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Main Pharmaceutical Classes Used in the Treatment of Depressive Disorder: A Bibliographical Analysis

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Abstract: *Depressive disorder or depression is a disease that affects thousands of people. In the acute phase of the disease, it is very common to be prescribed antidepressants of several classes, therefore the main classes were highlighted: 1) Selective Serotonin Recaption Inhibitors (SSRIs); 2) Tricyclic antidepressants. OBJECTIVE: To survey the most used classes of drugs. METHODS: We analyzed articles contained in Scielo, Pubmed, Google Academic and Ministry of Health websites. RESULTS AND DISCUSSIONS: The psychopharmacology of depression has evolved a lot, increasing the number of drugs available in the market. Where the pharmacokinetics of substances can alter the bioavailability and adverse effects, becoming a preponderant factor for not adhering to therapy. CONCLUSION: Through the studies evaluated, it is concluded that despite the controversy, the class of selective serotonin inhibitors (SSRI) comprises the first line of choice in depressive treatment.*

Keywords*: Psycho pharmaceuticals, Pharmacological treatment, Depression, Antidepressants.*

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I. INTRODUCTION

Sadness is a particular universal feeling through which people experience, throughout their lives, conflicts, frustrations, disappointments, failures and losses. Thus, in certain circumstances, it is normal to feel depressed. However, if these experiences persist over a long period, psychic suffering can arise along with mood disorders (TELLES FILHO, 2014).

Depression presents troubling behaviors that appear slowly and intensely, being the oldest and most frequent of the diagnosed psychiatric disorders (MATOS, 2019). A period of sadness or discouragement is common among individuals and is a normal response to day-to-day disappointments or frustrations. These are episodes of short duration while the process of adaptation to the loss, alteration, or failure (whether real or perceived) that has been experienced (FERREIRA, 2018).

Depression, as a pathological condition, occurs when this process of adaptation is not effective, characterized by a minimum period of two weeks, during which a depressed mood, loss of interest or pleasure in almost all activities predominates (MENEZES, 2017).

The symptoms of depression are divided into: Vegetative life (change in appetite, loss or increase in body weight, change in sleep, decrease in sexual desire); Cognitive (change in memory, attention deficit, learning difficulty, pessimistic thoughts); Behavioral (anhedonia or loss of satisfaction in pleasurable activities, excessive delay in decisions, ideas of suicide, use of drugs to circumvent the symptoms of depression, low self-esteem); Somatic (physical symptoms such as pain, fatigue, difficulty in food digestion and muscle tension) (MENEZES, 2017andJARDIM, 2011).

According to Duncan (2012) urbanization, population aging, and lifestyle changes form a combination of chronic and non-transmissible pathologies such as depression, which are increasingly important in morbidity and mortality. In children and adolescents, mood can present itself through irritability as a substitute for sadness.

The Psychosocial Care Centers (CAPS) are public units, articulated to the health network that attend users with mental disorders. The Psychiatric Reform represented a great advance in the area of Mental Health in Brazil, and the creation of CAPS, through Ordinance No. 224 of 1992, provided considerably for its implementation, with free access to psychopharmaceuticals facilitated to users (DE CASTRO, 2011 and BRAZIL, 2010).

Antidepressant drugs are drugs that have their action in the Central Nervous System, regulating the mood, when the person with depression is depressed, this medication does not act when the mood is normal, distinguishing itself from psychostimulants. They act on the brain, having the function of modifying and correcting the neurochemical transmission in the Nervous System that regulates the state of mood (DE ARAÚJO, 2012).

According to Lima (2013), the mode of consumption of antidepressants varies according to the drug and the patient, it is normal for such medications to take some time to take effect, and it may take weeks to feel the desired effect, some side effects decrease or even disappear throughout the treatment.

