

MULTIDISCIPLINARY APPROACHES IN MENOPAUSE PATIENTS TO IMPROVE THEIR QUALITY OF LIFE

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Abstract: Introduction: Menopause is a physiological process of amenorrhea for at least 1 year, which results from the loss of ovarian activity, between the ages of 45 and 55; Clinical studies from Latin America place Ecuador in the 4th position with the highest rate of menopausal women with 60.10% of cases. The most common clinical manifestations are vasomotor symptoms 75%, psychological symptoms 10%, hot flashes and insomnia. Currently, hormonal therapies have been developed for its management, as well as medicine and complementary alternatives that help improve the quality of life of patients in a large percentage. **Goal:** To determine the different types of multidisciplinary approach to the menopausal patient, through review of articles, which will contribute to scientific knowledge regarding the reality of this topic to improve the quality of life of patients. **Materials and methods:** Descriptive study through a systematic bibliographic review obtained in different scientific databases of evidence-based medicine in various digital repositories with high impact on health such as (Pub-Med, Scielo, Medisur, gynecology and obstetrics literature) of the latest 5 years. **Conclusion:** Strategies and complementary medicine in the management of menopausal women such as: cognitive-behavioral therapy, physical exercises, meditation, herbal medicine, hormonal therapy relieve symptoms and improve quality of life in patients in more than 80% of cases.

Keywords: Menopause, Women, Complementary Strategies, Hormonal Therapy, Symptoms.

INTRODUCTION

The climacteric is characterized by having several periods: first the premenopause stage, which is characterized by symptoms such as perspiration/sweating, emotional changes, palpitations, obesity, hot flashes and irritability, then the peri-menopause stage occurs, which is the manifestation of the biological effects., because the production of estrogen is irregular, which causes alteration of the menstrual cycle causing hot flashes, vaginal dryness and insomnia, after 1 year of amenorrhea it is known as menopause and then the postmenopause stage which is determined by the levels high levels of (FSH) and decreased levels of estrogen, affecting well-being, leading to the development of osteoporosis, fractures and cardiovascular diseases. (1,2)

The term Menopause is the interruption of menstruation for at least twelve continuous months that occurs as a result of the cessation of egg production, in female patients approximately 50 +/- 2 years of age, if this change occurs at 40 to 45 years of age, it is called early menopause due to greater involvement of diseases. At this stage, most patients may experience various vasomotor symptoms, involvement of the urogenital and cardiovascular systems. Other clinical manifestations include mood disorders, insomnia, memory impairment, among others. (1,3,4)

The most common clinical manifestations at this stage are vasomotor symptoms that occur in 75-85%; if these symptoms do not disappear spontaneously, they can persist in 25 to 50% for more than a year and 25% can remain up to for more than 5 years; while psychological alterations represent only 10%, remembering that these symptoms can last approximately 6 months to 5 years. (2)

In 2019, Medisur magazine published an article establishing that Latin America has

the highest numbers of menopausal women. According to its statistics, we have: Mexico and Colombia between 48.3% and 49.5%, Peru 51.60%, Dominican Republic and Panama 56.60%, Ecuador with 60.1%, Venezuela 62.70%, Uruguay with 67.40% and Chile 80%. Leaving Ecuador in position number 4 with more than 60%; which indicates that the patient must be cared for comprehensively in this phase of her life (5).

In 2020, two very important studies were carried out in Ecuador, the first about the Benefits of Foods With Phytoestrogens in a population of 102 menopausal patients at the Tulcán Sur Health Center in the province of Carchi, it was evident that a large part of the Respondents have information about some of the symptoms of menopause, but do not have a balanced nutritional diet with vegetables, seeds, legumes, fruits, among others; Rather, the vast majority consume them biweekly or almost never, with isoflavones being a satisfactory alternative to relieve hot flashes; as well as phytoestrogens to stimulate osteoblasts and inhibit osteoclasts, this favors bone apposition and increases bone density. In this sense, health educational strategies have been used to increase knowledge of this topic and alleviate clinical manifestations during this stage of life. (6) The second investigation was in the province of Esmeraldas, in the La Propicia neighborhood in a population of 50 women on the prevalence of osteoporosis in the climacteric, it was shown that 25 patients had an age range between 51-60 years, the 34% of the total study group (17 women), only 8 underwent the bone densitometry examination and 2 received hormone replacement therapy (HRT), meaning that the total 88.23% diagnosed with this disease (15 women) did not receive therapy. hormonal deteriorating their quality of life. (7)

This bibliographic review is carried out to determine the different types

of multidisciplinary approach for the menopausal patient, through a review of evidence-based medicine articles with high impact on health from the last 5 years, which will contribute with updated scientific knowledge about the clinical manifestations, risk/benefit of management and/or treatment, in order to change the lifestyle and well-being of the patients.

