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# Nuevas terapias para el manejo de los síntomas vasomotores en la menopausia

*New therapies for the management of vasomotor symptoms in menopause*

[1] Jeniffer Pamela Llumitasig Trujillo https://orcid.org/0009-0002-9179-7969
Medical student, Technical University of Ambato, Ambato, Ecuador.
jllumitasig9035@uta.edu.ec

[2] Veronica Elizabeth Padilla Vinueza https://orcid.org/0000-0001-6869-7738
Medical Specialist of the Medicine Department, Technical University of Ambato, Ambato, Ecuador
ve.padilla@uta.edu.ec

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**Palabras claves:**
Síntomas vasomotores, menopausia, sofocos, neuroquinina b, fezolinetant

**Resumen**

**Introducción.** La menopausia trae cambios físicos y psicológicos que pueden afectar las relaciones personales y familiares. Muchas mujeres no buscan ayuda médica debido a la falta de información, dificultades de acceso y preocupaciones sobre los efectos secundarios de las terapias hormonales. Los nuevos tratamientos no hormonales, como los antagonistas de la neuroquinina B, muestran promesas en aliviar eficazmente los síntomas vasomotores. **Objetivo.** Analizar el impacto de la menopausia en la vida de las mujeres, identificando las barreras que enfrentan para buscar ayuda médica y evaluar la efectividad de los tratamientos no hormonales recientes, como los antagonistas de la neuroquinina B, en la mejora de los síntomas vasomotores y la calidad de vida. **Metodología.** Esta revisión bibliográfica sirve como base para un estudio retrospectivo que evalúa críticamente la literatura seleccionada bajo diversos criterios. **Resultados.** Diversos estudios han investigado la eficacia de los antagonistas de la neuroquinina B, como el fezolinetant, en el tratamiento de los sofocos menopáusicos. La investigación ha demostrado que la vía de la neuroquinina B regula la secreción de GnRH y, por tanto, juega un papel crucial en el control de los sofocos. **Conclusión.** Durante décadas, la terapia hormonal ha sido eficaz para aliviar los síntomas de la menopausia, como los sofocos, aunque conlleva riesgos como el tromboembolismo venoso y el cáncer de endometrio. Esto ha llevado a la búsqueda de alternativas más seguras y efectivas, como los antagonistas de NK3R y la neuroquinina B, que se están evaluando en términos de eficacia, seguridad y tolerabilidad en comparación con la terapia hormonal tradicional. **Área de estudio general:** Medicina **Área de estudio específica:** Ginecología **Tipo de estudio:** Artículos originales

**Keywords:**
Vasomotor symptoms, menopause, hot flashes, neurokinin b, fezolinetant.

**Abstract**

**Introduction.**Menopause brings physical and psychological changes that can affect personal and family relationships. Many women do not seek medical help due to lack of information, access difficulties, and concerns about the side effects of hormonal therapies. New non-hormonal treatments, such as neurokinin B antagonists, show promise in effectively relieving vasomotor symptoms.**Objective.**To analyze the impact of menopause on women's lives, identifying the barriers they face in seeking medical

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help and evaluating the effectiveness of recent non-hormonal treatments, such as neurokinin B antagonists, in improving vasomotor symptoms and quality of life.**Methodology.**This bibliographic review serves as the basis for a retrospective study that critically evaluates the selected literature under various criteria.**Results.**Several studies have investigated the effectiveness of neurokinin B antagonists, such as fezolinetant, in the treatment of menopausal hot flashes. Research has shown that the neurokinin B pathway regulates the secretion of GnRH and therefore plays a crucial role in the control of hot flashes.**Conclusion.**For decades, hormone therapy has been effective in relieving menopause symptoms such as hot flashes, although it carries risks such as venous thromboembolism and endometrial cancer. This has led to the search for safer and more effective alternatives, such as NK3R and neurokinin B antagonists, which are being evaluated in terms of efficacy, safety and tolerability compared to traditional hormone therapy.

