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PREMENSTRUAL DYSPHORIC DISORDER - SELECTIVE SEROTONIN REUPPERATION INHIBITORS IN THE REGULATION OF SYMPTOMS AND THE POSITIVE EFFECTS OF PHARMACOTHERAPY ON THE QUALITY OF LIFE OF WOMEN WITH PMDD

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Abstract: Premenstrual dysphoric disorder (PMDD) is a severe and disabling form of premenstrual syndrome that affects an average of 5% of women during their period. Studies show that the intense symptoms present during PMDD involve multiple factors, from genetic, ovarian or uterine, hormonal, neurological and psychological causes. These symptoms significantly impact the quality of life of women who suffer from this disorder, and serotonin inhibitors are considered the gold standard treatment for these cases, since they inhibit the release of hormones that stimulate the emergence of the aforementioned disorders. Therefore, the purpose of this chapter is to present the effectiveness of selective serotonin inhibitors (SSRIs) in the treatment of Premenstrual Dysphoric Disorder (PMDD). It is understood that studies have shown that SSRIs have reduced PMDD symptoms significantly. Likewise, each SSRI can cause particular adverse effects, which makes it necessary to choose the agent according to the characteristics of each patient.
Keywords: premenstrual disorder. premenstrual dysphoric disorder. serotonin inhibitors

INTRODUCTION

Epidemiological data show that between 75% and 90% of women of childbearing age have symptoms associated with menstruation. Within this population group, 20% to 40% of cases correspond to Premenstrual Disorder (PMS), while between 2% and 10% of these patients meet the criteria for premenstrual dysphoric disorder (PMDD). According to available information, the prevalence of PMDD in Brazil is 1.9 to 5 million women (LIMA, ROMÃO, GOUVEIA, 2021; MOURÃO, ZANINI, 2020).

Premenstrual symptoms are considered multifactorial. Normal fluctuations in the production of ovarian hormones during

the menstrual cycle may be associated with cerebral and peripheral biochemical phenomena, which trigger the somatic and psychic symptoms that appear before menstruation in predisposed women. Thus, it is estimated that premenstrual symptoms are the result of the interaction between processes in the central nervous system (CNS), sex hormones, some neurotransmitters, and neurohormonal systems, including γ-aminobutyric acid (GABA), serotonin, and the renin- angiotensin-aldosterone (RAAS) (RIOS et al., 2020).

It is not known what factors lead women to develop PMDD, however studies show that decreased levels of the hormones estrogen and progesterone, after ovulation and before menstruation, can trigger PMDD symptoms. Serotonin, a neurotransmitter that regulates mood, hunger, and sleep, may also play an important role in the occurrence of PMDD, as serotonin levels, like hormone levels, change throughout your menstrual cycle (GOLDEN, 2017). We already have a prominent question: what is the effectiveness of selective serotonin inhibitors in the treatment of Premenstrual Dysphoric Disorder? The chapter will address this issue, seeking to direct to an elucidated understanding of treatment with antidepressants of the serotonin inhibitor class.

PATHOPHYSIOLOGY OF PREMENSTRUAL DYSPHORIC DISORDER – ETIOLOGY OF THE DISORDER

The menstrual cycle has an average period of 28 days, which can vary between 24 to 35 days, starting to be counted from the first bleeding, not referring to menarche. During the menstrual period, there is a cycle of hormone release, consisting of a hierarchy that begins with the release of gonodotropins (GnRH), released by the hypothalamus, in response, the pituitary gland releases follicle-stimulating (FSH) and luteinizing (LH) hormones. After these, the body responds with the ovarian hormones: estrogen and progesterone. There is no regularity in the secretion of these hormones, and there may be instability throughout the cycle, that is, there is a variability of symptoms among women (GUYTON and HALL, 2008).

Menstruation is a process of periodic shedding of the endometrium, characteristic of mammals, with cyclical hormonal changes that affect the entire woman's body and not just the endometrium. Therefore, there are normal variations in behavior, mood, weight, appetite, libido and body temperature, both in the follicular and luteal phases of the cycle (SILVEIRA et al., 2014).

Studies related to symptoms associated with the cycle show a multiplicity of factors involved: genetic factors, ovarian or uterine, hormonal and neurotransmitter changes, distress and eating behavior disorders. It is admitted that the etiology of these symptoms is not yet fully understood, but there is consensus on the interrelationship of psychosocial and biological factors, among which hormonal variations and changes in certain neurotransmitters are involved with the pathophysiology of dysphoric disorder of menstrual cycle origin. (CARVALHO, 2010).

