Número do Trabalho – Oral 1

The novel Mas agonist, CGEN 856S, promotes vasodilation through Akt/eNOS pathway and activates FOXO1 in cellular models.

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Biotechnology advances based on a computational platform developed by Compugen, Tel Aviv - Israel, allowed the discovery of a potential Mas agonist, CGEN 856S, which produces several effects resembling those produced by Angiotensin-(1-7) (Ang-(1-7)), such as vasodilation and anti-hypertrophy. At least, part of these effects is dependent of increased nitric oxide (NO) production. We have recently shown using time-resolved phosphoproteomics, that Ang-(1-7) phosphorylates several kinases in human endothelial cells. In addition, it dephosphorylates the transcriptional factor FOXO1 at serine 256, which promotes its activation and nuclear translocation. When activated, FOXO1 can increase transcription of genes involved, for instance, in apoptosis, cell arrestment and tumor suppression. However, is not known whether CGEN 856S is capable to activate the AKT/eNOS pathway and FOXO1, as previously demonstrated for Ang-(1-7). This study evaluated the effect of CGEN 856S on eNOS and FOXO1 activation, besides the participation of AKT to mediate these effects using different cell types. Mas-transfected CHO (chinese hamster ovary) cells were stimulated with CGEN 856S in different conditions, such as time and peptide concentration. Untransfected CHO cells were used as control and the proteins were used for phospho-Akt, phospho-eNOS, phospho-FOXO1 and Mas detection by western blot. These cells were also used for NO release assay by DAF-FM incorporation. Human aortic endothelial cells (HAEC), A549 and DU145 (human adenocarcinoma linages from lung and prostate, respectively) cells were treated with CGEN 856S with or without previous A779 treatment, used for immunolocalization of FOXO1, analyzed by confocal microscopy and the nuclear fluorescence intensity was quantified. The results showed a significant phosphorylation of AKT, eNOS as well as the dephosphorylation of FOXO1 in CHO-Mas cells treated with CGEN856S. Only Mas-CHO transfected cells showed an increase of NO release after CGEN 856S treatment. A significant nuclear translocation of FOXO1 in HAEC, A549 and DU145 cell types treated with CGEN 856S was also observed. The A779 blocked this effect, at least partly. These data suggest that CGEN 856S induces its effects similarly to Ang-(1-7), via Mas receptor.

Número do Trabalho – ORAL 2

The angiotensin-(1-7) Mas receptor and the bradykinin B2 receptor interact to form a hetero-oligomer: functional implications

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Objective: Angiotensin (Ang) (1-7) through Mas receptor (R), and bradykinin (BK) through B2 R, exerts vasodilator and blood pressure lowering effects. Both B2 and Mas R belong to the G protein-coupled receptor (GPCR) family. It has been shown that GPCRs exist as homo- or hetero-oligomers, which is essential for receptor function. Taking into account that BK actions were blocked by a Mas R antagonist or when Mas R was knocked-down, or that Ang-(1-7) responses disappeared when the BK receptor B2 was blocked, we hypothesized that Mas and B2 Rs on the plasma membrane may interact directly through hetero-oligomer formation. Our aim was to investigate the existence of heteromerization between Mas and B2 Rs by the fluorescence energy transfer (FRET) technique and the functional consequences of this oligomer formation

Methods: HEK293T cells were transfected with the coding sequence for Mas R fused to YFP and B2 R fused to CFP. After 48 h cells were incubated in the absence and presence of 1 μM Ang-(1-7) or BK during 15 min and interaction between Mas and B2 R was evaluated by FRET. Functional consequences of this interaction were determined by ligand binding assays.

Results: A positive FRET was observed in cells cotransfected with MasR-YFP and B2R-CFP, suggesting that both Mas and B2 Rs interact by a hetero-oligomer formation in a constitutive manner. The formation of this hetero-oligomer was not altered by the agonist because FRET was not modified when the cells were stimulated with BK or Ang-(1-7). Ang-(1-7) or BK induced internalization of this hetero-oligomer into early endosomes since MasR-YFP or B2R-CFP colocalized with Rab-5, an early endosome marker, after ligand stimulation. To further confirm that the oligomer is internalized, we evaluated the amount of receptor present in the plasma membrane after agonist stimulation. When MasR-YFP plus B2R-CFP transfected cells were stimulated with Ang-(1-7) there was a decrease of 82±6% in Mas R and 58±4% in B2 R present in the plasma membrane. Conversely, when MasR-YFP plus B2R-CFP transfected cells were stimulated with BK there was a decrease of 91±4% in B2 R and 53±3% in Mas R in the plasma membrane. This result clearly demonstrates that in co-expressing cells of both receptors the selective stimulation of one of the GPCRs promotes co-internalization of both receptors.

Conclusions: our results show that Mas and B2 Rs constitutively interact through an hetero-oligomer formation at the plasma membrane. This hetero-oligomer is internalized upon stimulation with either Ang-(1-7) or BK, leading to a decrease in the number of Rs present in the membrane. This hetero-oligomer may explain the cross-talk between Ang-(1-7) and BK.

Número do Trabalho – ORAL 3

AUMENTO DA EXPRESSÃO DO RECEPTOR MAS ATENUA A HIPERTENSÃO E REMODELAMENTO CARDÍACO E RENAL EM CAMUNDONGOS TRANSGÊNICOS

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INTRODUÇÃO. O sistema renina-angiotensina (RAS) está presente em diversos tipos de tecidos, além do sistema cardiovascular. O principal componente vasodilatador deste sistema é a angiotensina 1-7 que atua através do seu receptor específico o MAS. OBJETIVO. O objetivo deste trabalho foi avaliar se a superexpressão do receptor MAS atenua a hipertensão tipo DOCA-SAL. MÉTODOS. A hipertensão foi induzida pelo tratamento com DOCA-SAL em animais machos com idade entre 12-18 semanas UB8 e WT. Antes de iniciar o experimento todos os animais foram submetidos a exame ecocardiográfico e medida de pressão através de pletismografia de cauda. Todos os animais foram nefrectomizados unilateralmente e para os grupos tratados, um pellet contendo 50 mg de acetato de desoxicorticosterona foi implantado na região interescapular e a água substituída por NaCl 0,9%. Nos grupos controle um pellet contendo apenas o silicone foi implantado e fornecida água de torneira normalmente. Após 28 dias foram tomadas as medidas de pressão e os animais foram novamente submetidos ao exame ecocardiográfico. Amostras de tecido foram retiradas para análise morfométricas.RESULTADOS. Os camundongos UB8 que apresentam superexpressão do MAS apresentaram atenuação do aumento da pressão arterial sistólica com o tratamento com DOCA-SAL (UB8 148 ± 23 VS. WT 192 ± 13mmHg). Como esperado, o peso do rim remanescente nos animais WT-DOCA apresentou um aumento significativo, no entanto o mesmo não foi observado nos animais UB8 DOCA-SAL (WT sham 0,27 ± 0,03 WT DOCA-SAL 0,46 ± 0,07 g VS UB8 sham 0,32 ± 0,08; UB8/DOCA-SAL 0,29 ± 0,017). Para o coração, assim como para o rim, a alteração no peso foi observada somente em animais WT (WT sham 0,09 ± 0,01; WT DOCA-SAL 0,12 ± 0,01), nos animais UB8 o peso do coração não variou (UB8 sham 0,094 ± 0,01; UB8/ DOCA/SAL 0,087 ± 0,02). A análise ecocardiográfica evidenciou uma redução na função sistólica que pode ser observada pela diminuição da fração de encurtamento e fração de ejeção nos animais WT-DOCA. A espessura septal aumentada na diástole observada nos animais WT-DOCA indica hipertrofia cardíaca significativa, essas alterações foram diminuídas ou estavam ausentes no coração dos animais UB8-DOCA. CONCLUSÃO. Os resultados obtidos monstram que superexpressão do receptor MAS atenua a hipertensão e reduz o remodelamento de órgãos como o coração e o rim de camundongos submetidos ao tratamento com DOCA-SAL.

Número do Trabalho – ORAL 4

MODULATION OF ACE ACTIVITY BY HIGH GLUCOSE LEVELS IN CULTURE OF COLLECTING DUCT CELLS

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The diabetes mellitus, as well as its complications, has becoming the major health problem of Western Countries. It is well know that increased intrarenal renin-angiotensin system (RAS) activity contributes to diabetic nephropathy. Our group described that in mesangial cells the consistent upregulation of angiotensin converting enzyme mRNA (ACE) suggested that, besides renin, ACE was directly involved in the increased mesangial angiotensin II (Ang II) generation induced by high glucose (HG). However, this relationship in the collecting duct is not studied yet. The aim of this study was to evaluate the modulation of RAS in collecting duct cells (IMCD) induced by high glucose concentration.The IMCD were divided into three groups: 1. normal glucose (5 mM D-glucose, NG); 2. high glucose (30 mM D-glucose, HG); 3. mannitol (30 mM, MG). Cells were exposed during 48h in their respectively medium. The intracellular and extracellular ACE was measured using hippuryl-His-Leu as substrate using a fluorimetric assay. The ACE protein expression was analysed using the western blotting method .Our results showed that ACE activity was significantly lower at intracellular (27%) and extracellular (22%) content in the cells of HG group when compared with NG and MG. However, there was no difference in the protein expression between the groups studied. Thus, our data suggest that the high glucose concentration in the culture medium is not able to modify ACE synthesis in IMCD cells, but can modulate ACE activity that was decreased in HG when compared with NG and MG. The decrease in ACE activity may result in decreased levels of Ang II in an attempt to protect the IMCD against proliferative and inflammatory deleterious effects of this peptide. (Supported by Fapesp and Mackpesquisa).

