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Position of the Spanish Menopause Society regarding the management of perimenopause

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ABSTRACT

Perimenopause is an imprecise period in woman over 40 years of age, which comprises the time between the moment that the first changes in the menstrual cycle appear and the year following the definitive cessation of the menses. Besides irregular bleeding, many women also complain of hot flashes and other characteristic symptoms of postmenopause. Moreover, most of them are concerned about the future impact that these events may have on their health, such as needing health exams or continuing to use contraceptive methods. A panel of experts from the Spanish Menopause Society has met to establish diagnostic and therapeutic guidelines for this period based on the best available evidence.

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Review

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1. Introduction

Perimenopause or the *menopausal transition* is an imprecise period in a woman's life comprising the period between the time that the first changes in the menstrual cycle appear and the year following the definitive cessation of menstruation. Menopause occurs naturally in our country at 51.4 years on average; however, the transition period is more difficult to establish, as its starts between 47 and 48 years of age, with a duration varying between two and five years.

Menstrual cycle disorder is characteristic at this stage. It is the result of dysfunction of the ovary, as the hormone production does not follow the cyclical patterns of fertile life that exposes the endometrium to uneven stimuli by estrogen and progesterone. In addition to irregular bleeding and the deterioration of ovarian function, many women also complain of hot flashes and other symptoms described in postmenopause. Moreover, most women are concerned about the future impact that these events may have on their health.

2. Definitions

Classically, perimenopause has been defined as a period ranging from two to five years that includes all endocrine, clinical and biological manifestations occurring *around* menopause. Recently, the *Stages of Reproductive Aging Workshop* has proposed a terminological scheme and established perimenopause between the end of the regular cycles and the year after natural menopause, as follows [1]:

Perimenopause or menopausal transition – The menopausal transition is established from the moment of appearance of menstrual disturbances and elevation of the serum follicle-stimulating hormone (FSH) level, which is up to 12 months after the last menstrual period. Women in this stage often show vasomotor symptoms.

Menopause – Menopause is a condition that is reached when there has been more than 12 months from the last menstrual period. It indicates the complete follicular depletion and absence of ovarian estrogen secretion.

Postmenopause – Early postmenopause comprises the first five years after the last menstrual period. It is characterized by the definitive cessation of ovarian function, which is usually accompanied by an accelerated loss of bone mass. Many women show vasomotor symptoms during this stage. The late postmenopausal stage is a broad term that continues from the fifth year of the last menstrual period to the end of life.

3. Epidemiology

The age of perimenopause onset is usually set between 40 and 54 years of age. According to data from the National Statistics Institute [2], Spain has a population of over 4 million women in the perimenopausal period, representing more than 12% of the entire female population of our country.

4. Endocrinology

The menstrual cycle and hormonal patterns begin to change years before menopause. Perimenopause is accompanied by a complex process resulting from the cessation of ovarian activity. From the endocrine standpoint, inter- and intra-individual variability is the norm; therefore, hormonal determinations lack a clear clinical utility for diagnosis during this period. Although various neuroendocrine changes in the menopausal transition have been described, the central biological event of this period is the phasing out of ovarian activity, both in the number of follicles and the quality of oocytes. Consequently, perimenopause is a period of low fertility that is maintained by anovulation and poor oocyte quality [3,4]:

- In the early stage of the menopausal transition, menstrual irregularities begin to appear, although a plasmatic decrease of inhibin B or anti-Mullerian hormone and an elevation of FSH levels can be detected beforehand. Meanwhile, estradiol levels remain normal or are even elevated (by increased aromatase activity), and the levels of progesterone are decreased. Occasional spontaneous ovulations may occur. Although these findings may identify the perimenopausal period, their value is not specific and is only used for measurement of the follicular reserve.
- In the late stage of the menopausal transition, the menstrual irregularity and the fluctuation of serum FSH, inhibin B and estradiol levels increases; therefore, a single determination of these hormones might not be adequate, as normal premenopausal values might be shown. Therefore, the determination of the anti-Mullerian hormone level is more accurate during this period.
- After menopause, the production of estradiol ceases due to the depletion of ovarian follicles, but androgens still continue to be synthesized due to the constant stimulation by *luteinizing hormone* (LH).

