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Perspectiva

AEEM-SEGO position statement on menopausal hormone therapy

Posicionamiento AEEM-SEGO sobre la terapia hormonal de la menopausia

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Abstract

According to the latest data from the medical literature, the Spanish Menopause Society (Asociación Española para el Estudio de la Menopausia [AEEM]) has brought together a group of experts to re-evaluate the use of menopausal hormone therapy so that women can make an informed, evidence-based decision to determine the most appropriate dose, formulation, route of administration, and duration of menopausal hormone therapy.

There is some disagreement between scientific evidence on the efficacy and safety of menopausal hormone therapy and how this evidence is perceived by menopausal women and the clinicians who care for them, leading to an unnecessary loss of quality of life in those who reject it or in the unjustified fear of those who choose to use it.

A critical review of the most recent available literature was conducted. The review mainly covered randomized clinical trials and epidemiological studies published since January 2015.

This paper reviews clinical trials published since then, as well as new information on the potential risks and benefits of HT for the treatment of menopausal symptoms. Decisions about menopausal hormone therapy should be based on a woman's specific health risks, age, and time since onset of the menopause, as well as on the goals of therapy.

The Spanish Menopause Society (Asociación Española para el Estudio de la Menopausia) and the Spanish Society of Gynecology and Obstetrics (Sociedad Española de Ginecología y Obstetricia) updated their position statement on menopausal hormone therapy. This statement updates the clinical practice guidelines on the menopause.

Key words:

Estrogen. Hormone therapy. Menopause. Position statement. AEEM-SEGO.

Resumen

Conocidos los últimos datos de la literatura médica, la Asociación Española para el Estudio de la Menopausia ha reunido a un grupo de expertos para reevaluar el uso de la terapia hormonal de la menopausia con el fin de adoptar una decisión informada, basada en la evidencia que determina el tipo más apropiado de dosis, formulación, vía de administración y duración del uso de la terapia hormonal de la menopausia.

Existe una discordancia entre las evidencias de carácter científico, sobre la eficacia y la seguridad de la terapia hormonal de la menopausia y la percepción que tienen de ello las mujeres que están en la menopausia y los médicos que las atienden, lo que redunda en una pérdida innecesaria de la calidad de vida en las que lo rechazan o en el temor injustificado de las que optan por su utilización.

Se ha realizado una revisión crítica de la literatura disponible más reciente, fundamentalmente de ensayos clínicos aleatorizados y estudios epidemiológicos, publicados desde enero de 2015.

El presente documento revisa los nuevos ensayos clínicos publicados desde entonces, así como nueva información sobre los posibles riesgos y beneficios de la terapia hormonal de la menopausia para el tratamiento de los síntomas de la menopausia. Las decisiones sobre la terapia hormonal de la menopausia deben basarse en los riesgos de salud específicos de cada mujer, la edad o el tiempo desde la menopausia y los objetivos de la terapia. La Asociación Española para el Estudio de la Menopausia y la Sociedad Española de Ginecología y Obstetricia actualizaron su posicionamiento con respecto a la terapia hormonal de la menopausia. Dicho posicionamiento de la Asociación Española para el Estudio de la Menopausia/Sociedad Española de Ginecología y Obstetricia actualiza las guías de práctica clínica de menopausia ya publicadas.

Palabras clave:

Estrógenos. Terapia hormonal. Menopausia. Posicionamiento. AEEM-SEGO.

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RATIONALE

There is some disagreement between scientific evidence on the efficacy and safety of menopausal hormone therapy (HT) and how this therapy is perceived by women experiencing the menopause and by the physicians who care for them. This leads to an unnecessary loss of quality of life for those women who refuse menopausal HT and unjustified fear in those who choose to receive it.

A critical review of the most recent literature was performed. This comprised mainly randomized clinical trials and epidemiological studies published since 2015. The present document reviews the latest clinical trial results published since then, as well as information on possible risks and benefits of HT for the treatment of the symptoms of the menopause.

The symptoms of the menopause go beyond vasomotor effects (hot flashes and night sweats). Other symptoms associated with the onset of the menopause include potential alterations in sexual response, musculoskeletal complaints, mood swings, irritability, and sleep disorders, all of which affect quality of life and for which HT has proven beneficial.

LIFESTYLE MODIFICATIONS

A first step for women of any age with menopause symptoms is the recommendation of hygiene-dietary measures such as wearing loose clothing, drinking cold drinks, avoiding spicy food, and maintaining a lower ambient temperature. Furthermore recommends making lifestyle changes, maintaining an appropriate body weight, taking regular and suitably adapted physical exercise, and avoiding toxic habits.

Menopausal hormone therapy

The new recommendations in this position statement have been summarized as 10 basic concepts:

1. Vasomotor symptoms continue to be the main indication for HT. The most efficient approach for relief of the vasomotor symptoms of the menopause at any age comprises HT based on estrogens alone or in combination with gestagens, tibolone, and the combination of conjugated estrogens and bazedoxifene (CE/BZA).
2. Before HT is prescribed to symptomatic women, personal and familial risk factors should be taken into consideration, as should age and time since onset of the menopause.