Número do Trabalho – ORAL 5

INFLUENCE OF β-ADRENERGIC RECEPTOR BLOCKADE IN HEPATIC GLUCOSE RELEASE INDUCED BY ANGIOTENSIN II IN TWO MODELS OF HYPERTENSION

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INSTITUÇÃO: Universidade Federal de São Paulo

In the liver angiotensin II (AII) has hemodynamic (portal hypertensive response, PHR) and metabolic (glucose release, GR) effects. PHR is abolished by losartan whereas GR is only diminished, therefore AII metabolic response might be mediated by other(s) receptor(s) besides AT1. Models of hypertension as genetic (SHR) and pharmacologic (L-NAME) have related or unrelated pathophysiology with RAS. The aim of this work was to compare the hepatic effects induced by AII in the presence of losartan or a β-adrenoreceptor antagonist in these two different models of hypertension.Methods: Angiotensin II effects were studied in perfused livers: 1) L-NAME, Wistar rats received L-NAME (drinking water 0.5 mg/mL) for 10 days and 2) SHR and compared to 3) WIS, normotensive Wistar. The livers were perfused in the absence or presence of propranolol (β-adrenoreceptor antagonist) and/or losartan. Liver perfusion: portal vein and vena cava were cannulated and AII (2nmol) injected in bolus; the perfusion pressure was recorded before and during 10 minutes after the injection, the PHR (AUC: portal pressure increase vs perfusion time) calculated and expressed as cmH2O.min. Glucose was measured in aliquots of efferent perfusate collected in different times. Liver viability was evaluated by bile production and oxygen consumption. The liver glycogen content was determined from caudal lobe fragments removed after rapid exsanguination.Results: Bile production and oxygen consumption were similar in all groups. The liver glycogen content was similar between the groups. In the WIS group, the PHR induced by AII (cmH2O.min; 26.4±3.2) and GR (µmol/min; 8.5±1.3) were diminished (ANOVA, $p<0.0001$) in the presence of losartan (PHR: 8.5±1.3; GR: 2.8±0.4) while propranolol affected neither PHR (31.6±2.0) nor GR (15.3±1.2). In the presence of propranolol/losartan both the PHR (3.5±1.2) and the GR (3.4±0.5) induced by AII were diminished. Regarding to the L-NAME group, the profile obtained for AII effects were similar to the WIS group. Propranolol (PHR 38.5±1.9; GR 10.4±1.1) did not affect the AII effects (PHR 38.1±4.8; GR 11.2±1.5). On the other hand, AII effects were diminished in the presence of losartan (RHP 3.4±0.8; GR 3.4±0.3) or propranolol/losartan (PHR 4.2±2.4; GR 2.8±0.5). In the SHR group, PHR induced by AII (25.9±3.7) was similar but GR (5.4±0.6) was diminished when compared to WIS and L-NAME groups. In the presence of the antagonists, the PHR profile obtained for the SHR group was similar to the WIS and L-NAME groups. Interestingly, propranolol increased GR induced by AII (14.1±0.9) while neither losartan (4.6±1.1) nor propranolol/losartan (3.1±0.3) affected GR when compared to absence of antagonism in SHR groupConclusion: Our results suggest that the hepatic the PHR induced by AII is mediated only by AT1R but the glucose release might also be mediated by ²;-adrenergic receptor in SHR.Supported by: CNPq and FAPESP

Número do Trabalho – ORAL 6

Blockade of NMDA receptors in the dorsomedial hypothalamic region attenuates the cardiovascular response evoked by cage switch stress

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INSTITUÇÃO:UFMG

Evidence indicates that the dorsomedial hypothalamic region (DMH) plays a key role in the organization of the cardiovascular (CV) response to acute emotional stress. Blockade of EAA receptors in the DMH attenuates the physiological responses evoked by stress. However, all findings have been obtained in a single stress model (air-stress).We evaluated the contribution of NMDA receptors in the DMH on the CV response evoked by cage switch stress (CS stress).Wistar rats received guide cannulas for nanoinjections into DMH. Seven days later, a catheter was inserted into the femoral artery for HR and BP recording. On the next day, rats were subjected to bilateral nanoinjections into DMH (100nL) of vehicle (0.9% saline, n=7), the GABAA agonist muscimol (100pmol, n=8) or the NMDA antagonist AP-5 (100pmol, n=6) and, ten minutes later, subjected to CS stress. A control group without nanoinjection was also tested (intact group, n=9).In the intact and vehicle groups CS stress evoked tachycardic response (Δ119±12bpm and 121±11bpm) accompanied by a large increase in BP (Δ60±2mmHg and Δ60±3bpm, respectively). The tachycardic and pressor responses were markedly reduced by muscimol or AP-5 (ΔHR: 62±7bpm and ΔMAP: 37±4mmHg; ΔHR: 31±7bpm and ΔMAP: 39±3mmHg, respectively, $P<0.05$).These data suggest that the DMH is also important for controlling CV responses in other forms of acute emotional stress. Part of this response involves activation of NMDA EAA receptors.

Número do Trabalho – ORAL 7

Luminal Angiotensin II on porcine proximal tubule kidney cells (LLC-PK1) increases SERCA activity via AT1 and AT2 heterodimers and PLC/PKC pathway: a possible way for increased Na+ reabsorption.

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Angiotensin II (Ang II) is found in renal interstitium and tubular lumen at higher concentrations than systemic Ang II. At these compartments, this peptide can trigger an effect on intracellular Ca2+ homeostasis, inducing alteration on Na+ reabsorption. The aim of this study is to determine the effect of Ang II facing luminal membrane on the kidney Ca2+-ATPases and to elucidate its physiological effect. LLC-PK1 cells were cultivated in DMEM medium with 10% FBS at 37º C with 5% CO2. Cells were seeded in culture bottle, after reaching 90% of confluence, cells were treated with different conditions, harvested and lysed. Protein concentration was assayed (J. Biol. Chem. 193: 265, 1951) and total Ca2+-ATPases activity was calculated by difference between absence and presence of 2 mM EGTA (J. Biol. Chem. 202: 675, 1953). It was observed that Ang II in low concentrations stimulates SERCA activity (10-14 M - 10-10 M), in a rapid (30 s) and persistent (30 min) manner, while in higher concentrations (10-8 M - 10-6 M) this effect is not observed. Luminal Ang II decreased during time and no formation of metabolites was observed, indicating peptide internalization. Ang II increased AT1/AT2 heterodimerization by 140% and AT1 and AT2 receptors antagonists, 10 nM losartan and 10 uM PD123319, blocked luminal stimulus of SERCA by Ang II. Calphostin C (5 × 10-8 M; PKC inhibitor) and PMA (0,1 µM e 1 µM; PKC activator) blocked and mimicked Ang II stimulation of SERCA activity, respectively. Calphostin C –sensitive PKC activity is 40 % increased at 10-10 M and 37 % inhibited at 10-6 M Ang II. Moreover, pre incubation of 10-9 M Ang II for 30 min, induced a 10 times higher and 3 times longer Ca2+ mobilization than in absence of previous incubation with Ang II. We concluded that luminal Ang II induces the formation of AT1/AT2 heterodimer to activate PLC/PKC signaling pathway, increasing SERCA activity. The Ca2+ mobilization study indicates that increased Ca2+ intracellular store by SERCA activation, results in a more efficient response to agonist future stimulus contributing to increase fluid and solute reabsorption in renal proximal tubule cells.

Número do Trabalho – ORAL 8

INCREASED CIRCULATING ANGIOTENSIN-(1-7) LEVELS PREVENTS GLUCOSE INTOLERANCE AND EXCESS WEIGHT GAIN IN ADULT OFFSPRING OF FRUCTOSE-FED MOTHERS

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Maternal malnutrition during pregnancy adversely affects the health of the offspring later in their life. Studies have shown that the offspring of fructose-fed mothers present neuroendocrine and metabolic disorders on weaning and adult life. We sought to evaluate the effects of increasing circulating angiotensin (Ang)-(1-7) levels on metabolic parameters in adult offspring of fructose-fed mothers. Female Sprague-Dawley (SD) and transgenic-(A-1-7)3292 (L32) rats received either 10% fructose solution (-FF) or tap water (-CTL) to drink and fed regular chow from 5 weeks before mating to the end of lactation. Each mother remained with 7-8 pups after parturition. With 25-days age, pups were weaned and some male grew until 9-weeks age. Data was analyzed by Two-way ANOVA followed by Student-Newman-Keuls post-hoc tests, $p< 0.05$. The SD-FF mothers had increased relative weight of liver (LIVER, 2.58 ± 0.07 mg/cm tibia) and retroperitoneal adipose tissue (RETRO, 0.60 ± 0.08 mg/cm tibia) compared to SD-CTL (LIVER= 2.27 ± 0.05, RETRO= 0.43 ± 0.03 mg/cm tibia). Differently, it was comparable between L32-FF (LIVER= 2.20 ± 0.08 and RETRO= 0.31 ± 0.02 mg/cm tibia) and L32-CTL (LIVER= 2.03 ± 0.05 and RETRO= 0.27 ± 0.01 mg/cm tibia). The L32 mothers had improved response to glucose tolerance test (TTG) compared to SD. Fructose feeding did not alter TTG response in either in SD or L32 mothers. Adult SD-FF offspring had impaired glucose tolerance [TTG; area under curve (AUC)= 13363 ± 1256], increased body weight (BW, 310 ± 5 g) and LIVER (2.67 ± 0.04 mg/cm tibia) compared to SD-CTL (AUC= 9950 ± 1110, BW=290 ± 6 g, LIVER= 2.48 ± 0.08 mg/cm tibia). In contrast, TTG response (AUC=6235 ± 311), BW (224 ± 5g), and LIVER (2.06 ± 0.05 mg/cm tibia) were comparable between L32-FF and L32-CTL offspring (AUC= 7180 ± 633, BW= 234 ± 5 g, LIVER= 2.20 ± 0.07 mg/cm tibia). These data show that increased circulating Ang-(1-7) levels attenuates metabolic effects in fructose-fed mothers and glucose intolerance and excess body weight gain in their adult offspring. Financial support: CNPq, FAPEMIG and CAPES (INCT-Nanobiofar, Programa de Núcleos de Excelência - PRONEX-CBB-APQ-04758-10, and PMPD II 10/2013 postdoctoral fellowship to PSG).

