0)	-
Bipolar affective disorder (current manic episode without psychotic symptoms) and other bipolar affective disorders (F31.1, F31.8)	4 (1.7)	2 (1.5)	2 (2.0)	-
Schizotypic and schizoaffective disorder of the manic type (F21, F25)	3 (1.3)	1 (0.7)	2 (2.0)	-
Unspecified dementia (F03)	2 (0.9)	1 (0.7)	1 (1.0)	-
Others CIDs	9 (3.9)	5 (3.5)	4 (4.0)	-
**Total	233 (100.0)	132 (100.0)	101 (100.0)	

SD= standard deviation. *Statistically significant difference (Chi-square or Fisher exact, p≤0.05). ** More than one disease per patient. ICD= International Code of Diseases # Use of five or more drugs.

The number of patients, drugs prescribed and inappropriate prescriptions are presented in Table 2. Antipsychotics, benzodiazepines and lithium accounted for the bulk of prescriptions for the mental disorders, representing 84.0% (n= 2,938) of the drugs. Haloperidol was the most prescribed drug (n= 675 prescriptions for 97 patients), followed by diazepam (n= 623 prescriptions for 74 patients), chlorpromazine (n= 489 prescriptions for 62 patients) and lithium (n= 282 prescriptions for 32 patients).

A total of 61.6% (n= 2,157) of prescribed drugs were inappropriate. Haloperidol, diazepam, chlorpromazine and lithium were the drugs most frequently prescribed inappropriately. There were no inappropriate prescriptions for escitalopram or topiramate.

The inappropriate prescriptions due to risk of drug interactions, most of which were of major or moderate severity, are presented on Table 3. Antipsychotics were associated with the highest number of interactions (67.0%), particularly haloperidol (22.7%) and chlorpromazine (18.6%). Diazepam and lithium also accounted for a high number of interactions and those of greatest severity, classified as important interactions. The interaction of haloperidol with chlorpromazine was the most frequent drug-drug interaction, followed by haloperidol with promethazine and with lithium. These interactions can increase the risk of cardiotoxicity (haloperidol plus chlorpromazine and haloperidol plus promethazine) or brain damage (haloperidol plus lithium). The quality of information and severity of the interaction are factors which should be considered when assessing interaction risk for patients.

Table 2. Frequency of inappropriate prescription drugs by patients hospitalized in the CHS Psychiatric Unit, between August 2015 and December 2016

