EVALUATION OF THE FLUOXETINE DISTRIBUTION BY THE MUNICIPAL PHARMACY OF CAMPOS GERAIS – MG

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ABSTRACT

Fluoxetine is indicated specifically for the treatment of depression, but other applications have been established through clinical and controlled clinical studies and is also indicated for obsessive-compulsive disorders, nervous bulimia, premenstrual dysphoric disorder, panic disorder, bipolar disorder, and neuropathies. In recent years, antidepressants have been shown as one of the major classes of drugs marketed in the global pharmaceutical market. This study evaluated the therapeutic profiles of fluoxetine in the Municipal Pharmacy of Campos Gerais - MG from June to November 2013 through a questionnaire. The amount given for a semester was verified by P invoices, and prescriptions retained, making up an estimate for one year, since there are no variations in the amount, as it is not a product with seasonal distribution. The research showed that over 90 % of users are female, aged around 36 years, where most prescriptions were prescribed by a general practitioner. More than 70 % of the participants use the drug for more than one year. In addition to depression, anxiety disorder was the most cited as the reason for treatment. The drug was ineffective only in 3 % of users. The amount distributed was estimated at 11,200 tablets per month, benefiting an average of 400 people a month, suggesting the irrational use of medicines.

INTRODUCTION

According to the World Health Organization (WHO) (WANNMACHER, 2012), it is estimated that depression reaches more than 350 million people and is considered as the primary incapacitating agent in the world. Selective Serotonin Reuptake Inhibitors (ISRSs) are first-line drugs for the treatment of depression, obsessive-compulsive disorder, and panic disorder, as well as other conditions, being the rational

research result to discover drugs as active as tricyclic antidepressants (TADs), but with less tolerability and safety problems (DA SILVA; IGUTI, 2013). Fluoxetine hydrochloride, N-methyl-g- [4- (trifluoromethyl) phenoxy] benzenepropanamine, is an antidepressant drug, extremely active as a selective serotonin reuptake inhibitor in the central nervous system, being widely prescribed in the treatment of various medical conditions (SUAREZ *et al.*, 2009). According to Silva; Iguti, (2013), the psychotropic drugs consumption prevalence in Brazil is elevated. Fluoxetine, a second-generation antidepressant, deserves attention as it was considered the best selling drug in the United States from 1996 to 2000 (DA SILVA; IGUTI, 2013; DO NASCIMENTO; FREITAS; MOREIRA, 2013). Currently, the antidepressants constitute the second drug class more often prescribed, highlighting fluoxetine as one of the most prescribed (ARRUDA; MORAIS; PARTATA, 2012). Based in the increased consumption/prescription of Fluoxetine Hydrochloride this work aimed to identify this medication users profile and to evaluate the amount of this drug distributed in a year by the Municipal Pharmacy of Campos Gerais.

MATERIALS AND METHODS

Study characterization: The study is characterized by a descriptive, exploratory, and quantitative approach aimed to describe the amount of fluoxetine distributed to the Municipal Pharmacy of Campos Gerais, Minas Gerais, Brazil. A semi-structured questionnaire composed of 8 questions (4 multiple choice and 04 open questions) related to the fluoxetine use was applied.

Ethics: This work was carried out under the ethical precepts determined by resolution 196/96 of the National Health Council. Thus, it was submitted to the analysis of the Research Ethics Committee of the José do Rosário Vellano University (Unifenas) (protocol number: nº 419.078). Before the retained prescription verification at the Municipal Pharmacy of Campos Gerais - MG, the responsible pharmacist provided an authorization term for the research, as well as the Consent Term for the Use of the Database, based on the verification of retained prescriptions.

Local of study: Campos Gerais has an estimated population of 29,998 people, its primary economic source is agriculture and livestock, with emphasis on coffee production, being one of the largest state producers. The public network, which in Campos Gerais is the Municipal Pharmacy, is the main mechanism by which the psychotropics drugs are distributed to the population (IBGE, 2013).