Número do Trabalho – ORAL 9

AMYLOID SERUM AS A CANDIDATE OF ACUTE REJECTION IN KIDNEY TRANSPLANTATION

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Chronic kidney disease (CKD) has been regarded as "the new epidemic of the XXI Century", due to the exponential increase in the number of cases of hypertension and diabetes, with alarming projections for the coming years. The end-stage CKD generally affects less than 1% of the population and the treatment of choice is the kidney transplant or dialysis. After transplant, cases of acute rejection (AR) are considered a major complication in the function and survival of the transplanted kidney. When serum creatinine levels increase a renal biopsy is recommended to confirm acute rejection. Although serum creatinine has been widely used as a rejection indicator one of its weaknesses as a biomarker is that by the time increased levels are detected kidney damage is already seen. In addition besides being considered the gold standard AR graft diagnostic tool, this method is invasive, costly and uncomfortable to the patient. The aim of this study is to evaluate the Serum Amyloid A (SAA) protein as a possible biomarker in renal transplant AR.We analyzed the plasma profile of 16 renal transplant patients (10 with acute rejection and 6 with stable graft function) according to the inclusion and exclusion criteria and the immunosuppressive regimen that consisted of tacrolimus, azathioprine and prednisone. Samples were collected one day before renal transplantation (day 0), one day after transplantation (day 1), seven days (day 7), fourteen days (day 14), twenty one days (day 21), twenty eight days (day 28) and the day confirmation of rejection in Rej group, using the Western blotting technique. As a result, SAA was upregulated on day 14, 21 and 28 post-transplant in patients that had AR compare with patients without AR.We believe that the serial and routine monitoring of SAA in patients undergoing kidney transplantation can give us a broader profile of this protein to detect a premature AR and avoid a renal biopsy been this a protein a biomarker.

Número do Trabalho – ORAL 10

EFFECT OF ANGIOTENSIN-(1-7) ON BLOOD PRESSURE AND HEART RATE IN HEALTHY HUMANS

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INSTITUÇÃO: Instituto de Cardiologia de Porto Alegre

Introduction and Purpose In the modern concept of the Renin-angiotensin System (RAS), Angiotensin-(1-7) plays a key role and demonstrates promising therapeutic potential due to it is generally opposite effects to Angiotensin II. Once it is known that the cardiovascular and renal actions of Ang-(1-7) may effectively contribute to the prevention and improvement of cardiovascular diseases and the possibility of using this peptide as therapeutic agent is being increasingly investigated. However, the majority of these findings is usually assessed in animal models, denoting the necessity of a translational approach involving a larger number of clinical investigations related to patients in both physiological and pathological situations. Therefore, the aim of this study was to evaluate the effect of Ang-(1-7) administration on hemodynamic parameters such systolic and diastolic blood pressure (SBP and DBP) and heart rate (HR) in healthy subjects.Materials and MethodsEight normotensive healthy subjects (4 men), mean age of 35 years, BP: 110/63 mmHg and HR: 66 bpm, underwent over two distinct interventions: Ang-(1-7) and saline (placebo) infusion protocol through a continuous infusion pump on brachial vein (dose of 1 µg/Kg during 5 minutes), respecting at least seven days interval between infusions. The order of both interventions was randomly set. The assessment of the effects on SBP, DBP and HR was performed through a non-invasive and continuous blood pressure measuring instrument (Finapres Medical System®- Finometer) for 2 hours followed by 24 hours Ambulatory Blood Pressure Monitoring (24h-ABPM) after each of the following situations: (B) Baseline, (P) Placebo and (A) Ang-(1-7). The outcomes BP and HR are reported as average of each recorded time. Statistical analysis was performed using two-way ANOVA for repeat measure following Newman-Keuls posthoc test. Significance differences were defined at P≤0.05.Results and ConclusionsSBP evaluated by 24-ABPM was significantly lower in Ang-(1-7) administration when compared with Baseline and Placebo groups. Thus, in comparison to Baseline values, the results after administration were: 5 hours ((A) 108±8,7mmHg vs (B) 117±9,2mmHg, P=0,002) and 6 hours ((A) 109±4,7mmHg vs (B) 118±8,5mmHg, P=0,018) and in comparison to Placebo values the results were: 5 hours ((A) 108±8,7mmHg vs (P) 119±10,6mmHg, P=0,002), 6 hours ((A) 109±4,7mmHg vs (P) 116±10,1mmHg, P=0,021) and 7 hours ((A) 110±10,4mmHg vs (P) 118±11mmHg, P=0,045) after administration. The DBP was also significantly lower in Ang-(1-7) administration when compared with Placebo group and the results were: 2 hours ((A) 66±5,5mmHg vs (P) 70±4,6, P=0,029), 5 hours ((A) 67±4,8mmHg vs (P) 74±6,6, P=0,007) and 6 hours ((A) 68±3,2mmHg vs (P) 72±3,8, P=0,041) after administration. No significant different results were observed to HR and to the others hemodynamics parameters during the 24-ABPM. In conclusion, these findings suggest a long lasting slightly hypotensive effect of Ang-(1-7) administration in healthy humans.

Número do Trabalho – ORAL 11

SYMPATHETIC OVERACTIVITY IN HYPERTENSIVE PATIENTS WITH IMPAIRED CARDIAC FUNCTION

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Background: The presence of asymptomatic left ventricular diastolic dysfunction (LVDD) in hypertensive patients can be associated with the development of cardiac events. The increase in the sympathetic activity is considered one of the mechanisms that predisposes to this outcome. The aim of this study was to investigate sympathetic activity in hypertensive patients under therapy, divided in two groups, with and without left ventricular functions alterations. Method: After analyzing left ventricular function by echoDopplercardiography exam, 45 hypertensive patients were allocated into 2 groups: with normal cardiac function (H, n=15) and with LVDD (HD, n=30). In both groups muscle nerve sympathetic activity (MNSA by microneuragraphy), blood pressure (by FINOMETER® recording) and systolic blood pressure variability (SBPV) were evaluated in supine rest position. Statistics: Student's t and Fisher's Exact tests were used. The results were expressed as mean ± standard deviation, and values of $p < 0.05$ were considered significant. Results: Blood pressure values and use of antihypertensive drugs were similar among hypertensive groups. The LF component of SBPV was higher in HD when compared with H group (42.6 ± 22.4 and 28.3 ±11.1mmHg2). HD group had higher MSNA (32 ± 4 burst/min) when compared to H group (26 ± 5 bursts/min). Conclusions: 1- Treated hypertensive patients exhibiting LVDD showed increased sympathetic activity and sympathetic modulation of SBPV. 2- This increase was demonstrated by direct and indirect methods of evaluation of autonomic nervous system. 3- The clinical implication of this finding should be further evaluated, considering the worse prognosis already established when LVDD is present.

Número do Trabalho – ORAL 12

EFEITOS DA RESTRIÇÃO ENERGÉTICA SOBRE A APNEIA DO SONO, ATIVIDADE SIMPÁTICA, ESTRESSE OXIDATIVO, BIOMARCADORES INFLAMATÓRIOS, PRESSÃO ARTERIAL E FUNÇÃO ENDOTELIAL EM PACIENTES OBESOS COM APNEIA OBSTRUTIVA DO SONO

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Introdução: A intervenção nutricional para perda ponderal é uma das opções terapêuticas para a apneia obstrutiva do sono (AOS) em pacientes com excesso de peso. No entanto os efeitos da restrição energética moderada, recomendada pelas diretrizes atuais para o tratamento da obesidade, sobre a gravidade da AOS ainda não são conhecidos. Objetivos: Avaliar em indivíduos obesos com AOS os efeitos da restrição energética moderada sobre a adiposidade corporal; gravidade da AOS; pressão arterial (PA); atividade simpática; estresse oxidativo; biomarcadores inflamatórios; perfil metabólico; e função endotelial. Casuística e Métodos: Ensaio clínico randomizado, com duração de 16 semanas, envolvendo 21 indivíduos obesos grau I ou II, apresentando idade de 20-55 anos e IAH>5 eventos/h. Os participantes foram randomizados em 2 grupos: 11 no grupo restrição energética (GRE) e 10 no grupo controle (GC). O GRE foi orientado a realizar restrição energética (-800Kcal/dia) e o GC não modificou sua ingestão alimentar. No início e ao final do estudo, os participantes foram submetidos à avaliação do (a): AOS com o equipamento Watch-PAT 200® incluindo os seguintes parâmetros de gravidade da AOS: IAH, saturação mínima de O2 e número de dessaturações de O2>4%; adiposidade corporal; PA; atividade do sistema nervoso simpático (catecolaminas plasmáticas); biomarcadores inflamatórios (proteína C reativa e adiponectina); estresse oxidativo (malondialdeído); metabolismo glicídico (glicose, insulina e HOMA-IR) e lipídico; e função endotelial (índice de hiperemia reativa avaliado com Endo-PAT 2000® e moléculas de adesão). Resultados: O GRE, em comparação com o GC, apresentou redução significativamente maior no peso corporal (-5,57±1,81 vs. 0,43±1,21kg, p<0,001) e nos demais parâmetros de adiposidade corporal; no IAH (-7,22±2,79 vs. 0,13±1,88 eventos/h, p=0,04); no número de dessaturações de O2>4% (-33,70±15,57 vs. 1,80±7,85, p=0,04); nas concentrações plasmáticas de adrenalina (-12,70±3,00 vs. -1,30±3,90pg/mL, p=0,04); além de aumento significativamente maior na saturação mínima de O2 (4,60±1,55 vs. -0,60±1,42%,p=0,03). O GRE, em comparação com o GC, apresentou maior redução, porém sem alcançar significância estatística, na PA sistólica (-4,23±1,95 vs. 2,34±1,39mmHg, p=0,05), na insulina (-5,11±1,93 vs. -0,65±1,28□U/mL, p=0,07) e no HOMA-IR (-1,15±0,49 vs. -0,08±0,33, p=0,09). As demais variáveis não se modificaram de forma significativa após a restrição energética, em comparação ao GC. Durante o período do estudo, as modificações na adiposidade corporal apresentaram correlação significativa com as variações nos parâmetros de gravidade da AOS; na PA; no HOMA-IR; e nas concentrações de insulina, adiponectina e norepinefrina. Conclusões: Este estudo sugere que a restrição energética moderada em indivíduos com AOS é capaz de reduzir a adiposidade corporal, parâmetros de avaliação da gravidade da AOS e a atividade do sistema nervoso simpático.

