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ORIGINAL ARTICLE

Prevalence of psychotropic drug use and conformity of therapeutic dose among mental health users

Prevalência do uso de psicotrópicos e conformidade da dose terapêutica entre usuários de saúde mental

Prevalencia del uso de psicotrópicos y cumplimiento de la dosis terapéutica entre los usuarios de salud mental

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ABSTRACT

Objectives: to identify the prevalence of psychotropic drug use according to their Anatomical Therapeutic Chemical classification among Psychosocial Care Center users and assess their prescription compliance based on the recommended therapeutic dose. **Methods:** this is an analytical study, based on documents, from the study of 389 records between September 2017 and May 2018. Associations between the presence of underdose or overdose and participants' characteristics were assessed using the chi-square test, adopting a significant value of $p < 0.05$. **Results:** the most used drugs were antipsychotics (74.7%), 16.0% of users with at least one medication with a dose below the therapeutic level and another 3.6% above the recommended therapeutic dose. **Conclusions:** greater nonconformities in the prescribed dose were related to antihistamines, antipsychotics and antidepressants, with underdosage associated with females and overdose with the report of hearing voices.
Descriptors: Psychotropic Drugs; Mental Health; Services Community Mental Health; Prevalence; Administration and Dosage.

RESUMO

Objetivos: identificar a prevalência do uso de psicotrópicos conforme sua classificação Anatômico Terapêutico Químico entre usuários de um Centro de Atenção Psicossocial e avaliar a conformidade da prescrição dos mesmos com base na dose terapêutica recomendada. **Métodos**: estudo analítico, de base documental, a partir do estudo de 389 prontuários entre setembro de 2017 e maio de 2018. Associações entre a presença de subdose ou sobredose e as características dos participantes foram avaliadas por meio do teste qui-quadrado, adotando como valor significativo $p < 0.05$. **Resultados:** os medicamentos mais utilizados foram os antipsicóticos (74,7%), 16,0% de usuários com pelo menos uma medicação com dose abaixo da terapêutica e outros 3,6% acima da dose terapêutica recomendada. **Conclusões:** maiores inconformidades na dose prescrita se relacionaram aos anti-histamínicos, os antipsicóticos e antidepressivos, com subdosagem associada ao sexo feminino e sobredose com o relato de audição de vozes.
Descritores: Psicotrópicos; Saúde Mental; Serviços Comunitários de Saúde Mental; Prevalência; Administração & Dosagem.

RESUMEN

Objetivos: identificar la prevalencia del uso de psicofármacos según su clasificación Anatómica Terapéutica Química entre los usuarios de un Centro de Atención Psicosocial y evaluar el cumplimiento de su prescripción en base a la dosis terapéutica recomendada. **Métodos:** estudio analítico, basado en documentos, basado en el estudio de 389 historias clínicas entre septiembre de 2017 y mayo de 2018. Las asociaciones entre la presencia de subdosis o sobredosis y las características de los participantes se evaluaron mediante la prueba de chi-cuadrado valor significativo $p<0,05$. **Resultados:** los *fármacos más utilizados* fueron los antipsicóticos (74,7%), el 16,0% de los usuarios con al menos un medicamento con dosis por debajo del nivel terapéutico y otro 3,6% por encima de la dosis terapéutica recomendada. **Conclusiones:** las principales no conformidades en la dosis prescrita se relacionaron con antihistamínicos, antipsicóticos y antidepresivos, con infradosificación asociada a mujeres y sobredosis con el reporte de escuchar vocês.
Descriptores: Psicotrópicos; Salud Mental; Servicios Comunitarios de Salud Mental; Prevalencia; Administración & Dosificación.

INTRODUCTION

Psychotropic drugs are defined as chemical substances that act on psychological function and alter mental state, which includes drugs with antidepressant, hallucinogenic and/or tranquilizer action. These substances act on the central nervous system has the potential to produce changes in behavior, mood and cognition of those who use them[1].

