CLUSIONS: The levels of renal dysfunction and retinopathy are associated with a decrease in heart rate variability, especially LF components. Combination of power spectral analysis and cardiac MIBG becomes a powerful and interactive noninvasive assessment of autonomic nervous dysfunction in patients with EHT.

Key Words: End organ damage, MIBG, Heart rate variability

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LOSARTAN BUT NOT IRBESARTAN REDUCES SERUM URIC ACID IN HYPERTENSIVE PATIENTS WITH HYPERURICEMIA AND/OR GOUT

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Losartan has unique uricosuric properties and has been shown to decrease serum uric acid (SUA) levels in normal subjects as well as in hypertensive patients. The purpose of the present study was to compare the effects of losartan and irbesartan on serum uric acid in hypertensive hyperuricemic patients with or without gout.

Twelve hyperuricemic (SUA>420mmol/L), hypertensive patients (mean age: 58 yr) participated in this randomized, double-blind, cross-over study. After a 3-week run-in period during which patients received enalapril 20 mg o.d, patients were randomized to receive either losartan 50 mg o.d for 4 weeks followed by losartan 50 mg bid for another 4 week period or irbesartan 150 mg o.d followed by irbesartan 150 mg bid for 4 weeks. The losartan and irbesartan phases were separated by 3 weeks of the ACE inhibitor. All drugs were provided in an electronic pill container allowing to monitor compliance (MEMS system).

Losartan decreased SUA significantly from 539±28 mmol/L to 490±22 mmol/L ($p<0.01$) at 50 mg od and to 482±28 mmol/L at 50 mg bid, in contrast to irbesartan which had no effect on SUA. The first dose of losartan increased the urinary uric acid/creatinine ratio during the first 4h after drug intake, when compared with irbesartan (0.545±0.074 vs 0.361±0.049, $p=0.016$). This increase was still present at week 4 (0.494±0.092 vs 0.332±0.062, $p<0.01$) but was not found at week 8 when patients received a bid regimen (0.284±0.031 vs 0.329±0.032,p=ns). The monitoring of compliance showed that the adherence to the morning dose was good (90.4±1.7%) and significantly greater than that to the evening dose (81.30±2.2%, $p<0.001$). The changes in blood pressure induced by losartan and irbesartan were comparable.

These results demonstrate the potential benefits of using losartan in hypertensive patients with hyperuricemia and gout. They also suggest that losartan-treated patients reach a new uric acid steady-state during a sustained administration (>1 month). Hence, the uricosuric effect tends to decrease with time as SUA is reduced. Increasing the dose of losartan to 50 mg bid does not appear to induce a further decrease in serum uric acid.

Key Words: hypertension, uric acid, losartan

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REDUCTION OF BLOOD PRESSURE FROM CALCIUM SUPPLEMENTATION IN ADOLESCENT PREGNANCY: A RANDOMIZED TRIAL

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The incidence of gestational hypertension in adolescents less than 16 years of age is 3 times of that reported in the singleton pregnant adult. From previous mostly non-US investigations it appeared that calcium supplementation during pregnancy may decrease blood pressure and reduce the incidence of pregnancy-induced hypertension (PIH) and pre-eclampsia. However, a recent US multicenter clinical trial of calcium supplementation to prevent preeclampsia demonstrated no protective effect in normal pregnant adults. These contradictory studies could in theory be related to differences in basal dietary calcium intakes in diverse countries. We chose the high risk population of pregnant teens wherein there may be a theoretic increased need for calcium during pregnancy, to test the calcium supplementation hypothesis in a US high risk population.

We randomized 124 healthy pregnant teenagers into a calcium supplementation trial of 1000 mg/day of calcium or placebo by 20 weeks of gestation and followed them until delivery. In the trial, 62 "high risk" pregnant adolescents on calcium supplementation were compared to 62 "high risk" pregnant teens on placebo supplementation. Blood pressure measurements were conducted throughout pregnancy at each scheduled study visit. Blood samples were collected to study calcium metabolism.

There were no differences in age, 16.9 ± 1.4 years for adolescents on calcium and 16.7 ± 1.5 years for adolescents on placebo; nor height or weight at enrollment 161.9 ± 4.2 cm, and 67.2 ± 12.2 kg on calcium and 162.4 ± 5.8 cm and 70.6 ± 19.5 kg on placebo, respectively. There were no differences in daily consumption of calcium from the diet 976 ± 342 mg/day and 990 ± 366 mg/day respectively; nor plasma ionized calcium, 4.98 ± 0.16 mg/dL and 4.94 ± 0.14 mg/dL respectively. Parathyroid hormone, (PTH) was reduced on calcium 15.5 ± 9.2 ng/dL and 21.3 ± 10.8 ng/mL ($P = 0.05$) respectively. Calcitriol was reduced on calcium but did not reach significance, 75.1 ± 26.1 pg/dL and 81.6 ± 38.3 pg/dL ($P = 0.06$) respectively.

Systolic and diastolic blood pressures at 36 weeks of gestation were significantly lower ($P = 0.05$) in subjects receiving calcium Vs placebo: systolic blood pressure 120.7 ± 9.8 mmHg Vs 125.1 ± 9.3 mmHg, diastolic to 67.5 ± 6.5 Vs 70.2 ±6.8 mmHg, respectively. Mean blood pressure was significantly lower ($P = 0.05$) in adolescents receiving calcium 85.2 ± 7.6 mmHg Vs placebo 88.5 ± 6.6 mmHg.

Calcium supplementation significantly reduces the systolic and diastolic blood pressures in the USA of a high risk pregnant population, adolescents with singleton gestations.

Key Words: Blood Pressure, Calcium, Adolescent

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ANGIOTENSIN II DOES NOT AFFECT FIBRINOLYTIC FUNCTION IN HEALTHY SUBJECTS

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Numerous experimental studies have provided evidence for a direct functional link between the renin-angiotensin-aldosterone-system-(RAAS) and the fibrinolytic system. Angiotensin II (AII)has been suggested to mediate this interrelationship because this peptide was shown to stimulate plasminogen activator inhibitor-1 (PAI-1) in various tissues in vitro and in experimental animals in vivo. While an early study had revealed increased PAI-1 concentrations following AII infusion in a small number of healthy volunteers and in hypertensive patients, more recent infusion studies in man could not support these data. In the present study, we have therefore used AII at doses of 1,3 and 10 ng $kg^{-1}min^{-1}$, each over 45 min., in 9 healthy volunteer subjects with and without pre-treatment with a single dose of the angiotensin II(type 1)(AT_1)-receptor antagonist Valsartan (160 mg). All infusion increased arterial blood pressure from 121±6/81±mmHg to 153±8/101±5 mmHg ($p<0.001$). Over the time period investigated (11.00 AM-02.45 PM, plasma concentrations and activities of PAI-1 tended to decrease while the corresponding values for the tissue plasminogen activator (t-PA) tended to change in the opposite direction. In spite of the marked hemodynamic changes seen with the AII infusion, no effect could be demonstrated on the measured parameters of fibrinolytic function. Furthermore, pre-treatment of the volunteers with the AT_1-receptor antago-