Número do Trabalho – ORAL 13

PROGRAMA DE GESTÃO DE DOENÇAS CRÔNICAS AUMENTA ADESÃO AO TRATAMENTO: ESTUDO LONGITUDINAL EM UM GRUPO DE HIPERTENSOS

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Introdução A hipertensão arterial tem alta prevalência, porém o controle dos níveis pressóricos é pouco satisfatório, provavelmente devido à baixa adesão ao tratamento. Assim, faz-se necessário buscar estratégias para aumentar o controle e adesão ao tratamento e modificar o estilo de vida. Objetivos: Avaliar um grupo de hipertensos monitorados por enfermeiros dentro de um programa de gestão de doenças crônicas e identificar variáveis relacionadas.Casuística e Métodos Realizou-se estudo longitudinal retrospectivo com 283 hipertensos (62,5% mulheres, 73,4 (10,9) anos), em uma instituição particular na cidade de São Paulo, que praticava a gestão de doenças crônicas, por meio de contatos telefônicos e visitas domiciliares. Todas as atividades do programa foram realizadas por enfermeiros. Os hipertensos foram orientados por um período de 17 meses, com contatos telefônicos mensalmente e visitas domiciliares. A adesão ao tratamento medicamentoso foi avaliada pelo teste de Morisky Green. Valores de p< 0,05 foram considerado significantes.Resultados Comparando-se os momentos de ingresso no programa, com o final do seguimento dos hipertensos, houve mudança significativa no comportamento das seguintes variáveis (p< 0,05): Etilismo (10,2% vs 3,2%); Sedentarismo (96,8% vs 71,7%); Adesão ao tratamento medicamentoso (25,1% vs 85,5%); P Sistólica (128,8 (11,4) vs 125,1 (11,6) mmHg);e P Diastólica (78,9 (7,8) vs 77,2 (8,0) mmHg). Verificou-se que 76,3% estavam com a pressão controlada e o controle foi menor entre os tabagistas. Foram mais aderentes ao tratamento (p< 0,05) os hipertensos com insuficiência renal crônica e aqueles sob tratamento com Inibidores da Enzima Conversora de Angiotensina e os que usavam Bloqueadores dos Receptores de Angiotensina foram menos aderentes. Conclusão Os hipertensos monitorados por enfermeiros, em um programa de gerenciamento de doenças crônicas, apresentaram mudanças significativas na pressão arterial, nos hábitos de vida e adesão ao tratamento medicamentoso. Considera-se, que essas estratégias possam aumentar a adesão de hipertensos ao tratamento e dessa forma contribuir para o controle dos níveis tensionais, minimizando o perfil de morbimortalidade dessas pessoas.

Número do Trabalho – ORAL 14

Avaliação do controle autonômico cardíaco de crianças e adolescentes: implicações do peso ao nascer

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INTRODUÇÃO: Perturbações no padrão de crescimento fetal estão associadas ao desenvolvimento de enfermidades cardiovasculares na vida adulta. É evidenciado que alterações no sistema nervoso autônomo podem ser um dos mecanismos responsáveis pelo aumento no risco de desenvolver eventos cardiovasculares. Contudo, pouco se sabe sobre a influência do crescimento fetal no controle autonômico em crianças e adolescente. OBJETIVO: Avaliar a relação existente entre o peso ao nascer,e modulação autonômica cardíaca (MAC) em crianças e adolescentes. CASUÍSTICA E MÉTODOS: Foram avaliadas 71 crianças e adolescentes que foram divididos 4 grupos de acordo com o quartil de peso ao nascer (Q1< 2677g, Q2 2677g- 3100g, Q3 3100g - 3400g e Q4> 3400g) e pareados por nível de atividade física e antropometria. A MAC, foi avaliada por meio da variabilidade da frequência cardíaca (VFC) a partir dos índices do domínio do tempo, MNN, SDNN, RMSSD e pNN50, e domínio de baixa frequência (LF), alta frequência (HF) e razão baixa/alta (LF/HF). A FC foi medida continuamente pelo cardiofrequencimetro Polar RS800CX® durante 10 minutos em repouso na posição supina, com respiração espontânea. RESULTADOS: Em relação aos índices no domínio do tempo, observamos que crianças pertencentes aos quartis Q1 e Q4 apresentaram menores índices de pNN50 em relação ao terceiro quartil (P<0,01). Os índices HF e ln HF foram significativamente menores nos quartis Q1 e Q4 em relação ao terceiro quartil (HF: P<0,01; ln HF: P=0,01; respectivamente). Conclusão: Nossos resultados evidenciam que crianças tanto com baixo (quartil Q1) quanto com elevado (quartil Q4) peso ao nascer apresentam prejuízo na modulação autonômica cardíaca vagal, a qual pode contribuir precocemente para o maior risco de eventos cardiovasculares nesses indivíduos.

Número do Trabalho – ORAL 15

Respostas do controle autonômico cardiovascular ao treinamento muscular inspiratório e ao treinamento aeróbico em pacientes com hipertensão primária

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A hipertensão arterial sistêmica (HAS) é caracterizada por desequilíbrio dos componentes de controle nervoso autonômico cardiovascular, especialmente por hiperatividade simpática e redução de atividade vagal. O treinamento aeróbio (TA) é recomendado no tratamento desta população e, a prática de exercícios respiratórios demonstra efeitos benéficos na HAS. Neste trabalho, buscamos observar os efeitos das duas modalidades em uma população de pacientes portadores de hipertensão controlada. Desta forma, 13 pacientes (idade: 55±4 anos) foram incluídos e divididos em três grupos: TMI (n=4, 7dias/sem, 30min/dia, carga=30%PImax), TA (n=4, 2dias/sem, 1h/dia, carga=70ümax) e Controle (n=5). Os protocolos de treinamento foram realizados por 12 semanas. Sinais de pressão arterial (PA) e frequência cardíaca (FC) foram gravados antes e depois do treinamento através de sistemas de telemetria de pulso (Finometer®PRO) e ECG (3 derivações, PowerLab®). A avaliação dos componentes de controle nervoso autonômico cardiovascular foi realizada no domínio do tempo e da frequência e a função do barorreflexo arterial através do método da sequência. A análise dos componentes de variabilidade da pressão arterial antes e após o período de treino, demonstrou que o TMI reduziu a Variabilidade da PA (VPA) no domínio do tempo (SD: TMI=5.52(±3.04)vs11.93(±7.27)mmHg, TA=8.23(±1.8)vs5.16(±1.8) mmHg, além de reduzir o componente simpático de controle da PA (LFabs: TMI=4.4(2.55)vs10.09(±9.64) mmHg²; TA=7.15(±4.13)vs6.27(±2.03)mmHg²). Em relação aos componentes da VFC, observamos aumento da modulação vagal no grupo TMI (HFun: TMI=71.75(13.9)vs65.26(±36.2), TA=55.75(10.07) vs60(15.9)) e esta melhora repercutiu em benefícios sobre o balanço simpatovagal deste grupo (LH/HF: TMI=0.51(±0.2)vs2.22(±0.4), TA=1.2(±0.5)vs0.96(±0.5)). Adicionalmente, o TMI foi capaz de melhorar a sensibilidade barorreflexa de resposta taquicárdica e bradicárdica respectivamente (BRR Down Gain (mean): TMI=26.51(±1.7)vs15.57(±6.7), TA=13.94(±5.5)vs17.92(±1.6); BRR UpGain (mean): TMI=17.16(±1.2)vs16.28(±1.1), TA=12.39(±5)vs12.69(±3.3)). Nossos resultados demonstram, pela primeira vez, que apesar de o treinamento aeróbio apresentar benefícios sobre os componentes de controle e os níveis de pressão arterial, a prática de exercícios respiratórios e o treinamento específico da musculatura ventilatória é capaz de melhorar de maneira importante a interação cardiopulmonar na hipertensão, com repercussões ainda mais evidentes sobre o controle nervoso.

