A Novel Model of Care to Reduce Inflammation and Improve Cardiometabolic Measures in Perimenopausal and Postmenopausal Women

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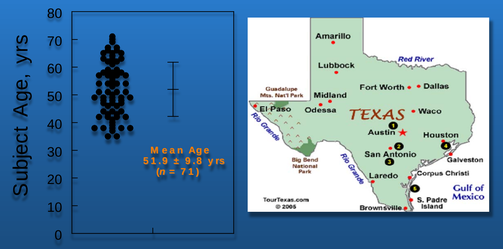
Introduction

Sex steroids have been recognized as key modulators of inflammatory and vascular activity in females, and low hormone levels may contribute to a significantly increased risk of cardiovascular mortality in menopausal women. In a novel model of care 75 healthy, perimenopausal and post menopausal women with low endogenous levels of sex steroid hormones received transdermal exogenous hormones of progesterone, estrogen, testosterone, and dehydroandrostenidione titrated to age specific physiologic ranges. Baseline, 2 month and 12 month values were obtained for inflammatory, cardiometabolic and quality-of-life measures.

Methods

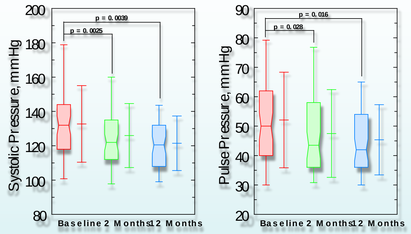
150 women of Caucasian, Black, Native American and Hispanic ethnic descent (mean age 51.9 yrs) who met strict inclusion & exclusion criteria were enrolled in our prospective, case-controlled study (75 controls, 75 interventional). The 2 month and 12 month effects of low dose daily transdermal progesterone and estradiol therapy on mood, quality-of-life, and gender-specific biomarkers of cardiovascular disease were measured.

Age and Demographic Distribution of Subject Population

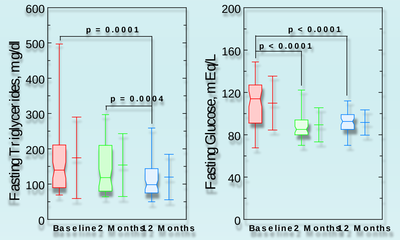


Results

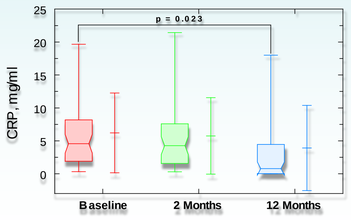
Blood Pressure Was Significantly Lowered at 2 Months and Remained Lower at 12 Months



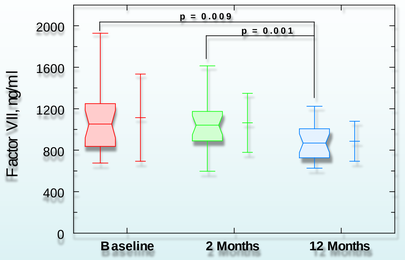
Fasting Triglycerides and Glucose Were Significantly Lowered at 2 Months and Remained Lower at 12 Months



C-Reactive Protein Was Significantly Lowered at 12 Months



Blood Coagulation Factor VII Levels Were Significantly Lowered at 12 Months



Summary of Data (Means ± SD)

Indicator	Baseline	8 Week	12 Month	12 Month p-value*
Systolic BP, mmHg	133 ± 22	126 ± 19	121 ± 16	0.004
Diastolic BP, mmHg	80 ± 10	79 ± 16	76 ± 9	0.010
Pulse Pressure, mmHg	52 ± 16	48 ± 15	45 ± 12	0.016
Fibrinogen, mg/ml	4.5 ± 1.3	4.4 ± 1.1		
PAI-1, IU/ml	9.6 ± 14.6	5.8 ± 8.5		
Factor VII, µg/ml	1.11 ± 0.42	1.11 ± 0.28	0.89 ± 0.19	0.009
Triglycerides, mg/dl	175 ± 115	154 ± 89	120 ± 64	< 0.001
Fasting Glucose, mEq/L	110 ± 25	89 ± 16	92 ± 12	< 0.001
HOMA-IR index	2.7 ± 3.3	2.1 ± 2.4	2.0 ± 3.2	0.25
Body Mass Index (BMI)	27.8 ± 5.9	27.4 ± 6.0	26.2 ± 5.3	0.107
CRP, mg/ml	6.2 ± 6.1	5.8 ± 5.8	3.9 ± 6.5	0.023
Interleukin-6, pg/ml	1.1 ± 3.7	10 ± 39	0.2 ± 0.4	0.068
Greene score	17.7 ± 8.9	13.7 ± 6.1	12.9 ± 6.5	0.001
Hormone score	31 ± 12	21 ± 12	18 ± 12	< 0.001
Hamilton-D score	6.6 ± 4.7	4.9 ± 3.8	5.0 ± 4.2	0.054
Hamilton-A score	9.6 ± 4.9	7.0 ± 4.1	6.5 ± 4.3	< 0.001
Vis-Analog Pain Scale	1.5 ± 1.0	1.2 ± 0.9	0.9 ± 0.8	< 0.001

* Using a paired Student's t-Test. Significant beneficial effects are highlighted in Green and significant adverse effects are highlighted in Red. Significance is based on p-values less than 0.05.

Conclusions

Dysfunction and dysregulation of endocrine/immune/inflammatory responses in aging women affects the incidence and progression of cardiovascular disease. The Hormone Restoration Model of Care is an expansion of conventional clinical models via individualized evaluation and treatment of the hormonal milieu, and it reveals the integral role of sex steroid hormones in regulatory processing of immune and inflammatory responses. Clinical trials in peri/postmenopausal women have demonstrated disconcordance with experimental data regarding hormonal factors in cardiovascular disease, likely related to differences in pharmacology of hormone therapies. By replacing the hormone that is deficient via transdermal dosing it may be possible to more closely mimic normal physiology and favorably impact cardiometabolic clinical biomarkers.

Related References

1. Stephenson, K., Neuenschwander, P., Kurdowska, A., Price, C. (2008). *Int. J. Pharm. Compound.* (in press).

2. Stephenson, K., Kurdowska, A., Neuenschwander, P., Loewenstein, I., Olusola, P., Pinson, B., Stephenson, D., Kinsey, R., Stephenson, J., Kapur, S., Zava, D. (2007) *Circulation* 115,e277.

3. Stephenson, K., Price, C., Kurdowska, A., Neuenschwander, P., Stephenson, J., Pinson, B., Stephenson, D., Alfred, D., Krupa, A., Mahoney, D., Zava, D., Bevan, M. (2004) *Blood,* 104(11), 414b-415b.

***Author Disclosures**: K. Stephenson -- Progesterone Research Foundation, International Academy of Compounding Pharmacists.*