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108390

MODALITY: BEST POSTER - YOUNG RESEARCHER
CATEGORY: CARDIORESPIRATORY PHYSIOLOGY/ BASIC SCIENCE
D: 14/10/2022 H: 16:10 / 16:50
L: ÁREA DE EXPOSIÇÃO DE PÔSTERES

TITLE: DOXORUBICIN-INDUCED CARDIOTOXICITY ATTENUATION BY OMEGA-3 FATTY ACID SUPPLEMENTATION IN RATS IS NOT MEDIATED BY SPHINGOMYELIN-CERAMIDE PATHWAY

MARINA GAIATO MONTE [1], CAROLINA RODRIGUES TONON[1], ANDERSON SEIJI SOARES FUJIMORI[1], ANA PAULA DANTAS RIBEIRO[1], KATASHI OKOSHI[1], PAULA SCHMIDT AZEVEDO[1], MARCOS FERREIRA MINICUCCI[1], LEONARDO ANTONIO MAMEDE ZORNOFF[1], SERGIO ALBERTO RUPP DE PAIVA[1], BERTHA FURLAN POLEGATO[1]

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Introduction: Doxorubicin (DOX) is widely used effective chemotherapy drug; however, it can cause cardiotoxicity which is a very serious side effect. There is no effective therapy for cardiotoxicity. Omega-3 fatty acid (O3) supplementation may act in the sphingomyelin-ceramide pathway. We aimed to evaluate the influence of O3 in attenuating DOX-induced cardiotoxicity. Methods: male Wistar rats (n=60) were divided into 4 groups: control (C), administration of O3 only (O3), DOX only (D), and DOX and O3 (DO3). O3 (400 mg/kg/day, gavage) was administered for 6 weeks. DOX (3.5 mg/kg, IP, once a week) was administered for the last 4 weeks of the experiment. At the end of 6 weeks, rats were submitted to echocardiogram and euthanized (thiopental 120 mg/kg, ip). Statistical analysis: 2-way ANOVA (pi: p value for the interaction between DOX and O3; pD: p value for the effect of DOX; pO3: p value for the effect of O3). Results: Group D exhibited increased left atrium diameter/aorta diameter ratio (C 1.31±0.11; D 1.45±0.11; O3 1.36±0.11; DO3 1.27±0.11; pD=0.467, pO3=0.028, pi<0.001) and decreased left ventricular fractional shortening (C 0.57±0.07; D 0.46±0.07; O3 0.56±0.08; DO3 0.53±0.08; pD=0.002; pO3=0.164; pi=0.046) compared to Group C, characterizing diastolic and systolic dysfunction, respectively. DOX increased neutral sphingomyelinase activity (nSMase, C 2283±412; D 2879±680; O3 2461±639; DO3 3319±284 UI fluorescence; pD<0.001, pO3=0.087, pi=0.461) and decreased myocardial nSMase protein quantification (C 0.05±0.03; D 0.04±0.02; O3 0.05±0.02; DO3 0.03±0.02 arbitrary units; pD=0.009, pO3=0.455, pi=0.275). There were no differences between groups in myocardial ceramide deposition evaluated by immunohistochemistry. Conclusion: O3 supplementation attenuates DOX-induced diastolic and systolic dysfunction with no changes in neutral sphingomyelinase activity or expression in the myocardium. Financial support: FAPESP 2018/25677-7 and CNPq 407201/2021-1.