5. Diagnosis

Menopause is usually diagnosed clinically and retrospectively after one year of amenorrhea. In terms of its diagnosis, there is no single biomarker that is independent of perimenopause. The serum levels of FSH, estrogen and progesterone fluctuate around menopause, while the LH levels are maintained within the normal range. An increase in FSH stimulates ovarian folliculogenesis at an accelerated rate until the onset of menopause, at which point all follicles are depleted.

Increased folliculogenesis causes a greater production of estrogens, which can contribute to irregular bleeding and symptoms such as bloating and breast tenderness. An elevated level of serum FSH indicates a certain degree of ovarian failure but is not predictive of definitive infertility. The woman's age and the menstrual bleeding pattern may be the most useful factors in determining the likelihood of approaching menopause, unless the menstrual bleeding pattern is altered by hormonal contraception [5–7]:

- Menopause can be diagnosed clinically as 12 months of amenorrhea in a woman over 45 years of age in the absence of other biological or physiological causes. A further diagnostic evaluation for women in this group is not recommended.
- The menopause transition can be diagnosed for women over 45 years of age with irregular menstrual cycles and menopause symptoms such as hot flashes, mood swings and sleep disorders, and no further diagnostic evaluation is suggested. Although FSH is often measured, it offers no additional information and may be misleading.
- Women younger than 45 years who present with irregular menstrual cycles and menopause symptoms may be in the menopausal transition. However, for women in this age group, with or without symptoms of menopause, the same endocrine evaluation as for any woman with oligo/amenorrhea is recommended, as follows: serum human chorionic gonadotropin (hCG), prolactin, thyroid-stimulating hormone (TSH) and FSH.
- For women under 40 years of age with irregular menses and menopause symptoms, we recommend a full assessment for premature ovarian failure.

6. Clinical manifestations

6.1. Bleeding pattern

The chronic anovulation that is characteristic of this period causes the endometrium to be exposed to estrogen for long periods *unopposed* by gestagen and, consequently, to abnormal bleeding and a risk of hyperplasia. This process has been called *abnormal* uterine bleeding (AUB) and is not related to a normal menstrual period; however, from the age of 40, both the duration and the amount or timing of the menstrual cycle lack a uniformity that allows a distinction between normal and pathological. Due to the inconsistency that has existed in the nomenclature used to describe AUB during the reproductive age and because there are many causes, some of which can coexist in the same woman, the International Federation of Gynecology and Obstetrics (FIGO) has approved a new classification system to define the cause of AUB that is not related to pregnancy. The basic system consists of four categories that are defined by structural objectifiable criteria (PALM: polyp; adenomyosis; leiomyoma; and malignancy and hyperplasia), four that are unrelated to structural anomalies (COEI: coagulopathy; ovulatory; endometrial; and iatrogenic) and one that is reserved for non-classified entities (N) [8].

In the presence of any AUB, the medical history should be addressed to discard general disorders, blood dyscrasias or the consumption of drugs with anticoagulant or hepatotoxic effects and to detect other habits that could influence the occurrence of bleeding or indicate an inherited disorder of hemostasis. In terms of exploration, we recommend a gynecological exam and a bimanual palpation. Analytical determinations, except for a hemogram or the determination of ferritin, are not necessary in the study of cases of heavy bleeding unless suggested by the medical history. In terms of efficiency, a transvaginal ultrasound is the best method to complement the medical history and clinical examination for the diagnosis of AUB. In cases where endometrial pathology is suspected (after the ultrasound) or where the disorder has not been resolved with medical treatment, a hysteroscopy may be more effective than endometrial aspiration or curettage [9].

6.2. Symptomatology

Although perimenopause affects most women, it is estimated that in 20% of women, their quality of life is affected in a meaningful way. There are other common psychological symptoms, sleep disturbances, irritability, premenstrual syndrome, mood changes, changes in the skin, musculoskeletal disorders, balance disorders and vaginal dryness that are associated with the hot flashes and hormonal dysfunction of perimenopause [10,11].