Número do Trabalho – ORAL 16

A MEDIDA CASUAL DA PRESSÃO ARTERIAL EM ADOLESCENTES É CONFIÁVEL AO DIAGNÓSTICO? COMPARAÇÃO E CONCORDÂNCIA COM MEDIDA AMBULATORIAL E RESIDENCIAL

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INTRODUÇÃO: A pressão arterial (PA) apresenta variações em razão de estímulos fisiológicos e ambientais, sendo necessários métodos de múltiplas medidas, além da medida casual, como a monitorização ambulatorial da PA (MAPA), padrão-ouro, mas de custo elevado e como alternativa, a medida residencial da PA (MRPA), menos onerosa, porém, menos estudada em adolescentes. OBJETIVOS: comparar os valores de PA de adolescentes obtidos pela MRPA, MAPA e medida casual e verificar a concordância entre os métodos. CASUÍSTICA E MÉTODOS: estudo transversal, avaliados escolares de 12 a 17 anos de Goiânia, Goiás, selecionados a partir da pressão arterial alterada (sistólica e/ou diastólica com percentil>90 para a respectiva idade, sexo e estatura de acordo com a 4th Task Force, 2004) em uma amostra de 1025 adolescentes, representativa dos adolescentes da cidade. Incluídos também adolescentes normotensos, os quais compuseram o grupo controle da segunda fase do projeto original. Realizada a medida casual e a MRPA com aparelhos semiautomáticos, Ohmron, HEM-705CP e protocolo de 06 dias, sendo 02 medidas pela manhã e 02 no fim do dia, e consideradas para análise ?12 medidas no total. A MAPA foi realizada com o equipamento Spacelabs, 90207 e no presente estudo foi considerada para análise a medida diurna. Dados digitados em duplicata no Epi-Info (versão 3.5.3), feita a validação dos dados neste mesmo software e utilizado o SPSS (20.0) para a análise estatística. Testes utilizados: Kolmogorov Smirnov (análise da distribuição dos dados); t-student dependente e Wilcoxon (comparação das médias dos valores pressóricos), e feita a análise de Bland Altman para a avaliação da concordância entre os métodos. Considerado significante p< 0,05. Projeto aprovado pelo Comitê de ética em Pesquisa Humana e Animal do Hospital das Clínicas da UFG e financiado pelo Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ). RESULTADOS: total de 162 adolescentes avaliados (131 com PA alterada e 31 normotensos), idade média de 14,9 ±1,6 anos, 61,2 % do sexo masculino, IMC médio de 23,6±7,1kg/m2. Valores da medida casual (PAS:127,3±13,8; PAD:74,4±9,5 mmHg); MRPA (PAS:120,3±12,6; PAD:69,4±7,7mmHg) e MAPA-diurna (PAS:121,5±9,8; PAD: 70,2±6,6mmHg). Os gráficos de Bland Altman mostraram boa concordância entre MRPA e MAPA-diurna. A medida casual não teve concordância com a MAPA-diurna. CONCLUSÕES: A medida casual deve ser usada como método de triagem, em adolescentes com PA acima dos valores de normalidade, e os valores devem ser confirmados pela MRPA, ou pela MAPA, sendo a última o padrão-ouro.

Número do Trabalho – ORAL 17

INFLUÊNCIA DE VARIANTES GENÉTICAS PARA ENOS EM PACIENTES COM HIPERTENSÃO ARTERIAL SISTÊMICA -

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Introdução - Óxido nítrico sintase endotelial (*eNOS*), representada pelo polimorfismo *eNOS*-G894T, pode interferir na disponibilidade de óxido nítrico e, consequentemente, na pressão arterial. **Objetivo -** Avaliar a influência do polimorfismo *eNOS*-G894T na hipertensão arterial (HA) e pré-hipertensão (PH) e no perfil bioquímico em casuística brasileira. **Métodos -** Foram estudados 224 indivíduos: HA=100 com hipertensão (≥140/≥90mmHg); PH=70 com pré-hipertensão (120-139/80-89mmHg); 54 normotensos (NT). Variantes de *eNOS* foram analisadas por PCR/RFLP. O perfil bioquímico consistiu em colesterol total (CT) e frações (LDLc, HDLc, VLDLc), triglicérides (TG) e glicemia. Admitiu-se nível de significância para P<0,05. **Resultados -** O genótipo TT prevaleceu em HA (41%), versus PH (9%; P<0,0001) e NT (22%; P=0,030), e o genótipo GG em PH (38%) e NT (32%), versus HA (11%; P<0,0001; P=0,003, respectivamente). A presença do alelo T associou-se a valores aumentados de pressão arterial diastólica (PAD) em HA (84,7±12,0 mmHg) e PH (83,1±3,3 mmHg), comparado a NT (74±6 mmHg; P<0,01, para ambos). Notaram-se valores nos limites de referência para o perfil bioquímico em todos os grupos, exceto para TG e glicemia em HA versus PH (P=0,002; P=0,0008, respectivamente) e NT (P=0,012; P=0,025, respectivamente). Acréscimo significante de CT foi observado em HA e PH, comparado a NT (P=0,017; P=0,001, respectivamente), enquanto PH mostrou acréscimo nos níveis de LDLc, comparado a HA (P=0,004) e NT (P=0,001). Valores aumentados de TG foram observados principalmente na presença do alelo T em HA, versus PH (P=0,015) e NT (P=0,003). **Conclusão -** O polimorfismo *eNOS*-G894T parece influenciar na pressão arterial, destacando-se o acréscimo nos valores de PAD, já na pré-hipertensão, na presença do alelo T, que provavelmente potencializa também distúrbios metabólicos, tanto em hipertensos como pré-hipertensos. Tornam-se necessários estudos em casuísticas mais numerosas para confirmar essa associação, contribuindo na identificação de grupos de risco e, consequentemente, prevenção e controle da doença e suas consequências.

Número do Trabalho – ORAL 18

REINNERVATION OF RENAL AFFERENT AND EFFERENT NERVES AT 5.5 AND 11 MONTHS AFTER CATHETER-BASED RENAL DENERVATION IN SHEEP

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Previous studies indicate that catheter-based renal denervation (RDN) reduces blood pressure and renal noradrenaline spillover in human resistant hypertension. The effects of this procedure on afferent sensory and efferent sympathetic renal nerves, and the subsequent degree of reinnervation, have not been investigated. We therefore examined the level of functional and anatomical reinnervation immediately and at 5.5 and 11 months after RDN using the Symplicity Flex catheter. In normotensive anesthetized sheep (n=6), electrical stimulation of the renal nerves increased arterial pressure (afferent response) and reduced renal blood flow (efferent response). In a separate group (n=5), renal sympathetic nerve activity (RSNA) was abolished after RDN, as were the responses to electrical stimulation. At eleven months post-RDN (n=5), RSNA and the responses to electrical stimulation had returned to normal levels. Immunohistochemical staining for renal sympathetic efferent nerves (tyrosine hydroxylase) and renal sensory afferent nerves (calcitonin gene related peptide), as well as renal noradrenaline levels, were normal 11 months post-denervation. Findings at 5.5 months post-denervation (n=5) were similar, with a tendency for incomplete reinnervation.Catheter-based RDN effectively ablated the renal afferent and efferent nerves in normotensive sheep. By 11 months after denervation RSNA had returned and the functional afferent and efferent responses to electrical stimulation were normal. Reinnervation at 11 months post-denervation was supported by the normal anatomical distribution of markers of afferent and efferent renal nerves. In view of this evidence the mechanisms underlying the prolonged hypotensive effect of catheter-based RDN in human resistant hypertension need to be reassessed.

Número do Trabalho – ORAL 19

CHRONIC HYPERLEPTINEMIA RESULTS IN THE DEVELOPMENT OF HYPERTENSION IN PREGNANT RATS

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Introduction: Although the etiology of preeclampsia (PE) remains unclear, impaired cytotrophoblast invasion followed by placental ischemia is thought to cause the placental release of anti-angiogenic factors such as soluble fms-like tyrosine kinase (sFlt)-1 and inflammatory cytokines such as tumor necrosis factor (TNF)-alpha into the maternal circulation that ultimately leads to hypertension and proteinuria. Obesity is a major risk factor for PE; however, the mechanisms whereby obesity and metabolic factors such as leptin increase the risk for developing PE are unclear. While correlative data in humans have shown that hyperleptinemia is associated with the development of hypertension in PE, the long-term effect of hyperleptinemia on blood pressure during pregnancy is unknown.Objective: This study aimed to determine the effects of chronic elevations in circulating leptin on blood pressure and placental factors in pregnant rats.Methods: On gestational day (GD) 14, Sprague Dawley rats were assigned to receive leptin where an osmotic minipump with leptin (0.5 µg/Kg/min) was implanted intraperitoneally (pregnant+leptin group) or to the non-infused group (normal pregnant group). On GD 19, mean arterial pressure (MAP) was assessed via carotid catheter in conscious rats. Rats were then euthanized, and blood, placentas, and fetuses were collected. Leptin, insulin, TNF-alpha, and sFlt-1 were measured by ELISA. Glucose, total cholesterol, triglycerides, and free fatty-acids were assessed by colorimetric assays.Results: Serum leptin concentration was elevated in pregnant+leptin compared with normal pregnant rats (18.0 ± 2.8 vs. 0.8 ± 0.1 ng/mL, $P<0.05$), which was associated with an increased in MAP (121.3 ± 8.1 vs. 102.4 ± 2.4 mmHg, $P<0.05$). Food intake (11.3 ± 1.2 vs. 25.2 ± 1.1 g/day, $P<0.05$) and body weight (284.1 ± 3.9 vs. 310.3 ± 6.6 g, $P<0.05$) were reduced following leptin infusion by the end of pregnancy compared to the normal pregnant group. Circulating insulin and glucose levels were similar, whereas total cholesterol (111.8 ± 27.7 vs. 250.5 ± 21.9 mg/dL, $P<0.05$), triglyceride (91.1 ± 33.7 vs. 494.5 ± 92.1 mg/dL, $P<0.05$), and free fatty acid (33.7 ± 11.8 vs. 105.1 ± 27.9 mg/dL, $P<0.05$) concentrations were decreased in pregnant+leptin rats compared with normal pregnant rats. Although litter size was similar, placentas (0.5 ± 0.0 vs. 0.6 ± 0.0 g, $P<0.05$) and fetuses (2.1 ± 0.1 vs. 2.3 ± 0.1 g, $P<0.05$) of pregnant+leptin rats were lighter than those of normal pregnant rats. While placental expression of sFlt-1 was similar, TNF-alpha was significantly greater in the pregnant+leptin group versus normal pregnant group (1.6 ± 0.1 vs. 1.1 ± 0.1 pg/mg, $P<0.05$).Conclusion: In summary, leptin increases blood pressure and placental TNF-alpha levels in pregnant rats despite its effect of reducing food intake, body weight, and circulating lipids, and represents a mechanism whereby obesity can promote the development of hypertension during pregnancy.

