Hormonal treatments during the climacteric and beyond

Portuguese Menopause Society

THE PORTUGUESE MENOPAUSE SOCIETY (PMS) STRONGLY RECOMMENDS THAT:

1. Hormone replacement therapy (HRT) or hormone substitution therapy (HST) is considered appropriate nomenclature only in cases of premature or surgical menopause. Otherwise hormonal treatments (HTs) during and after the climacteric are not aimed at a substitution but rather at a specific pharmacological effect.

2. HTs are mainly used to treat vasomotor and other symptoms felt by most postmenopausal women, which have marked negative effects in their quality of life. When initiated early after the menopause they may also prevent cardiovascular diseases and osteoporosis, although they should not be primarily used for this purpose.

3. The absolute and relative contraindications of HT are those stated in “Health Plan for the Adult Woman” (IMS), Bikhäuser MH, Barlow DH, Notelovitz M and Rees MC (eds). Taylor & Francis, London and New York, 2005

4. Systemic treatment, when needed, should be started as soon as possible after the menopause, and finished by 60 years of age. Local treatment, for cases of vaginal atrophy, has no age limit.

5. Progestagens should always be used in women with an intact uterus. Synthetic progestagens should not be used in hysterectomized women undergoing HT. However, micronized progesterone may have a protective effect according to some studies. Synthetic progestagens should be as similar as possible to the effects of natural progesterone, such as retroprogesterone. Drospерinone is a progestagen with antiglucocorticoid and antimineralocorticoid effects, devoid of androgenic effects which make it suitable for women with hypertension. Tibolone is a prodrug with mixed progestagenic, androgenic and estrogenic effects that does not stimulate the breast and endometrium. Some studies suggest that it may be associated with a very small increased risk of breast cancer. Combined estrogens and progestagen regimens may be also associated with a very small increased risk of breast cancer.

6. Micronized estradiol or estradiol esthers are used by the oral route. Natural 17 β estradiol can be delivered transdermally (gel or patches) or by subcutaneous implants. Estrogens should always be used in combination with progestagens in the presence of an intact uterus. The use of conjugated estrogens alone was shown to protect from breast cancer up to 7 years of treatment. But other studies suggest that estradiol alone may cause some risk that might be counteracted by micronized progesterone.

7. The oral route may be used to start treatment and when a stimulatory effect on the hepatic synthesis of Apolipoprotein A1 is desired. It may have a more pronounced initial effect on the eradication of vasomotor symptoms and on the arterial wall.

8. The transcutaneous route leads to a better bioavailability of estradiol, avoiding a first pass by the portal circulation. Is preferable when avoiding direct stimulation of triglyceride synthesis and angiotensinogen is desired (cases of hypertension).
9. The duration of the HT cannot be stipulated. If there are no adverse effects and the objectives are fulfilled, it may continue as long as needed.

10. The lowest effective doses should be used. Patches and gels have the advantage of allowing the tailoring of estrogen dose.

11. Mammographies every 1-2 years, preferably digital, are obligatory. Transvaginal ultrasound scanning of the endometrium should be used, especially in the presence of spotting. A cut-off of 5 mm for endometrial double layer appears to be safe to exclude malignancy. Monitoring of blood pressure, lipid profile, and C-reactive protein is also important.

12. A persistent side effect, such as elevated blood pressure, spotting and weight gain, is an indication to stop HT.

13. All women, symptomatic or not, after the age of 50 should avoid smoking, maintain a normal weight and blood pressure, exercise regularly, adopt a proper diet, as these measures save more lives than any pharmacological treatment. HTs do not substitute these fundamental principles of health care.

14. The initial conclusions of the WHI Study should be rejected, because they do not apply to symptomatic menopausal women and because the protocol design is clinically unrealistic. The conclusions of the Million Women Study are also not acceptable, in view of the methodological problems that invalidate them. Conversely, the Nurse’s Health Study is considered an important reference for this type of treatment.