7. Desire for pregnancy

Fertility declines over time, especially after 35 years of age. Along with the decline of ovarian reserve is a worsening of oocyte quality (with higher aneuploidy by meiotic nondisjunction phenomena), which increases the risk of spontaneous abortions and fetuses with chromosomal abnormalities. Age is the factor that most influences the rate of spontaneous pregnancies and the results obtained with fertility treatments. When consulting for infertility, the study begins at six months if the woman has reached the age of 35 and immediately if she has exceeded 40 years of age [12].

The application of assisted reproduction techniques is common in this age group, with a significant trend toward oocyte donation, which avoids the increased risk of fetuses with chromosomal abnormalities because the age of the oocyte is the same as that of the donor. This is not the case, however, with other pregnancy complications that remain dependent on the maternal age such as gestational diabetes, hypertension, growth restriction, placental pathology and prematurity. As a result, both the number of operative or instrumental deliveries and the perinatal and maternal mortality and morbidity are increased during perimenopause. As a result of these issues, reproductive counseling is necessary to inform women about the risks that age causes for conception [13–15].

8. Contraception

Although age is the most crucial predictor of a woman's reproductive capacity, it is assumed that there is still a risk of pregnancy in perimenopause as occasional spontaneous ovulation is possible. Moreover, age alone is not sufficient to contraindicate the use of any contraceptive method, whether hormonal or not.

8.1. Nonhormonal contraception

Nonhormonal contraceptive methods that are available to women in the menopausal transition are the same as those for women of other ages. From the standpoint of efficacy, both fertility awareness methods and the barrier methods require adequate compliance and, therefore, are categorized as having low efficacy (Pearl index >10). Due to hormonal changes, the effectiveness of natural methods for the relief of vasomotor symptoms and menstrual cycle control is low in this period [16].

8.2. Combined hormonal contraception

Age is associated with an increased risk of venous thromboembolism, which increases after age 39 among women using combined oral contraceptives. Epidemiological studies have reported an increase in myocardial infarctions, which are believed to be associated with a thrombotic mechanism rather than the development of atherosclerotic plaques, and in cardiovascular mortality in users of the combined pill who smoke and are 35 years of age. The relationship between smoking, the use of oral contraceptives and cardiovascular disease may be associated with high concentrations of intravascular plasma fibrinogen and fibrin deposition and the enhanced expression of tissue factor from monocytes. However, for healthy non-smoking women, age is not an obstacle for the use of hormonal methods. Besides providing menstrual cycle regularity and high contraceptive efficacy, combined contraceptives are associated with specific non-contraceptive benefits in perimenopause (Table 1). Transdermal and vaginal routes of administration have been granted the same status as the oral route. It is considered that both the contraceptive efficacy and indications and benefits and risks of the different hormonal methods, regardless of the route of administration, are similar in women over 35 years of age [17-21].

8.3. Hormonal contraception with progestin only

The main side effect of this type of method is the alteration in the bleeding pattern. The long-term reversible methods are an alternative to sterilization. The levonorgestrel IUD is indicated for the treatment of heavy menstrual bleeding. The enzyme-inducing drugs do not alter the effectiveness of the levonorgestrel IUD and depot medroxyprogesterone acetate [22,23].

8.4. Monitoring of hormonal contraception [24]

To start hormonal contraception, it is recommended that a medical history aimed at identifying facts that contraindicate or do not recommend its use be performed, especially a personal and family history of thromboembolism.

When monitoring hormonal methods, there is a consensus in not recommending specific periodic check-ups due to the use of contraceptives, but, if any, recommending contact with the patient at three or six months from the start of the treatment to improve adherence to it. A decision on the discontinuation of hormonal contraception should be based on an individualized contraceptive counseling, as currently there is no evidence that confirms the time at which ovarian function ceases, and fertility in women over 50 years of age is extremely low.

Before using the combined methods or progestin-only injections, it is advisable to measure the blood pressure and body mass index. For levonorgestrel IUD users, a check-up will be performed three to six weeks after its insertion.