DEVELOPMENT

ETIOLOGY OF MENOPAUSE

It is defined according to its presentation, which can be in two ways:

Natural: It occurs gradually and progressive, that is, due to the aging of the ovary, decreasing the number of ovarian follicles and ovarian granulosa cells; which are the main ones in producing estradiol and inhibin, increasing the production of hormones FSH and LH. Low levels of estrogen alter the Hypothalamic Pituitary-Ovarian axis, affecting the development of the endometrium and menstrual cycles until their complete Cessation. (3)

Artificial: Caused by surgical procedures, for example: Oophorectomy or hysterectomy), can also appear due to mechanisms that destroy germ cells such as radiation or chemotherapies. (3)

EPIDEMIOLOGY OF MENOPAUSE

This stage occurs in women between 45 and 55 years old; But if it occurs between the ages of 40 and 45, it is known as early menopause where they have a high risk of suffering from osteoporosis and cardiovascular diseases related to hypoestrogenism. It can also occur in women with a family history of early menopause; smokers; who have undergone surgery such as ovarian-sparing hysterectomy and surgical sterilization; even in women of low socio-economic level. (1)

The World Health Organization shows that around 25 million women around the world begin the menopause stage earlier each year, by 2030 it is estimated that there will be more than 1.2 billion postmenopausal women worldwide. Studies indicate that the beginning of menopause in white Caucasian women is 51 years old, in Asians it can begin at a variable age, but that they also depend or vary depending on the ethnicity and region where they live, as do the symptoms, for example in the United States. The most common clinical manifestations are related to joint and muscle pain, in South Africa surveys are related to mood disorders, musculoskeletal pain and sexual dysfunction, in Australia they are vasomotor symptoms and genitourinary dysfunction, in European countries they are sleep disorders, depressive disorders and in Asia depressive disorders are more common. (8)

Worldwide, in 2019, Medisur magazine ranked Ecuador as number 4 with the highest rate of menopausal women with a percentage of 60.10%. (5) In Ecuador in 2022, nursing students carry out a study from the months from September to December, titled Climaterium and Menopause with 105 women that they were provided medical care by the Gynecology and Obstetrics staff of the Teófilo Dávila General Hospital in the city of Machala, through a survey, of the total, 52.38% showed a high predisposition of psychological factors and 24.76% led to depression, affecting the quality and lifestyle of the users. (9)

The origin of menopause began in the year 1729 where John Freind described that the interruption of menstruation occurs at the age of 49, in which year 1776 John Fothergill (doctor English, naturalist and collector flora), suggested that the interruption of menstruation occurred due to iatrogenesis. At the time of the French Revolution, menopause was considered an equivalent of social death

(because in the society of the time, a woman's status depended on her physical appearance and her sexual capacity). In 1816 the French doctor De Gardanne defined this stage as "the critical age" and "the hell of women"; together with the Frenchman Wilbush in 1816 he defined it as (Ménopause), after 5 years it He calls it Ménopause. At the beginning of the 19th century, it stood out for the clinical manifestations that accompanied it, such as psychological symptoms and changes in temperament. In the 20th century Robert Benjamin Greenblatt (was a Canadian physician and researcher specialized in endocrinology), and Fuller Albright (was aendocrinologistAmerican), for the first time they were able to demonstrate that estrogens exert a very important action, both in the gynecological area, as well as outside in the reproductive system, the doctor Greenblatt in 1987 before dying, announced that in the postmenopausal stage the woman could maintain dignity and youth. (5)

INSTRUMENTS USED TO ASSESS QUALITY OF LIFE

MENOPAUSE RATING SCALE (MRS)

The scale (MRS) is the most used and allows us to outline the symptoms, where it is made up of eleven items or groups of symptoms and is made up of three domains, which are:

Somatic: It is associated with vasomotor discomfort, sleep disorders, arthralgia and palpitations.

Psychological: It is associated with depressive symptoms such as irritability, anxiety and fatigue

Urogenital: It is associated with symptoms of the sexual and genital area

Symptoms are rated on a scale of 0 (when there is no symptoms), 4 points (when there are severe symptoms). To calculate the score, it is done by domain and also as a total sum.

That is, if a final or total score is obtained that is ≥ 15 points, it suggests that the quality of life is severely compromised and it is necessary to start treatment.