Use must take into account some criteria such as diagnosis, the profile of symptoms, users' age, the presence of clinical problems, the concomitant use with other drugs and especially the doses that will be implemented, as such considerations will have direct interference on the effectiveness or not the drug used, and, consequently, in users' quality of life[2]. It should also be noted that using inadequate doses exposes to the risk of side effects, without providing therapeutic benefit, and it is recommended that "subtherapeutic doses and incomplete therapeutic experiments" be avoided[3].

The Psychosocial Care Center (CAPS - *Centro de Atenção Psicossocial*) is an open and community health service of the Unified Health System (SUS – *Sistema Único de Saúde*) that has a multidisciplinary team to provide care to people in psychological distress[4]. Several intervention resources are used for the production of life, autonomy and health, existing in the territory and in service, which may include medication use[5].

When necessary, the drug resource must be rationally selected, prescribed and used to bring better efficacy and safety, with less cost to users, cooperating for comprehensive care[6]. However, studies demonstrate weaknesses in the use and prescription process[7-8], and that psychotropic drug use should not be exclusive but added to other care resources[9]. This reinforces the importance of monitoring psychiatric drug use in Psychosocial Care services, avoiding harm to users.

OBJECTIVES

To identify the prevalence of psychotropic drug use according to their Anatomical Therapeutic Chemical classification among Psychosocial Care Center users and assess the compliance of their prescription based on the recommended therapeutic dose.

METHODS

Ethical aspects

The research protocol was approved by the Research Ethics Committee of the Faculty of Medication of *Universidade Federal de Pelotas*. It was carried out in compliance with the Brazilian rules and guidelines for the regulation of research involving human beings, CNS (*Conselho Nacional de Saúde* – Brazilian National Health Council) Resolution 466/2012, guaranteeing participnats' anonymity.

Study design, period, and location

This is an analytical study, based on documents, conducted from the study of medical records of CAPS users in the city of Pelotas, RS. This is an excerpt from the survey "*Ouvidores de vozes - novas abordagens em saúde mental*", which took place between September 2017 and May 2018.

The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines were followed in this study.

Population and sample; inclusion and exclusion criteria

We sought to include in the study all medical records of users active in the service during the data collection period, i.e., users who maintained a link with the service, attending consultations, visits, groups, workshops and for withdrawing medication prescriptions. Thus, after surveying the lists of users at the service, data obtained from 400 medical records were accessed, of which 11 were excluded due to incomplete information, resulting in 389 medical records of participants in this study.

Study protocol

The outcome of this study was psychotropic drug use classified based on the Anatomical Therapeutic Chemical (ATC) classification of the World Health Organization[10] as well as the compliance of the prescribed dose with the recommended therapeutic dose.

In the ATC system, drugs are arranged in different groups according to their sites of action and their therapeutic and chemical characteristics. There are five different levels; medications are divided into 14 main anatomical groups (level 1), which house two therapeutic/pharmacological subgroups (levels 2 and 3), level 4, therapeutic/pharmacological/chemical subgroup and level 5, the chemical itself[10-11]. For each individual, the presence of psychotropic drugs was identified according to the substance (last ATC level) and therapeutic/pharmacological class (level 3 of ATC).

It was analyzed whether medications were in conformity or not, from the comparison between the doses prescribed in the sample of this study with the therapeutic doses described in literature[2,12-13], classifying them in sub-dose, therapeutic dose, and overdose.

The study variables used the information related to users' gender (female; male), age (continuous/18 to 30 years; 31 to 40 years; 41 to 50 years; 51 to 60 years; 61 years or more), marital status (single; with partner; separated or widowed), education (0 to 4 years of study; 5 to 8 years of study; 9 years of study or more), source of income (paid work; family income; aid or benefits), primary diagnosis (schizophrenia; bipolar affective disorder; depression; mental retardation; other neurotic disorders; other unspecified disorders), hearing voices (absent; present), history of violence (absent; present).

