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EFFECT OF HORMONE REPLACEMENT THERAPY AND RALOXIFENE ON EXERCISE TESTING AND DISPERSION OF VENTRICULAR REPOLARIZATION IN TREATED HYPERTENSIVE POSTMENOPAUSAL WOMEN
Lillian S Costa, Monica A Oliveira, Valeria M Rubin, João Carlos Tress, Jose M Aldrighi, Mauricio Wajngarten, Cantidio Drumond Neto, Otavio E Gebara. Cardiology, Rio de Janeiro Santa Casa de Misericordia Hospital, Rio de Janeiro, RJ, Brazil; Cardiogeriatry, INCOR Sao Paulo Heart Institute, Sao Paulo, SP, Brazil.

Publish data have suggested that hormone replacement therapy (HRT) can result in delays after depolarizations and ventricular tachycardia. One consequence of these findings has been an interest in therapy with raloxifene (R), a selective estrogen-receptor modulator, because of its potential to retain most of the beneficial effects of estrogen while avoiding most of its adverse effects. In a randomized single-blind crossover study, in order to evaluate the effect of R and HRT on time of exercise and peak oxygen uptake (VO2max) on Bruce protocol exercise testing (ET) and QT interval on electrocardiogram, we studied 30 hypertensive women age of 69.13 (61-82 yrs) after a run-in period with hydrochlorothiazide 12.5mg once-a-day. The QT interval was corrected (QTc) for heart rate and QT dispersion (QTd) was defined as the difference between the maximal and minimal QT intervals in any 2 leads. Measurements were performed at baseline, after 8 weeks of HRT (transdermal estradiol+norethisterone) and after 8 weeks of R (60mg) with a 4-week wash-out period between therapies. As shown, R and HRT increased QTc as the same extension compared with baseline levels(p<0.05), although there were not significant differences between them regarding the QTd and ET data. Our results suggesting the same effects of R and HRT on QTc in hypertensive postmenopausal women and not demonstrating any effect on ET and QTd should encourage future trials to evaluate its impact on clinical events.

Exercise test and QT interval data

<table>
<thead>
<tr>
<th></th>
<th>basal</th>
<th>HRT</th>
<th>R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET time</td>
<td>5.91 ± 1.66</td>
<td>6.05 ± 1.84</td>
<td>6.43 ± 1.90</td>
<td>0.123</td>
</tr>
<tr>
<td>VO2 max</td>
<td>21.27 ± 5.54</td>
<td>21.79 ± 6.13</td>
<td>23.17 ± 11.0</td>
<td>0.007</td>
</tr>
<tr>
<td>QTc</td>
<td>0.42 ± 0.04</td>
<td>0.44 ± 0.03</td>
<td>0.45 ± 0.06</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>QTd</td>
<td>0.06 ± 0.01</td>
<td>0.06 ± 0.02</td>
<td>0.06 ± 0.01</td>
<td>0.987</td>
</tr>
</tbody>
</table>

HRT: hormone replacement therapy; R: raloxifene; ET: exercise test; QTc: QT interval; QTd: dispersion of QTc

Key Words: Menopause, QT Interval, Raloxifene

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LEFT VENTRICULAR MASS IS INFLUENCED BY CHRONIC HORMONE REPLACEMENT THERAPY

The present study was performed to investigate the effect of six months of hormone replacement therapy (HRT) on left ventricular mass (LVM) in post-menopausal hypertensive women.

In a randomised double-blind placebo controlled study, 20 post-menopausal women (age 52 ± 3 years, mean ± SEM) received six months therapy with 0.625 mg conjugated estrogen + 0.5 mg medroxyprogesterone acetate (Premelle®) compared with placebo. Anti-hypertensive therapy was kept constant. Two-dimensional M-mode was performed at baseline, after six and twelve months.

From baseline both placebo and HRT induced reduction of LVM (p<0.05 for both). A small additive reduction of LVM in response to HRT was not significantly separated from placebo. The order in randomisation between placebo and HRT had a significant influence on LVM (baseline - HRT - placebo; baseline - placebo - HRT: <0.01 ANOVA).

In women without blockade of the renin-angiotensin-aldosterone system (RAAS) LVM was reduced in response to HRT (p<0.05) without any change after placebo (ns). When treatment with drugs blocking RAAS was used, the response in LVM was similar comparing HRT and placebo.

In conclusion we found significant influence of HRT and placebo on LVM after six months treatment. The most profound decrease in LVM was seen after HRT treatment in women without RAAS blockade.

Key Words: Hormone Replacement Therapy (HRT), Hypertensive Women, Left Ventricular Mass (LVM)

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THE INFLUENCE OF ESTROGEN STATUS ON MICROALBUMINURIA IN HYPERTENSIVE WOMEN
Eva A Karpanou, Gregory P Vyssoulis, Maria-Sevasti I Chaloudpi, Dimitris S Mendrinos, Konstantinos A Azaouridis, Socrates A Dimitrakopoulos, Christodoulos I Stefanadis, Dennis V Kokkinos. 1st Department of Cardiology, Onassis Cardiac Surgery Center, Athens, Greece; 1st Cardiology Department of Athens University, Hippokration Hospital, Athens, Greece.