In the present work, we highlight a bibliographic survey on the main classes of drugs indicated for depressive treatment such as: 1) Selective Serotonin Recaption Inhibitors (SSRIs); 2) Tricyclic antidepressants. Evidencing what effects these drugs cause in the body of the person being treated, their side effects and treatment time.

II. MATERIALS AND METHODS

This work consists of qualitative exploratory research, through a bibliographic review of scientific articles referring to the pharmaceutical classes most used for depressive treatment. To obtain the articles, we used, among others, the bibliographic survey conducted in the database of Scientific Electronic Libray Online (SciELO), National Library of Medicine of the USA (PubMed) and Google Academic and websites of the Ministry of Health, available in Portuguese and English, published between 2010 to 2020. Terms such as: Pharmacological treatment, depression, antidepressants, and psychopharmaceuticals were used. Articles that did not fit the objectives or were not included in the specific period were discarded.

The present work has not exposed any risks to the subject, as it is research conducted with materials already published and made available in the literature, therefore there is no interference or direct approach with humans. Thus, it was not necessary to be submitted for approval with the Committee of Ethics in Research, according to the resolution CNS 466/2012.

III. RESULTS AND DISCUSSIONS

Based on bibliographical analyses, a question raised by authors says that most antidepressants are prescribed by general practitioners, justified by the facilitated access to primary health care, where they try to alleviate the first symptoms of the patients, but that, the minority of this population of patients go through a psychologist or psychiatrist (FIGUEIREDO, 2018 and NEVES, 2015). Given this reality, the creation of CAPS with Ordinance 336/2002 began to aim at integral attention, coming from therapeutic actions and proposals, aimed at family, social and cultural reinsertion and providing clinical care in a daily care regime, thus avoiding hospitalizations in psychiatric hospitals (SOUSA, 2015 and BRAZIL, 2010).

The most used antidepressant classes according to the literature are tricyclic antidepressants (TADs) (amitriptyline, clomipramine, imipramine, nortriptyline) and selective serotonin reuptake inhibitors (SSRIs) (fluoxetine, paroxetine, sertraline, citalopram, and escitalopram) (PINTO, 2009, CANCELLA, 2012 and SCHENKEL, 2016). The SSRI is considered the first-choice treatment for anxiety and depression disorders, especially sertraline and citalopram due to their pharmacokinetic advantages, midlife, less drug interaction, and side effects, in addition to having its use defended in the elderly (SOUSA, 2016).

However, Araújo Aguiar (2016) refers to fluoxetine as the drug of the ISRS class with the lowest capacity to produce side effects, potentially safe in the treatment of depression associated with anxiety. Scoring

the pharmacological similarity of fluoxetine and sertraline, the Ministry of Health says sertraline is more successful in treating depression (MINISTRY OF HEALTH, 2019).

Tricyclic antidepressants (TADs) share with the ISRS the indication of the first choice. However, their side effects still represent their main disadvantage of use. Motivating patients to discontinue treatment (SANTOS, 2016 and FREDERICO, 2016). In addition to their action on monoamine transport, the TADs interact with adrenergic (α1), muscarin (M) and histamine (H1) receptors (table 1). The antagonization of these receptors leads to a series of side effects that include: cardiovascular effects, antimuscarinic effects (dry mouth, constipation, urinary retention, tachycardia, dizziness, palpitations and blurred vision), antihistamine effects (increased appetite and sedation) (SOUSA, 2015).

According to the facts, the use of TADs in the elderly should be cautious, especially in cardiac patients (CANCELLA, 2012). As amitriptyline and nortriptyline present in recent studies, the lower intensity in side effects and can be used in the elderly (SOUSA, 2015, PIGNARRE, 2012 and DE ARAÚJO AGUIAR 2016). However, it is worth mentioning that nortriptyline has greater selectivity in the inhibition of noradrenaline reuptake about serotonin reuptake inhibition, and there is not enough information that can prove superior or inferior efficacy, compared to amitriptyline (SCHENKEL, 2016).