To collect the data, a form designed for the purposes of the research was used, composed of objective and discursive questions. They were answered by collectors, previously trained, based on the information available in the medical records.

Analysis of results, and statistics

The data were entered into Microsoft Excel software and later converted to the Stata 11 statistical package (StataCorp., CollegeStation, United States), where the analyzes were conducted. Inconsistencies in data were assessed and corrected when necessary.

Initially, descriptive statistics were used, by means of which the averages for continuous variables were calculated, as well as their respective standard deviations, in addition to the calculation of prevalence over each of the studied variables' strata. For conducting hypothesis tests, in the case of categorical variables, a chi-square test was used to identify whether there was an association between independent variables, arranged in line, and the outcome variable, arranged in the column in a contingency table constructed from sample data. The null hypothesis was that the variables were not associated and the alternative hypothesis that the variables were associated. Statistical significance was defined as a p value <0.05.

RESULTS

Through this study, data were collected on 389 users of a CAPS in the municipality of Pelotas. Among these, 66% were female. The average age found for the studied population was 47.7 years, with a standard deviation of 12.5, with a range from 19 to 86 years. Among the users studied, 59.6% had up to 4 years of study, while 19.9% had studied between 5 and 8 years and 22.5% 9 years or more. Most users (60.5%) received some aid or benefit paid by the state, another 17.4% were in a paid job and 22.1% depended on family income. Regarding marital status, 40.7% of users had a partner, 31.6% were single and 27.6% were widowed or divorced. The most frequent diagnosis was depression (36.6% n=133), followed by schizophrenia (25.1% n=91), mental retardation (14.33% n=52), bipolarity (10.5% n=38), other neurotic disorders (8.3% n=30) and other unspecified disorders (5.2% n=19).

There was a prevalence of antipsychotic use in 74.7% of the users assessed; this psychotropic class was the most used by them. Then, antidepressants, used by 60.6% of users, and antiepileptics, used by 51.5%, stand out. Anxiolytic use was also observed by 48.2% of users studied, followed by anticholinergic agents, sedative hypnotics and antihistamines by 28.6%, 16.5%, and 5.7%, respectively. The prevalence of use of each medication belonging to the examined classes can be seen in Table 1.

As noted in Table 1, the five most used drugs by the population studied were Diazepam (44.3%), Haloperidol (29.1%), Biperiden (28.6%), Fluoxetine (26.3%), and Clonazepam (24.7%).

With regard to the compliance of the prescribed dose with the recommended therapeutic dose, it was observed that 80.9% (n=314) of users had received a prescription for all drugs within the recommended therapeutic dose. However, 16% (n=62) of users had received indication of at least one medication with a dose below the therapeutic dose, and another 3.6% (n=14) received prescriptions with at least one medication with a dose above that recommended therapeutic dose. It is noted that in 2 cases (0.5%), users had received indication of at least one medication with a dose below the therapeutic dose and at least one medication with a dose above the recommended therapeutic dose concomitantly. Table 2 shows the prevalence of compliance or not with the recommended therapeutic dose for each psychotherapeutic class studied.

As seen in Table 2, the psychotherapeutic class with the highest prevalence of prescribing a dose below the recommended therapeutic dose was that of antihistamines (27.3% n=6), followed by antipsychotics (17.6% n=51) and antidepressants (17.4% n=41). The psychotherapeutic classes for which there was a higher prevalence of prescription above the therapeutic dose, were those of antihistamines (13.6% n=3), antiepileptics (6% n=12) and sedative hypnotics (4.7% n=3).

With regard to the sociodemographic and clinical characteristics that were related to the prescription of a dose above or below the recommended therapeutic dose, there were sex, marital status and hearing of voices. The meaning of these relationships as well as the other variables studied can be seen in Table 3.