Classification	ATC	Patients (N= 509) n (%)	Total of prescription drugs (N= 3,500) n (%)	Inappropriate prescription drugs (N= 2,157) n (%)
Antipsychotics		**249 (48.9)**	**1,877 (53.6)**	**1,104 (51.2)**
Aripiprazole	N05AX12	2 (0.4)	7 (0.2)	7 (0.3)
Chlorpromazine	N05AA01	62 (12.2)	489 (14.0)	312 (14.5)
Clozapine	N05AH02	13 (2.6)	242 (6.9)	135 (6.3)
Haloperidol	N05AD01	97 (19.0)	675 (19.3)	387 (18.0)
Levomepromazine	N05AA02	3 (0.6)	8 (0.2)	7 (0.3)
Olanzapine	N05AH03	26 (5.1)	203 (5.8)	145 (6.7)
Periciazine	N05AC01	1 (0.2)	1 (0.0)	1 (0.0)
Quetiapine	N05AH04	18 (3.5)	111 (3.2)	65 (3.0)
Risperidone	N05AX08	20 (3.9)	111 (3.2)	30 (1.4)
Zuclopenthixol	N05A505	7 (1.4)	30 (0.8)	15 (0.7)
Benzodiazepines		**103 (20.2)**	**779 (22.3)**	**392 (18.2)**
Clonazepam	N03AE01	3 (0.6)	18 (0.5)	12 (0.6)
Diazepam	N05BA01	74 (14.5)	623 (17.8)	334 (15.5)
Midazolam	N05CD08	26 (5.1)	138 (4.0)	46 (2.1)
Mood Stabilizer		**32 (6.3)**	**282 (8.1)**	**269 (12.5)**
Lithium	N05AN01	32 (6.3)	282 (8.1)	269 (12.5)
Anticonvulsants		**38 (7.5)**	**201 (5.7)**	**150 (6.8)**
Valproic acid	N03AG01	23 (4.5)	145 (4.1)	98 (4.5)
Carbamazepine	N03AF01	10 (2.0)	45 (1.3)	44 (2.0)
Phenytoin	N03AB02	1 (0.2)	1 (0.0)	1 (0.0)
Phenobarbital	N03AA02	2 (0.4)	6 (0.2)	4 (0.2)
Gabapentin	N03AX12	1 (0.2)	3 (0.1)	3 (0.1)
Topiramate	N03AX11	1 (0.2)	1 (0.0)	0 (0)
Antihistamines		**53 (10.4)**	**181 (5.2)**	**137 (6.4)**
Dimenhydrinate	R06AA02	1 (0.2)	2 (0.1)	2 (0.1)
Promethazine	R06AD02	52 (10.2)	179 (5.1)	135 (6.3)
Antidepressants		**25 (4.9)**	**109 (3.1)**	**86 (4.0)**
Amitriptyline	N06AA09	12 (2.3)	55 (1.6)	43 (2.0)
Citalopram	N06AB04	1 (0.2)	16 (0.5)	16 (0.7)
Escitalopram	N06AB10	1 (0.2)	2 (0.1)	0 (0)
Fluoxetine	N06AB03	2 (0.4)	5 (0.1)	5 (0.2)
Imipramine	N06AA02	1 (0.2)	8 (0.2)	8 (0.4)
Sertraline	N06AB06	2 (0.4)	4 (0.1)	4 (0.2)
Venlafaxine	N06AX16	6 (1.2)	19 (0.5)	10 (0.5)
Antiparkinsonian		**9 (1.8)**	**71 (2.0)**	**19 (0.9)**
Biperiden	N04AA02	9 (1.8)	71 (2.0)	19 (0.9)
Total		***509 (100.0)**	***3,500 (100.0)**	***2,157 (100.0)**

Inappropriate prescription Information according to Dynamed® (EBSCO, MA, USA) and Micromedex® 2.0.

*More than one prescription of drug used per patient. ATC: Anatomical Therapeutic Chemical.

Table 3. Drug interactions with risk of occurrence in patients hospitalized in the CHS Psychiatric Unit, between August 2015 and December 2016 (n= 1,712)