Arterial hypertension is a common finding in climacteric woman even though the role of reduced estrogen levels in promoting this condition remains unclear. From the other side it is known that the level of microalbuminuria is an independent risk factor for CAD in hypertensive patients. The aim of the present study was to investigate whether estrogen status influences microalbuminuria in hypertensive women.

We studied 757 women, aged 45-55 years old, with untreated, uncomplicated essential hypertension. Premenopausal were 326, post-menopausal were 306, while 115 women had undergone hysterectomy. The 3 groups were age-matched, with similar office BP values, plasma renin activity levels (p=NS) and hypertension history. Microalbumin and α1-microglobulin excretion was measured in 24-hour urinary collection.

The 3 groups differentiated in both 24h microalbumin (F=13.8 p<0.0001) and α1-microglobulin excretion (F=9.9 p<0.0001). Thus, hysterectomized hypertensives had higher microalbumin values compared to pre- and post-menopausal ones (29.5 vs 20 vs 21.9 mg/l, p<0.0001 and p=0.008), as did in α1-microglobulin (7.16 vs 5.93 vs 6.6 mg/l, p=0.0001 and p=NS). Thus, the incidence of microalbuminuria was higher in hypertensives with hysterectomy compared to pre- and post-menopausal women (50.4 vs 25.8 vs 33.7 %), as was the incidence of α1-microglobulinuria (34.8 vs 13.8 vs 24.5%).

Menopause and hysterectomy in hypertensive women probably increase microalbuminuria. Therefore, the reduction of estrogens may play an additional role in hypertensive women influencing microalbuminuria and microglobulinuria, contributing to the harmful effects of hypertension.

Key Words: Hysterectomy, Menopause, Microalbuminuria

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PERCEPTION OF SODIUM CHLORIDE TASTE IN PREGNANT WOMEN WITH AND WITHOUT ESSENTIAL HYPERTENSION
Joanna Niegoswa, Nina Barylko-Pikielna, Michal J Wac. Louis G Keith. Outpatient Hypertension Clinic, National Institute of Cardiology, Warsaw, Poland; Polish Academy of Sciences, Warsaw, Poland; Center for Study of Multiple Births, Chicago, IL.

The aim of this study was to examine the relation between the perception of taste of sodium chloride, craving for salt, and values of blood pressure...
in pregnant women with hypertension. A group of normotensive pregnant women served as controls.

We examined 144 pregnant women with the diagnosis of essential hypertension (including a group of women with blood pressure <140mmHg and a group with blood pressure >140/90 mmHg), and 60 healthy women (control group) on 3 occasions: between 8-12, 24-28, and 34-38 weeks of pregnancy. We used NaCl solutions of 0.08%-0.96% concentrations to test two types of taste response: a) perception of salt taste, and b) craving for salt. Results were recorded on a unstructured linear scale and a nine-point interval scale, respectively.

The perception of salt taste in pregnant women with hypertension, BP>140/90 mmHg, was significantly decreased compared to the group of normotensive women in all 3 trimester of pregnancy (p<0.05). Craving for salt in the group of pregnant women with hypertension, BP>140/90mmHg, was increased compared to the control group; however, the differences were statistically significant (p<0.01) only in the first and third trimester of pregnancy.

The perception of salt taste and craving for salt in pregnant women with essential hypertension may be related to the BP changes in pregnancy. Changes in the perception of salt taste in the early pregnancy may predict the BP values later in pregnancy.

Key Words: Essential Hypertension, Perception of Salt Taste, Pregnancy

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CORRELATION OF NON-HDL CHOLESTEROL TO ANKLE–BRACHIAL SYSTOLIC INDEX IN PRE- AND POST- MENOPAUSAL UNTREATED NEWLY DIAGNOSED ESSENTIAL HYPERTENSION WOMEN

Maria V. Papavasiliou, Konstantinos Thomopoulos, Athanasios Anadiotis, Spiillos Karas. Department of Cardiology, Hypertension Clinic, Sismanoglion General Hospital, Athens, Greece.

Measured simply, easily reproduced and well associated assays to cardiovascular risk (CVR) in hypertensive subjects are non-HDL-C estimation and ankle-brachial systolic index (ABSI) determination. Menopause constitutes a period of abrupt change in CVR.

In this setting, we investigated the possible correlation of non-HDL-C with ABSI in pre-menopausal and post-menopausal essential hypertensive women.

For this, we used 81 untreated newly diagnosed essential hypertensive women (48 premenopausal and 33 postmenopausal) mean aged 52.6±11.1 years, with office blood pressure (BP) 159.3/99.6±19.8/9.25 mmHg and body mass index 26.4±2.6 kg/m². All women underwent measurements of total cholesterol (TC) and HDL-C levels (non-HDL-C=TC-HDL-C) and determination of ABSI with a hand-held Doppler according to established methods. The lower ABSI value was used for our study between right and left limb side measurements.