Table 1 - Description of the psychotropic drugs used in the Psychosocial Care Center studied according to the therapeutic/pharmacological subgroup - levels 2/3 of the Anatomical Therapeutic Chemical classification

	n	%
(N03A) Antiepileptics	200	51.5
Oxcarbazepine	53	13.7
Carbamazepine	64	16.5
Clonazepam	96	24.7
Phenytoin	10	2.6
Phenobarbital	16	4.1
Lamotrigine	1	0.3
Oxcarbamazepine	4	1.0
Topiramate	11	2.8
(N04A) Anticholinergic agents	111	28.6
Biperiden	111	28.6
(N05A) Antipsychotics	290	74.7
Aripiprazole	1	0.3
Chlorpromazine	69	17.8
Clozapine	1	0.3
Fluphenazine	23	5.93
Haloperidol	113	29.1
Levomepromazine	12	3.1
Lithium	40	10.3
Olanzapine	11	2.8
Pimozida	10	2.6
Quetiapine	25	6.4
Risperidone	87	22.4
Sulpiride	4	1.0
Thioridazine	2	0.5
(N05B) Anxiolytics	187	48.2
Alprazolam	9	2.3
Bromazepam	1	0.3
Clobazam	1	0.3
Bromazepam	172	44.3
Lorazepam	6	1.5
(N05C) Sedative hypnotics	64	16.5
Flunitrazepam	8	2.1
Flurazepam	5	1.3
Midazolam	4	1.1
Nitrazepam	48	12.4
(N06A) Antidepressants	235	60.6
Amitriptyline	47	12.1
Bupropion	6	1.5
Citalopram	12	3.1
Clomipramine	14	3.6
Duloxetine	3	0.8
Escitalopram	5	1.3
Fluoxetine	102	26.3
Imipramine	13	3.3
Mirtazapine	4	1.0
Nortriptyline	31	8.0
Paroxetine	7	1.8
Sertraline	32	8.2
Trazodone	7	1.8
Venlafaxine	8	2.1
(R06A) Antihistamine	22	5.7
Promethazine	22	5.7

** Most subjects used more than one psychotropic, sometimes from the same medication class.*

Table 2 - Conformity of the prescribed dose for psychotropic drugs used by users of the Psychosocial Care Center studied according to the therapeutic/pharmacological subgroup - levels 2/3 of the Anatomical Therapeutic Chemical classification

	Within the therapeutic dose		Below the therapeutic dose		Above the therapeutic dose	
	n	%	n	%	n	%
(N03A) Antiepileptics	156	78.0	33	16.5	12	6
(N04A) Anticholinergic agents	94	84.7	13	11.7	5	4.5
(N05A) Antipsychotics	230	79.3	51	17.6	11	3.8
(N05B) Anxiolytics	154	82.3	29	15.5	5	2.7
(N05C) Sedative hypnotics	55	85.9	6	9.4	3	4.7
(N06A) Antidepressants	187	79.6	41	17.4	8	3.4
(R06A) Antihistamine	14	63.6	6	27.3	3	13.6

** Most subjects used more than one psychotropic, sometimes from the same medication class.*

Table 3 - Prevalence of dosage below and above the therapeutic dose among users of a Psychosocial Care Center in the city of Pelotas, Rio Grande do Sul, according to strata of the variables selected for the study

		Below		Above	
	n	(%)	*p* value	(%)	*p* value
Sex					
Male	144	9.1	0.005	4.2	0.635
Female	245	20.0		3.3	
Age					
18 to 30 years	42	16.7	0.622	0	0.430
31 to 40 years	59	18.6		6.8	
41 to 50 years	104	12.5		3.8	
51 to 60 years	122	15.6		4.1	
61 years and over	55	21.8		1.8	
Marital status					
Single	111	8.2	0.032	3.6	0.522
With a partner	143	18.9		4.9	
Separated or widowed	97	19.6		2.1	
Education					
0 to 4 years of study	140	16.4	0.183	3.6	0.402
5 to 8 years of study	42	7.1		7.14	
9 years of study or more	53	20.7		1.9	
Source of income					
Paid work	45	6.7	0.207	2.2	0.069
Family income	57	14.3		0	
Aid or benefits	156	17.3		7.1	
Diagnosis					
Schizophrenia	91	11.0	0.069	5.5	0.473
Bipolarity	38	23.7		7.9	
Depression	133	17.3		3.0	
Intellectual disability	52	11.5		3.8	
Other neurotic disorders	30	20.0		0	
Other disorders not specified	19	36.8		0	
Hearing voices					
Absent	208	16.4	0.798	0.5	**<0.001**
Present	181	15.5		7.2	
History of violence					
Absent	263	15.2	0.548	3.8	0.766
Present	126	17.6		3.2	
TOTAL	389	16.0		3.6	