Inappropriate prescribing drugs N (%)	Associated drug	Consequence of the association of drugs	Quality of information	Severity
		Antipsychotics 1,146 (67.0)		
Chlorpromazine 319 (18.6)	Clozapine	May result in the risk of prolonging the QT interval	*Fair	*Major
	Lithium	May lead to encephalopathy syndrome, especially when lithium concentrations are high in plasma	**Not available	**Not available
	Promethazine	May result in the risk of prolonging the QT interval	*Fair	*Major
Clozapine 143 (8.4)	Benzodiazepines	Severe hypotension, cardiac arrest, and loss of consciousness may result	**Not available	**Not available
	Lithium	May result in weakness, dyskinesia, increased extrapyramidal symptoms, encephalopathy and brain damage	*Good	*Major
Haloperidol 388 (22.7)	Chlorpromazine	May result in an increased risk of cardiotoxicity (prolonged QT interval, torsades de pointes, cardiac arrest)	*Fair	*Major
	Promethazine	May result in an increased risk of cardiotoxicity (prolonged QT interval, torsades de pointes, cardiac arrest)	*Fair	*Major
	Lithium	May lead to encephalopathy syndrome followed by irreversible brain damage. In addition to increased risk of developing weakness, dyskinesia and increased extrapyramidal symptoms	*Good	*Major
	Olanzapine	May increase risk of developing parkinsonism	*Good	*Moderate
	Clozapine	May result in increased plasma clozapine concentration	*Fair	*Major
Levomepromazine 7 (0.4)	Lithium	Increases risk of developing encephalopathy syndrome, extrapyramidal reactions, brain damage	**Not available	**Not available
Olanzapine 178 (10.4)	Valproic acid	May result in decreased olanzapine concentration in plasma	*Excellent	*Moderate
	Diazepam	May potentiate the sedative effect and cause cardiorespiratory depression	*Fair	*Major
	Lithium	May lead to weakness, dyskinesia, increased extrapyramidal symptoms, encephalopathy and brain damage	*Good	*Major
	Midazolam	May potentiate the sedative effect and cause cardiorespiratory depression	*Fair	*Major
Periciazine 1 (0.0)	Lithium	May lead to weakness, dyskinesia, increased extrapyramidal symptoms, encephalopathy and brain damage	**Not available	**Not available
Quetiapine 65 (3.8)	Carbamazepine	May cause increased plasma carbamazepine and decrease the efficacy of quetiapine	*Fair	*Major
Risperidone 30 (1.8)	Valproic acid	May increase plasma valproic acid concentration	*Good	*Moderate
	Carbamazepine	May promote increased risperidone release in the form of excretion, thereby decreasing plasma levels of the active antipsychotic fraction of risperidone	*Good	*Moderate
	Haloperidol	May increase risk of prolonged QT interval	*Fair	*Major
Zuclopenthixol 15 (0.9)	Lithium	May lead to weakness, dyskinesia, increased extrapyramidal symptoms, encephalopathy and brain damage	*Good	*Major
		Benzodiazepines 334 (19.5)		
Diazepam 334 (19.5)	Carbamazepine	Decreased plasma diazepam concentration	**Not available	**Not available
	Fluoxetine	Increased serum concentration of diazepam	*Good	*Minor
	Lithium	May cause hypothermia	**Not available	**Not available
	Phenobarbital	May result in respiratory depression	*Good	*Major
		Anticonvulsants 144 (8.4)		
Valproic acid 99 (5.8)	Chlorpromazine	Increases plasma valproic acid concentration	**Not available	**Not available
	Diazepam	Inhibits the metabolism of diazepam by increasing its plasma fraction	**Not available	**Not available
Carbamazepine 45 (2.6)	Haloperidol	May decrease plasma haloperidol concentration	*Good	*Moderate
	Midazolam	May result in reduced effectiveness of midazolam	*Good	*Moderate
Phenytoin 1 (0.0)	Diazepam	Can change plasma phenytoin concentration	*Good	*Major

Continue

Table 3. Drug interactions with risk of occurrence in patients hospitalized in the CHS Psychiatric Unit, between August 2015 and December 2016 (n= 1,712) Continue

Inappropriate prescribing drugs N (%)	Associated drug	Consequence of the association of drugs	Quality of information	Severity
		Antidepressants 88 (5.1)		
Amitriptyline 43 (2.5)	Antipsychotics	May result in an increased risk of cardiotoxicity (QT prolongation, bridge torsades, cardiac arrest)	*Fair	*Major
	Diazepam	May result in psychomotor deficit (decreased reaction time and decreased wakefulness)	*Good	*Moderate
Citalopram 16 (0.9)	Lithium	May result in increased plasma lithium concentration and also serotonergic syndrome	**Not available	**Not available
Fluoxetine 6 (0.4)	Antipsychotics	May increase the risk of developing cardiotoxicity (prolonged QT interval, cardiac arrest, torsades de pointes)	*Reasonable	*Major
Imipramine 8 (0.5)	Lithium	May result in neurotoxicity	**Not available	**Not available
Sertraline 4 (0.2)	Lithium	May result in increased plasma lithium concentration and serotonergic syndrome	**Not available	**Not available
Venlafaxine 11 (0.6)	Haloperidol	May result in increased concentrations of haloperidol in plasma as well as possible increased the risk of cardiotoxicity (prolonged QT interval, cardiac arrest, torsades de pointes)	*Good	*Major

*Drug interaction described in Micromedex® 2.0. **Drug interaction described only in Dynamed® (EBSCO, MA, USA), but without classification of the quality and severity of the interaction).