## Introduction

The World Health Organization (WHO) describes natural or physiological menopause as the "permanent termination of the menstrual cycle, confirmed retrospectively after a continuous period of 12 months without menstruation due to non-pathological causes." It symbolizes a moment in the sequence of women's lives and marks the end of their reproductive capacity.as a natural part of the biological aging process with a gradual transition period that begins with alterations in the menstrual cycle and can occur between the ages of 45 and 55 (1).

Globally, according to reports from the PAHO, it is estimated that by 2030, more than one billion women will have reached menopause by the age of 50, representing 10% of the global population. Another known stage is perimenopause, which refers to the period from the first appearance of these symptoms until one year after the last menstrual cycle, continuing with the postmenopausal stage. These phases can extend for several years and have an impact on physical, emotional, mental and social health.(2).

In the United States, according to data obtained from the Registry of Aging, Menopause and Sexuality, 18% of women who sought help for menopause-related issues, the age of assistance seeking help, were women over 60 years of age. Of this group, a considerable

41.2% reported significant discomfort due to vasomotor symptoms (VMS). Women experienced moderate to severe vasomotor symptoms during their seventh and eighth decades of life. African-American women were more likely than other groups. In addition, 10% of women continued to have symptoms up to 12 years after their last menstrual period.(3).

In Latin America, the age of onset of menopause varies slightly, generally occurring between 43.8 and 53 years. However, cases have been recorded that occur before the age of 40, which is known as early or premature menopause. In Mexico, according to data from the 2020 Population and Housing Census, it is estimated that there are around 14 million 847 thousand women aged 50 years or older. The average age of onset of menopause ranges between 45 and 48 years.(4, 5).

In Ecuador, menopause usually occurs around the age of 46-47, according to data collected in the study entitled 'Ecuadorian epidemiology of menopause, climacteric and osteoporosis'(6).Furthermore, in a study carried out in Latacunga on the impact of menopause in a group of 80 women, the most frequent discomforts wereLow mood (66%), irritability (66%), muscle and joint pain (65%), anxiety (65%), physical fatigue (60%), difficulty falling asleep (59%), hot flashes (56%), bladder problems (54%), heart problems (53%), sexual difficulties (50%) and vaginal dryness (50%) (7).

*Justification*

Menopause represents a complex period in a woman's life.characterized by physical and psychological changes that often cause personal discomfort and can influence interactions with the environment. These changes can be so significant that, on some occasions, they cause personal dissatisfaction derived from the difficulties in adjusting to them, even generating tensions in family and romantic relationships.

Vasomotor symptoms can interfere with women's daily lives. It is common to hear comments about the discomfort caused by menopause and even more so the reasons why they do not go to the doctor. Some women decide to wait for relief without treatment, they do not have enough information on the subject, while other women know about the adverse effects of hormone therapy such as loss of bone density, decreased sexual desire, vaginal dryness, among others. Most of them cannot easily access a medical appointment due to their place of residence located in remote areas of the city, long work hours, personal factors, insufficient shifts. Through research, it is intended to provide sufficient information to improve the quality of life in women who go through the process.

In recent years, considerable progress has been made in understanding the treatment of neuropeptides and tachykinins and their involvement in hypothalamic function, especially in the regulation of the reproductive axis and the release of gonadotropin-releasing

hormone. Neurokinin B, in association with kisspeptin, appears to be crucial in the control of these systems. Neurokinin B antagonists have been developed and have shown promising efficacy in the treatment of hot flashes in menopause. Although data are still limited, these non-hormonal drugs show rapid results, evident within the first or second day of administration, and have benefits in reducing hot flashes and improving sleep. If their long-term safety and efficacy are confirmed, they will represent a significant advance in the treatment of vasomotor symptoms.

The purpose of the research is to collect and analyze information on new treatment options. By covering this need, it will serve to make informed decisions about the management of these symptoms, as well as to provide help to health professionals so that they have reliable and safe information, allowing for quality medical care by offering new treatment options.