108392

MODALITY: BEST POSTER - YOUNG RESEARCHER
CATEGORY: CARDIORESPIRATORY PHYSIOLOGY/ BASIC SCIENCE
D: 14/10/2022 H: 16:10 / 16:50
L: ÁREA DE EXPOSIÇÃO DE PÔSTERES

TITLE: NETOSIS IS INVOLVED IN THE PATHOPHYSIOLOGY OF ACUTE DOXORUBICIN-INDUCED CARDIOTOXICITY

MARINA GAIATO MONTE [1], CAROLINA RODRIGUES TONON[1], TATIANA FERNANDA BACHIEGA PINELLI[1], ANDERSON SEIJI SOARES FUJIMORI[1], ANA PAULA DANTAS RIBEIRO[1], NAYANE MARIA VIEIRA[1], NATALIA FERNANDA FERREIRA[1], DANILO MALMONGE BARBOSA LUCIANO[1], RONNY PETERSON CABRAL[1], KATASHI OKOSHI[1], BERTHA FURLAN POLEGATO[1], LEONARDO ANTONIO MAMEDE ZORNOFF[1]

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Background: Doxorubicin (dox) is used in the treatment of several types of cancer. However, cardiotoxicity is a common side effect of the drug. The pathophysiology of cardiotoxicity is not clearly understood. Neutrophils produce attractant substances such as NETs (neutrophil extracellular traps), that are involved in immune response and inflammation which could mediate myocardial extracellular matrix remodeling. Purposes: To analyze the role of NETs in the pathophysiology of acute dox-induced cardiotoxicity. Methods: 60 male Wistar rats were allocated into 3 groups: Control (C), Dox (D), and Dox + DNAse (DD). D and DD groups received an intraperitoneal injection of dox 10mg/kg, and 2h later, DD received a subcutaneous injection of DNAse 20mg/kg (NETs inhibitor). Rats were submitted to cardiac function evaluation and euthanasia 48h after dox injection. Statistical analysis: one-way ANOVA. Results: D showed increased NETs production compared with C and DD (C=2997±810; D=5955±1906; DD=4108±1674 pg/mL; p<0.001). Transthoracic echocardiogram showed no differences in systolic parameters, but isovolumetric relaxation time corrected by heart rate was higher in D and DD than C (C=46±4.6; D=51±7.9; DD=51±7.7, p=0.039). Additionally, in isolated heart study, area under curve for diastolic pressure-volume ratio was reduced in D, indicating lower ventricular compliance, compared with C and DD (C=827±74; D=670±109; DD=966±218; p=0.007). Dox induced increased malondialdehyde myocardial concentration in D and DD compared to C (C=48±28; D=73±32; DD=82±25 nmol/mg of protein; p<0.05). Regarding extracellular matrix, dox increased and DNAse attenuated collagen in cardiac tissue (C=2.88±0.97, D=3.51±0.7, DD=2.99±0.66%; p<0.05). Additionally, dox increased matrix metalloproteinase activity (MMP)-2 (C=1.01±0.28, D=2.04±0.47, DD=2.36±0.6; p<0.001), but DNAse did not interfere with this parameter. Evaluation of protein expression of |Type 2 and 4 MMP tissue inhibitors (TIMP) showed no differences between groups. Conclusions: Dox-induced cardiotoxicity is associated with diastolic dysfunction, cardiac fibrosis, increased MMP-2 activity, and oxidative stress. NETs are involved in the pathophysiology of dox-induced cardiotoxicity. Netosis inhibition improved diastolic function, associated with decreased myocardial collagen content. However, this effect was not mediated by oxidative stress, MMP-2 activation, or TIMP-2 and -4 protein expression.

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MODALITY: BEST POSTER - YOUNG RESEARCHER
CATEGORY: CARDIO-ONCOLOGY
D: 14/10/2022 H: 16:10 / 16:50
L: ÁREA DE EXPOSIÇÃO DE PÔSTERES