Premenstrual dysphoric disorder (PMDD) is a severe and disabling form of premenstrual syndrome that affects 1.8–5.8% of women in their menstrual cycle. There is a variety of symptoms linked to the disorder, such as affective, behavioral and somatic, which recur monthly during the luteal phase of the menstrual cycle (COSTA et al., 2020).

Conditions throughout the menstrual cycle are often a reason for concern and a frequent cause of medical and/or psychological consultation. The first description of a set of mood and behavior changes associated with the luteal phase was made in 1931 by

Robert Frank. From Frank's studies (1931), he reported a wealth of scientific evidence about conditions throughout the menstrual cycle. This series of symptoms and signs were finally grouped together constituting nosological categories described in the ICD-10 (WHO, 1992) and DSM-IV (APA, 1994) as Premenstrual Syndrome (PMS) and when the symptoms are severe, Premenstrual Dysphoric Disorder. menstrual cycle (PMDD).

The etiology of PMDD is an active area of investigation. Potential biological contributors include central nervous system (CNS) sensitivity to reproductive hormones, genetic factors, and psychosocial factors such as the stress. Sex steroids produce different effects, estrogens have neuromodulatory activity, through receptors that are located in various nervous structures, and they can also modify the concentration of neurotransmitters by different mechanisms. On the one hand, they produce an increase in catecholamine synthesis, affecting their metabolism by increasing the rate of degradation of monoamine oxidase (MAO), an enzyme related to the catabolism of norepinephrine, dopamine and serotonin, neurotransmitters involved in mood stabilization. However, estrogens, by increasing the blood release of tryptophan, promote the synthesis of serotonin, a neurotransmitter related to depression (MARIANO, 2012).

The timing of onset and end of symptoms in PMDD suggests that hormonal fluctuation is a key component in the pathogenesis of PMDD. Paradoxically, women with PMDD cannot be distinguished from asymptomatic women in terms of peripheral ovarian hormone levels. Instead, research suggests that women with PMDD have altered sensitivity to normal hormonal fluctuations expected in the cycle, particularly estrogen and progesterone, neuroactive steroids that influence CNS function (SILVEIRA et al., 2014).

According to Oderich (2017) progesterone levels are low during menstruation and the follicular phase and reflected by the main progesterone metabolite, allopregnanolone (ALLO), also a neuroactive steroid. Progesterone and ALLO increase in the luteal phase and decrease rapidly during menstruation.

Chronic exposure (due to cycles) followed by rapid withdrawal of ovarian hormones may be a key factor in the etiology of PMDD. In a developed animal model of PMDD based on progesterone withdrawal, rats in withdrawal from physiological doses of progesterone exhibited social withdrawal and anhedonia, characteristic symptoms of PMDD. In fact, preclinical research demonstrates that chronic exposure to progesterone followed by rapid withdrawal is associated with increased anxiety behavior and changes in the function of the γ-aminobutyric acid (GABA) A receptor, the main inhibitory neurotransmitter in the CNS. Studies carried out suggest that this effect may not be due to progesterone itself, but to the main progesterone metabolite, ALLO, since blocking the conversion of progesterone to ALLO blocks the aforementioned effects of progesterone. ALLO is a potent positive allosteric modulator of the GABA A receptor, similar to alcohol or benzodiazepines, with anxiolytic, anesthetic and sedative properties.

It is possible that women with PMDD developed tolerance to the arousal-lowering and GABA-boosting effects of ALLO. Although suboptimal luteal phase GABA A receptor sensitivity to neuroactive steroids is a potential mechanism for PMDD pathogenesis, another potential mechanism is through direct effects on ALLO biosynthesis. In preclinical studies, manipulations that produce depressive and anxiety symptoms in mice are associated with decreased levels of ALLO in the amygdala, hippocampus, and medial prefrontal cortex. Modifying the

formation of neuroactive steroids, such as ALLO, which affect GABAergic tone, may be an important avenue for the development of treatment for PMDD (MOURÃO; ZANINI, 2020).

Estradiol exerts potent effects on several neurotransmitter systems involved in regulating mood, cognition, sleep, eating, and other aspects of behavior. With selective serotonin reuptake inhibitors (SSRIs) being the gold standard treatment for PMDD, the general effects of increased estradiol on serotonergic function in particular are important to consider in the pathophysiology of PMDD.