This tool is of utmost importance because it allows us to determine the current condition of the patient, in addition to evaluating the evolution of symptoms over time and thus being able to objectiveize the effect of the therapeutic interventions required. (1,2)

KUPPERMAN-BLATT INDEX (IKB)

Tool that was developed in 1953, used to measure the intensity of climacteric symptoms such as: excessive sweating, irritability, mood, sleep disorders, attention disorders, hot flashes, headaches, arrhythmias, paresthesias, bone pain and joints; which are evaluated on a scale from 1 to 4, where each symptomatology is assessed at three levels if it is mild, moderate and severe; This way, it is based on the diagnosis of the intensity of the symptoms. (10)

The results of this test are interpreted as follows: no symptoms from 0 to 16 points, mild symptoms from 17 to 25 points, moderate symptoms from 26 to 30 points and severe symptoms when the score is greater than 30 points. (10,11)

MULTIDISCIPLINARY APPROACHES TO IMPROVE QUALITY OF LIFE IN MENOPAUSAL PATIENTS

NON-HORMONAL MEDICAL THERAPY WITH FEZOLINETANT

It is a selective non-hormonal antagonist of the neurokinin 3 receptor, it contributes to reducing the neuronal activity of kisspeptin-neurokinin B/dynorphin, relieving vasomotor symptoms; It is still being studied today and could become an alternative to hormone replacement therapy. In doses of (15-30-60 or 90 mg 2 times a day orally), or (30-60

or 120 mg only once a day in the morning), accompanied by placebo in the evening or placebo twice a day for twelve weeks. (8)

Neal-Perry G, Cano A, Lederman S, et al. carry out a controlled, randomized, phase 3, double-blind trial, entitled Safety of Fezolinetant in vasomotor symptoms associated with menopause, 1830 postmenopausal women who were seeking treatment to reduce the discomfort caused at this stage participated in this study, the inclusion criteria to evaluate the research were adverse events, the percentage of patients with endometrial hyperplasia and endometrial cancer, placebo, Fezolinetant 35 mg and 45 mg daily were used; found as a result that Fezolinetant demonstrates safety and tolerability during the 52 weeks, adverse events occurred in 64% of the placebo group (391 of 610 patients), 67.9% of the Fezolinetant 30mg group (415 of 611) and 63.9% of the Fezolinetant group 45mg (389 of 609). Treatment interruption occurred in 4.3% of the placebo group (26 of 610 women), 5.6% of the Fezolinetant 30mg group (34 of 611) and 4.6% of the Fezolinetant 45mg group (28 of 609 women); in the endometrial safety assessment of 599 women; The result was that 1 of 203 patients had endometrial hyperplasia in the Fezolinetant 45 mg group, 1 of 210 had endometrial malignancy in the Fezolinetant 30 mg group, there was also an increase in liver enzymes three times the normal limit, 6 of 583 women who were administered placebo, 8 of 590 who received Fezolinetant 30 mg and 12 participants of 589 with Fezolinetant 45 mg.(12)

Another RCT study (Randomized Controlled Trial), double blind, phase 3; conducted by Johnson KA, Martin N, Nappi RE, et al, titled Efficacy and Safety of Fezolinetant in Moderate to Severe Vasomotor Symptoms Associated with Menopause, which was conducted with a total population

of 500 menopausal women aged 40 to 65 years with moderate to severe vasomotor symptoms who received treatment with placebo (167 participants), Fezolinetant 30 mg (166 participants) and 45 mg (167 participants) for 12 weeks plus a 40-week extension. The result was that both doses of Fezolinetant reduced symptoms by more than 50% between 2 to 3 episodes per day, from the first week of initiation to the end of treatment compared to placebo. (13)

ALTERNATIVE TECHNIQUES

They are of utmost importance and allow us to provide a comprehensive health approach in the management of climacteric symptoms, for example, we have mind and body practices such as hypnosis, cognitive therapy, aromatherapy, meditation; as well as the use of natural products such as herbs, minerals, vitamins among others. (14,15)

Currently, thanks to clinical research on the implementation of alternative therapies such as: physical activity, acupuncture, ear therapy, and reflexology, they have made it possible to reduce vasomotor, psychological, genitourinary, and joint symptoms in women during the menopause period; while epidemiological studies consider the consumption of phytoestrogens as one of the best options, because it is part of foods that are of plant origin, allowing the estrogenic effect to be induced in the patient, relieving vasomotor symptoms such as night sweats and hot flashes.(16)