**Methodology**

This literature review is the basis of a retrospective study in which a critical evaluation is carried out by selecting literature based on various selection parameters. Data were collected from sources such as PubMed, Scielo, Springer, DynaMed, Scopus, Chocrane, as well as information from the National Institute of Statistics and Census (INEC), Ecuador en Cifras and The Institute for Health Metrics and Evaluation (IHME). Documents from the World Health Organization (WHO) were also considered, and a time frame was established between the years 2019 and 2024.

Inclusion criteria for literature selection included literature reviews, clinical trials, and meta-analyses focused on the study population, specifically on people going through the onset and transition of menopause. Texts that were not fully accessible were excluded.

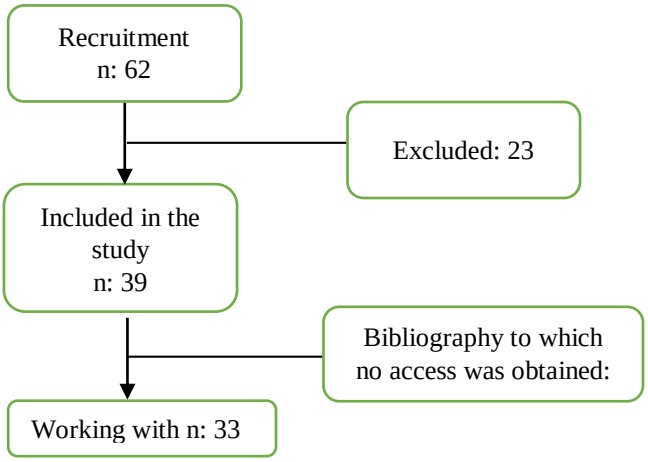


**Figure 1.***Search strategy and selection of scientific documents*

**Results**

Menopause is defined as the "permanent termination of the menstrual cycle, confirmed retrospectively after a continuous period of 12 months without menstruation due to non-pathological causes." The transition is a gradual process that begins with alterations in the menstrual cycle, refers to the period from the first appearance of these symptoms until one year after the last menstrual cycle, continuing with the postmenopausal stage, these phases can extend for several years and have an impact on physical, emotional, mental and social health.(8)

*Stages*

The transition to menopause is divided into four stages:

First stage. - “late reproductive stage” is mainly characterized by a reduction in the remaining follicles in the ovaries, i.e. the reserves are depleted so the hormones compensate for this reduction so that the cycle is not altered and maintains its normal rhythm. This reduction in the ovarian reserve does not yet affect the menstrual cycle.(9).

Second stage. - It is characterized by an increase in the general symptoms of menopause and minimal alterations in menstruation that is presented as a menstrual cycle in the last 3 months. An average that guides us on when a woman enters this stage is that she has a difference greater than or equal to 7 days in the arrival of her next period. This stage is known as "early transition", and the compensatory mechanism is a greater production of follicle-stimulating hormone on the surplus ovarian follicles and increased activity of follicular aromatase, in order to maintain the normal cycle.(10)

Third stage - during the "late transition" phase, the woman experiences amenorrhea for about 60 days, lasting 1 to 3 years, the symptoms become more pronounced, this phenomenon occurs because the production of hormones (follicle-stimulating hormone increases, while estrogen decreases), these hormones can no longer compensate for ovarian failure, resulting in an increase in the typical symptoms of menopause.

Fourth stage - the "early postmenopausal" phase begins one year after the last menstruation and is characterized by an undetectable, i.e. greatly reduced, ovarian reserve. During this period, the follicle-stimulating hormone continues to increase, while estrogen levels continue to decrease, requiring a period of two years to reach equilibrium.(9).

*Pathophysiology*

*Central nervous system changes in the menopausal transition*

Pituitary gonadotropins (FSH and LH) are regulated by estrogen (by positive and negative feedback) through estrogen receptors in the hypothalamus, which in turn regulate the release of GnRH. During the menopausal transition, there are changes in the hypothalamic-pituitary axis, which results in decreased sensitivity to this estrogen feedback, producing anovulatory cycles.(11).