Procedures and sample: The present study was performed in the Municipal Pharmacy of Campos Gerais – MG. The incoming receipts and retained prescriptions of fluoxetine hydrochloride from June to November 2013 were verified. From the data recorded, a year estimate was calculated, as the fluoxetine use is not seasonal. Furthermore, the questionnaire was applied to 100 users to delineate the user's therapeutic profile. All participants signed a free informed consent form.

Inclusion and exclusion criteria

All prescriptions containing the drug fluoxetine hydrochloride 20 mg, and users over the age of 18 who agreed to participate in the study were included. Those prescriptions that did not contain the fluoxetine hydrochloride and/or from patients aged under 18 years old and/or without the proper authorization were excluded.

Critical analysis of risks and benefits risks: Since all research involving human subjects involves risks, the following study has the risks of embarrassment or discomfort when the volunteer is answering the questionnaire. This risk will be minimized by the fact that the interview takes place individually after consent. Before the interview, the Free and Informed Consent Form was provided to aware the participants of the importance and relevant aspects of the study. Benefits: The research will bring more knowledge about the consumption of fluoxetine hydrochloride by the patients that use Unique Health System medication distribution, as well as the users profile. The work can also help to improve the assistance provided to users when necessary.

Data analysis: An analysis is the attempt to evidence the relations between the studied phenomenon and other factors (MARCONI; LAKATOS, 2011). The data analysis was performed with the database codification and elaboration, which consists in establishing the connection between the results obtained with others already known, regardless of whether they are derived from theories or previously performed (GIL, 2002). The results were provided in percentage.

RESULTS AND DISCUSSION

Dispensation of Fluoxetine Hydrochloride: The amount of Fluoxetine Hydrochloride dispensed by the Municipal Pharmacy of Campos Gerais – MG in the period from November 2012 to November 2013, was estimated as 11,200 pills per month, benefiting 400 people per month. The pharmacy drugs request is quarterly performed via Integrated Pharmacy Assistance Management System (SiGAF), and in case of system failure, the requisition is performed in the City Hall. In cases of unavailability or delay in the delivery of the medicines by the suppliers, the dispensed number may be even greater since continuous users may acquire the pills in the private network. Nascimento, Freitas, and Moreira (2013), also observed these variations in the dispensation and justified the lack of medication in the pharmacy, due to the purchases being made through bidding that is commonly associated to drug delivery delays (DO NASCIMENTO *et al.*, 2013). Once there is no guaranteed regularity of stock replacement by the Municipal Health Department, the above-mentioned number may be smaller, and there is a suppressed demand in the Municipal Pharmacy.

User profile: The data collection period related to the user's profile was performed from October to November 2013, being interviewed, 100 people. Most of the participants were female, as presented in graph 1. This finding may be justified by the increased frequency of anxiety, depressant, and hormonal alterations disorders observed in periods such as puberty, menopausal, pre-menstrual period, postpartum and affective issues, besides the fact that women seek more medical treatment than men (DO NASCIMENTO *et al.*, 2013). Another reason that might justify this great gender difference would be the influence of this medication in the sexual libido inhibition. It is known that while dopamine improves sexual function, serotonin inhibits the desire, ejaculation and orgasm,

leading to resistance in the use by the male gender patients. This is the reason why ISRSs may be important causes of sexual dysfunction. Because of the high incidence of sexual dysfunction caused by these drugs, they are being used in patients with premature ejaculation, paraphilia and excessive libido (MORENO; MORENO; SOARES, 1999).
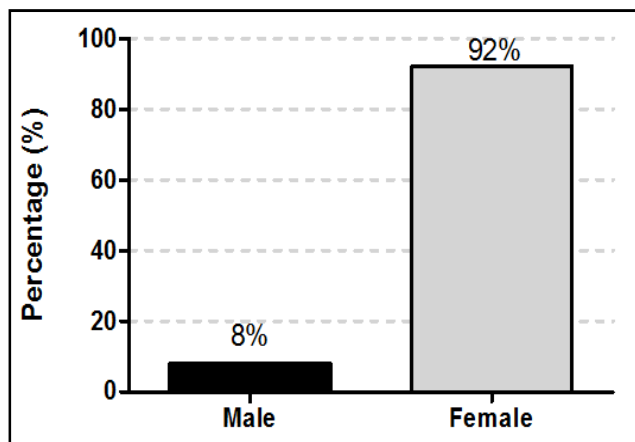
**Graph 1. Users distribution by gender**