Hypnosis

Johnson A, Roberts L, Elkins G. carry out a critical review that includes several RCTs, entitled Complementary and alternative medicine for menopause, where hypnosis is considered as a mind and body intervention, which has come to have an effect that is clinically significant in reducing hot flashes in 5 sessions

of hypnotherapy, obtaining good results in 70% of cases and even helps to improve the quality of sleep and sexual function. Reason why the North American Menopause Society recommends it as an alternative treatment for symptoms in menopausal women. Based on two important studies, the first involving 187 women with menopausal symptoms, hypnosis therapy was performed with results of a 74% reduction in the frequency of hot flashes, and sexual function and sleep quality in the patients also improved. Another pilot study with 71 women who were randomly assigned to 4 groups; the first received venlafaxine 75 mg + hypnosis, the second received venlafaxine 75 mg + sham hypnosis, the third took a placebo pill + hypnosis and the last took a placebo pill + sham hypnosis; As a result, 50% of cases were reduced when receiving hypnosis or venlafaxine alone, while in patients who received placebo, symptoms decreased by only 25%. (15)

Cognitive – Behavioral Therapy

It is considered a psychological technique of approximately six weeks of intervention, which is associated with various climacteric symptoms such as hot flashes, depression and others; It is of limited duration due to its focus that involves changing cognitive evaluations and behavioral options to alter symptoms. This strategy can include motivational interviews – relaxation, controlled breathing, among others. (15)

Through a systematic literature review carried out by Johnson A, Roberts L, Elkins G; based on an RCT with 96 women on the use of CBT (Cognitive Therapy –Behavioral) in women with menopausal symptoms, after breast cancer treatment; Visualizing the effects of this strategy for 6 weeks compared to usual care (standard follow-up), the result was that the interference of hot flashes decreased in 52% of the cases with CBT, while the patients

who received usual therapy There was a 25% discussion and regarding the frequency of hot flashes in both groups they were reduced by 38%. This way, the North American Menopause Society has recommended this technique to help reduce the vasomotor clinical picture of women, but not for the frequency. (15)}

John JB, Chellaiyan DVG, et al, conduct a randomized, double-blind trial, from January to June 2021, entitled How Effective is Mindfulness-Based Cognitive Behavioral Therapy on the Quality of Life of Menopausal Women; in a tertiary care hospital, with a population of 50 menopausal women divided into two groups; one intervention (25 patients) and another control (25 patients), where Mindfulness-based cognitive therapy (MBCT) was administered once a week, for 8 sessions of 1 hour each session only to the first group; It was concluded that with the MBCT technique, based on mindfulness to improve the severity of vasomotor symptoms, it can improve the quality of life of the patients.(17)

Aromatherapy

It is considered a natural treatment method that is carried out with essential or volatile oils, using aromatic essences that are naturally extracted from flowers, herbs or trees, influencing various physiological and psychological imbalances; helping to relieve climacteric symptoms. Chien LW, Cheng SL, Liu CF carried out a crossover clinical trial with a population of 100 menopausal women, they concluded that applying 12 weeks of lavender inhalation reduced hot flashes and sleep disorders in 50% of the patients, and also reduced stress, anxiety and insomnia, improving mental health. Currently, despite obtaining good results in some scientific articles, there is not enough evidence to support this technique in relieving menopause symptoms. (15)

Cao X, Zhou J, Liu J, et al; perform a bibliometric analysis of aromatherapy as a management of mood disorders worldwide over the last two decades; finding as a result that it helps the limbic system and the reticular formation of the brain, analyzing the particular aroma that is associated with emotions and behavior, the decrease in olfactory acuity is related to sexual dysfunction, aromatherapy improves sexual function and increases olfactory acuity modulating vegetative, visceral and sexual activity in patients.(18)

Relaxation-Yoga

Progressive muscle relaxation, stimulated breathing, applied relaxation help by controlling stress responses and have been used to relieve climacteric symptoms, reducing hot flashes and improving psychological symptoms in women going through this stage of life. In a randomized controlled trial on the effects of applied relaxation on vasomotor symptoms in postmenopausal women, it was shown that patients who received the treatment.

Immediately with this relaxation technique, hot flashes decreased in 55% of cases twelve weeks after treatment. (15)

Yoga originated as a Hindu discipline, where physical postures, sequence of various movements, breathing and attention techniques are applied; They are a set of concentration exercises; An analysis carried out by Elavsky and McAuley, on the effect of yoga on psychological symptoms, with a population of 481 menopausal women, no negative side effects were found after practicing yoga; on the contrary, it was beneficial to receive 90 minutes (2 times a week for 4 months), to reduce psychological symptoms; Like another study focused on adopting 75 minutes of this technique (2 times a week for 12 weeks), they reduce stress and depression. This strategy must be included in

work programs to help menopausal patients; considered a safe, effective practice to treat psychological symptoms, improving style and quality of life by increasing energy. (16)