8.5. Interruption of contraception [24]

Generally, contraception can be discontinued at the age of 55 years; however, this advice must be tailored to each woman. Women who do not use a hormonal contraceptive method and continue to have regular menstrual bleeding at the age of 55 should continue with some form of contraception. Women who use nonhormonal methods can stop contraception after one year of amenorrhea if they are 50 years or older or at two years if the woman is less than 50 years of age (Table 2).

Women carrying a copper IUD inserted after the age of 40 can keep the device until menopause or until contraception is no longer needed.

Women who use hormonal contraceptives should be advised that amenorrhea is not a reliable indicator of ovarian failure. For them, the FSH levels can be used to help diagnose menopause but should be restricted to women over 50 and those using progestinonly methods. FSH is not a reliable indicator of ovarian failure in women using combined hormones, even if measured during the *hormone-free interval*.

FSH levels can be assessed in women over 50 years of age who are amenorrheic and want to interrupt progestin-only methods. If the FSH level is \geq 30 IU/L, the measurement should be repeated after six weeks. If the second measurement of FSH level is \geq 30 IU/L, contraception can be discontinued after one year.

Women carrying an LNG-IUD (levonorgestrel-releasing intrauterine device) that was inserted for contraception at the age of 45 years or older can use the device for seven years or, if amenorrheic, until menopause, after which the device must be removed.

9. Perimenopause screening programs

9.1. Breast cancer

The breast is a hormone-dependent organ that responds to the hormonal changes of perimenopause. It presents radiological characteristics more similar to those of younger women, which reduces the sensitivity and specificity of a mammography on subsequent stages, and will require other tests to diagnose a condition. Screening should target women of 50–75 years of age. Breast cancer screening should also be discussed with women from age 40, although fewer women in this age group are likely to benefit from it. Screening every two years provides almost the same benefits as an annual evaluation but with far fewer false positive tests and fewer overdiagnoses of cancers that never become clinically evident. Women with a strong family history should be counseled on options that may include genetic testing for BRCA-1 and BRCA-2 and a more intensive screening for breast cancer. Despite the

Table	1
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Benefits of different methods of contraception in perimenopause.

	Tubal ligation	Vasectomy	Condom	IUD	Hormonal
Prevents unwanted pregnancy	Yes	Yes	Yes	Yes	Yes
Minimizes hormonal fluctuations	No	No	No	No	Yes
Provides additional health benefits	Yes, ovarian cancer and protection from PID	No	Yes, STIs and HIV	Early detection of cervical cancer with all IUDs. Possible protection of endometrial cancer, reduces anemia, dysmenorrhea and PID with LNG-IUD	Yes (ovarian or endometrial cancer, bone protection, relief from hormonal fluctuations, cycle control, dysmenorrhea and others)

PID: pelvic inflammatory disease; STIs: sexually transmitted infections; HIV: human immunodeficiency virus; LNG-IUD: levonorgestrel-releasing intrauterine device.

controversies, the breast cancer screening with mammography reduces mortality from breast cancer to a small but clinically significant degree. The absolute benefit of detection increases with age, whereas the false positive rate decreases with age. We support regular clinical examinations, even if based on weaker evidence. Some breast cancers are not detected by mammography, and a positive clinical examination requires further investigation even if the mammography is negative [25–27].

9.2. Cervical cancer [28-31]

The incidence of cervical cancer has two peaks, with the first being between five and ten years after the first sexual intercourse and the second beginning at the age of 40. It is unknown whether the latter is caused by the reactivation of a latent infection or by a new contact with human papillomavirus (HPV). Changes in sexual behavior among women of this age have been observed. Although cytology alone is a reasonable strategy, the co-test, which associates the cytology with a test for 12 or 13 oncogenic HPV types, has been shown to be superior to cytology alone in the identification of preinvasive lesions, which allows women with negative cytology and HPV results to be safely screened less frequently. The best detection rate of cervical cancer is not clear, but studies suggest that screening every three years achieves the same benefits as annual screening with fewer false positives and fewer procedures. However, women with abnormal screening results should be examined more frequently than every three years.

