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EFFECTIVENESS AND SAFETY OF HORMONAL THERAPY IN IMPROVING SEXUAL FUNCTION IN WOMEN IN MENOPAUSE

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Abstract: Goal: To discuss the effectiveness of hormone therapy in improving female sexual function during menopause, as this phase plays an integral role in women's lives. Methodology: Bibliographic review carried out through searches in the PubMed and Scientific Electronic Library Online (SciELO) databases, with 11 articles selected to compose the collection. Results: Menopause, the female post-reproductive period, is associated with symptoms resulting from hypoestrogenism, such as mood swings, vaginal dryness, dyspareunia, among others, which significantly impact the woman's quality of life and can generate a feeling of loss of femininity. In order to minimize these impacts on sexual life, hormone replacement therapy has been widely used, due to its many benefits, including improvement in vaginal dryness, regulation of libido and female sexual arousal, increased bone mineral density and improvement in lipid profile. Final considerations: It was observed that hormone replacement therapy is currently considered the most effective and safe treatment for menopausal women, providing relief from vasomotor symptoms, reduction of hot flashes and other benefits related to female sexual health.
Keywords: Menopause; Sexuality; Hormone replacement therapy.

INTRODUCTION

Menopause represents an inherent stage in the evolutionary process of female life, intrinsic to advancing age, leading to substantial transformations. The progressive decrease in estrogen levels during the preliminary stages of menopause triggers a wide variety of symptoms capable of compromising women's physical, mental and sexual health. In addition, such a condition can have repercussions on professional performance, social interactions, emotional stability, interpersonal communication and

the perception of pleasure in living, therefore affecting the quality of life of these women (HEIDARI et al., 2019). Women undergo hormonal and metabolic changes during the climacteric, a transition period in the female life cycle marked by the biological shift from the reproductive to the non-reproductive period. This period includes the loss of reproductive capacity and is composed of perimenopause and postmenopause. Menopause is characterized by the end of the menstrual period for 12 consecutive months (CREMA et al., 2017). The duration of the climacteric is variable and influenced by socioeconomic and environmental factors, being commonly reported at 50 years of age, but symptoms can start earlier (GUTIÉRREZ et al., 2020).

During the climacteric, there is a decrease in estrogen levels and ovarian activity, resulting in an increase in the secretion of pituitary gonadotropic hormones as a compensatory mechanism to induce oocyte maturation (GUTIÉRREZ et al., 2020). The most common signs and symptoms during this period are hot flashes, vaginal dryness, loss of libido, sweating and changes in sexual functioning. These symptoms are influenced by personal and contextual factors (CREMA et al., 2017). In addition, changes in vaginal tissues can cause pain, burning, irritation, cracks and decreased lubrication, in addition to affecting the appearance of the genitals (SAMPAIO et al., 2021).

Female sexuality is a complex phenomenon and influenced by several factors, such as the social, cultural, economic, religious, educational and psychological context (CREMA et al., 2017). In this context, hormone replacement is a therapeutic option that plays an integral role in women's lives, improving the quality of sexuality. Testosterone administration, for example, can increase libido and slow down the aging process. In addition to the health-disease aspect, hormone replacement is also related to general well-being (SAMPAIO et al., 2021). During the climacteric, many women are in a process of growth and personal fulfillment, but the problems related to this period can affect physical appearance, reduce self-confidence and destabilize emotional balance (GUTIÉRREZ et al., 2020).

Given this context, the objective of this literature review is to evaluate the efficacy and safety of hormone therapy in improving sexual function in menopausal women, considering the effects of hormone therapy on sexuality, in addition to analyzing the risks and benefits associated with hormone therapy in the treatment of sexual dysfunction in menopause.

METHODOLOGY

This is a literature review developed according to the criteria of the PVO strategy, an acronym that represents, respectively, population or research problem, variables and outcome. Thus, the following guiding question was elaborated for the research: "What is the efficacy and safety of hormone therapy in improving sexual function in menopausal women?". In this sense, according to the parameters mentioned above, the population of this research refers to menopausal women who use hormone therapy, in order to identify the efficacy and safety of this therapy for this population. The searches were carried out using PubMed and Scientific Electronic Library Online (SciELO) databases. The following descriptors were used in different associations with the Boolean operator "AND": menopause, sexuality, hormone replacement therapy, libido, risk, benefit. Then, the following inclusion criteria were established: articles in English and Portuguese; published between 2012 and 2023; and that addressed the themes proposed for this research, such

as meta-analysis studies, randomized clinical trials and cohort studies available in full. The exclusion criteria were: duplicate articles, available in the abstract form, that did not directly address the proposal studied, and that did not meet the other inclusion criteria. After the association of the descriptors used in the researched databases and the application of the inclusion and exclusion criteria, seven articles were selected from the PubMed database and four articles from SciELO, totaling 11 studies used to compose the collection.