Auriculotherapy

Considered a branch of reflexology and acupuncture, it is an ancient technique of traditional Chinese medicine to eliminate certain pathologies. It stimulates reflex points in different areas of the ear using, for example, spheres, seeds, metal crystals, electric current, laser, semi-permanent or filiform needles, has no side effects and is used as a safe, non-invasive alternative for sleep quality. Women have lighter sleep during this period, night sweats and hot flashes increase. This happens because magnesium promotes muscle relaxation and sweating, reducing estrogen levels, limiting serotonin levels, causing melatonin to decrease. It is a very important substance to be able to fall asleep. (19)

Eidani M, Montazeri S, et al; carry out a clinical trial, entitled The effect of auriculotherapy on improving sleep quality in postmenopausal women aged 45 to 60 years, which was carried out in 2021 to 2022 with a population of 82 postmenopausal women, divided into two groups; the intervention group received 4 weeks of auriculotherapy, except for the control group, both completed the sleep quality questionnaire at the beginning and after 4 weeks of therapy, as a result no negative side effects were found and the conclusion was reached that auriculotherapy can be used as an effective, safe and low-budget technique to improve sleep quality in menopausal patients. (19)

Exercises

Exercises help reduce insomnia and relieve sleep disorders. In 2019, thanks to the electronic search review by Daly et al, it was concluded that with the help of intense

exercises performed 2 to 4 times per week, muscle strength, bone density and physical function are improved, improving quality of life between 70% to 90% of menopausal women. (20)

In 2021, information was collected from four scientific studies that evaluated the benefit of exercise and physical activity on the psychological symptoms of a population of 635 menopausal patients. It was evidenced that walking 3 times for 1 hour a week, for a period of four months, helps improve mental health and reduce psychological symptoms. (16)

High volume exercises help reduce cholesterol, muscle performance and lean mass; while jumping exercises improve bone density (femoral neck) and strength exercises decrease heart rate, hot flashes in menopausal women. They are an alternative to pharmacological treatment, they help increase muscle strength, bone mineral density (reducing kyphosis), intervene in motor control, balance - muscular coordination and reduce the risk of falls in menopausal patients. (16)

Sleep disorder is a common symptom in menopause; it alters hypothalamic and pituitary function, desynchronizing the release of growth hormone (GH); negatively affecting the quality of life, increasing insomnia from 46 to 48%, causing a greater risk of high blood pressure, diabetes mellitus and even suffering from cardiovascular diseases. Exercises at this stage help increase energy expenditure, release endorphins, improving sleep and intervene in the recovery of the human body. (21)

Exercise can override the attenuation of GH release during sleep deprivation, i.e. during recovery from exercise, this hormone returns to baseline within 2 hours, regardless of aerobic or high-intensity exercise; Multiple updated meta-analyses focus on exercise intervention to significantly reduce the severity of insomnia and alleviate sleep problems in patients; they encompass a set of

diverse activities that have a physiological and psychological benefit. (21)

Reflexology

Complementary technique that consists of applying pressure to areas such as hands and feet that are reflex points associated with other areas of the human body; When pressure is applied, these disease-causing energy blockages are removed from the area of the body.(15) A study by Asltoghiri et al; compared reflexology with non-specific foot massage, to reduce sleep disorders and depressive symptoms, obtaining a result of 41.5% symptom relief, unlike foot massage with a percentage of 19.1%. Eman et al, made a comparison between aerobic exercise and reflexology, the result was that aerobic exercise was more effective in reducing average depression scores than reflexology.(22)

Another RCT study that was carried out with a population of 120 women randomly assigned to two groups, the first group received foot reflexology therapy and another control group (foot massage), the result was that vasomotor symptoms and sexual dysfunction improved significantly. in the first group and even reduces the frequency of hot flashes by 56%, after 12 sessions applied 2 times a week. (15)

Acupuncture

Invasive physiotherapy technique, it is a traditional Chinese therapeutic alternative, it consists of applying small needles to the skin that are connected to certain points of the body, with a follow-up of more than 8 weeks, it is used to relieve pathologies that affect humans such as diseases metabolic, endocrine, nervous system, musculoskeletal-connective tissue and disorders (mental, neurological, behavioral and skin). They help improve vasomotor symptoms, hot flashes, sleep disorders, insomnia; Electro-

acupuncture is the passage of electrical current between acupuncture needles that significantly improves mood only. (23)

Avis NE, Coeytaux RR, et al; carried out a controlled, randomized, pragmatic trial, entitled Study of acupuncture in menopause with 209 peri-menopausal and post-menopausal women, the effects of acupuncture in the short and long term were investigated, the results in this study revealed a positive effect of acupuncture on anxiety and memory for 6 months after completing the treatment, together with a meta-analysis, it is defined as a safe and effective alternative in the management of psychological symptoms.(16)