As noted in Table 3, the women who composed the sample received a prescription for a psychotropic agent below the recommended therapeutic dose more frequently. Among women, this prevalence was 20.0%, while in men, 9.1%. The same is observed among individuals who reported marital status as separated or widowed, whose prevalence of this outcome was 19.6%. Among singles, in turn, this prevalence was 8.2%.

As for the prescription of a psychotropic drug in a dose higher than the recommended therapeutic dose, it was possible to observe that users who had a report of hearing voices were more prone to this outcome. Among users who did not report hearing voices, the prevalence of prescription above the therapeutic dose was 0.5%. Among voice listeners, this prevalence was 7.2%.

DISCUSSION

Initially, it is possible to verify in the sample studied subjects' biological variability (age, sex, among others) as well as socioeconomic conditions and family structure, and these factors may interfere with the choice of medication and its dosage. In this sense, many variables must be considered in psychopharmacology regarding the choice of medication, prescription, administration, psychic representation of the medication for users and family and environmental issues[3].

Another aspect pointed out in the research is that, as observed in other studies, health services are mostly accessed by women[14-15], which may justify the prevalence (36.6%) of depression diagnosis in the studied sample, considering that it is the psychopathological disorder that most affects women as a result of biological, social, and gender factors[8,16-17]. Such prevalence is similar to a study carried out in substitute mental health services in the southern region, in which the diagnosis of depression was identified in 34.3% of the sample[18]. It is worth mentioning that in depressive conditions, users may present a multiplicity of symptoms, including psychotic symptoms[19]; this would justify the high rate of psychotropic drugs belonging to the class of antipsychotics (74.7%) and to the class of antidepressants (60.6%).

When associating the most prevalent diagnoses with the medications most used by the sample, hypotheses for use arise: diazepam (44.3%), used as an adjunct in treatment of schizophrenia, or associated with antidepressants in cases of depression with anxiety; haloperidol (29.1%), used to treat exacerbation of schizophrenic conditions and psychotic depression; biperiden (28.6%), for treatment of extrapyramidal symptoms caused by psychotropic use; fluoxetine (26.3%), as the first choice for the treatment of depression; clonazepam (24.7%), as an adjunct to sedation with antipsychotics[2].

The more frequent use of diazepam, in a sample of female predominance, is also justified by the social constructions of gender, as they are directly associated as determinants of consumption. Anxiolytics are widely used in the clinic as a "tranquilizer", although it is a medication to treat specific anxiety attacks[20].

In mental health, antihistamines are prescribed for sedative-hypnotic purposes, in isolation or in combination with other medications, for treatment of insomnia, extrapyramidal manifestations of antipsychotics or to control agitation. It should be considered that antihistamines reduce tolerance as age advances, i.e., their sedative effect is prolonged, with the need to decrease the therapeutic dose[21-22], which could explain the prevalence of underdosing found in our study.

It is observed that antihistamines are the class with the highest non-conformity in this sample, also showing prevalence for overdose. A justification would be that antihistamines, whose main action is anti-allergic and commonly used for their sedative action, are well-known medications among health professionals, users, and family members, and may generate overdoses prescription, paying little attention to the effects, safety, and effectiveness. It is worth highlighting the alert with this class, because although it is of low dependence, doses above therapy are potentially lethal[22]. The search for enhancing a medication also explains why the hypnotic-sedative class is the third most prevalent of overdoses.