Discussion

The data collected on 160 patients of the CHS Psychiatric Unit revealed a predominance of adults, not in use polypharmacy. Similar results were obtained in a retrospective study carried out in Barcelona, Spain, involving a population of 71,004 patients in use of antipsychotics. The study showed that most patients used monotherapy (66.7%) and were predominantly women (55.4%) and adults (52.2%).[15]

Although no statistically significant difference between men and women was evident in the present study, changes in women´s role in society, such as greater engagement in the formal job market together with household duties and family care, are factors that may contribute to the higher prevalence of mental health problems observed in the female population.[16]

Polypharmacy was not a common practice in the present study. This finding contrasts with the results of a survey carried out in a province of Spain based on electronic data from medical records, in which polypharmacy was common with the use of antipsychotics.[17] This practice can improve treatment efficacy, but must be employed with caution given that concomitant use of several medications can increase the risk of undesirable drug-drug interactions, such as treatment failure and adverse reactions.[1,7,18,19]

The present study found a predominance of prescriptions with antipsychotics (53.6%), benzodiazepines (22.3%) and lithium (8.1%) for the treatment of mental disorders. These results are similar to those of a previous study evaluating individuals with psychotic disorders living in the city of São Paulo, in which around 90% of patients used antipsychotics regularly.[7] Another study in 39 psychiatric hospitals, 11 psychiatric wards of a general hospital and 61 emergency departments was performed, collecting information from 550 psychiatrists about their preferences regarding drug prescriptions. Antipsychotics (59.3%) proved the most used drugs class for rapid tranquilization, followed by benzodiazepines (40.7%).[15]

A study evaluating 2,246 prescriptions used in the treatment of bipolar affective disorder found that 85.0% of prescriptions were dispensed with more than one psychotropic drug. Lithium was the most prescribed, given it is the drug of choice for treating bipolar affective disorder.[20] In the present study, bipolar affective disorder was the most commonly diagnosed condition at the CHS Psychiatric Unit, and lithium was one of the most frequently prescribed drugs.

Regarding prescription adequacy, over half of the prescriptions were inappropriate (61.6%). This result differs to a cross-sectional study conducted in a psychiatric sector of a university hospital in the United Kingdom, which found that less than half (27.0%) of prescriptions were inappropriate and 59.0% of patients used an inappropriate drug (33.0% potentially serious and 12.0% fatal).[21]

In the present study, inappropriate prescriptions due to risk of drug-drug interactions were also found. These combinations principally involved haloperidol plus chlorpromazine, followed by haloperidol plus promethazine, and haloperidol plus lithium, commonly used for rapid tranquilization of patients hospitalized with mental disorders.[22]

Rapid tranquillization is a method adopted in situations where fast control of agitation, aggression or excitement in patients with mental disorders is necessary.[22] The prescription of antipsychotics, alone or in combination with other drugs, is widely practiced because it promotes effective and safe action in patients. However, there is a need for further studies to establish the relationship between level of agitation and type of first-choice drugs prescribed.[15]

The association of haloperidol with promethazine is considered a possible risk because it promotes cardiotoxic effects.[14] However, an overview of systematic reviews of randomized controlled clinical trials that investigated the effectiveness and safety of medications used for rapid tranquillization in psychiatric patients, found that this association was an effective and safe alternative for the rapid tranquillization of patients with psychomotor agitation.[22] In addition, although this interaction is classified as important, the information documenting the phenomenon is of fair quality.[14]

The combination of haloperidol plus promethazine promotes the desired effect in a shorter timeframe compared to the combination of haloperidol with lorazepam or the use of other atypical antipsychotics.[22] The onset of tranquilization is faster using midazolam compared to the use of haloperidol plus promethazine, but must be administered more often to maintain the desired effect. Consequently, midazolam exposes the patient to a greater risk of respiratory depression, potentially precluding its use for rapid tranquilization.[23]