RESULTS

SEXUAL DYSFUNCTION IN MENOPAUSE

Menopause, which is the female post-reproductive period, starting one year after the last menstruation, is associated with symptoms resulting from the decrease in estrogen levels, known as hypoestrogenism. These symptoms include hot flashes, sweating, fatigue, headache, myalgia, arthralgia, vaginal dryness, dyspareunia, changes in sleep patterns, mood swings, among others (CABRAL et al., 2012). These symptoms have a significant impact on women's quality of life and are often the starting point for a series of side effects (HEIDARI et al., 2019).

Recent studies have shown that these symptoms affect the sexual function of women after menopause, both physically, mentally and socially. The lack of estrogen, in addition to being related to an increased risk of cardiovascular disease, can lead to decreased sensitivity, loss of libido, reduced lubrication and, consequently, pain during sexual intercourse. In addition, aging can lead to an altered body image, along with a feeling of loss of femininity and a high incidence of depression and anxiety, which negatively impacts women's sex lives (HEIDARI et al., 2019).

In this context, to assess the occurrence of sexual dysfunction, since many women do not report spontaneously or do not have access to regular medical care, some questionnaires have been used. However, it can be difficult to establish a direct link between sexual dysfunction and menopause. For the Brazilian reality, the questionnaire for evaluating female sexuality after menopause - QSFM - proved to be a valid instrument, with relevant psychometric attributes, aimed at analyzing the sexual function of menopausal and postmenopausal women, taking into account the symptoms presented and their impact on sexual life. It is important to emphasize that the use of this questionnaire is based on self-report, and sociodemographic conditions and the absence of clinical diagnosis of organic causes in menopause can affect the results, masking the occurrence or not of sexual dysfunction (LIMA et al., 2020).

In order to minimize impacts on sexual life, randomized placebo-controlled trials have shown that hormone replacement therapy with low-dose testosterone is effective in postmenopausal women with sexual dysfunction. However, while this approach has shown short-term safety and there have been no controversies about its safety to date, the cardiovascular risks and potential increased incidence of breast cancer in the long term are not yet fully understood (VEGUNTA et al., 2019).

HORMONE THERAPY

Menopausal hormone therapy (MHT) is considered the first-line treatment for the relief of menopausal symptoms such as vasomotor and genitourinary symptoms. However, its effects on various health outcomes remain uncertain, presenting a complex balance between benefits and harms (ZHANG et al., 2021). Often, health professionals are asked about hormone replacement therapy to deal

with female alterations after menopause, such as vulvovaginal atrophy and decreased libido, among others. Vaginal atrophy occurs due to the decrease in systemic estrogen during menopause, leading to the involution of the vaginal epithelium and the tissues of the vulva and vagina. According to the North American Menopause Society, women with genitourinary symptoms of menopause must use vaginal moisturizers, lubricants and continuous sexual activity or vaginal exercises as a first line of treatment. If there is no success, the discussion about the use of hormone therapy must be considered (PARAISO et al., 2020).

One subject under discussion is the use of fractional CO2 laser therapy, which acts through thermal shock activating proteins and growth factors, resulting in tissue remodeling and production of collagen, elastic fibers and angiogenesis in different parts of the body. It was observed that, after 6 months, fractional CO2 laser therapy showed similar results to vaginal estrogen treatment with regard to the improvement of menopausal symptoms and sexual function (PARAISO et al., 2020).

Sexual dysfunction is a prevalent problem in postmenopausal women and significantly affects quality of life. Several studies show that endogenous testosterone therapy can influence the sexual behavior of these menopausal women, resulting in a moderate effect of approximately one additional satisfying sexual activity per month. Although testosterone therapy is well tolerated in the short term, with adverse effects such as skin reactions, unwanted hair growth, acne, and vaginal bleeding, the Endocrine Society Clinical Practice Guideline states that there is insufficient evidence to recommend this therapy in women in general. Therefore, it is important for the physician to provide full advice on the risks and benefits before opting for this approach (JAYASENA et al., 2019).

Androgens play an important role in regulating sexual desire and arousal in women. Testosterone, the primary ovarian androgen, has been used in the treatment of carefully selected women with hypoactive sexual desire disorder, with support from the Endocrine Society and the American College of Obstetricians and Gynecologists. However, non-oral use of testosterone in women has not been approved by the United States Food and Drug Administration (FDA) due to uncertainties about its long-term efficacy and safety. The FDA has only approved the intravaginal use of androgens (VEGUNTA et al., 2019). The risks and adverse effects depend on the duration and dose used, with hirsutism and increased acne being the most common effects. Absolute contraindications for the use of androgens include pregnancy, lactation, neoplasms dependent on this hormone, severe acne, and hirsutism (JAYASENA et al., 2019).