According to Vicente (2015), tricyclic antidepressants (TADs) are the most widely used, and amitriptyline is the most consumed active ingredient. The usual prevalence of these drugs may be related to the morbidity of the population, in general, there has been an increase in the prescription and consumption of this class of drugs if confronted with older studies. In these older studies, the most used class is the ISRS, with the highest consumption of fluoxetine (SOUSA, 2015, CANCELLA, 2012 and ESMERALDO, 2017).

However, another factor that may influence the consumption pattern of this class of antidepressants is the therapeutic indication. Selective serotonin reuptake inhibitors (SSRIs) are preferably used in the management of major depressive and anxiety disorders, unlike tricyclic ones that offer a broader spectrum of clinical indication, such as in the approach of insomnia, chronic pain, among other various indications in medical practice (MEDAWAR, 2012, PIGNARRE, 2012 and VICENTE, 2015).

The quality of life of people with depressive symptoms may improve if there is a specific treatment. With the option of using Selective Serotonin Recaption Inhibitors (SSRI), different from tricyclic antidepressants, it has a lower degree of intoxication. For the same author, the high consumption of ISRS by the degree of professional and patient acceptability, due to its adverse effects are lower compared to other classes of antidepressants.

ISRSs have a lower abandon rate. However, their negative effect is associated with high rates of suicidal thoughts at the beginning of the treatment, due to their two-week period of latency. Even so, the difference in adverse effects and dropout rates are lower (ESMERALDO, 2017).

Fluoxetine, citalopram from the ISRS class, and tricyclic antidepressants: Amitriptyline, Clomipramine and Nortriptyline, are included in the list of essential drugs prepared by the World Health Organization (WHO) and in the National List of Essential Medicines (RENAME), made available by the Unified Health System (SUS) in municipal and state health units. For the treatment of anxiety, insomnia and moderate pain (MINISTRY OF HEALTH, 2019).

Table 1- Effect of ant depressive on blocking of receptors.

Drugs	**Class**	**Find**	**Alpha-1**	**H1**	**5-HT1**	**5-HT2**
Amitriptyline	TAD	+++	+++	+	+/-	+
Imipramine	TAD	+	+	+	0	+
Nortriptyline	TAD	+	+	+	+/-	+
Clomipramine	TAD	+	+	+	0	+
Fluoxetine	ISRS	0	0	0	0	+/-
Paroxetine	ISRS	++	+	+/-	+/-	+/-
Sertraline	ISRS	++	++	+/-	+/-	+
Citalopram	ISRS	-	+	++	+/-	+

ISRS= Selective Serotonin Recaptation Inhibitors; TAD= Tricyclic Antidepressants; Acha= cholinergic, alpha-1= alpha-adrenergic, H= histamine type 1/5, 5HT1= serotonergic type 1, 5HT2= serotonergic type 2, 0= no effect, +++= marked effect. Source: adapted, Cardoso, 2018.

IV. CONCLUSION

From this bibliographical review study, it was possible to see that there is increased use of psychopharmaceuticals all over the world. One of the reasons for this is related to the increase in diagnoses of depression. Where the advances of pharmacological research of antidepressants, bring to the patient's substances with pharmacokinetic profiles, of tolerance and interactions with other different drugs between each class and active principle.

Besides, the mechanisms of action proposed for each one of them are still linked to monoamine theories, of increasing the supply of neurotransmitters in the synaptic cleft, and sub-sensitization of postsynaptic receptors.

It is concluded then that there are divergences regarding the first line of choice for the treatment of depressive disorders since there is a difficulty because of the acceptability of the treatment because of the side effects of each therapeutic class. However, most of the authors describe that the selective serotonin receptor inhibitors (SSRI) are the pharmacological intervention of the first choice, due to the balance between its effectiveness and its side effects, as the second line is formed by the tricyclic antidepressants class (TAD).

Conflict of interest

There is no conflict to disclose.

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