Non-HDL-C levels were higher in postmenopausal women compared to premenopausal (201.9±38.46 vs. 166.1±41.9 mg/dL, p=0.0001). Increased levels of ABSI were noticed in postmenopausal women compared to premenopausal group (1.13±0.1 vs. 1.08±0.1, p=0.05). Non-HDL-C was correlated to ABSI only in the population of postmenopausal women (r=0.354, p<0.05) as well as in the total study population (r=0.241, p=0.036) but not in premenopausal hypertensive women (r=0.143, p=NS). By applying a multivariate regression analysis model in the population of postmenopausal hypertensive patients including age, BMI, systolic and diastolic office BP, ABSI and non-HDL-C levels as independent variables it was revealed that non-HDL was significantly correlated to BMI and ABSI (p<0.05 for both cases). In conclusion, non-HDL-C was significantly correlated to ABSI in middle aged hypertensive women. This correlation remains significant in postmenopausal hypertensive women but not in premenopausal hypertensive women. In this setting, postmenopausal women with impaired ABSI and higher levels of non-HDL-C might be considered a possible group of increased CVR. Furthermore, the use of low cost accurate methods like the ones used above, may prove effective for initial screening assessment of CVR in such subjects.

Key Words: Ankle-Brachial Systolic Index, Lipids, Menopause

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EFFECTS OF NOVEL HORMONE THERAPY WITH ALDOSTERONE ANTAGONIST ACTIVITY DROSPIRENONE/ESTRADIOL ON BLOOD PRESSURE, RENAL FUNCTION, AND POTASSIUM IN HIGH RISK SUBGROUPS OF HYPERTENSIVE POSTMENOPAUSAL WOMEN

Richard A Preston, William B White, Bertram Pitt, Paul M Norris, Vladimir Hanes. Division of Clinical Pharmacology Clinical Research Center, Department of Medicine, University of Miami School of Medicine, Miami, FL; Division of Hypertension and Clinical Pharmacology, University of Connecticut School of Medicine; University of Michigan Medical School; Division of Gynecology, Department of Obstetrics and Gynecology, University of Miami School of Medicine; Berlex Laboratories, Inc, Montville, NJ.

Purpose: The novel hormone therapy Drosiprone/17-β-estradiol (DRSP/E2) has aldosterone antagonist activity and has been shown to lower both systolic and diastolic blood pressures (SBP/DBP) in hypertensive postmenopausal (PM) women. We assessed its effects on creatinine clearance (Ccr) and potassium (K) in high risk subgroups of hypertensive PM women.

Methods: Multicenter, randomized trial of DRSP/E2 versus placebo in PM women aged 45-70 years, with (n=82) or without (n=148) diabetes mellitus treated with an ACE inhibitor (ACEI) or ARB. Changes from baseline in Ccr (ml/min) and K (mEq/L) were analyzed overall and for subjects with renal impairment and age≥60.

Results: Overall, DRSP/E2 reduced SBP/DBP -8.8/-5.8 versus placebo -3.7/-2.9 mmHg (p=0.0001/0.003). There was no deterioration in creatinine clearance. There were small and clinically insignificant differences in change from baseline K only on day 15 in the overall group and age≥60 group. There were no differences in K in subjects with renal impairment.

Conclusions: DRSP/E2 lowered both SBP and DBP when added to an ACEI or ARB and was not associated with significant changes in renal function or K compared to placebo in high risk PM women.

<table>
<thead>
<tr>
<th>Change from baseline in K (mEq/L)</th>
<th>Day 15</th>
<th>Day 17</th>
<th>Day 25</th>
<th>Study End</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRSP/E2 Overall (N = 112)</td>
<td>0.099</td>
<td>0.123</td>
<td>0.121</td>
<td>0.097</td>
</tr>
<tr>
<td>Placebo Overall (N = 118)</td>
<td>0.005</td>
<td>0.080</td>
<td>0.105</td>
<td>0.073</td>
</tr>
<tr>
<td>P-value</td>
<td>0.004</td>
<td>0.340</td>
<td>0.800</td>
<td>0.650</td>
</tr>
<tr>
<td>DRSP/E2 renal impaired (n = 28)</td>
<td>0.161</td>
<td>0.243</td>
<td>0.284</td>
<td>0.197</td>
</tr>
<tr>
<td>Placebo renal impaired (n = 28)</td>
<td>0.019</td>
<td>0.106</td>
<td>0.056</td>
<td>0.122</td>
</tr>
<tr>
<td>P-value</td>
<td>0.20</td>
<td>0.25</td>
<td>0.15</td>
<td>0.45</td>
</tr>
<tr>
<td>DRSP/E2 age &gt;60 (n = 47)</td>
<td>0.138</td>
<td>0.158</td>
<td>0.123</td>
<td>0.164</td>
</tr>
<tr>
<td>Placebo age &gt;60 (n = 47)</td>
<td>-0.01</td>
<td>0.059</td>
<td>-0.013</td>
<td>0.033</td>
</tr>
<tr>
<td>P-value</td>
<td>0.03</td>
<td>0.18</td>
<td>0.10</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Key Words: Aldosterone, Drosiprene, Potassium