The difference in hypothalamic structure between postmenopausal and premenopausal women is in the infundibular nucleus. Lack of estrogen and aging cause a group of neurons in the infundibular nucleus to hypertrophy reflecting changes in the estrogen receptor, kisspeptin and neurokinin B (NKB), and are accompanied by increased compatibility of the kisspeptin and NKB genes. Neurons that express kisspeptin and neurokinin B are responsible for regulating the GnRH hormone causing an effect on the production of LH and FSH.(9).

Estrogen deficiency intervenes in thermoregulation and there are also investigationssupporting the involvement of kisspeptin and neurokinin B in vasomotor symptoms such as hot flashes. The gene responsible for encoding kisspeptin and NKB (tachykinin receptor 3) has been found to be associated with the manifestation of hot flashes. Consequently, studies indicate that kisspeptin and neurokinin B antagonists have the effect of reducing the frequency of hot flashes.(12).

*Signs and symptoms*

The transition period lasts approximately 4 years, the intensity of the symptoms starts from mildwith a gradual increase over the years, determining that during theThe first two years the symptoms are much more severe and are correlated with amenorrhea and low estrogen levels. One of the first indicators of the beginning of the transition to menopause is irregular menstrual cycles and a change in the duration of bleeding.(13).

The duration of hot flashes is approximately 4 to 5 years, there are some cases that persist up to 10 years. It is characterized by starting with a sensation of heat that lasts a few minutes, and spreads throughout the upper part of the body, they occur due to a narrowing of the thermoregulatory system of the hypothalamus, in response to the deprivation of estrogen, which is responsible for regulating body temperature. While estrogen levels are low, we will find high levels of norepinephrine and low levels of serotonin, on the contrary, 5-HT receptors are responsible for positive regulation.(14).

Changes in the genitourinary system are evidenced by the response to the reduction of estrogens, and may include vaginal dryness, vaginal narrowing, atrophy of the vagina and

vulva, uterine prolapse, and urinary incontinence. These changes may lead to patients having recurrent urinary tract infections and dyspareunia.(15).

The decrease in estrogen causes less vaginal flow, a decrease in the amount of vaginal secretions, and therefore an increase in pH and parabasal cells. This lack of secretions causes the anatomy of the vagina to atrophy. Several studies have shown that most symptoms are relieved by the administration of estrogen, except for urinary incontinence.(15).

During the transition stageHormonal changes produce an imbalance in gamma aminobutyric acid (GABA) resulting in a greater likelihood of developing depressive episodes during this stage, the symptoms associated with this are due to the variability in the patient's mood, increasing in late perimenopause. There are factors that intervene in a higher risk of depression in women approaching perimenopause, among which may influence,a breakup, smoking, or premenstrual symptoms. Women with a history of depression are more likely to develop depression during menopause, and women without a history are at risk for developing depression during this time.(16).

The reduction in sleep is noticeable as the years advance, sleep is impaired by the menopausal transition, in a study carried out in Canada, postmenopausal patients between 45 and 60 years of age mentioned problems falling asleep, but it was discovered that this alteration is not completely justified by the association with vasomotor symptoms, but rather this imbalance in sleep is observed in the early transition and as it progresses to its maximum point it appears in the late transition.(17).

Sexual desire is affected in about 10% of women with decreased libido in the transition stage. ThisIt is attributed to aging and the reduction of hormone levels such as estrogen and testosterone. Testosterone replacement has provided a slight solution regarding sexual desire, but there is a lack of studies to support testosterone replacement as it can lead to unwanted effects such as breast cancer. The approved drugs are bremelanotide and flibanserin.(18).

At the bone level, the decrease in estrogen causes greater bone resorption. Fractures due to osteoporosis are more frequent in women over 50 years of age. Estrogen allows the formation of osteoblasts and greater absorption of calcium in the intestine. As estrogen levels decrease, bone remodeling is affected, creating an imbalance that results in bone loss.(19).

*Treatment*

Treatments available to relieve menopausal symptoms range from hormonal therapies to non-pharmacological options and hormone-free medications. Estrogen hormone therapy

stands out as the most effective option for treating vasomotor and genitourinary symptoms associated with menopause.(20).