Clinically, women with PMDD exhibit low mood, cravings for specific foods, and impaired cognitive performance during the luteal phase, all cognitive-affective characteristics that may be influenced by serotonin. Previous work has established that ovarian steroids alter the expression of 5-HT2A receptor and serotonin transporter (SERT) genes, and the vesicular monoamine transporter, that estrogen administration increases serotonin transporter (SERT) mRNA, particularly in brain areas involved with emotion and behavior, and low estrogen states were associated with decreased SERT gene expression. Estradiol also decreases the expression of monoamine oxidase A (MAOA) and catechol-O-methyltransferase (COMT) and may impact brain-derived neurotrophic factor (TRIBÉSS, 2020).

Given the model of CNS sensitivity to PMDD, it is possible that women with PMDD are more sensitive to these effects of estrogens on serotonergic function. Women with PMDD have specific serotonin (5-HT) abnormalities that are particularly apparent in the late luteal phase, when estrogen levels have decreased. These include a deficiency of 5-HT in whole blood, decreased production of 5-HT in response to L-tryptophan challenge, and worsened premenstrual symptoms during tryptophan depletion.

Recent work has focused on polymorphisms in genes encoding sex steroid hormone receptors, such as estrogen receptor alpha (ESR1), which may confer differential sensitivity to hormones. Single nucleotide polymorphisms in the ESR1 gene were associated with PMDD in preliminary research, and a 5HT1A gene polymorphism associated with reduced 5-HT neurotransmission and major depression was found to be associated with PMDD (COSTA, 2014).

The serotonin transporter gene polymorphism (5 - HTTLPR), which is associated with reduced transcriptional efficiency of SERT, was associated with certain psychological characteristics in women with PMDD, but was not associated with PMDD itself. Most studies exploring genes associated with premenstrual symptoms used small samples, and more epidemiological studies on the genetics of PMDD are needed (TRIBÉSS, 2020).

As seen throughout this chapter, premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) include several somatic and mood symptoms that appear regularly before menstruation begins, disappear quickly when menstruation begins, and can be mild. or cause very adverse effects on behavior and consequently on the quality of life of women who have this disorder, justifying pharmacological treatment as a support measure for women, not neglecting the needs that these patients have, as well as psychotherapeutic treatment. if necessary.

QUALITY OF LIFE OF WOMEN WITH PMDD - DETERMINING FACTORS ACCORDING TO DSM-IV

Currently, taking into account a highly competitive postmodern context, the various

symptoms associated with the menstrual cycle can interfere in different areas of life, decreasing physical, cognitive and emotional well-being, bringing with it a lower performance in several areas (CARVALHO, 2010).

Throughout the menstrual cycle, a significant number of women experience changes in their daily lifestyle (food consumption, sleep-wake cycle, sexual desire, among other factors). These changes are related to physiological, psychological, cultural and social aspects. The search for cognitive, emotional and behavioral relationships during the menstrual cycle makes it possible to link two coincident phenomena at the temporal level, changes and emotional and behavioral hormonal changes that occur in this period (COSTA, 2014).

Premenstrual dysphoric disorder is a complex diagnosis, which is why women who have PMDD, over the years of their symptoms, receive a variety of diagnoses, from anxiety and depression to more complex mental health conditions, such as the bipolar disorder. and Borderline personality disorders, causing negative impacts on the quality of life of these women. As a consequence of these diagnoses, these women are often prescribed a variety of psychotropic drugs, with a long therapeutic duration, causing drug resistance and, as a consequence, the change of pharmacotherapy (MARIANO, 2012).

Premenstrual dysphoric disorder (PMDD) is a severe mood disorder characterized by cognitive-affective and physical symptoms in the week before menstruation and affects millions of women worldwide. In 2012, an international expert committee on the pathophysiology and treatment of PMDD submitted to the American Psychiatric Association's DSM-V Executive Committee a review of the current science on PMDD and gave its recommendation for the inclusion of PMDD in the DSM-V as a complete diagnosis. category (RIOS et al., 2020).

In defining PMDD, mood symptoms are key. The DSM-IV and DSM-V diagnoses are based on a perimenstrual pattern of at least five physical, affective, and/or behavioral symptoms, with a requirement for at least one of the main affective symptoms of affective lability (mood changes, crying, sensitivity to rejection); irritability or anger that is usually characterized by heightened interpersonal conflicts; marked depressed mood, hopelessness, or self-deprecating thoughts; or anxiety, tension or feeling on the edge (SILVEIRA et al., 2014).