• For women between 40 and 65 years of age with negative cytology and HPV test results:

- A co-test is recommended every five years. If the HPV test is unavailable, cytology should be continued every three years.
- The cytologic finding of *atypical squamous cells of undetermined significance* (ASCUS) that is accompanied by a negative HPV result should be managed as a normal screening result.
- For women with negative cytology but positive HPV results, there are two possibilities, as follows:
 - One option would be to repeat the co-test in one year. At that time, for women whose new HPV test is again positive or shows a change to a low-grade squamous intraepithelial lesion in the cytology, a colposcopy should be practiced. Women with normal cytology or ASCUS and a negative HPV test at one year should return to routine screening.
 - Another option would be to immediately perform a test for HPV types 16 and 18. Women who test positive for either of these viral types should undergo a colposcopy. Women who obtain a negative result for both viral types should undergo a co-test at 12 months, with the management of the results as indicated in the previous option.
- Women with *all* other abnormalities should be managed according to the SAGO (Spanish Association of Gynecology and Obstetrics) guidelines. Most women can stop screening at age 65 years or after a hysterectomy. Once suspended, the screening should *not* be resumed even when the woman reports having had a new sexual partner. After spontaneous regression or proper treatment, women with a history of CIN2 (cervical intraepithelial neoplasia grade 2) or a more serious injury should continue to undergo screenings for at least 20 years, even if they exceed 65 years of age.

Table 2

Advice for women who wish to discontinue contraception.

Contraceptive method	Advice on the interruption of contraception			
	Age	Age		
	<50 years	>50 years		
Nonhormonal	Stop contraception after two years of amenorrhea	Stop contraception after one year of amenorrhea		
СНС	May be continued until 50 years of age ^a	Stop CHC at 50 years and switch to a nonhormonal method or with progestin only, then follow the advice for your own case		
DMPA	May be continued until 50 years of age ^a	Stop DMPA at 50 years of age and choose from the following options: Switch to a nonhormonal method and stop after two years of amenorrhea Switch to a POP, implant or LNG-IUD and follow the advice for your own case		
Implant POP LNG-IUD	May be continued until 50 years of age or more ^a	Continue with the method of choice		
		If amenorrhea, assess FSH levels and stop method after one year if serum FSH is \geq 30 IU/L on two occasions with an interval of six weeks.		
		Stop at 55 years when the majority of women can assume a natural loss of fertility.		
		If no amenorrhea, consider looking for abnormal bleeding or changes in bleeding pattern and continue to use contraceptives after 55 years until one year of amenorrhea.		

^a If a woman wishes to stop hormonal contraception before age 50, she should be advised to switch to a nonhormonal method that should be interrupted after 2 years of amenorrhea (or three years if a switch to DMPA is due to a possible delay in the return of ovulation) CHC, combined hormonal contraception; DMPA, depot medroxyprogesterone acetate; FSH, follicle-stimulating hormone; IU, international units; LNG-IUD, levonorgestrel-releasing intrauterine device; POP, progestin-only pill.

9.3. Colorectal cancer

Inquires should be performed about first- and second-degree relatives who have had colorectal cancer. There are screening and prevention recommendations specifically for women with a family history of colorectal cancer, as well as a genetic analysis. Colorectal cancer screening reduces disease mortality. Screening should begin at age 50 for women who are at average risk for colorectal cancer and earlier for people at increased risk. There are several strategies for early detection, although there is controversy in the recommended tests. Women should be involved in deciding which test to undergo. Although there is a trend toward a screening colonoscopy as opposed to other tests, it is reasonably safe for low-risk women to choose a fecal occult blood test, flexible sigmoidoscopy, or a combination of both [27].

10. Diagnostic tests used in perimenopause [32,33]

Ultrasonography is the most simple and economical test that is recommended for any suspected uterine or ovarian pathology. In perimenopausal women, the endometrial thickness is highly variable; therefore, ultrasonography should be performed during the first days of the cycle by measuring the thickest part in a sagittal section.

• **Hysterosonography** increases the diagnostic accuracy of ultrasonography because it differentiates focal endometrial pathology from that affecting the entire cavity, but it is only indicated when ultrasound suggests a disorder.