Zhao FY, Zheng Z, Fu QQ, et al; conducted an (RCT), entitled Acupuncture for comorbid depression and insomnia in perimenopause, with a population of 70 women in transition to menopause in an age range of 45 to 55 years, assigned into 2 groups: one of real acupuncture and another of simulated acupuncture; They received 17 sessions for 8 consecutive weeks divided into three sessions a week for three weeks; then two sessions a week for three weeks and finally one session a week for the last two weeks, without evidence of serious adverse effects, it was concluded that acupuncture is a safe technique and helps improve the clinical symptoms of depression and insomnia. (2. 3)

Herbal Products and Vitamins

Phytoestrogens

They are plant substances, derived from plants that have estrogenic properties that were discovered at the end of the 19th century and are currently still used as an alternative to pharmacological therapy; Several clinical studies since ancient times detail that black Cohosh and Red Clover help reduce climacteric symptoms, but can cause long-term adverse reactions. (15)

Black cohosh is a phytopharmaceutical plant from North America, it has historically been used as an indigenous treatment to treat climacteric symptoms, both neurovegetative and psychological, its side effects are rash, acute hepatitis and gastrointestinal disorders; Several randomized trials, using the Kupperrman index, have obtained significant improvements in quality of life. (24)

In European countries, the black cohosh rhizome preparation is marketed as a medicine based on other herbs to relieve symptoms such as hot flashes, sexual dysfunction, and vulvovaginal symptoms; While in the United Kingdom it is used to relieve rheumatic pain, it is considered a traditional drug. (24)

In a systematic literature review carried out by C. Castelo Branco, a total of 35 clinical trials and 1 meta-analysis were found in which around 43,759 women were included, of which only 13,096 received isopropanol extract of black cohosh, reducing neurovegetative and psychological symptoms unlike the participants who did not receive it. but in higher doses and in combination with the herb *Hpericum perforatum* or also known as St. John's wort, the result is significantly effective. (24)

The benefits of using black cohosh or in combination with St. John's wort are beneficial, without risks, which is why it is recommended in the treatment of clinical manifestations in menopause and including in patients with hormone-dependent disorders; and the effect of the isopropanol extract can be compared with low doses of transdermal estradiol or even tibolone, having a better result in benefit-risk than tibolone, with few side effects and no hepatotoxic effects were observed.(24)

Trifolium pretense or also called red clover, isIt originated in Asia, Africa, Europe, but is currently found in all other continents. It is characterized by containing isoflavones, genistein and daidzein that produce effects

similar to estrogen. (15)

In 2019, several clinical studies were compiled, demonstrating that administering dried leaves of this clover in doses of 40 mg over the course of 12 weeks relieved the symptoms in these patients, reducing 10 points in the assessment of the menopause rating scale, unlike of using placebos, which is why they are considered safe and no side effects have been found after a year of use; without forgetting that due to its estrogenic activity, attention must be paid to any adverse effects in patients with hormone replacement therapy, contraceptives, or a history of cancer.(15)

In August 2023, an Analysis of the safety problems of herbal products with alleged phytoestrogenic activity was published, specifying that black cohosh, soybeans, chaste tree, red clover; They are plant species that have been reported to cause mild adverse reactions such as pruritus, nausea and pyrexia in various results of scientific reports, which are consistent with data from the World Health Organization. But today they continue to be used due to their popularity over time, such as *Actaea racemosa* L, also called black cohosh, which has been used since 1956 in Germany. (25)

Vitamins

Vitamin D:It is a fat-soluble steroid hormone, it acts in the maintenance of bone metabolism, it regulates the growth of vaginal epithelial cells, alleviating genitourinary tract problems; but if there is a vitamin D deficiency, it is related to the risk of cardiovascular diseases, metabolic syndrome, dyslipidemia, type II diabetes mellitus, especially elevated triglycerides in postmenopausal women. In conclusion, its decrease leads to secondary hyperparathyroidism, which in turn induces changes in the bone metabolism causing reduction in bone mass and osteoporotic fractures. (26)

The role of vitamin D is to regulate the growth of vaginal epithelial cells, relieve genitourinary tract problems, modulate the production of adipokines, and have an anti-proliferative effect on tumor cells; It has been shown in clinical studies that their normal levels decrease in depressed patients, they intervene in the production of proinflammatory cytokines, activating a stress response; They also have a regulatory and protective effect on the dopamine system of the brain, similar to the so-called antidepressants, so low values of Vitamin D are related to cognitive deterioration in menopausal women.(26,27)