Women who experience noticeable sleep or mood disturbances during the menopausal transition may also find benefit from hormone therapy (HT). HT is considered safe and effective for women who are at low risk, without underlying coronary artery disease or history of breast cancer, who are younger than 60 years of age, and who are less than 10 years past the onset of menopause.(20).

Hormone therapy is not recommended for primary or secondary prevention of cardiovascular disease (CVD). The Women's Health Initiative (WHI) Study, a trial focused on primary prevention, compared the use of conjugated equine estrogen (CEE) at 0.625 mg together with 2.5 mg medroxyprogesterone acetate (MPA), or CEE alone in women without a uterus, versus a placebo group for CVD. The CEE+MPA group was discontinued early due to an increase in rates of invasive breast cancer. The use of CEE alone or in combination with MPA was found to increase the risk of blood clots and stroke, but to reduce the risk of hip fracture. In addition, CEE+MPA also increased the rate of CVD and showed a protective effect on colon cancer.(21).

Before starting hormone therapy, it is also crucial to consider the risk of breast cancer. Women with a history of breast cancer or a high baseline risk are advised to opt for non-hormonal alternatives to relieve bothersome symptoms. The Women's Health Initiative (WHI) Study revealed an increased risk of invasive breast cancer associated with the use of conjugated equine estrogen (CEE) and medroxyprogesterone acetate (MPA). This risk became detectable after 3 years of treatment.(22).

*Hormonal therapy*

Estrogen is available in several forms of administration such as oral, topical, and vaginal. For vasomotor symptoms, oral or topical estrogen is recommended, while for genitourinary symptoms, vaginal estrogen is recommended. However, the route of administration with the lowest risk is transdermal due to the lower risk of venous thromboembolism compared to women who use oral estrogen. Estrogen should be administered with a progestin or an estrogen receptor antagonist to reduce risks such as cancer and endometrial hyperplasia. In addition, the combination of estrogen and progestin (cyclic or continuous) is recommended. The dose of cyclic progestin consists of 200 mg of progesterone for 12 days per month. While the dose of continuous progestin consists of 100 to 200 mg each day(23).

Among the effects of hormone therapy we have the presence of irregular bleeding that will resolve in 2 or 3 months, however, this bleeding should be observed to rule out neoplasia in the endometrium.(23).

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**Table 1**. Estrogen treatment

| Drug | Route of administration | Dose | |
|---|---|---|---|
| 17 B-estradiol | 1. Patch<br>2. Oral<br>3. vaginal | 1. 1-2 patches per week.<br>2. 1-2 milligrams day<br>3. 1 time a day for 2 weeks and then 2 times a week. | 1. Preferred route already reduces the risk of venous thromboembolism.<br>2. It is similar to biological estradiol.<br>3. Preferred route in case of genitourinary symptoms during menopause. |
| Conjugated estrogen | Oral | 0.3-1.25 milligrams per day | |
| Synthetic estrogen | Oral | 0.3-1.25 milligrams per day | |
| Ethinyl estradiol | Oral | 0.2 – 0.05 milligrams day | |

**Fountain:** (23)

*Non-hormonal therapies*

They are an alternative for patients who have a contraindication to hormonal therapy or patients who have doubts about it, paroxetine (selective serotonin reuptake inhibitor) is the only option approved by the FDA. Selective serotonin reuptake inhibitors

Norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine and desvenlafaxine do help improve vasomotor symptoms compared with low doses of estradiol. Neurokinin B is a promising alternative for vasomotor symptoms as it is more effective and has fewer adverse symptoms.(24).