Número do Trabalho – ORAL 20

Sodium overload in the pregnant rats induces vascular dysfunction in adult offspring

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High sodium intake is associated with a greater risk of hypertension and other cardiovascular disease in susceptible people. In this study mechanisms underlying perinatal sodium overload-programmed vascular dysfunction (contractile and relaxation responses) were investigated. Dams were fed a diet with normal sodium content (NS, 1.3% NaCl), moderate (MS, 4% NaCl) or high (HS, 8% NaCl) during pregnancy and lactation periods. Blood pressure, acetylcholine-induced relaxation, phenylephrine- and angiotensin I and II-induced contraction, lipid peroxidation, reduced glutathione levels and angiotensin converting enzyme (ACE) activity were performed in aorta from 6-month-old NS, MS and HS offspring. Blood pressure was similar in all groups. Relaxation to acetylcholine was impaired, while the phenylephrine-induced contraction was increased, in HS aorta compared to NS. Aortic relaxation and contraction were not altered in MS group. Pre-treatment with Tempol, Apocinin or Indomethacin restored acetylcholine and phenylephrine responses in aorta from HS group. Contraction to angiotensin I was increased, while response to angiotensin II remained unmodified in HS aorta compared to NS. Aortic TBARS malondialdehyde and reduced glutathione levels were similar in HS compared to NS. Aortic ACE activity was increased in the offspring HS group compared to NS. All together, these results demonstrate that maternal sodium overload programmed vascular dysfunction in the offspring. These vascular changes seem to be produced by a NADPH oxidase-dependent oxidative stress and by an enhanced formation of vasoconstrictor prostanoids. These mechanisms are possibly stimulated by angiotensin II in the aortic wall, whose production is increased in the HS group.

Número do Trabalho – ORAL 21

Reduced uterine perfusion pressure (RUPP) elicits increased sFlt-1 levels not only in the placenta but also adipose tissue

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Preeclampsia is a pregnancy-specific disorder characterized by new-onset hypertension. Placental ischemia is causative in this disorder with the release of antiangiogenic factors such as sFlt-1 into the maternal circulation promoting endothelial dysfunction and hypertension. Obesity is a major risk factor for preeclampsia, but the mechanisms are far less understood. Recent evidence suggests that adipose tissue is a source of sFlt-1. This study tested the hypothesis that placental ischemia produced by RUPP elicits an increase of sFlt-1 levels in both placental and adipose tissue from normal pregnant rats. Timed-pregnant Wistar-hannover rats (20 wks old) on NIH31 standard chow were subjected to RUPP (N=15) on gestational day (GD)14 or remained normal pregnant (NP, N=14). Rats were implanted with carotid catheters on GD18 and fasted overnight. On GD19, mean arterial blood pressure (MAP) was assessed in conscious, restrained rats. Statistical significance was $P<0.05$. MAP was greater in RUPP (114±2 v 101±1mmHg) with reduced fetal weight (1.73±0.02 v 1.88±0.01g) but similar placental weight (RUPP: 0.45±0.03 v NP: 0.47±0.03g). Although RUPP reduced body weight (297±7 v 343±6g), visceral adipose tissue weight was not altered (RUPP: 11.5±1 v NP: 13.2±1g). Total cholesterol was increased (RUPP: 223±35 v NP: 156±6mg/dL) but there was no difference in free fatty acids (RUPP: 8±2 v NP: 8±2mg/L) but reduced triglyceride levels (RUPP: 265±38 v RUPP: 659±100mg/dL). RUPP reduced leptin (3.2±0.2 v 4.2±0.4ng/mL) and adiponectin (2.8±0.2 v 3.3±0.2ug/mL) with increased fasting glucose levels (191±6 v 163±8mg/dL). Very interestingly, RUPP increased sFlt-1 levels in placenta (4702±375 v 3903±309pg/g tissue) and retroperitoneal adipose tissue (179±28 v 76±22pg/g tissue). These data indicate that RUPP-induced hypertension in normal pregnant rats promotes metabolic disturbances along with increases in sFlt-1 not only the placenta but in the adipose tissue. In conclusion, we propose that placental ischemia-induced hypertension is exaggerated in states linked to increased accumulation of adipose tissue, such as in diet-induced or genetic obesity, due to amplified metabolic derangements and increases in sFlt-1 levels from both placental and adipose sources. Funding: HL105324, HL51971.

Número do Trabalho – Oral 22

BIOLOGICAL AND INFLAMMATORY CHARACTERISTICS OF HEART TISSUE IN POSTMENOPAUSAL AND OBESE RATS

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Introduction/objectives: B-type natriuretic peptide (BNP) acts on the heart promoting antiproliferative and antifibrinolytics effects. Estrogen has been associated with preventing the development of cardiac hypertrophy, once pre-menopausal women are much less likely to have cardiovascular disease. Despite well-established models of myocardial hypertrophy, there has been a lack of suitable animal models to study postmenopausal hypertrophic cardiac remodeling. We present some biological and inflammatory characteristics of postmenopausal hypertension and hypertrophic remodeling in high fat diet-fed ovariectomized rats. We also analyzed the BNP participation in the myocardial hypertrophy in these animals.
Methods: Twenty-four 10-wk-old female Wistar rats (210 g) intact (sham-operated) or ovariectomized were housed in 12-h light, 12-h dark lighting. They were divided into four groups (n=6) according to diet: diet containing 54.4% of total calories from fat (high fat diet) or standard diet. During 24 weeks we measured body weight and blood pressure. At the end of the experiment the rats were decapitated and hearts were removed for gene expression determination, hydroxyproline determination and immunohistochemistry. The trunk blood was removed for measured plasma estradiol, tumoral growth factor (TGF-β) and BNP levels.
Results: The high-fat diet associated with ovariectomy was able to produce a greater weight gain (510±20 vs. 270±19g, $p<0.05$, n=6 per group), higher systolic (130±1 vs. 98±0.5mmHg, $p<0.05$, n=6 per group) and mean blood pressure than control group (111±1 vs. 92±2mmHg, $p<0.05$, n=6 per group) as well as an increase in ventricle weight and hydroxyproline ventricular concentration.This group also showed a ventricular myocytes hypertrophy (20.7±0.4 vs. 15.7±0.3μm, $p<0.05$, n=6 per group), an increased synthesis and release of BNP (about 105% increase, $p<0.05$, n=6 per group) and a decrease in A-receptor gene expression in the ventricle (about 67% decrease, $p<0.05$, n=6 per group) than control group. The ovariectomized group and high fat diet-fed group also presented an increase alpha smooth muscle actin (α-SMA) and showed presence of miofibroblasts and the beginning of heart remodeling.The high-fat diet associated with ovariectomy was the only group presenting increase of TGF-β (45.3±1.6 vs. 22±0.9 ng/mL)and this can be the stimulus to initiate the remodeling heart.A strong positive correlation was observed between plasma BNP levels and both cardiomyocyte diameter ($r=0.914$, $p=0.004$) and body weight ($r=0.89$, $p=0.007$) in high fat diet-fed rats. The cardiac ER-β gene expression was reduced in ovariectomized groups compared with the control group.
Conclusions: This study establishes a new postmenopausal model of hypertrophy and obesity and showed the role of BNP as a marker of hypertrophy in this model. The key molecular event in the hypertrophic response observed may be the reduced expression of NPR-A and ER-β and increased of TGF-β.

Número do Trabalho – ORAL 23

PERIVASCULAR ADIPOSE TISSUE REDUCES ACETYLCHOLINE RELAXATION IN AORTA AND FEMORAL ARTERY FROM OBESE MICE

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Introduction: Obesity causes serious metabolic derangements and is closely related to high risk of cardiovascular disease. The role of perivascular adipose tissue in vascular function has recently been recognized. The aim of this study was to investigate the role of perivascular adipose tissue in macro- and micro-vascular responsiveness in obese mice. Methods: Male mice (C57BL6/JUnib; body weight: 20.5±0.5) were divided into: control (CT, n=5) and obese (OB, n=5). During 16 weeks the CT mice were fed with standard chow and to induce obesity the OB mice were fed with high fat diet (37% carbohydrate, 20% protein, 38% fat and 5% vitamin/mineral). Concentration-response curves to acetylcholine (ACh) were obtained in aorta and femoral artery s in the absence (PVAT-) or presence (PVAT+) of perivascular adipose tissue. The potency (pEC50) and maximal responses (EMAX) were calculated. The glycaemia and serum total cholesterol were measured. Results: As expected, in OB group the body weight (46±0.9 g), epididymal fat pad (1.4±0.07 g), glycaemia (157±9 mg/dl) and total cholesterol (226±45 mg dl) were increased when compared to CT (28±1 g, 0.3±0.03 g, 98±0.5 mg/dl and 80±4 mg/dl; respectively). The amount of perivascular adipose tissue (mg/mm) in rings of aorta and femoral artery were markedly increased in OB (aorta: 3.55±0.6; femoral: 2.83±0.64) when compared to CT (aorta: 0.76±0.41; femoral: 0.14±0.02). The PVAT+ did not modify the relaxation response to ACh in CT group for both preparations. However in OB mice the rings PVAT+ showed a reduction in pEC50 (aorta: PVAT+:6.09+0.2 versus PVAT-:6.63+0.2, approximately 3.5 fold; femoral PVAT+:6.58+0.2 versus PVAT-:7.24±0.1; approximately 4.6 fold) and in EMAX to ACh (aorta: PVAT+:57+3% versus PVAT-:78+3%; femoral PVAT+:83+5% versus PVAT-:96±1%). Conclusion: The presence of perivascular adipose tissue causes endothelial dysfunction in aorta and femoral artery from obese mice.

