S8

PROGESTERONE AND CARDIOVASCULAR RISKS: THE STATUS OF THE ART

G. Rosano

There is now evidence that the arterial effects of progestins are mediated through progesterone receptors as well as through down-regulation of estradiol receptors. Progestin therapy can stabilize arteries in a state of vasomotor instability, but may also induce vasoconstriction of estrogenized vessels and precipitate arrhytmia. According to their chemical structure progestins have different metabolic and vascular effect that may enhance or abolish those induced by estrogen therapy on cardiovascular risk factors and on vascular functions.

Lipid, glucose and insulin metabolism are imporved by estrogen replacement therapy but this effect may be reversed by androgenic progestins while non andorgenic progestins have a more favorable metabolic profile.

Estrogens improve endothelial function and reduce the progression od coronary atherosclerosis both in animals and in early post-menopausal women. When administered in combination with estrogens, progestins may, in some istances, interfere with the effect of estrogens. However, in postmenopausal women, data on the anti-atherogenetic effect of progestins other than medroxyprogesterone acetate and gestodene are not available at present. The adjunct of more androgenic progestins to estrogens negatively affect peripheral vascular resistances. On the other hand progesterone has a beneficial or neutral effect on cardiovascular functions and on metabolic parameters suggesting that the lack of androgenicity may potentiate the cardiovascular effects of estrogens. Furthermore, the careful selection of the dose and scheme of administration of progesterone and progestins to use in hormone replacement is crucial in order to preserve and possibly enhance the benefical vascular effects of estrogens.

In conclusion, the cardiovascular effect of progestins may be different depending on type, dosage and route of administration of progestins. Natural progesterone is the progestin with less metabolic impact and neutral or beneficial effect on cardiovascular functions.

S9

PROGESTERONE SUPPLEMENTATION ON MOOD AND SEXUAL WELL-BEING

R.E. Nappi[1], A. Sommacal[1], G. Sances[2,3], I. Abbiati[1], F. Ferdeghini[1], C. Vercesi[1], F. Albani[1], F. Polatti[1]

[1]Dept Ob/Gyn, IRCCS Policlinico S. Matteo, University of Pavia & [2]Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH) IRCCS C. Mondino Institute of Neurology, Pavia, Italy

A vulnerable mood during the premenstrual phase has been highly related to luteal function. A complex interaction between estrogen and progesterone is operating within the CNS and a peculiar sensitivity to progesterone metabolites seems to be present in women with PMS and PMDD. The pattern of mood changes during sequential HRT shows some similarities with premenstrual cyclic mood swings and is modulated by estrogen dose and type of progestogens. Even though data from the literature at regard are mixed, it is reasonably to affirm that progestogen-related negative side-effects affect the compliance with HRT, particularly in those women suffering of PMS/PMDD during fertile age. In addition, recent data suggest a significant positive correlation between progesterone metabolites and sexual function in fertile women confirming indirectly the evidence that negative mood is strictly related with poor sexual well-being.

That being so, we have recently investigated the effect of oral micronized progesterone (P) supplementation (200 mg, os for 12 days) for 3 months in premenopausal women (n°18) with menstrual irregularities suffering from mood changes and sexual dysfunction. In addition, we studied mood and sexual function in a group (n°22) of perimenopausal women treated with transdermal E_2 (50 mcg) + P (200 mg, vaginal per 12 days) in a continuous combined regimen for 6 months.

In premenopausal women we obtained a significant improvement of libido, arousal and pain (measured by the female sexual function index) in those women reporting a concomitant significant improvement in anxiety, irritability, increase of appetite, but not in women who remained significantly depressed

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(evaluated by the Calendar of Premenstrual Experiences, Zung questionnaires). A similar result was observed in perimenopausal women which showed an amelioration of sexual behavior only when HRT was able to significantly improve anxiety, panic and tension, but not when depression was still present (evaluated by Greene Scale and Zung questionnaires). Therefore, P may be considered an effective treatment to improve mood and sexual well-being in pre- and postmenopausal women, but clinically relevant depression should be always rule out.

S10

PROGESTERONE INSTEAD OF PROGESTINS IN HRT: POTENTIAL DIFFERENCES IN THE IMPACT ON BREAST CANCER RISK.

C. Campagnoli, C. Abbà, S. Ambroggio, C. Peris

Endocrinological Gynecology, Sant'Anna Gynecological Hospital, Torino, Italy

At least 12 epidemiological studies on HRT and breast cancer risk have been published in the last five years. Most of them suggest that the addition of a progestin to the estrogen causes an increase in breast cancer risk three-four times higher than that observed with the estrogen alone. Most "in vivo" findings do suggest that natural progesterone is not a mitogen for breast epithelium and could even decrease the proliferative effect of estrogen (deLignières, 2002). Possibly, the increased risk seen in the epidemiological studies is due to non-progesterone-like effects of the progestins widely used in the countries where these studies were done (Sweden, UK and US), i.e. 19-Nortestosterone derivatives (norethisterone, levonorgestrel) and/or medroxyprogesterone acetate (MPA). Actually, these progestins differ from progesterone because they have: 1. an estrogenic action, through metabolites or directly (the 19-Nortestosterone derivatives); 2. a different influence on the enzyme reducing estrone to estradiol (possibly, MPA); 3. hepatocellular actions (opposing those of estrogen): decrease of the level of Sex Hormone Binding Globulin (SHBG) and increase of circulating Insulin-like Growth Factor-I (the 19-Nortestosterone derivatives, and, to a lesser extent, MPA); 4. property to bind to SHBG, with further reduction of its binding capacity (the 19-Nortestosterone derivatives). Progesterone is widely used in HRT in some European countries. Unfortunately, epidemiological data on its effect on breast cancer risk are not available so far. These kind of data would be more suitable in orienting therapeutical choices. Meanwhile, even if on theoretical basis only, the use of progesterone seems to be preferable.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.