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VISCERAL PERIVASCULAR ADIPOSE TISSUE REGULATES ARTERIAL TONE OF SMALL MESENTERIC ARTERIES

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Increased visceral adipose tissue in obesity is associated with adverse cardiovascular events and hypertension. Visceral adipose tissue surrounds mesenteric arteries and may produce vasoactive substances that influence vascular contraction. We tested the hypothesis that perivascular adipose tissue modulates contraction of small, resistance-sized mesenteric artery ring preparations. We studied mesenteric rings surrounded by periadventitial adipose tissue from adult male Sprague-Dawley rats. The contractile response to serotonin, phenylephrine, and endothelin I was markedly reduced in intact vessels compared to vessels without periadventitial fat. The contractile response to U46619 or depolarizing high K+ containing solutions (60 mM) was similar in vessels with and without periadventitial fat. The K+ channel opener cromakalim induced relaxation of vessels precontracted by serotonin but not by U46619 or high K+ containing solutions (60 mM), suggesting that K+ channels are involved. The intracellular membrane potential of smooth muscle cells was more hyperpolarized in intact vessels than in vessels without periadventitial fat. Both the anti-contractile effect and membrane hyperpolarization of periadventitial fat were abolished by inhibition of delayed-rectifier K+ channels with 4-aminopyridine (2 mM). Blocking other K+ channels with glibenclamide (3 mM), apamin (1 μM), TEA (1 mM), TPeA (10 μM) did not restore the vascular response in intact vessels. Longitudinal removal of 50% of perivascular tissue reduced the anti-contractile effect to serotonin by almost 50% while removal of the endothelium did not affect the anti-contractile effect. Using Vivaspin filters, we separated and isolated the visceral adventitia-derived relaxing factor. We suggest that visceral perivascular adipose tissue controls mesenteric arterial tone locally. It induces vasorelaxation by activating delayed-rectifier K+ channels in vascular smooth muscle cells.

Key Words: ion channels, adipocytes, arterial tone

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HIGH NACL DIETS INJURE ARTERIES AND HYDROCEPHALUS PROTECTS ARTERIES

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High NaC1 diets raise blood pressure (BP) and thereby accelerate arterial lesions. Study I: 100 uninephrectomized Dahl salt-resistant rats were given DOCA implants (250 mg/kg) and drink 1% NaC1 water for 6 weeks. Following 4 weeks of recovery after removal of the DOCA and NaC1, rats were divided into 2 matched groups with BP160 mm Hg (0.3% low vs 8% high NaC1). After 5 weeks on these diets, BP averaged 158 in both groups. Although the 8% high NaC1 produced no further rise in BP, 51% of the rats had died after 8 weeks on 8% NaC1 vs. none in 3% low NaC1 ($p<0.001$). The chief cause of death appears to be cerebral arterial injuries although they had no further rise in BP. Seemingly, salt's infany goes beyond BP. Study II: Following a true or sham aqueductal block on 4 week old Sprague Dawley rats, DOCA hypertension was induced by DOCA (150mg/kg) and 6% high NaC1 for 5 weeks, showed similar BPs, 175 vs 171. After 7 weeks, 27 sham BP averaged 189 ± 2.5 vs 175 ± 3.6 mm Hg in 25 blocked rats ($p<0.005$). In 14 weeks, 20 sham rats averaged much higher BP than that of 19 blocked rats, 203 ± 4.5 vs 187 ± 5.9 mm Hg ($p<0.05$). At 11 weeks postsurgery, the sham group showed much higher mortality: 8 out of 32 sham vs none in 25 truly blocked rats ($p<0.01$). Furthermore, averaged wet and dry weights of hearts and kidneys were significantly heavier in the sham group as compared to the blocked group. In summary, high NaC1 causes arterial lesions, especially in cerebral and mesenteric arteries, and organic cellular damages, thus, increased BP and mortality, which are markedly reduced by induced-hydrocephalus.

Key Words: Blood Pressure, Mortality, Vascular Injury

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SALT, ENDOGENOUS OUABAIN AND BLOOD PRESSURE INTERACTIONS IN THE GENERAL POPULATION

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Background: Nothing is known about the physiologic determinants of endogenous ouabain and its relationship to blood pressure in the general population. Accordingly, we investigated the association of circulating ouabain with blood pressure and other critical variables in the Belgian population.

Methods: Plasma ouabain was measured by a specific radioimmunoassay in 379 subjects enrolled in a Belgian population study. We also determined anthropometrical characteristics, blood pressure, serum and urinary electrolytes, urinary aldosterone excretion, various lifestyle factors and the Gly460Trp polymorphism of the α–adducin gene.

Results: In multivariate analysis, plasma ouabain (median, 140 pmol/L) increased significantly and independently with male gender ($N=182$; $P=0.002$), smoking ($N=116$; $P=0.05$), urinary potassium excretion (mean, 69 mmol/day; $P<0.001$) and the mutated α–adducin (Trp allele carriers, $N=161$; $P<0.001$). After adjustment for confounders, in both continuous and categorical analyses, systolic and diastolic blood pressures (mean, 123/76 mm Hg) were dependent on a significant interaction between plasma ouabain and urinary sodium excretion (mean, 194 mmol/day). In individuals with plasma ouabain values below the median, blood pressure increased by 2.2 mm Hg systolic and 1.4 mm Hg diastolic for each 50 mmol/day increment in urinary sodium excretion ($P\leq0.01$). No association between blood pressure and urinary sodium excretion was found when plasma ouabain exceeded the median.

Conclusions: Endogenous ouabain behaves in the general White population as a blood pressure modulating factor that is secreted in response to potassium. This endogenous steroid likely counteracts the depressor action of low salt intakes and appears also to reduce the pressor effect of excessive dietary sodium.

Key Words: endogenous ouabain, sodium, potassium

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SYNERGISTIC EFFECT OF UROTENSIN II WITH SEROTONIN ON VASCULAR SMOOTH MUSCLE CELL PROLIFERATION

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Urotensin II (U-II), the most potent vasoconstrictor known to date, and serotonin (5-HT) have been recently shown to play a crucial role in pulmonary hypertension. However, little is known about the effect of U-II and its interaction with 5-HT on vascular smooth muscle cell (VSMC) proliferation. We assessed the interaction between U-II and 5-HT in inducing VSMC proliferation. Growth-arrested rabbit VSMCs were incubated in serum-free medium with different concentrations of U-II and 5-HT. VSMC proliferation was examined by the increase in [^{3}H]thymidine incorporation into cellular DNA and cell number. U-II or 5-HT induced [^{3}H]thymidine incorporation in a concentration-dependent