Número do Trabalho – ORAL 24

PAPEL DO TREINAMENTO FÍSICO NA PREVENÇÃO DE DISFUNÇÕES CARDIOVASCULARES E DE ESTRESSE OXIDATIVO INDUZIDAS PELA SOBRECARGA DE FRUTOSE DESDE O DESMAME EM RATOS

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O aumento do consumo de produtos industrializados contendo grande quantidade de frutose e sua associação com maiores índices de sedentarismo têm aumentado a preocupação de órgãos da saúde em relação ao aumento da prevalência de doenças crônicas. A associação de vários fatores de risco no período de desenvolvimento da criança pode ter uma influência no desenvolvimento de síndrome metabólica na vida adulta. Neste sentido, a prática de atividades físicas na infância pode ser uma estratégia preventiva para o manejo desse risco e para melhorar a qualidade de vida. O objetivo deste estudo foi avaliar o papel do treinamento físico em parâmetros hemodinâmicos e de estresse oxidativo cardíaco em ratos tratados com frutose no período de desenvolvimento. Foram utilizados 32 ratos machos Wistar divididos em 4 grupos (n=8 cada grupo), sendo: água sedentário (AS), água treinado (AT), frutose sedentário (FS) e frutose treinado (FT). O tratamento com frutose foi iniciado após o desmame. O grupo treinado foi submetido a um programa de treinamento físico em esteira ergométrica (1 hora/dia, 5 dias/semana, 8 semanas, 40-60% da velocidade máxima no teste de esforço). Ao final do protocolo foram analisados: glicemia, teste de tolerância a glicose, registro direto da pressão arterial e da frequência cardíaca, sensibilidade barorreflexa e estresse oxidativo no tecido cardíaco (VE) e sistêmico (S) com avaliação do razão GSH/GSSG, capacidade antioxidante total (TRAP), dano à proteínas (CARB) e lipoperoxidação. Testes estatísticos foram devidamente aplicados para comparação dos dados. Os grupos AT e FT apresentaram maior capacidade física, analisado por meio do teste de esforço (AS: 1,5 ± 0,05; FS: 1,9 ± 0,07 vs. AT:2,15 ±0,05; FT: 2,2 ± 0,07 km/h). A pressão arterial média do grupo FS foi maior que nos outros grupos (FS: 122 ± 3 vs. FT: 117 ± 3; AS:112 ± 1; AT:115 ± 2 mmHg), contudo o AT e FT apresentaram bradicardia de repouso (AT: 339 ± 6 e FT:340 ± 6 bpm) comparado com os grupos sedentários (AS: 366 ± 13 e FS: 378 ± 8 bpm). A resposta barorreflexa taquicárdica foi maior no grupo FT em comparação ao grupo AS (FT: 2,4 ± 0,1 vs. AS: 2 ± 0,15 bpm/mmHg). O perfil de estresse oxidativo apresentou mudanças desfavoráveis no grupo FS (CARB-S FS:3,30±0,09 vs. AS:1,45±0,08 nmol/mg protein; TRAP-VE FS:~2,5 vs. AS:~12,7 uM trolox), que foram atenuadas no grupo FT. Concluindo, nossos dados sugerem que a prática de exercício físico durante o desenvolvimento pode ser uma ferramenta não farmacológica para prevenção de disfunções cardiometabólicas induzidas pelo alto consumo de frutose na fase adulta.Apoio Financeiro: FAPESP (2012/01873-5).

Número do Trabalho – ORAL 25

The relationship between training status, blood pressure and uric acid in older-adults

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Background: Due to the high hypertension incidence and prevalence, especially in the elderly population, several studies have searched to understand the relationship between etiological factors and blood pressure control. In this sense it has been observed in the literature that the most of hypertensive population tend to present a status of hyperuricemia. These results suggest that there is a relationship between blood pressure values and uric acid concentrations. The purpose of this study was to investigate the relationship between hypertension and uric acid concentration pointing oxidative stress as the main factor of this relationship and, whether this relationship may be mediated by the functional fitness index, benefiting the blood pressure control. Method/Results: All participants (n= 123) performed the following tests: indirect maximal oxygen uptake (VO2max), AAHPERD Functional Fitness Battery Test to determine the general fitness functional index (GFFI), systolic and diastolic blood pressure (SBP and DBP), body mass index (BMI) and blood sample to evaluate the total-cholesterol (CHOL), LDL-cholesterol (LDL-c), HDL-cholesterol (HDL-c), triglycerides (TG), uric acid (UA), nitrite (NO2) and thiobarbituric acid reactive substances (T-BARS). All participants were allocated into three groups according the GFFI results: G1 (regular), G2 (good) and G3 (very good). All participants were allocated into two groups according the UA values: participants with normal UA values (2,0-5,0 mg/dl) and elevated UA values (>5,0 mg/dl). Baseline blood pressure was higher in G1 compared to G3 (SBP: 129.3±14 vs 114±12; DBP: 83.4±14 vs 74.2±8,9 mmHg; p<0.05) and the subjects who had higher values of UA also presented higher values of blood pressure (SBP: 128.8±10; DBP: 85.5±10 mmHg), compared with the subjects who had normal values of UA (SBP: 119.7±16.3; DBP: 72.1±12 mmHg). T-BARS and UA were not different between groups. Although UA was not different among GFFI groups, it presented a significant correlation between GFFI and VO2max (r = 0.8; p < 0,01). Nitrite concentration was elevated in G3 compared to G1 (140±29 μM vs 111± 29 μM respectively; p<0.0001). As far as the lipid profile, G3 presented better values when compared with G1 in CHOL (168.9 ± 31 vs 203.4 ± 36 mg/dL) and TG (94.2 ± 39 vs 157.7 ± 59 mg/dL). In the general, it can be observed that people with better training status have better profile in blood pressure, nitrite concentration, lipid profile and good correlation with UA concentration.Conclusion: These results suggested that the most subjects with higher blood pressure had elevated values of UA and lower values of nitrite, and the relationship between blood pressure and oxidative stress can be mediated by training status.

Número do Trabalho – ORAL 26

Melhora de parâmetros morfofuncionais e de estresse oxidativo cardíacos em ratas diabéticas ooforectomizadas submetidas a treinamento físico combinado.

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Introdução: A incidência de doenças cardiovasculares e de diabetes aumenta significativamente em mulheres após a menopausa. Dentre as complicações crônicas do diabetes destaca-se a cardiomiopatia, a qual aumenta muito o risco de mortalidade cardiovascular. Por outro lado, o treinamento físico aeróbio induz atenuação de disfunções cardiometabólicas que acometem mulheres menopausadas e/ou diabéticas. Entretanto, estudos envolvendo os efeitos cardíacos do treinamento físico aeróbio em associação com o resistido (combinado) são escassos e controversos.

Objetivo: Avaliar o efeito do treinamento físico combinado em parâmetros de morfometria, função cardíaca e estresse oxidativo em ratas ooforectomizadas diabéticas.

Métodos: Ratas Wistar (200-220g) foram divididas em 4 grupos: euglicêmico sedentário (ES), diabético (estreptozotocina, 50 mg/kg, iv) sedentário (DS) e diabético ooforectomizado (retirada bilateral dos ovários) (n=8) sedentário (DOS) ou submetido a treinamento físico combinado (DOTC). O treinamento físico foi realizado em esteira e escada adaptadas, 8 semanas, 5 x/semana, 1 hora/dia de forma alternada. As medidas ecocardiográficas foram realizadas ao final do protocolo de treinamento de 8 semanas e seguiram as recomendações do Comitê de Padronização do Modo M da Sociedade Americana de Ecocardiografia. O estresse oxidativo cardíaco foi avaliado por quimiluminescência iniciada por t-BOOH (QL) e pela dosagem de proteínas carboniladas.

Resultados: O peso corporal foi menor e a glicemia foi maior (ES: 102±4; DS: 442±15; DOS: 475±15; DOTC: 422±23mg/dl) nos grupos diabéticos em relação ao ES. Houve redução de massa do ventrículo esquerdo (MVE), da espessura relativa de parede (ERP) da velocidade de encurtamento circunferencial (VEC), bem como aumento da cavidade do VE na diástole e do tempo de relaxamento isovolumétrico nos animais diabéticos sedentários. O treinamento físico combinado atenuou tais disfunções morfométricas e funcionais. Houve aumento de estresse oxidativo, tanto pela QL (DS: 1107 ± 110; DOS: 2371 ± 330; DOTC: 777 ± 46 cps/mg proteína) quanto pelas carbonilas (ES: 3,00 ± 0,23; DS: 5,94 ± 1,59; DOS: 13,31 ± 3,27; DOTC: 9,63 ± 1,48 nmoles/mg proteína) no grupo DOS em relação ao DS, o que foi atenuado pelo treinamento.

Conclusão: os resultados do presente estudo evidenciam que o treinamento físico combinado induziu atenuação das disfunções morfométricas e funcionais cardíacas associado à redução de estresse oxidativo neste tecido em um modelo experimental de diabetes e menopausa, sugerindo impacto positivo desta abordagem no manejo do risco cardíaco nessa condição.