Few inappropriate prescriptions containing valproic acid occurred due to its restricted use in patients with affective bipolar disorder. Although valproic acid in combination with atypical antipsychotics is recommended by the American Psychiatric Association guideline for the treatment of affective bipolar disorder; monitoring of this drug is necessary because it can cause increased suicidal ideation and behavior in these patients.[14,24]

In the present study, there were few inappropriate prescriptions (2.4%) with haloperidol, olanzapine and risperidone used in elderly. The use of antipsychotics in this population is associated with an increased risk of patients suffering a stroke or of worsening dementia. The recommendation is to avoid prescribing this class of drugs to treat dementia, unless other drug treatments have failed.[25]

Missing information in the medical records on diagnoses and patient age led to the exclusion of 12.7% of the prescriptions. In addition, the absence of other information that could have improved the study may be considered a limitation, but is inherent to data collection studies of drugs records. On the other hand, it is important to emphasize that the present study collected data from all hospitalized patients during the data collection period stipulated.

The cross-sectional design of the study precluded the establishment of a causal relationship. It is important to highlight that this study compared the results obtained based on recommendations from sources supported by scientific evidence, such as Dynamed® and Micromedex® 2.0,[13,14] databases recommended for consultation by the World Health Organization.[26]

This study contributes with information about the possible risks involved in prescribing drugs for the treatment of mental disorders. This knowledge allows a more critical view of prescribers and other health professionals involved in the care of psychiatric patients and can help reduce the costs involved in treatment. The development of clinical protocols for the treatment of mental disorders can be a useful strategy to provide better clinical results, minimize risk and improve resource allocation.[7,27]

Conclusions

The study revealed a high number of inappropriate prescriptions in adult patients with mental disorders. Haloperidol, diazepam, chlorpromazine and lithium were the drugs most frequently prescribed inappropriately. Therefore, the adequacy of such prescriptions should be improved to ensure effective and safe treatment of psychiatric patients.

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Contributors

MRGF and CCB planned the study, performed the analysis and interpretation of data, wrote and reviewed the article. MRGF, TRF, LJEL, MPPR, LPAZ and CBR collected the data, wrote and reviewed the article. All authors approved the final version of the manuscript.

Conflict of Interest

The authors have no conflict of interest.