FDA-approved estrogen-free options include:

**Table 2.**FDA-approved non-estrogen drugs

| Drug | Route of administration | Dose | |
|---|---|---|---|
| Paroxetine | Oral | 7.5 milligrams per day | Helps with vasomotor symptoms |
| DHEA | Vaginal | 6.5 milligrams per day | Genitourinary symptoms in menopause. |
| Ospemifene | Oral | 60 milligrams day | It acts on the breast and endometrium, and for genitourinary symptoms in menopause. |

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| | | | |
|---|---|---|---|
| Gabapentin | Oral | 900 milligrams per hour of sleep | Helps with vasomotor symptoms |
| Clonidine | Oral, patch | 0.1 – 0.4 milligrams day | In patients with hypertension. |
| Neurokinin B (nk3) | Oral | 90 milligrams day | It helps more effectively with vasomotor symptoms. |

**Note.**Gray: drugs not approved by the FDA(23)

*Non-pharmacological therapies*

In studies, it has been observed that cognitive-behavioral therapy for insomnia in patients with insomnia for 6 months has helped to reduce this discomfort. The authors have concluded that this therapy should be applied as a first line for women with insomnia from an early age. Other activities such as yoga help reduce insomnia, but not vasomotor symptoms as such. Omega-3 helps improve mood and aerobic activities help improve sleep and mood. As general recommendations, it is suggested to avoid stressful situations, use a fan while sleeping, consume refreshing drinks, and avoid caffeine, spicy food and alcohol. For genitourinary symptoms, lubricants are a valid option.(25).

*The neurokinin B pathway in the treatment of menopausal hot flashes*

Administration of an NK3R antagonist reduced LH secretion in postmenopausal women, although lack of response to kisspeptin-10 limited research on the relationship between the NKB and kisspeptin pathways at this stage. Studies have shown that treatment with NK3R antagonists decreased self-reported menopausal hot flashes and reduced LH pulse frequency in these women. These results suggest that NKB signaling plays a role in regulating LH secretion during the hypergonadotropic phase of menopause, and provide indirect evidence linking vasomotor symptoms and high GnRH pulse frequency to the NKB pathway.(26).

The neurokinin B pathway is important in the reproduction and regulation of GnRH secretion in men and women. Neurokinin B antagonists have been shown to be effective in reducing vasomotor symptoms such as hot flashes, both in frequency and magnitude. A drug developed by AstraZeneca (AZ4901) is a specific antagonist of the NK3R receptor, responsible for suppressing luteinizing hormone (LH) secretion. This drug now known as (MLE4901) administered for 4 weeks resulted in the reduction of hot flashes in menopausal women.(27).

MLE4901 was administered to postmenopausal women for 7 days, resulting in a decrease in hot flashes both at night and in the morning. The effect was faster compared to other therapies already mentioned, so much so that on the second day the effects of this new alternative could already be observed, observing a decrease in the LH pulse. Patients who were administered MLE4901, 80 milligrams a day for 7 days, underwent an MRI before

and after treatment, where less connectivity was observed, which translates into fewer hot flashes.(27).

This confirms that fezolinetant is an effective alternative to significantly reduce vasomotor symptoms of moderate to severe intensity. Positive changes can be noticed from the first day of treatment, making it a promising option according to the FDA, which considers a decrease of 2 episodes per day as an important difference compared to other available therapies. In addition to relieving vasomotor symptoms, fezolinetant also improves the quality of life of patients. Regarding side effects, an improvement is observed compared to hormonal therapy, which tends to cause more bleeding. The most common adverse effects are related to the gastrointestinal tract, such as diarrhea, due to the presence of NK3 receptors in this system. However, in general, fezolinetant is supported as a safe and effective option for the treatment of vasomotor symptoms of menopause.(28).

**Discussion**

In the study on the neurokinin B pathway in the treatment of menopausal hot flashes published in 2021, where they carried out a study in order to verify the intervention of the neurokinin B pathwayfor the reproductive process, proving that it plays an important role in regulating the secretion of GnRH in both sexes, controlling physiological functions related to reproduction. It has also been proven that it is responsible for regulating hot flashes in the menopausal process. Neurokinin B antagonists have shown remarkable effectiveness in reducing both the frequency and intensity of vasomotor symptoms, both during the day and at night. Therefore, they represent a promising non-hormonal treatment option for this frequent and debilitating symptom of menopause.(29).