The woman may also have difficulty concentrating or a feeling of being overwhelmed or out of control. These cogno-affective symptoms may be accompanied by behavioral and somatic symptoms such as loss of interest in usual activities, lack of energy, changes in appetite or food cravings, changes in sleep, and physical symptoms unique to premenstrual such as the breast tenderness, breast swelling or abdominal distension (RIOS et al., 2020).

According to the DSM-V criteria, these symptoms must have occurred during most menstrual cycles in the previous year to meet criteria for a diagnosis of PMDD. Community data and clinical samples from women with a prospectively confirmed diagnosis of PMDD report the greatest symptom severity from 3-4 days before the onset of menstruation to 3 days after the onset of menstruation. Symptoms must be absent in the post-menstrual week.

While it may seem like a slight difference between DSM-IV and V, mood lability and irritability are listed first in the latest version due to findings that these symptoms are considerably more common among women with PMDD than depressed mood, which was listed first in the DSM-IV. Another subtle difference between the DSM-IV and V

criteria is that the latter included the concept of distress in addition to impairment due to PMDD symptoms. Anguish and/or disability must be present in the area of work, school, social activities or relationships with other people (DOURADO, 2017).

Of particular importance, symptoms must be confirmed by prospective daily assessments for at least two symptomatic cycles; this can be accomplished through tools such as the Daily Problem Severity Record (RDGP), the Premenstrual Experience Calendar, or the Premenstrual Assessment Form. Although a presumptive diagnosis of PMDD can be made based on history alone, prospective daily assessments are invaluable in ruling out premenstrual exacerbation of other psychiatric disorders that are present to some extent throughout the menstrual cycle (RIOS et al., 2020).

Regarding PMDD, a greater proportion of women have milder premenstrual symptoms. Recently, attempts have been made to distinguish between mild premenstrual symptoms experienced by many women and the more severe symptoms present in PMDD (SILVEIRA et al., 2014).

The American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization have published descriptions of premenstrual mood changes. While lay language often refers to any unpleasant or undesirable physical, emotional, or behavioral symptom that occurs before or during menstruation such as premenstrual syndrome or "PMS", the ACOG provides specific criteria for its diagnosis, including a physical symptom. or psychological in the 5 days before menstruation (ALMEIDA and SIQUEIRA, 2015).

Symptoms must occur in three consecutive menstrual cycles and subside within 4 days of the start of menstruation. As with PMDD, the symptom(s) must (m) cause significant impairment and must be verified by prospective assessment for diagnosis. Given this continuum of severity, future research may focus on the etiology of symptoms shared between PMDD and PMS (COSTA et al., 2020).

With no obvious factors to explain the sudden negative changes in their emotions, women may have doubts about their mental health diagnosis, as they may not accurately match their psychological experiences. As a result, women with PMDD have a lower quality of life, experience higher somatization, obsessive-compulsive, depressive and anxiety symptoms, have poor emotions, family relationships and social functioning, and the disease is highly compromised. The appropriate recognition of the disorder and its impact leads to the treatment of these women, a point that highlights the need for pharmacological and non-pharmacological treatment (MASRY and ABDELFATAH, 2014).

A study carried out with women from the department of Xàtiva-Otinyent in Spain, with premenstrual dysphoric syndrome (PMDS) showed that throughout the study there was a high incidence of irritability, anger or an increase in interpersonal conflicts in a marked and persistent way. Furthermore, crying was the only psychological symptom that appeared in all menstrual cycles over the course of a year. The researchers found that all women who participated in the study had one or more defining symptoms of PMDD for more than one year (CATALÁ et al., 2018).

Although there is a high prevalence of symptoms, both physical and psychological, they end up not having the diagnosis directed, which makes treatment inadequate and, for the most part, self-medication becomes one of the alternatives. PMDD is not seen as a whole as a syndrome, which means that different professionals (family doctors,

psychiatrists and gynecologists) attend to the woman partially, and treatments are applied according to the different symptoms or causes independently (LIMA, ROMÃO, GOUVEIA, 2021).

In view of what has been exposed in this chapter, it is important to emphasize that, given the impacts caused by PMDD and because it occurs in almost all cycles, it is essential that there is Health Education, in order to help detect PMDD early, its adequate treatment and a better quality of life. It is also highlighted the need to carry out an awareness campaign and health professionals, to detect, diagnose or treat this syndrome in an adequate way, giving it visibility and not trivializing the symptoms or stigmatizing the woman who presents it.

