

Title: Topical Progesterone Cream Does Not Increase Thrombotic and Inflammatory Factors in Postmenopausal Women

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BACKGROUND AND OBJECTIVE

Postmenopausal women have an increased risk of cardiovascular disease and heart disease is the leading cause of death in postmenopausal American women. Conventional hormone replacement therapy has been shown to result in an increase in thrombotic events in large prospective clinical trials including HERS I, and the recently halted Women's Health Initiative. One possible mechanism for this observed increase is the unfavorable net effects of conjugated equine estrogens and medroxyprogesterone acetate on hemostatic and inflammatory factors. An estimated 40 million American women are peri or postmenopausal and clinical therapies for menopausal symptoms remain a significant challenge in light of thrombotic risks. In this prospective, randomized, blinded, placebo-controlled, crossover study of 29 healthy postmenopausal women we examined the short term effect of topical progesterone cream on menopausal symptom relief, hemostatic and inflammatory factors, and nocturnal cortisol.

METHOD

29 postmenopausal women were randomized to receive 20 mg. of topical progesterone cream or placebo cream for 4 weeks. Subjects then underwent a 4 week washout period before crossing over to placebo cream or active drug. Baseline, 4 week follow-up, and end of study values were obtained for: the Green Climacteric Scale, total Factor VII, Factor VIIa, Factor V, Fibrinogen, Antithrombin III, PAI, and CRP. Subjects also underwent salivary sampling for measurement of progesterone and cortisol levels.

RESULTS

Greene Climacteric Scale Scores were significantly decreased over baseline demonstrating a significant improvement in menopausal symptoms with

administration of 20 mg. of topical progesterone daily for 4 weeks. In contrast there were no changes in hemostatic components: total Factor VII; Factor VIIa, Fibrinogen, Factor V, Antithrombin III, and PAI. CRP levels were unchanged with administration of topical progesterone. In hypercortisolemic women, topical progesterone was associated with a decrease in nocturnal cortisol.

CONCLUSION

Topical progesterone cream administered in a daily dose of 20 mg. significantly relieved menopausal symptoms in postmenopausal women without altering prothrombotic potential. Thus, topical progesterone cream should be seriously considered as an effective and safe clinical therapy for women with menopausal symptoms due to its neutral effects on hemostatic and inflammatory factors, and its favorable effect on nocturnal cortisol.