TITLE: RESISTANCE TRAINING PRESERVES LEFT VENTRICLE ULTRASTRUCTURE AND FUNCTION IN DOXORUBICIN-INDUCED CARDIOTOXICITY

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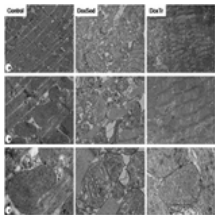
Introduction/aim. It is well known that doxorubicin (DOX) elicits toxic effects on the heart limiting its use in cancer treatment. Here, we investigated the effects of resistance training on left ventricle (LV) ultrastructure and function in DOX-induced cardiotoxicity in rodents. Methods. Male adults Sprague Dawley rats were divided into three groups (n=10): control, DOX that remained sedentary (DoxSed), or DOX submitted to resistance training (DoxTr). Resistance training (5 d/wk for 8 wks) consisted of climbing a ladder with weights placed on the tail, with progressive increase in the training load (number of repetitions and weight). DOX was administered for 10 consecutive days (1 mg/kg/d, i.p.) and it initiated concomitantly with training. At the end, cardiac function was measured by echocardiography, and LV fragments were processed for transmission electron microscopy. Results. There was a reduction in mortality in DoxTr compared to DoxSed (20 vs. 38%, P < 0.001, log rank test). The decrease in LV ejection fraction observed in DoxSed was attenuated in DoxTr (control: 76 ± 1; DoxSed: 64 ± 1; DoxTr: 71 ± 1%; P < 0.05, one-way ANOVA). The most striking effects were seen in LV ultrastructure (Fig 1). The control group showed a normal structural arrangement, with myofibrils arranged in parallel, preserved sarcomeres with uniform distance between Z lines. Intact mitochondria were seen in parallel arrangement to the myofibrils. The cardiomyocytes of the DoxSed group showed severe cellular disruption, with fragmentation of the myofibrils, disappearance of some sarcomeres, increased electron-lucid cytoplasmic content and the presence of autophagosomes, and degenerated mitochondria. Resistance training resulted in positive effects on the ultrastructural morphology of cardiomyocytes, with intact mitochondria and large areas of preservation of the structural organization of the sarcomere, although it was still possible to observe a non-linear arrangement and reduction in the density of myofibrils. Conclusion. Resistance training can be a non-pharmacological strategy to prevent the deleterious effects of DOX on the heart.



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MODALITY: BEST POSTER - YOUNG RESEARCHER
CATEGORY: CARDIOLOGY OF SPORTS, EXERCISE, ERGOMETRY AND CARDIOVASCULAR REHABILITATION
D: 14/10/2022 H: 16:10 / 16:50
L: ÁREA DE EXPOSIÇÃO DE PÔSTERES

TITLE: PHYSIOLOGICAL ELECTROCARDIOGRAPHIC FINDINGS IN A BRAZILIAN COHORT OF YOUNG FOOTBALL PLAYERS: B-PRO FOOT ECG PILOT STUDY

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Introduction: The 12-lead ECG is a useful tool for screening cardiac abnormalities in athletes. We aimed to describe physiological ECG findings in young Brazilian football players (YBFP) based on the “2017 International Criteria for Electrocardiographic Interpretation in Athletes”. Methods: Cross-sectional/descriptive study. Intra-group differences were estimated by linear models or binomial and multinomial logistic regressions. Results: 3.490 YBFP from 41 clubs, aged 15-35 years (median: 19 y) were evaluated. 1.668 were Caucasians, 1.154 Mixed-race (MR) and 668 Afro-Brazilians (AB). Prevalence: sinus bradycardia (50%), incomplete RBBB (12%), first-degree AV block (3%), Mobitz type I AV block (0.1%), and increase QRS voltage for left or right ventricular hypertrophy (34% and 15%, respectively). ST-elevation followed by T-wave inversion confined to V1–V4 leads were identified in 2% of AB. Early repolarization (ER) was present in 35% of athletes (AB versus Caucasians and MR: P=0.002 and P=0.004, respectively), which was similar to the PR interval (P<0,001 for both comparisons). There was no difference between Caucasians and MR for ER or PR intervals. For all remaining variables, there was no difference among races. Conclusions: This is the first large study to describe the prevalence of physiological electrocardiographic findings in YBFP. Further studies comparing the frequency of these findings with the prevalence observed in other cohorts are welcome.