Número do Trabalho – ORAL 27

EXPRESSÃO GÊNICA DE DIFERENTES PROTEÍNAS COM AÇÃO ANTIOXIDANTE E ENVOLVIDAS COM A INFLAMAÇÃO EM NEURÔNIOS DO NÚCLEO DO TRATO SOLITÁRIO COMISSURAL (NTSC) E REGIÃO ROSTROVENTROLATERAL DO BULBO (RVL) EM RATOS SUBMETIDOS AO TREINAMENTO FÍSICO EM ESTEIRA

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INSTITUÇÃO: Faculdade de Medicina do ABC

Introdução: Espécies reativas de oxigênio (ROS) estariam relacionadas com o desenvolvimento da hipertensão. A inflamação tem sido associada ao aparecimento de doenças cardiovasculares e o ponto chave envolvido neste processo seria a geração de ROS. Os exercícios físicos aeróbios influenciam o controle autonômico cardiovascular. Não é sabido se o treinamento físico é capaz de induzir alterações na produção de ROS e de marcadores inflamatórios em neurônios bulbares envolvidos com o controle cardiovascular.Objetivo: Avaliar a expressão gênica de proteínas protetoras contra o estresse oxidativo e de proteínas envolvidas na inflamação no NTSc e RVL em ratos submetidos ao treinamento físico.Metodos: Ratos Wistar foram treinados em esteira (GT, n=7) ou mantidos sedentários (GS, n=7) por 10 semanas (protocolo CEEA-FMABC#002/2010). Após esse período, foram coletados o encéfalo (NTSc e RVL) e coração para extração do RNA total com kit Qiagen e posterior obtenção do cDNA. A expressão gênica de superóxido dismutase (SOD), catalase (CAT), neuroglobina (Ngb), citoglobina (Ctb), NADPH oxidase, cicloxigenase-2 (COX-2), tirosina hidroxilase (TH), oxido nítrico sintetase neuronal (NOSn) no NTSc e RVL; e mioglobina no coração como marcador de treinamento físico, foi realizada por RT-PCR (tempo real). Os dados foram analisados pelo método comparativo de Ct e estão expressos como média±EP e submetidos ao teste t-Student não pareado (p<0,05).Resultados: A expressão de SOD no NTSc (1,38±0,13 GT vs. 0,90±0,10 GS) e RVL (1,43±0,11 GT vs. 1,00±0,08 GS), bem como de CAT no NTSc (1,31±0,13 GT vs. 0,89±0,10 GS) e RVL (1,34±0,09 GT vs. 1,00±0,08 GS) estavam aumentadas no GT comparado ao GS. Não foram observadas diferenças na expressão de TH no RVL e de Ngb, Ctb e TH no NTSc do GT e GS. Porém, tanto a Ngb (1,29±0,04 GT vs. 1,00±0,07 GS) quanto a Ctb (1,18±0,02 GT vs. 1,02±0,07 GS) estavam aumentadas no RVL do GT. A expressão da NADPH oxidase foi similar no NTSc do GT e GS, mas observou-se diminuição no RVL (0,55±0,15 vs. 1,00±0,08 GS). Houve diminuição da expressão de COX-2 no GT no NTSc (0,39±0,11 vs. 1,0±0,15 GS) e no RVL (0,26±0,02 vs. 0,97±0,09 GS) e da NOSn no NTSc (0,15±0,05 vs. 1,0±0,62 GS) e no RVL (0,38±0,08 vs. 0,97±0,23 GS). A expressão de mioglobina aumentou no GT (1,42±0,10 vs. 1,02±0,07 GS). Conclusão: Após 10 semanas de treinamento físico, houve redução da expressão de proteínas envolvidas com o processo inflamatório e aumento da expressão gênica de diferentes proteínas com ação antioxidante no NTSc e RVL, sugerindo diminuição do estresse oxidativo em cascatas intracelulares que envolvem a participação do óxido nítrico.

Número do Trabalho – ORAL 28

Increase in exercise tolerance in trained rats supplemented with L-arginine is associated with improvement in mitochondrial biogenesis and cardiometabolic biomarkers in gastrocnemius muscle

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INSTITUIÇÃO: Universidade Estadual Paulista Júlio de Mesquita Filho

Mitochondria are organelles which plays an important role in energy metabolism. It is known that either nitric oxide or exercise promotes mitochondrial biogenesis. However, no study has evaluated the interaction between of L-arginine (L-arg) and exercise on mitochondrial biomarkers. Objective: to assess exercise tolerance, redox state and mitochondrial biomarkers in trained rats supplemented with L-arg. Methods: Wistar rats were divided into four groups: sedentary with and without L-arg (SD; SDLA) and trained groups with and without L-arg (TR; TRLA). Aerobic physical training was conducted in sessions of 60 min. 5 days a week for 8 weeks. L-arg was administered orally by gavage (62.5 mg/ml/day/rat). Exercise tolerance test (ET) was performed in the 8th week after physical training. The gastrocnemius muscle was isolated and protein expressions of PGC-1α, mtTFA, ATP synthase subunit c, cytocrome c oxidase (COXIV), AMP-activated protein kinase (AMPK), superoxide dismutase isoenzymes: Cu/Zn-SOD and Mn-SOD and both neuronal and endothelial nitric oxide synthase (eNOS and nNOS) were measured in the cytoplasm (cyt) and extract enriched in mitochondria (mit) by Western Blott. Fasting glucose, lipid profile, nitrite and nitrate (NOx-) and MDA levels were also analyzed. Results: We found a significant increase in ET in both trained groups (TR: 21±1 and TRLA: 25±0.6) as compared with sedentary. Furthermore, in TRLA group showed an enhancement of ET in comparison to TR (20%). Physical training per se increased the COXIV (TR: 1.7±0.2 and TRLA: 2±0.2) and Cu/Zn-SOD (TR: 1.8±0.2 and TRLA: 2±0.3) protein expressions. Interestingly, the association exercise and L-arg caused a significant increase in mtTFA (2.6±0.2 cyt; 1.5±0.1 mit), ATP synthase c (2.7±0.4) as compared with SD. AMPK expression was increased in L-arg groups (SDLA: 1.6±0.2 and TRLA: 2.1±0.3) compared with non-supplemented groups. The TRLA group showed increased NOx- concentration (2.4±0.2) and protein expression of PGC-1α (1.6±0.1) and Mn-SOD (1.5±0.1) compared to all other groups. The nNOS and eNOS expressions were not different between groups. MDA levels were decreased in SDLA (62±5 μM), TR (60±1 μM) and TRLA (63±2 μM) compared to SD group (86±4 μM). Conclusion: Physical training and L-arg supplementation promoted greater exercise tolerance that was positively associated with increased protein expressions of PGC-1α, AMPK, Cu/Zn-SOD, Mn-SOD, mtTFA, COXIV and the ATP synthase subunity c that was accompanied by increased NO production and reduction in lipid peroxidation biomakers in rat gastrocnemius muscle. These findings may provide new strategies for the prevention of cardiometabolic diseases since this interaction promotes greater resistance to physical exercise.Financial Support: FAPESP

Número do Trabalho – ORAL 29

STUDY OF CARDIAC AUTONOMIC AND MORPHOFUNCTIONAL ADAPTATIONS INDUCED BY PHYSICAL TRAINING IN OVARIECTOMIZED RATS TREATED WITH AN ANGIOTENSIN-CONVERTING ENZYME INHIBITOR

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INSTITUÇÃO: Universidade de São Paulo - Faculdade de Medicina de Ribeirão Preto

ABSTRACT Aim: We investigated the effects of the treatment with angiotensin-converting enzyme inhibitor (enalapril) and/or aerobic physical training-induced adaptations on cardiac autonomic control and cardiac morphofuncional parameters using different approaches in ovariectomized rats: 1) pharmacological autonomic blockade double (methylatropine/propranolol); 2) heart rate and arterial pressure spectral analysis; baroreflex sensitivity; and cardiac morphological and functional analysis by echocardiography. Female Wistar rats (N=48) were divided into 3 groups: SHAM Sedentary Vehicle group (SHAM-Sed-Veh), N=8; ovariectomized Sedentary Vehicle group, (OVX-Sed-Veh), N=8; OVX treated with enalapril maleate (10 mg-1.kg-1.d-1) group, (OVX-Sed-Enal group); N=8. In each group, half of the rats were subjected to swimming training (Train), SHAM-Train-Veh (N=8); OVX-Train-Veh (N=8) and OVX-Train-Enal (N=8). Results: The OVX-Sed-Veh group showed no differences in autonomic control and cardiac hemodynamics, compared to SHAM-Sed-Veh group. However, only the SHAM-Train-Veh group showed increased vagal after physical training. Moreover, when the sedentary rats were treated by enalapril and when there was an association between enalapril treatment and physical training, the OVX-Sed group and OVX-Train-Enal groups, respectively, exhibited increased sympathetic participation in cardiac autonomic balance. Regarding the morphological and functional parameters, the OVX-Sed-Veh group showed a reduction of the ratio of left ventricle (LV) mass / body weight and the interventricular septum thickness (IVST), resulting in decreased cardiac index, ejection fraction and fractional shortening. The physical training and treatment with enalapril, independently, promoting a few changes on these parameters. However, this association promoted the beginning of cardiac remodeling evidenced by increased relative LV wall thickness, IVST and posterior wall thickness of LV, however, without altering the cardiac function. Conclusion: Ovariectomy promoted changes on cardiac remodeling and cardiac function without affect the autonomic modulation and these changes were not reverted by physical training. The enalapril treatment associated with exercise training did not reverse these changes, but induced a marked compensatory response in sympathetic autonomic drive.Keywords: angiotensin-converting enzyme inhibitor; cardiovascular autonomic control; cardiac function; cardiac morphometry; exercise training; ovarian failure.