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www.clearspringrx.com

CHERRY CREEK
201 UNIVERSITY BOULEVARD, #105
DENVER, CO 80206
T 303.333.2010
F 303.333.2208

LITTLETON
8031 SOUTHPARK CIRCLE, SUITE B
LITTLETON, CO 80120
T 303.707.1500
F 303.707.1717

PCAB ACCREDITED® Compounding Pharmacy
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Bio-Identical Hormones for Women

Is Transdermal Estradiol + Progesterone the Preferred Postmenopausal HRT?[1]

The selection of hormones used for symptom control and hormone replacement therapy (HRT), as well as doses and routes of administration, ultimately determine the potential for clinical benefits as well as adverse effects. The transdermal route of estrogen administration and the use of natural progesterone might offer significant advantages. Transdermally administered estrogens minimize the hepatic induction of clotting factors and other proteins associated with first-pass metabolism following oral administration. The risk of developing deep vein thrombosis (DVT) or pulmonary thromboembolism (TE) with transdermal estrogen therapy is negligible in comparison to that associated with oral estrogens.[2,3,4,5] Also, studies suggest potential advantages for blood pressure control with natural progesterone.[6]

The addition of a progestogen (a class of drugs which includes synthetic progestins as well as natural progesterone) to estrogen therapy is required for endometrial protection. The PEPI trial[7] demonstrated that micronized progesterone is as effective as the synthetic progestin medroxyprogesterone acetate (MPA) in preventing endometrial hyperplasia. A growing body of medical literature suggests that various progestogens are not equivalent. Furthermore, recent trials indicate that the use of natural progesterone does not increase the risk of breast cancer, as opposed to synthetic progestins.[8,9]

Metabolic syndrome and/or diabetes mellitus (DM) are important risk factors for cardiovascular disease, especially when combined with hypertension. The incidence of DM increases with age and menopause. Estrogen deficiency during menopause contributes to the development of abdominal obesity and insulin resistance, and could represent a major step in diabetogenesis in women. In a 2006 meta-analysis of 107 trials, Salpeter et al.[10] concluded that appropriate HRT reduces abdominal obesity, insulin resistance, new-onset diabetes, lipids, pro-inflammatory adhesion molecules and pro-coagulant factors in women without diabetes. Glucose metabolism and insulin sensitivity can be improved by estrogen replacement therapy but the addition of an androgenic progestin, such as MPA or NETA, may reduce the beneficial effect of estrogens. While MPA is known to increase insulin resistance and impair glucose tolerance, natural progesterone does not.[11]

Neuroprotective effects of progesterone include prevention and reversal of age-dependent changes and dysfunction. Some of these actions, particularly those mediated by conversion to neurosteroids such as allopregnanolone, may not be shared by synthetic progestins. Progesterone promotes the formation of new myelin sheaths after injury or lesions. Progesterone behaves differently in the brain than synthetic progestins (particularly MPA), through direct effects, as well as indirectly through effects on the vascular endothelium. This may have important implications for the effective use of HRT in the maintenance of neuronal function during menopause and aging and for protection against neurodegenerative diseases.[12]

In conclusion, evidence indicates that individualizing the selection of hormone, dose, and route of administration, based on a careful risk/benefit assessment for each patient, can result in significant benefits while minimizing the risk of side effects.

Testosterone Therapy for Women

Androgens, including testosterone and DHEA, enhance libido, provide cardiovascular protection (lower cholesterol), enhance bone building (increase calcium retention), and improve energy levels and mental alertness. Recently, attention has turned to the addition of the androgens testosterone and dehydroepiandrosterone (DHEA) to ERT in order to alleviate recalcitrant menopausal symptoms and further protect against osteoporosis, loss of immune function, obesity, and diabetes. ERT may represent incomplete preventive hormonal treatment in postmenopausal women because it does not directly address the declines in serum testosterone associated with hysterectomies and age-related gender-independent decline in DHEA and DHEA sulfate. Additionally, ERT may cause relative ovarian and adrenal androgen deficiency, creating a rationale for concurrent physiologic androgen replacement.[13] The addition of testosterone to conventional hormone therapy for postmenopausal women does not increase and may indeed reduce the hormone therapy-associated breast cancer risk, thereby returning the incidence to the normal rates observed in the general, untreated population.[14]

T4 plus T3 versus T4 alone

Bunevicius and colleagues compared the effects of thyroid hormone replacement with T4 alone (levothyroxine) versus T4 plus T3 in patients with hypothyroidism either caused by autoimmune thyroid disease or removal of the thyroid gland due to thyroid cancer. In a randomized, double-blind, crossover study design, each patient was studied for two five-week periods. During one period, the patient received his or her usual dose of T4. During the other, the patient received a regimen in which 50 micrograms of the usual dose of T4 was replaced by 12.5 micrograms of T3. Performance on tests of incidental learning was significantly better after T4 plus T3 treatment, indicating improved mental flexibility and attention. Patients scored their mood and physical symptoms as significantly better after T4 plus T3 treatment, and tended to be less depressed than after treatment with T4 alone. When asked at the end of the study, two-thirds of patients preferred T4 plus T3, saying they were more energetic, better able to concentrate, and simply felt better. This study concluded that partial substitution with T3 improved cognitive performance, mood, physical status, and neuropsychological function in hypothyroid patients.[15]

Research indicates there is a need for sustained-release T3 preparations in order to avoid adverse cardiac effects due to high serum T3 levels which can result if the hormone is absorbed too rapidly. Physicians may wish to consider the inclusion of sustained-release T3 in the treatment of hypothyroidism, particularly when the response to levothyroxine (T4) has not been complete. For more information about sustained-release T3 formulations, please contact our compounding pharmacist.

Every woman is unique. Therefore, it is a sensible approach for the patient to work together with health care professionals to customize hormone replacement therapy. Bio-identical HRT can be customized in the needed strength and dosage form and administered via the most appropriate route to meet each woman's individual needs.

References:

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Drugs, dosage, and dosage form are patient-specific. Please call one of our ClearSpring Pharmacy locations and speak to one of our pharmacists for more information.

Sample Prescription

Compounded Medication

Estradiol 0.5mg/ Estriol 2mg/ Progesterone 100mg per gram
Quantity: 30 grams
Sig: Apply one gram to skin daily as directed

Sample Prescription

Compounded Medication

Estradiol 0.5mg/ Estriol 2mg/ Progesterone 100mg per lozenge
Quantity: 30 lozenges
Sig: Dissolve one lozenge between cheek & gum daily as directed