Long-term low-dose administration has significantly inhibited the formation of neutrophils in tissues, positively regulating vascular endothelial growth factor, reducing the production of pro-inflammatory cytokines, improving microvascular growth of the tissue and thus relieving the inflammatory response. (27)

Vitamin E: It is a fat-soluble, exogenous substance, it belongs to the group of antioxidant tocopherols and tocotrienols that can be found in the human body, in plasma lipoproteins, as a component of cell membranes, having a main dietary source (vegetable oils, meat, eggs, cereals). It has an important effect on the clinical manifestations of the climacteric, especially on postmenopausal vasomotor symptoms, vaginal, neurological and vascular changes. (28)

Radnia N, Hosseini ST, et al; carried out a randomized clinical trial with a population of 64 postmenopausal women who presented genitourinary syndrome, they were divided into 2 teams (1 study and 1 control). The study group used vaginal creams combined with vitamins D and E, and the control group was treated with vaginal creams based on conjugated estrogens for a period of 12 weeks, regular visits were made where libido,

vaginal symptoms (pruritus, dryness and dyspareunia) improved in both trials, it was concluded in this research that the use of vaginal creams of vitamins D and E have the same positive and beneficial effect as creams with conjugated estrogens.(29)

HORMONAL THERAPY IN MENOPAUSE

It is contraindicated in patients with a history of cancers that are dependent on estrogen, such as breast cancer. (28) Clinical studies consider that women can spend approximately 40% of their lives in the menopause stage, which is why it has been Considered very helpful, Hormone Replacement Therapy (HRT) allows you to supplement with hormones that are lost during the menopausal transition, to relieve associated symptoms (vasomotor, genitourinary and osteoporosis). There are several options for estrogens and progestogens, which can be administered by different routes, both oral and transdermal (creams, patches, inserts, among others); (30)

In conclusion, the administration of oral estrogens causes greater resistance to activated protein C, increasing the risk of blood clot formation. Transdermal Estrogen is characterized by avoiding hepatic metabolism, which produces resistance to activated protein C, canceling the risk of blood clotting. And the administration of progestin is also usually taken orally, although they are also combined with estrogens in the form of patches. (31)

Management of Hormone Replacement Therapy (HRT) in Vasomotor Symptoms

The relief of vasomotor symptoms is due to the implementation of hormonal therapy, in which low doses of estrogen are used, either alone or combined in low doses, a randomized, double-blind study, with a population of 339 perimenopause and menopausal women, placebo was compared with the two therapies

(17 β -estradiol orally in low doses 0.5 mg/day) and venlafaxine XR (75 mg/day), it was concluded that they reduce symptoms between 80 to 85% of cases or in standard doses reduce symptoms between 85 to 90% of cases, while the results with the placebo effect are 40-45%.(8)

There are other alternatives in moderate to severe hot flashes, such as Sulpiride (antipsychotic) 50 mg/day or placebo for eight weeks and in cases of moderate to severe vasomotor symptoms we have the placebo, Esmirtzapine 2.25 mg, 4.5 mg, 9 mg or 18.0 mg, which is characterized as a specific noradrenergic and serotonergic antidepressant. (8)

Another RCT, double-blind, phase 3 trial, with a sample of 459 postmenopausal women, with vasomotor symptoms, evaluated the effect of (CE/BZA/MPA) conjugated estrogens/bazedoxifene/ Medroxyprogesterone acetate on sleep and quality of life. One group was randomly selected with (CE/BZA) 0.45mg/20mg, the second (CE/BZA) 0.625mg/20mg, the third (BZA/CE/MPA) 20mg/0.45mg/1.5mg or placebo for 1 year. All three showed beneficial results (obtained during the third and twelfth months); improving sleep and quality of life in postmenopausal women. The results of CE/BZA had no adverse reactions on lipid metabolism and hemostatic balance, but in venous or cardiovascular thromboembolic events the incidence was similar to that of the placebo group. (8)

Hormone Replacement Therapy (HRT) in Genitourinary Symptoms

It all depends on the severity of the symptoms that occur. In these cases, the implementation of treatment with estrogens is very helpful to relieve moderate or severe symptoms; Lubricants that are non-hormonal treatments provide relief in mild symptoms, as well as ospemifene, which is the estrogen receptor modulator indicated in dyspareunia.(30)

Kingsberg SA, Derogatis L, et al; conducted an RCT in relation to vaginal estrogen in soft gel capsules (solubilized 17 β -estradiol) as an effective treatment to treat dyspareunia, vulvar or vaginal atrophy in doses (4, 10 or 25 μ g improved sexual function).(8)