It is noteworthy in this sample the fact that antipsychotics are the second drug class with the highest prevalence of underdose, in contrast to literature, in which it is presented as the main class used with doses above the therapeutic level[23-24]. It is observed that currently using antipsychotics in underdoses in the clinic is for hypnotic purposes, since the idea is to decrease the prescription of benzodiazepines, which are prescribed in great majority by general practitioners in Basic Health Units[25].

The presence of the antidepressant class in therapeutic underdoses may be related to individuals' adaptation to medication doses. This can be verified in another study[26], which found cases of sub-therapeutic doses of antidepressants without mentioning them in the medical record, if the dose would be increased gradually, stating that the records need to be improved.

As for the association of overdose with hearing voices, it can be neurochemically justified based on the biomedical model, in which they consider the experience of hearing voices as a psychotic symptom. The prescription of higher doses occurs as a result of antipsychotics blocking most of the brain's D2 receptors, and neurons, in order to compensate, increase the density of these dopaminergic receptors, making the pathways dysfunctional, which aggravates psychotic symptoms (psychosis belated). Moreover, morphological changes (in the ganglia, thalamus, and frontal lobe) caused by antipsychotics have been found, which are related to the worsening of positive and negative symptoms, causing increasing doses of these psychotropic drugs to be used, thus occurring prescription of overdoses[1].

Also, approximately one third of people who are diagnosed with schizophrenia are resistant to drug treatment even in high doses of psychotropic drugs[27-28], i.e., hearing voices remains even with the constant use and increase of psychotropic drugs.

It should be noted that using psychotropics related to the discrepancy in therapeutic doses, whether in the case of underdoses or overdoses, may be related to a service performed in a prescriptive way, without taking into account a person's uniqueness, neither the periodicity of reassessment nor the need to continue using these medications.

A survey carried out in an emergency department of a mental health clinic resulted in the majority of people who arrive at the service already having a prescription for psychiatric medications, and the complaints presented are often not taken into account, which causes maintenance of the prescribed medications[29].

It is necessary to point out the need for the CAPS nursing team to guide users on the prescribed medication, monitor the establishment of users' relationship with their medications, as well as clarify the expected therapeutic effects, frequency of use and probable side effects[30]. Furthermore, it is important that monitoring users regarding the prescribed medications needs to occur in an interdisciplinary way so that their rational use happens considering the participation of users and family in planning this therapeutic resource, in a co-management of medication use.

Study limitations

Little research can be considered as limitations of this study that address the prescription of psychotropic drugs and the analysis of their doses (in underdoses or overdoses). It is identified the lack of bibliographies that allow assessing the justification for the use or not of these dosages, which brings to reflection the importance of criteria for the rational use of psychotropics.

Contributions to nursing, health, and public policies

Psychotropic drug use as one of the care strategies must win the contribution of all the actors involved in this process. The study reaffirms the responsibility and the importance of nursing to actively participate in team discussions regarding the rational use of medications, to contribute in an interdisciplinary way in monitoring, in addition to their duties in guidance and administration of these medications.

CONCLUSIONS

In this study, the prevalence of antipsychotics was evidenced as the psychotropic class most used by CAPS users, followed by antidepressants and antiepileptics. Considering the compliance of the dose, antihistamines, antipsychotics, antidepressants, antiepileptics and sedative hypnotics were the ones that presented the greatest nonconformities, underdosing or overdosing, highlighting a higher frequency of underdosing in women.

According to the study, people who reported hearing voices presented therapeutic doses above the recommended, bringing to reflection the imperative need to search for perspectives that explore other approaches related to the phenomenon of hearing voices.

Thus, the need for monitoring and continuous reviews of medication by the team of service professionals, especially nursing, is highlighted. Also, it is important to use psychotropics appropriately and responsibly, recognizing them and using them as one of the resources available at CAPS added to others and not as a focus of care developed by these services.

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