Regarding the age group, it was observed that the majority of respondents were between 30 and 40 years old (Graph 2). According to Weiss *et al*. (2012), the young and the elderly have a lower chance of developing depression. The research of these authors was carried out in several countries, and the result showed a U-shaped graph, where the top represents the contentment state and the lowest level represents sadness, reaches mainly middle-aged people. For Weiss *et al*. (2012), children and the elderly feel better because they suffer less social pressure (WEISS *et al.*, 2012). In a study performed by Medeiros; Sougey (2010), patients with depression present mean age of 36 years old. Another research conducted by WHO, in 2011, pointed Brasil as the third country more depressed in the world, with 18.4% of the population with at least one depressant episode during life (MEDEIROS; SOUGEY, 2010).
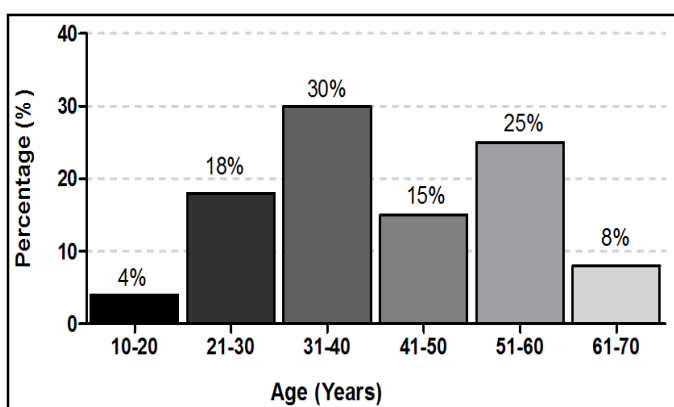
Graph 2. Users age range

According to the results presented in graph 3, it was observed that more than 90% of the fluoxetine prescriptions were performed by a general clinician. According to Laranjeira (2005), the rational use of psychotropic drugs has surpassed the specialty area of psychiatrists and has become a public health problem. Researchers with various distortions in the prescriptions of psychotropics, made by different medical specialties such as neurologists, cardiologists, gynecologists