The **endometrial aspiration biopsy** has a sensitivity of 95% and a specificity of 81% in the diagnosis of endometrial cancer, but it should be reserved for situations such as a history of persistent AUB in women over age 45 or with risk factors for endometrial adenocarcinoma, such as a failure of medical therapy, sonographic suspicion of endometrial pathology, presence of endometrial cells in cervical cytology in patients with AUB, or presence of atypical glandular cells on cervical cytology.

An outpatient **hysteroscopy** for diagnosing endometrial pathology has been proven to be cost-effective and provide higher rates of satisfaction for patients undergoing the same procedures in an operating room. It shows a sensitivity of 94% for diagnosing endometrial pathology and a specificity of 89% with a 96% rate of satisfaction for procedures in premenopausal women.

11. Healthy habits for perimenopause

Body weight increases due to declining physical activity during perimenopause. Furthermore, hypoestrogenism produces a redistribution of body fat with a greater shift toward the abdominal depot. Fundamentally, this change comes at the expense of adipose tissue, which increases the risk of metabolic syndrome and cardiovascular events. For this reason, the principles of a healthy lifestyle focus on physical exercise along with a proper diet to achieve a proper body weight and the elimination of toxic habits [10].

Risk modifications through healthy lifestyle habits include increased physical activity (30–60 min per day), smoking cessation, maintaining a moderate alcohol consumption and heart-healthy diet and incorporating dietary supplements, or pharmacological supplements if necessary, of calcium and vitamin D [34,35].

12. Symptomatic treatment

12.1. Treatment of menstrual cycle disorders

In "nonstructural" abnormal uterine bleeding, the guidelines described in Algorithm 1 are recommended. Hormonal and nonhormonal medical treatments (Tables 4 and 5) are recommended for patients with a non-objectified organic disorder. Other hormonal treatments such as danazol, gestrinone or gonadotropin-releasing hormone (GnRH) analogs are in disuse due to their side effects. Surgery is reserved for a failure of medical treatment or when there is an associated organic pathology [36].

12.2. Treatment of vasomotor symptoms

Most women do not need treatment for vasomotor symptoms, or the symptoms are relieved after following the recommended healthy habits. Nevertheless, the quality of life will be affected in one out of every four women and will require some type of medical treatment. In this case, hormonal treatment (HT) is the first choice and the one that has the more favorable risk/benefit ratio. Given the indication of its use, use of the effective dose for the time necessary to achieve the treatment goal is recommended.

Other treatments such as selective inhibitors of serotonin reuptake (venlafaxine, paroxetine and fluoxetine) or gabapentin have been shown to be effective in the relief of hot flashes, although this indication has not been approved for their technical specifications. Phytotherapy is an alternative therapy in women with vasomotor symptoms who are unable or unwilling to use estrogens. When using phytoestrogens, it is recommended that the preparation contain a dose of 40–80 mg with at least 15 mg/day of genistein. *Cimicifuga racemosa* (Black Cohosh) is used at a dose of 40 mg/day [37–42].

12.3. Treatment of urogenital symptoms

It is necessary to identify the problem and routinely assess for signs and symptoms of vaginal atrophy and its interference in sexual activity and quality of life. Measures are recommended to prevent irritation of the vagina and to maintain the proper balance of flora that can be caused by harsh soaps or deodorants or synthetic fiber underwear. Maintaining sexual activity prevents the development of vaginal symptoms. The use of a polycarbophil- or liposomes-based vaginal moisturizer is considered as a first choice. These moisturizers remain while the epithelium peels off (48-72 h)and are effective for symptomatic relief. They must be used regularly, with two to three applications per week. Similarly, the use of vaginal lubricants during sexual activity provides relief from vaginal dryness and irritation in a short period of time, thereby making sexual activity more comfortable by reducing tissue friction. Topical estrogen therapy by the vaginal route effectively treats the symptoms of urogenital atrophy. There is little systemic absorption or effects on the endometrium; therefore, it does not require any specific medical monitoring during use. Topical estrogens restore the normal pH of the vagina, reestablish the normal flora of lactobacilli, increase the vaginal transudate and prevent a recurrence of urinary tract infections [43,44].