PHARMACOLOGICALAPPROACH - SEROTONIN INHIBITORS IN THE TREATMENT OF PMDD

Serotonin is a neurotransmitter closely related to the control of emotions and mood, although it also performs other types of functions, among them, regulating appetite causing a feeling of satiety, controlling body temperature, regulating sexual appetite, controlling motor activity, perception and cognitive function. Along with other neurotransmitters such as dopamine and norepinephrine, it participates in the mechanisms that govern anxiety, fear, anguish and aggression. Serotonin regulates the secretion of some hormones, such as melatonin, a protein whose many functions include the regulation of circadian rhythm and sleep (FEIJÓ; BERTOLUCI; REIS, 2011).

In addition, it plays an important role in the formation and maintenance of bone structure and is also involved in the functioning of the vascular system. Serotonin is also known as the happiness hormone, because by increasing its levels in neural circuits, it generates feelings of well-being, relaxation, satisfaction and increases concentration and self-esteem.

Selective serotonin receptor inhibitors (SSRIs) antidepressants are the treatment of choice for depression, anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder, bulimia nervosa, and premenstrual dysphoric disorder (GANEO and NETO, 2021).

Selective serotonin reuptake inhibitors (SSRIs) are a class of antidepressants that share a major pharmacological mechanism but have a highly heterogeneous secondary pharmacology. Blocking serotonin reuptake increases its levels in the central nervous system and throughout the body and explains the therapeutic actions of SSRIs as well as their side effects, mainly gastrointestinal, such as nausea; also neuropsychiatric symptoms, headache and tremor (NEVES, 2015).

SSRIs antagonize the presynaptic serotonin reuptake pump. This reuptake inhibition initially increases the availability of serotonin in the synaptic space, which subsequently produces a "down" regulation of the same receptors, eventually increasing net serotonergic transmission. It has been suggested that the effect of 5-HT would produce its therapeutic actions through the stimulation of 5-HT receptors in four basic pathways that start from the raphe nuclei: for depression, the pathway that goes to the cortex would be prefrontal stimulated; for obsessive compulsive disorder (OCD), one that goes to the basal ganglia would be uninhibited; in panic disorder, it goes to the limbic cortex and hippocampus, and for bulimia, it is directed to the hypothalamus (FEIJÓ; BERTOLUCI; REIS, 2011). Currently, SSRIs replace benzodiazepines in the treatment of generalized anxiety disorder, just as they replaced tricyclic antidepressants in the past. Depressed patients have less

serotonergic neurotransmitter activity than normal (serotonergic depression hypothesis) and blocking reuptake at the presynaptic serotonergic receptor site 5HT1A, 5HT2C and 5HT3C increases neurotransmission in this system (BRAGA et al., 2012). Desensitization of 5HT1A autoreceptors and downregulation of G protein-coupled 5HT2 receptors, a late effect of SSRIs, results in improvement of depressive symptoms. The mechanism that explains the relatively late antidepressant effect seems to be different from the acute and rapid serotonergic effect responsible for the improvement of premenstrual dysphoric disorder (SILVA, 2012).

SSRIs used in the treatment of PMDD include fluoxetine, sertraline, citalopram, and paroxetine. Studies showed that SSRIs reduced PMDD symptoms significantly compared to placebo; Between 60 and 75 percent of women with PMDD improve with an SSRI. Adverse effects of most SSRIs include gastrointestinal disturbances, anxiety, sexual dysfunction, cognitive impairment, and serotonin syndrome.

The individual properties, especially those not related to serotonin reuptake, make it possible to distinguish the drugs from this group and choose the most suitable for each particular case. Fluvoxamine has an affinity for receptors that regulate dopamine release. This drug has been shown to produce an important anti-amnestic effect with a positive action in memory disorders; and may be beneficial in treating depressed patients with symptoms of anxiety or stress and memory disorders, as well as psychotic depression. The most frequent adverse effect of fluvoxamine is nausea, which tends to disappear after a few days, with drowsiness, asthenia and headaches also being observed. It does not present active metabolites that prolong its effects (GALLI, 2018).

Fluoxetine, a potent inhibitor of 5-HT2C receptors, by this mechanism, acts as a modulator of the dopaminergic and noradrenergic brain systems, which produces increased activity and weight loss. These properties can cause undesirable effects such as restlessness and insomnia in anxious patients; but they are beneficial for cases with decreased activity. There is an active metabolite, norfluoxetine, which has activity similar to the parent drug and a half-life of 4 to 16 days (BRILHANTE et al., 2010)

Sertraline has a significant inhibitory effect on dopamine reuptake, although decreased for serotonin; because of this characteristic, it is very useful in the treatment of patients with certain types of depression, especially melancholic ones; they can also cause adverse cardiovascular, extrapyramidal symptoms, and in some cases sexual dysfunction; in addition, because it has an active metabolite, the effects can be prolonged (GALLI, 2018).