Another multicenter, randomized, double-blind study, with a total of 576 postmenopausal women, who presented vaginal dryness, received treatment with 0.003% estradiol vaginal cream (15 μ g of estradiol) applied twice a week, demonstrating efficacy in symptoms of vulvar atrophy and vaginal. The combination of estrogens with intravaginal fractional CO₂ laser is of great help in relieving genitourinary symptoms. (8)

Management of Hormonal Therapy in Osteoporosis

Osteoporosis is a prevalent pathology with a high degree of morbidity and mortality in postmenopausal women. An effective, timely diagnosis and bone densitometry have made it possible to reduce the risk of fractures; Studies have shown that hormonal therapy can be used to prevent osteoporosis; several medications are used to prevent this pathology, such as bone resorption inhibitors (which are estrogens, calcitonin, bisphosphonates) and bone formation stimulants. (30)

Estrogens are what help stabilize bone mass in women at the beginning of postmenopause, reducing bone loss and the risk of fractures by 40% of cases; Based on updated clinical studies, they act in conjunction with estradiol, which helps improve bone mineral density. A study with a sample of 22 osteoporotic women with osteopenia showed that therapy with bisphosphonates combined with scaling and root planing for 12 months obtained positive results in postmenopausal women who suffer from diseases such as chronic periodontitis. (8)

Management of Cardiovascular Diseases with Hormone Therapy

An updated multicenter, randomized trial demonstrated that estrogen-based hormonal therapy on the accumulation of cardiac adipose tissue; with a population of 727 women who received oral conjugated equine estrogen (o-CEE) 0.45 mg/day, micronized progesterone, transdermal estrogen 17 β -estradiol (t-E2) 50 mcg/day or placebo (could be pills and inactive patches), the Patients who received o-CEE or t-E2 were also administered oral micronized progesterone at a dose of 200 mg/day for the first 12 days of each month, concluding that the accumulation of epicardium adipose tissue could be delayed with oral conjugated equine estrogen treatment., but the group that received t-E2 increased the progression of coronary artery calcification and pericardial adipose tissue.(8)

The use of transdermal estradiol in a randomized trial, with a population of 44 menopausal women (non-diabetic and with a body mass index greater than 25), divided into 2 groups, the first received estradiol hemihydrate gel treatment and another placebo gel. a time of three months; showing that if administered in low doses in a short period it proved to be very effective, with a beneficial effect on endothelial function and decreased blood viscosity unlike the placebo gel. (8)

A double-blind RCT, with 64 healthy postmenopausal women, treated with 0.625 mg of conjugated equine estrogens and another group with only placebo for a period of 28 days; It was shown that o-CEE improves vascular dilation that is mediated by brachial artery flow. (8)

Of all the approaches used since ancient times such as non-hormonal and/or hormonal therapies, relaxation, vitamins and even herbal products used to improve the quality

of life in menopausal women, they have been effective in 70% of cases in reducing of clinical manifestations, especially in vasomotor symptoms.

Currently, the management indicated in these cases is attributed to the use of hormonal therapy as the most valuable therapeutic resource, limiting vasomotor, genitourinary and even cardiovascular symptoms, but it is also advisable to modify the lifestyle by reducing the incidence of the effects. during the transition to menopause.

CONCLUSIONS

- Thanks to the implementation of different techniques and complementary medicine such as cognitive behavioral therapy, physical exercises, yoga, herbal medicine and hormonal therapies, it has been possible to reduce the clinical manifestations that appear in the menopause stage, affecting the quality and lifestyle of women. women; It is extremely important to provide more information, as well as guidance and support programs on this topic that help women in the transition period to menopause since there is a lack of knowledge in certain populations in both Ecuador and Latin America to be able to address climacteric symptoms.

- Through the techniques that are applied to relieve the symptoms of menopausal patients, we have physical activity using a range of alternatives such as yoga, meditation, mild to high intensity exercises that are recommended to reduce clinical manifestations by more than 40%. such as hot flashes, stress, insomnia, sleep disorders, which are the most common at this stage; as well as Hormonal Therapy, which is considered the main treatment applied to sleep disorders in menopausal women, helping to reduce hot flashes in approximately two weeks by improving sleep patterns.

- The use of different approaches in menopausal patients has been of great help from its origins to the present, demonstrating effectiveness in reducing climacteric symptoms through non-pharmacological strategies such as yoga, acupuncture, phytoestrogens, vitamins and hormonal therapies that have been able to reduce the clinical manifestations to a greater percentage at this stage, but at the same time, unfortunately, women choose not to use it for fear of adverse effects such as cancer and this is where the health professional must look for the latest updates on this topic and treat patients within the safety margins, achieving the benefit of the therapy and their quality of life.

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