In a study conducted at the Centre for Reproductive Health at the University of Edinburgh's Institute of Medical Research in the United Kingdom in 2018, 11 postmenopausal women aged between 46 and 62 years were investigated, with laboratory results within normal parameters. These participants received a dose of 40 milligrams of NK3R MLE4901 every 12 hours. The results showed good tolerance to the treatment, and no alterations were observed in blood tests, including blood count and blood chemistry. Regarding hormonal levels, a decrease in the secretion of luteinizing hormone (LH) was observed, although a similar effect was not recorded on follicle-stimulating hormone (FSH), after evaluating the suppressive effect on LH secretion daily for 7 days.(30).

In the studioSKYLIGHT 1 is a phase 3 trial,Conducted in the US, Canada, Czech Republic, Hungary, Poland, Spain and the UK, women aged 40 to 65 years with hot flashes on average 7 were included in the study, divided into three groups 175 to the placebo group, 176 to the fezolinetant 30 milligrams group and 176 to the fezolinetant 45 milligrams group day to receive for 12 with an extension of treatment of 40 weeks, where

it was shown that the fezolinetant 30mg and 45 mg group had a significant reduction of vasomotor symptoms at week 4 versus the placebo group(31).

In the study carried out at the Breast and Menopause Clinic of the Corneel Heymanslaan University Hospital in 2021, they conducted a study in which the treatment of vasomotor symptoms of menopause was evaluated using fezolinetant, a neurokinin receptor antagonist. This drug selectively blocks neurokinin B (NKB) signaling, slowing down the pulse of gonadotropin-releasing hormone (GnRH) and reducing neuronal activity.(32).

For the study, 21 premenopausal women were considered, who were administered fezolinetant (90 mg twice a day) for a period of 12 weeks. During the study, the dose of this drug was increased without observing any alteration in laboratory results or vital signs. It was found that fezolinetant caused a 49.8% reduction in luteinizing hormone levels, compared to 16.4% recorded in the placebo group, just 3 hours after administration of the drug. In terms of side effects, fezolinetant was positioned as a safe and effective alternative for the treatment of vasomotor symptoms of menopause, in contrast to placebo, which generated more adverse effects such as bleeding. Therefore, it was concluded that fezolinetant offers a rapid and significant reduction in the frequency and severity of vasomotor symptoms, resulting in improvements in the quality of life of patients.(33).

**Conclusions**

- Hormone therapy, used for decades to mitigate menopausal symptoms, comes in various forms of application and has been shown to be effective in controlling hot flashes and other related symptoms. However, it also involves risks, such as an increased risk of venous thromboembolism and endometrial cancer. This has prompted the search for safer and more effective alternatives, such as NK3R antagonists and neurokinin B, which raise important considerations regarding their efficacy, safety and tolerability compared to traditional hormone therapy.
- In summary, the results show that NK3R antagonists and drugs that intervene in the neurokinin B pathway offer a promising and original perspective in the treatment of vasomotor symptoms. These drugs have been shown to significantly reduce the frequency and intensity of hot flashes, while improving the quality of life of patients. In addition, they appear to entail fewer serious side effects compared to conventional hormone therapy.
- In conclusion, the evidence suggests that neurokinin B signaling plays a crucial role in regulating hormone secretion and vasomotor symptoms during menopause. This supports the investigation of new drugs that act on this pathway to offer safer and more effective treatments. However, studies on NK3R antagonists and related drugs are still in early stages, requiring further research to confirm their long-term

efficacy and safety. Individualization of treatment is essential, considering the needs and preferences of each patient. The choice between hormonal therapy and new approaches should be based on a careful assessment of risks, benefits and individual preferences.

## Conflict of interest

The authors declare that there is no conflict of interest.

## Authors' contribution statement

Jeniffer Pamela Llumitasig Trujillo. Conducted the bibliographic search taking into account selection and exclusion criteria. Structured, wrote and corrected the bibliographic review.

Verónica Elizabeth Padilla Vinueza. Review of the first drafts through critical comments in order to contribute to the development of the writing.

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