BENEFITS AND RISKS ASSOCIATED WITH HORMONE THERAPY

Many climacteric women are seeking professional help to deal with the symptoms of this phase, especially those experiencing changes in their sex life. Vulvovaginal atrophy is a common problem in postmenopausal women and is associated with symptoms such as irritation, vaginal dryness, dysuria and dyspareunia, which are related to the development of female sexual dysfunction. Hormone replacement therapy is often considered the most effective treatment for alleviating vasomotor symptoms and sexual changes in menopausal women. However, there is a portion of women who cannot benefit from this treatment, and although the true effectiveness of other methods is still not fully understood, some of them have shown improvements in symptoms with mild to moderate adverse effects, without serious ones (SARMENTO et al, 2023).

In addition to alleviating menopausal symptoms, MHT has been linked to a reduced risk of bone fractures, diabetes mellitus, and esophageal, gastric, and colorectal cancer. However, it also increases the risk of stroke, venous thromboembolism, gallbladder disease, breast cancer and ovarian cancer. Symptoms such as hot flashes and night sweats, characterized as vasomotor symptoms, affect approximately 75% of women. Furthermore, up to 84% of postmenopausal women experience genitourinary symptoms such as vulvovaginal atrophy and incontinence (ZHANG et al., 2021).

When weighing the risks and benefits, it is known that women have a percentage of androgen hormones in their bodies, which makes testosterone treatment a viable option, as this hormone plays a role in regulating female libido and sexual arousal. In addition to the positive effects on sexual function, studies on the subject have also reported additional benefits of testosterone use, such as increased bone mineral density and reduced serum high-density lipoprotein cholesterol. However, as testosterone is a typically male hormone, adverse effects such as hirsutism, acne and vaginal bleeding have also been observed (JAYASENA et al., 2019).

The benefits of hormone therapy are diverse, and some of them are more pronounced when given orally, except in the case of women taking only estrogen replacement, where transdermal or topical routes are more appropriate. Estrogen helps relieve vasomotor symptoms such as hot flashes, vaginal dryness and dyspareunia, improving women's sexual health at this stage of life. In addition, estrogen reduces breast cancer risk and mortality, but may increase blood clotting, inflammatory markers, hypertriglyceridemia, gallstone formation, and the risk of endometrial cancer in women without a hysterectomy, as well as the risk of venous thromboembolism, especially when administered orally (METHA et al., 2021).

When it comes to the cancer risk associated with hormone therapy, the hormone estrogen is responsible for the cell proliferation of ovarian cells, which may explain the potential risk of hormone therapy. However, progesterone is responsible for the apoptosis of ovarian surface cells. Therefore, when combined hormone therapy with estrogen and progesterone is used, the risk of ovarian cancer is reduced (LIU et al., 2019).

In view of the above, the best approach for the treatment of vasomotor symptoms would be combined estrogen and progesterone hormone therapy, with the exception of women who underwent hysterectomy. When hormone replacement is started early, that is, in women younger than 60 years or with less than 10 years of climacteric, and there are no contraindications for the use of hormones, the benefits certainly outweigh the risks. Hormone therapy can have a neutral or beneficial effect on women's cardiovascular health, reducing the prevalence of coronary heart disease and cardiovascular mortality. There is no significant influence on the risk of stroke and heart attack. In addition, hormone therapy can improve the lipid profile by lowering LDL and increasing HDL. It also has positive effects on type 2 diabetes mellitus, reducing fasting blood glucose, glycated hemoglobin and improving insulin sensitivity, in addition to reducing the incidence of osteoporosis and, consequently, the number of fractures in this age group. Combination hormone therapy is also associated with a reduction in the incidence of cervical cancer and endometrial cancer. However, continuous use for more than 5.2 years increases the risk of breast cancer, although it does not affect mortality from this disease. When started late, hormone therapy has a negative effect on cognitive function, increasing the risk of Alzheimer's

(METHA et al., 2021). For women who have contraindications, especially those with first-degree relatives with a history of breast cancer, other treatment options may be considered, such as the use of vaginal lubricants and moisturizers, phytoestrogens, ospemifene, pelvic floor muscle exercises, oxytocin, CO2 laser in the vaginal region, lidocaine, and vitamin E vaginally (SARMENTO et al., 2023).

FINAL CONSIDERATIONS

The present study aimed to analyze the efficacy and safety of hormone replacement therapy in improving sexual function in menopausal women, considering the effects of this therapy on sexuality. In addition, we sought to assess the risks and benefits associated with this therapy in sexual dysfunction resulting from menopause. It has been observed that hormone replacement therapy is currently considered the most effective and safe treatment for menopausal women, providing relief from vasomotor symptoms, reduction of hot flushes and other benefits related to female sexual health. Despite the specific contraindications for the continuous, prolonged or delayed use of hormone replacement, this treatment is considered safe and advantageous. Based on the findings of this study, it can be concluded that hormone replacement therapy has a high degree of efficacy and safety in relation to the potential risks associated with drug treatment.

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