References

1. Fernandes MA, Affonso C, Sousa L, ***et al***. Interações medicamentosas entre psicofármacos em um serviço especializado de saúde mental. Comissão de publicação. 2012:9.
2. Leonardo BC, Cunha DF, Sakae TM, ***et al***. Prevalência de Transtornos Mentais e Utilização de Psicofármacos em Pacientes Atendidos em um Ambulatório médico de Especialidades. ACM Arq Catarin Med. 2017;46(2):39-52.
3. OMS, Organización Mundial de la Salud. Plan de acción sobre salud mental 2013-2020. Ginebra: Organización Mundial de la Salud. [Internet].2013. Available from: http://apps.who.int/iris/bitstream/10665/97488/1/9789243506029_spa.pdf. Acessed in December 1st 2019.
4. Rocha BSd, Werlang MC. Psicofármacos na Estratégia Saúde da Família: perfil de utilização, acesso e estratégias para a promoção do uso racional. Ciênc Saúde Colet. 2013;18:3291-300.
5. Da Silva XM, Terra MG, Da Silva CT, ***et al***. A utilização de psicofármacos em indivíduos com transtorno mental em acompanhamento ambulatorial. Enferm Glob. 2014;13(4):114-37.
6. Gonçalves RW, Vieira FS, Delgado PGG. Política de Saúde Mental no Brasil: evolução do gasto federal entre 2001 e 2009. Rev de Saúde Pública. 2011;46:51-58.
7. Razzouk D, Kayo M, Sousa A, ***et al***. The impact of antipsychotic polytherapy costs in the public health care in Sao Paulo. PloS one 2015;10(4):1-13.
8. Baldoni Ade O, Ayres LR, Martinez EZ, ***et al***.Factors associated with potentially inappropriate medications use by the elderly according to Beers criteria 2003 and 2012. Int J Clin Pharm 2014;36(2):316-24.
9. Masnoon N, Shakib S, Kalisch-Ellett L, ***et al***. What is polypharmacy? A systematic review of definitions. BMC Geriatrics. 2017;17(1):230.
10. Magalhães MS, Santos FSd, Reis AMM. Fatores associados ao uso de medicamentos potencialmente inapropriados para idosos na alta hospitalar. Einstein. 2019;18.
11. CID 10. [Internet]. 2013 [Cited 2019 Dec. 01]. Available from: https://www.cid10.com.br/. Acessed in December 1st 2019.
12. ATC/DDD Index. [Internet]. 2013 [Cited 2019 Dec. 01]. Available from: https://www.whocc.no/atc_ddd_index/. Acessed in December 1st 2019.
13. Dynamed Editorial Team. [Internet]. [Cited 2019 Dec. 01]. Available from: http://www.dynamed.com/home/. Acessed in December 1st 2019.
14. Micromedex® 2.0. [Internet]. 2016 [Cited 2019 Dec. 01]. Available from: https://psbe.ufrn.br/index.php#. Acessed in December 1st 2019.
15. Bernardo M, Coma A, Ibanez C ,***et al***. Antipsychotic polypharmacy in a regional health service: a population-based study. BMC Psychiatry 2012;12:42.
16. Prado MA, Francisco PM, Barros MB. Uso de medicamentos psicotrópicos em adultos e idosos residentes em Campinas: um estudo transversal de base populacional. Epidemiol Serv Saúde. 2017;26:747-758.
17. Gaviria AM, Franco JG, Aguado V, ***et al***. A Non-Interventional Naturalistic Study of the Prescription Patterns of Antipsychotics in Patients with Schizophrenia from the Spanish Province of Tarragona. PloS one 2015;10(10):1-15.
18. Moura CS, Ribeiro AQ, Starling S. Avaliação de interações medicamentosas potenciais em prescrições médicas do Hospital das clínicas da Universidade Federal de Minas Gerais. Latin Am J Pharm 2007;26(4):596-601.
19. Manso MEG, Biffi ECA, Gerardi TJ. Prescrição inadequada de medicamentos a idosos portadores de doenças crônicas em um plano de saúde no município de São Paulo. Rev Bras Geriatr Gerontol 2015;18(1):151-164.
20. Haeberle A, Greil W, Russmann S, ***et al***. Mono- and combination drug therapies hospitalized patients with bipolar depression. Data from the European drug surveillance program AMSP. BMC Psychiatry 2012;12:153.
21. Soerensen AL, Nielsen LP, Poulsen BK,***et al***. Potentially inappropriate prescriptions in patients admitted to a psychiatric hospital. Nord J Psychiatry 2016;70(5):365-373.
22. De Almeida CG, Del Grossi Moura M, Barberato-Filho S,***et al***. Rapid Tranquilization for Psychiatric Patients with Psychomotor Agitation: What is Known About it? Psychiatr Q 2017;88(4):885-895
23. Bak M, van Os J, Marcelis M. [Rapid tranquillisation; review of the literature and recommendations]. Tijdschr Psychiatr. 2011;53(10):727-37.
24. Ketter TA. Monotherapy versus combined treatment with second-generation antipsychotics in bipolar disorder. The Journal of clinical psychiatry 2008;69 Suppl 5:9-15.
25. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc 2015;63(11):2227-2246.
26. Ferreira TR, Lopes LC. Analysis of analgesic, antipyretic, and nonsteroidal anti-inflammatory drug use in pediatric prescriptions. J. pediatr 2016;92(1):81-87.
27. Kharadi D, Patel K, Rana D, ***et al***. Off-label drug use in Psychiatry Outpatient Department: A prospective study at a Tertiary Care Teaching Hospital. J Basic Clin Pharm. 2015;6(2):45-49.