and psychiatrists were reported in the literature (FERRARI *et al.*, 2013; LARANJEIRA *et al.*, 2005). Regarding the usage period, more than half interviewed users used fluoxetine for more than one year, due to the great recurrence probability and by the fact that depression commonly evolves from an acute to a chronic disorder (Graph 4).
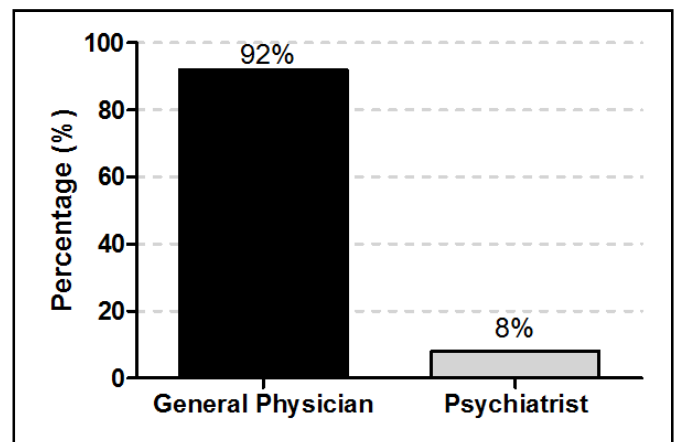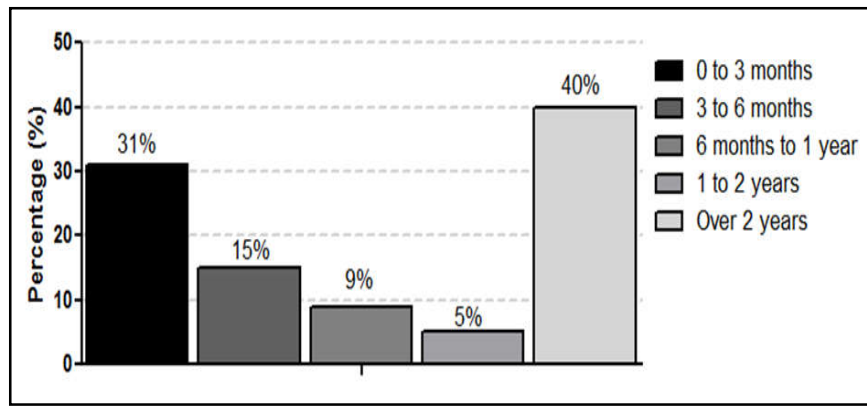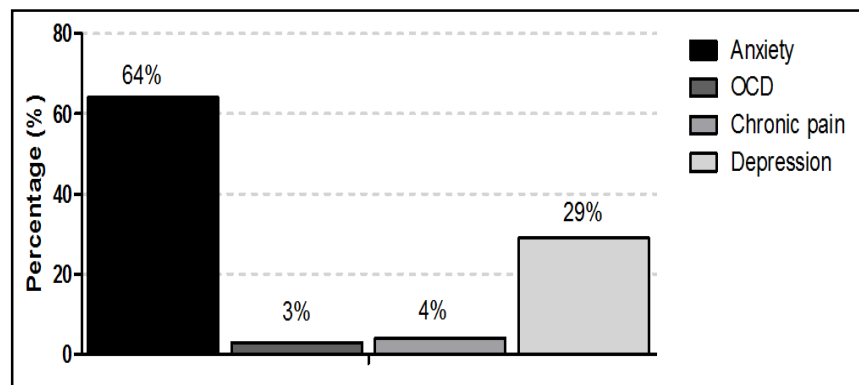

Graph 3.

According to FLECK *et al.* (2003), there are three phases:

- Acute phase: including the two and three first months and is aimed at reducing depressive symptoms (response) or ideally the full dimming with the return of the level of pre-morbid functioning (remission).
- Continuation phase: corresponds to the fourth and sixth months following acute treatment and aims to maintain improvement, avoiding relapses. At the end of the continuation phase, the patient who remains with the initial improvement is considered recovered from the episode index.
- Maintenance phase: The goal of the maintenance phase is to prevent new episodes from occurring (recurrence). Therefore it is recommended for those users with a probability of recurrence.

Relapse rates are estimated to be 20% to 24% in the first two months, 28% to 44% in the fourth month, 27% to 50% in the sixth and 37% to 54% in one year. Similar results were reported for depressed patients in general practice outpatient clinics with a 37% relapse in one year. A meta-analysis of studies with depressed patients treated with an antidepressant for two to six months beyond remission shows a relative risk of 0.5% when compared to placebo. The benefit of treatment for more than six months after remission has been demonstrated only for groups with a history of recurrent depressive episodes (FLECK; LAFER; SOUGEY; PORTO*; et al.*, 2003). Follow-up studies show that up to 30% of people are still depressed after one year, 18% after two years and 12% after five years of treatment. Many treated patients maintain residual and subsyndromal symptoms that lead to unfavorable outcomes, such as a higher risk of relapse and suicide, impoverishment of psychosocial functions and high mortality due to other clinical diseases. Among patients who recover from a depressive episode, more than 50% experience newer depressive episodes. The return of depressive symptoms during maintenance treatment with antidepressants occurs at rates ranging from 9 to 57% (DO NASCIMENTO *et al.*, 2013; POWELL *et al.*, 2008).