   HT may not be suitable for some women with a greater risk of cardiovascular disease, greater risk of thromboembolic disease (eg, those with obesity or a history of venous thrombosis) or a greater risk of some types of cancer, such as breast cancer.

   Age and duration of estrogen deficiency at initiation of HT should be taken into account. In fact, available scientific evidence supports the hypothesis that HT halts progression of atherosclerosis in women whose menopause is of recent onset, but that it would have a neutral or adverse effect in older women or if it is started more than 10 years after onset of the menopause.

   There is greater support for the possibility that the metabolic effects of estrogens can vary with age and time since onset of the menopause, and there is evidence that estrogen receptors may be more functional and sensitive at the initiation of the menopause than afterwards.

   - Women aged under 60 years, or in the first 10 years after onset of the menopause, with no contraindications, are ideal candidates for treatment of troublesome vasomotor symptoms and high risk of bone mineral loss and even fracture.
   - For women who start HT after more than 10 years after onset of the menopause, or after age 60 years, the risk-benefit ratio is less favorable owing to the greater absolute risks of coronary heart disease, cerebrovascular accident, and venous thromboembolism.

   Dose. Dose and time of administration seem to be the main indicators of safety in HT. The importance of the type of estrogen and the route of administration remains open to debate.

   Even if women whose menopause is of recent onset have similar and substantial reductions in hot flashes and night sweats with doses of oral or transdermal estrogen that are lower than the standard doses, it is important to transmit the message that the dose necessary to obtain the desired effect must be used. We suggest starting at the lowest dose possible for the formulation and adjusting according to response.

   All routes of administration of estrogens seem to be equally efficient for relief of symptoms, although their metabolic effects differ.

   Transdermal formulations should be taken into consideration because of their less severe adverse effects: as they avoid the first-pass effect in the liver, there may be no accumulation of metabolites with estrogenic activity. Data suggest that transdermal estrogen formulations are as effective as, and potentially safer than, oral therapy.
3. When use of gestagens, natural progesterone, or its synthetic alternative dehydrogesterone, is necessary (administered at appropriate doses via the route chosen [oral or vaginal]), this is considered the safest approach.

   In women using an LNG-IDU that is active at onset of symptoms, addition of another gestagen is not necessary. This alternative may be valid—albeit

off-label—for women who do not tolerate oral gestagens.

Another option can be found in the combination of bazedoxifene with conjugate estrogens. In this combination, bazedoxifene prevents the endometrial hyperplasia induced by estrogens; therefore, it is not necessary to administer a gestagen.

4. In the absence of other factors, age is not a limitation for the duration of HT. Decisions on a longer or shorter duration of HT should be taken on an individual basis and according to the risk for various diseases (venous thrombosis, stroke, and some types of cancer). HT can be interrupted if symptoms disappear. The duration of treatment-free periods should be as short as possible and will depend on the reappearance of symptoms.
5. Both systemic estrogen and vaginal estrogen are effective for the symptoms of genitourinary atrophy, although in women who only have genitourinary syndrome of menopause with no other menopausal symptoms (eg, flashes), vaginal estrogens are more efficient. Vaginal estrogens can be used at any age. When administered locally, they improve vaginal comfort and trophism. These biological improvements alone do not guarantee a good sexual response.
6. HT is not indicated for primary or secondary prevention of cardiovascular diseases or for prevention of cognitive impairment in postmenopausal women. However, new findings in young postmenopausal women who take HT point to a favorable cardiovascular risk-benefit ratio.

   Given the lack of validated primary prevention strategies other than lifestyle changes for younger women (< 60 years), HT is considered a good strategy—taking into account current knowledge thereof—for reducing the risk of osteoporosis fractures in menopausal women and for reducing the frequency of coronary heart disease and general mortality of women in their sixth decade (or in the 10 years since onset of the menopause), unless there are specific contraindications.
7. The use of HT during the menopause does not imply the need to carry out tests other than those corresponding to basic health tests in this age group.
8. The AEEM/SEGO does not recommend the use of alternative HT (also incorrectly known as "Bioidentity").

   There is no scientific evidence in favor of greater safety with these products. Very often, the content or release of the components is inconsistent; consequently, lower or higher quantities of the biologically active hormone are administered. No controlled clinical trials support efficacy or rule out concern over safety.
9. Except in the case of contraindications, HT is recommended for women with early-onset menopause (primary ovarian insufficiency) and those who undergo bilateral salpingo-oophorectomy before age 50 years, at least until they reach the age for spontaneous menopause in the general population.

   The long-term consequences of early menopause include adverse effects on cognition, mood, cardiovascular health, bone health, and sexual health, as well as a greater risk of early death.

   HT should be administered on an individual basis in the case of women with early estrogen deficiency, since they may require higher doses in order to reach the physiological doses recorded for premenopausal women. It is also important to address the psychological impact of early menopause, review fertility options, and consider the potential need for contraception if the ovaries are intact.
10. As with any medical intervention, treatment should be on an individual basis using the best available evidence to maximize benefits and minimize risks, with regular re-evaluation of the risks and benefits of continuing or suspending menopause HT.

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