12.4. Treatment of sexual dysfunction

Topical HT may improve *sexual dysfunction* related to pain, thinning and vaginal dryness. In addition to the increase of irrigation of the vagina, clitoris and urethra due to its vasodilator effect, it shows a beneficial effect on sexual function [11].

12.5. Treatment of premenstrual syndrome

During perimenopause, the same measures as in premenopause have been proposed (dietary habits, vitamin supplements, evening primrose oil or combined hormonal contraceptives in nonsmoking women). When other psychological symptoms or mood disturbances prevail, selective inhibitors of serotonin receptors can be used [45].

13. List of recommendations

The Spanish Menopause Society considers it appropriate to develop its own recommendations based on the GRADE (*Grading of Recommendations Assessment, Development and Evaluation*) system to elaborate clinical practice guidelines and to classify the quality of the evidence and the strength of the recommendations [46].

14. Summary

14.1. Overview

- Women should be informed of the risks of chromosomal abnormalities, spontaneous abortion, pregnancy complications and increased maternal morbidity and mortality after the age of 40.
- Heavy or irregular bleeding ("nonstructural" abnormal uterine bleeding) is a common problem during the menopausal transition.
- During the menopausal transition, women appear to have a higher frequency of mood changes than pre- or postmenopausal women.
- Menopause can be diagnosed clinically as 12 months of amenorrhea in a woman over 45 years of age in the absence of other biological or physiological causes. Although FSH is often measured, it offers no additional information and may be misleading.

14.2. Contraception

- No contraceptive method is contraindicated by age alone (Grade 2B).
- There are a number of absolute and relative contraindications to oral contraceptive use. The World Health Organization has published medical eligibility criteria for contraceptive use.
- Women who are age 35 or older and smoke should be advised that the risks of using combined hormonal contraception generally outweigh the benefits. There is no contraceptive method contraindicated by age alone (<u>Grade 2B</u>).

14.2.1. Hot flashes

- Most postmenopausal women, with the exception of women with breast cancer or known cardiovascular disease, who have symptoms of vaginal atrophy and/or vasomotor instability are good candidates for estrogen therapy (Grade 1B).
- For postmenopausal women with moderate to severe vasomotor symptoms and no history of breast cancer or cardiovascular disease, we suggest a short-term estrogen therapy as the treatment of choice (<u>Grade 2B</u>).
- A short-term therapy is considered to be for two to three years and, in general, no more than five years.
- For women with moderate to severe vasomotor symptoms for which HT is contraindicated or not well tolerated or for women who have discontinued HT and again experience recurrent symptoms but wish to avoid estrogen resumption, phytotherapy treatment or inhibitors of serotonin reuptake are advised (Grade 2B). Because hot flashes disappear gradually without

treatment in most women, any drug may be reduced gradually after being administered for one or two years.

• For women with breast cancer and hot flashes, we suggest not using phytoestrogens or *cimicifuga racemosa* (Black Cohosh) (Grade 2C).

14.3. Vaginal atrophy

- For women with mild symptoms of urogenital atrophy, we suggest vaginal moisturizers on a regular basis and lubricants during intercourse (<u>Grade 2B</u>).
- For women with moderate to severe symptoms or those in which moisturizers and lubricants do not work, we recommend a low dose of vaginal estrogen (<u>Grade 1B</u>).
- With the exception of women with breast cancer, almost all postmenopausal women are candidates for vaginal estrogen therapy.

14.4. Disease prevention

- The importance of detecting and preventing illness and that routine controls (with the reported frequency) provide health benefits should be noted.
- Currently, no estrogen therapy should be indicated for the prevention of chronic diseases, including osteoporosis.

Contributors

N Mendoza, R Sanchez Borrego and MJ Cancelo: conception and design of the idea, data interpretation and preparation of manuscript.

All authors participated in the statement and approved the final version of the manuscript.

Competing interest

None of them have conflict of interest with.

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Provenance and peer review

Spanish Menopause Society Position Statement can the title have a minor alteration i.e. to Consensus Paper Position of the Spanish Menopause Society regarding the management of the perimenopause.

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