Antidepressant effects and some adverse reactions such as gastrointestinal disturbances may occur. The other pharmacological actions of SSRIs distinguish them from each other, and knowledge of these variations allows us to understand why some patients respond better to an SSRI than to another drug. Choosing the treatment that best suits each patient is essential, since the choice of the first SSRI may not always be so effective, that is, adaptations and changes in pharmacotherapy may occur (HENZ, 2016).

Treatment of Premenstrual Disorder (PMDD) with a serotonergic antidepressant significantly improves functioning and quality of life, in all studies that have systematically examined quality of life issues in this disorder, this quality is reflected in family life, social and work context of this patient. While data show that PMDD is effectively treated with serotonergic antidepressants and that the functional impairment that

accompanies the disorder also improves with treatment, the social and economic burden of PMDD remains largely unknown, this means more studies addressing this context of unfamiliarity. There is a need for greater awareness of the effectiveness of treatments and reliable measures, in addition to the direct and indirect costs of the health disorder, as the treatment is not restricted to drugs alone, psychotherapy also enters as a treatment for these patients (NEVES, 2015).

Hofmeister (2016) reviewed 31 randomized controlled trials that compared SSRIs with placebo for the relief of PMS symptoms. Each of the five SSRIs studied had statistically significant benefits in patient-reported symptoms when taken continuously or only during the luteal phase, but more direct studies comparing luteal phase administration with continuous administration are needed. Adverse effects include nausea, asthenia, fatigue, and sexual dysfunction. All doses of SSRIs appeared to be effective for psychiatric symptoms and, ultimately, could be titrated according to patient tolerability. Higher doses are needed for the relief of physical symptoms.

All SSRIs share the same mechanism of action, namely the inhibition of serotonin reuptake. However, they differ in terms of their action profile on other targets. In general, all SSRIs have similar efficacy, which is superior compared to other drugs (GANEO and NETO, 2021).

Likewise, each SSRI can cause particular adverse effects, which makes it necessary to choose the agent according to the characteristics of each patient. In this sense, it is important to consider the possibility of pharmacological interactions at the level of the cytochrome P450 (CYP450) enzyme system, since these enzymes are primarily responsible for the biotransformation of SSRIs. In turn, SSRIs can affect the activity of CYP450 isoenzymes (BRASIL, 2012).

As seen, many women suffer from a variety of varied symptoms before menstruation and only a minority have PMDD. Therefore, it is important to make an accurate diagnosis by criteria (DSM-V) before initiating therapies that may be inappropriate if patients do not meet criteria for PMDD, and the diagnosis is left to the physician.

FINAL CONSIDERATIONS

In this chapter, we understand the effectiveness of selective serotonin inhibitors in the treatment of Premenstrual Dysphoric Disorder (PMDD). PMDD has been found to be a disease responsible for serious psychological effects in women during the luteal phase (the period between ovulation and menstruation). Its periodicity makes it particularly challenging for this patient to face her life in society, since the symptoms reappear every month, with each menstruation.

Furthermore, the literature shows that due to the various extreme illnesses and sometimes with serious consequences caused by premenstrual dysphoric disorder, affected women face disruptions in their daily, social and professional life. It is also noteworthy that the reason why some women suffer from PMDD, while others do not have symptoms, remains unknown and under study. On the other hand, some risk factors are known: stress, obesity, as well as a history of trauma or sexual abuse. It is also known that dietary and lifestyle adjustments can lessen the intensity of symptoms.

In addition, it is necessary to assess its severity and the consequences on the patient's social and relational life in order to devise an appropriate therapeutic plan. This therapeutic plan consists of different steps, each of which must be discussed with the patient.

As it was seen in this chapter, serotonin reuptake inhibitors (SRIs) are the most

commonly prescribed antidepressants in the treatment of DSM-V Characterized Depressive States. These serotonergic antidepressants are numerous, due to an efficacy similar to that of imipramines, and the most indicated for the treatment of PMDD are fluoxetine, sertraline, citalopram and paroxetine.

SSRIs are currently the treatment of choice when non-pharmacological strategies do not show positive effects. The administration of hormonal treatments must be limited to specific cases, taking into account the patient's history and existing underlying diseases. The combination of psychotherapy is helpful in most cases and can even be significantly minimized in some situations.

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