Graph 4. Fluoxetine usage
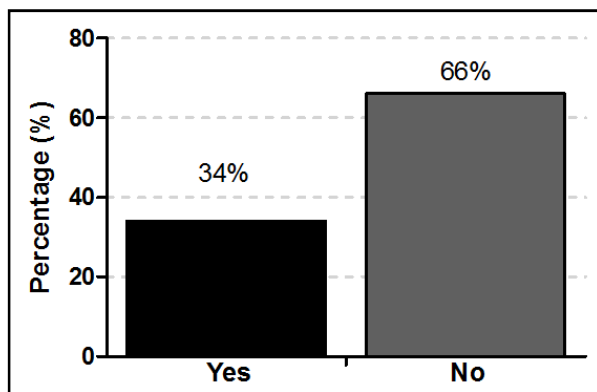

Graph 5. Treatment reason

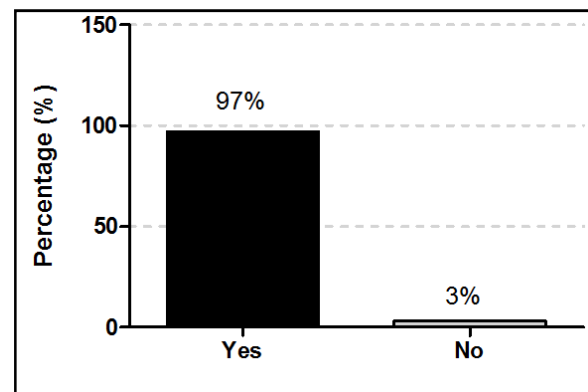**Gráfico 6. Use of other psychotropic substances**

Gráfico 7. Improvement of clinical status

In this study, anxiety has been the leading cause for the use of fluoxetine, identifying the possible irrational use of medications, since the prescriptions are made by general practitioners in the vast majority (Graph 5). Although fluoxetine is an antidepressant drug, anxiety has come to prominence in medical prescriptions. Anxiolytics were the controlled substances most consumed by the Brazilian population in the period from 2007 to 2010, according to the National System of Controlled Products Management (SNGPC) of the National Agency of Sanitary Surveillance, Anvisa (DA SILVA; IGUTI, 2013). In the systematic review of the pharmacological therapy efficacy in generalized anxiety disorder, Tomé (2011) analyzed the results for nine treatments: duloxetine, escitalopram, fluoxetine, lorazepam, paroxetine, pregabalin, sertraline, tiagabine, and venlafaxine. Fluoxetine was the first in the classification, most likely to be the most effective treatment (62.9%).

Regarding tolerance, the treatment with a lower percentage of dropouts was sertraline, with a probability of 49.3% being the best choice (TOMÉ, 2011). Graph 6 the use or not of another of other psychotropic drugs. The antidepressant choice must be based in the depression characteristics, suicide rate, collateral effects, other clinical disturbances, concomitant therapy, tolerability, cost, cognitive damage, etc. (FLECK; LAFER; SOUGEY; DEL PORTO; *et al*., 2003). The following medications were mentioned by the interviewers as previously or concomitantly used: Lithium carbonate, Bromazepam, Diazepam, Paroxetine, Amitriptyline, Bupropion, Risperidone, Clonazepam, and Sertraline. In addition to replacing the medication, other factors that are directly related to depression, such as affective, biological and social factors, should be considered taking into consideration the human being as a whole (WIRZBICKI *et al*., 2013). Fluoxetine was effective in

most cases (Graph 7), but for some users, there is a need for medical reassessment when the expected results are not obtained.

Conclusion

The present study findings suggest that there is a broad dispensation of fluoxetine hydrochloride in Campos Gerais - MG, a fact that can be associated with the increase of people suffering from depression and anxiety, a condition that affects all age groups. However, it is relevant to verify the irrationality in the medical prescriptions of this drug. Also, it was possible to delineate the user's profile during the survey period where the majority of users are women with a mean age of 36 years old. Most of the users suffer from depression and anxiety and have used the medication for more than one year and have already tried treatment with other psychotropic drugs, but obtained better results with fluoxetine and that although this is a psychoactive drug, most of the prescriptions were prescribed by a general practitioner. Thus, we must seek to improve the quality of prescriptions to achieve the rational use of medicines.

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