Impact of exercise in high-humidity on heart rate variability and salivary oxidative stress in obese and lightweight asthmatic children

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ABSTRACT

Background: Asthma and obesity are becoming increasingly common among children. Such conditions are known to negatively affect both cardiac autonomic function and oxidative stress. We therefore investigated the heart rate variability (HRV) and oxidative (malondialdehyde, MDA) response to exercise within a high humidity environment (~65%) in obese and lightweight asthmatic children.

Methods: Forty-two children participated in this study and were categorized into four groups: obese asthmatic (OA, n = 10), obese non-asthmatic (ONA, n = 15), lightweight asthmatic (LA, n = 10), and lightweight non-asthmatic (LNA, n = 7). Time-domain and nonlinear indices of HRV were assessed at rest, during, and immediately after exercise. Further, saliva samples were collected immediately before and after exercise and analysed for the determination of MDA.

Results: HRV significantly decreased during and after exercise compared to baseline ($P < 0.05$) with short-term fractal scaling exponent ($\alpha1$) for the LNA group significantly smaller than the OA group after exercise ($P < 0.05$). In contrast, the long-term fractal scaling exponent ($\alpha2$) was greater after exercise compared to baseline and during exercise for all groups ($P<0.05$). MDA significantly decreased after exercise compared to baseline ($P<0.05$). We also found significant correlations after exercise between salivary levels of MDA with HRV components (i.e., RMSSD, SD1, and $\alpha2$) in asthmatic groups (all $P<0.05$).

Conclusions: Our findings showed that exercise in high humidity environment does not significantly differentiate the autonomic response among children with various conditions (i.e., obese, asthmatic and healthy). However, a significant relationship was found between HRV and MDA in asthmatic children after exercise, highlighting the inter-relationship between oxidative stress markers and autonomic function in asthmatic children.

Keywords: cardiac autonomic activity; asthma; chronic disease; youth; exercise, humidity.

Introduction

Chronic respiratory disease (CRD), including asthma and chronic obstructive pulmonary disease (COPD), represents a wide range of serious conditions which have a deleterious effect on health for millins of people worldwide [1, 2]. Asthma and its exacerbations are characterized by airway edema, remodelling, hyper-responsiveness, shortness of breath, cough, chest tightness, and/or wheezing [3]. The incidence of asthma is significantly greater in children, compared to adults, due in part to the irreversible impairments in lung function resulting from repeated and cumulative injury caused by various respiratory infections (e.g., rhinovirus, respiratory syncytial virus, etc.)[4]. Therefore, effective management programs to improve health for those children suffering for early-life asthma are important.

While asthma is a common condition during childhood [5], obesity incidence among children has also been increasing with prevalence rates in some countries reaching >30%[6]. Obesity incidence has been suggested to be linked to asthma incidence in children[5], with obesity-induced, abnormal circulating inflammatory and oxidative stress markers being potentially associated with chest restriction and air-way narrowing[5]. The relationship between obesity and asthma remains a crucial topic for clinicians and researchers that warrants further investigations. A greater understanding of these relationships and the factors that influence them, including treatment regimes, will enable greater management and health care for obese and asthmatic children.

The first line of treatment for paediatric obesity is a family-based intervention that involves a combination of lifestyle strategies to reduce energy intake, increase physical activity and reduce sedentary activities[6]. Regular exercise can also assist children by reducing the incidence and/or severity of asthma[7]. However, acute exercise, and particularly vigorous exercise, can induce asthmatic symptomology (i.e. exercise-induced asthma, EIA) such as intermittent narrowing of the airways, chest tightness, cough, wheezing, and dyspnea [8]. Additionally, the local environment has also been reported as a factor that may influence EIA response [9]. Environmental triggers such as temperature and humidity have been reported to impact on water and heat loss through the airways [10] that need to be considered for EIA responses. Consequently, vigorous exercise, particularly in hot and dry environments, has not been recommended for children with asthma, despite its potential beneficial effects on health [11]. Together, very little information is available regarding the effects of acute progressive exercise and high-humidity on physical performance among asthmatic and/or obese and non-obese (lightweight) children. Given the benefits of regular exercise for the management of asthma and obesity [12], it is important to consider the effect of environmental conditions on

exercise responses in children with these conditions, and the mechanisms responsible for such changes.

Alterations in oxidative stress and antioxidant responses, and cardiac autonomic activity have been reported as important mechanisms that contribute to the enhanced long-term management of health and chronic conditions/diseases[13]. Previously, regular, moderate exercise training was reported to be beneficial for overall oxidative stress levels and general health[11]. In contrast, acute exercise has been reported to increase oxidative stress via erythrocyte malondialdehyde (MDA)[14]. Similarly, acute exercise has been shown to reduce cardiac autonomic function with supramaximal exercise suppressing cardiac autonomic function as indicated by heart rate variability (HRV) measurements[15]. While exercise-induced changes in oxidative stress and cardiac autonomic activity are common[11], the degree of change for children with asthma and/or obesity may be crucial for long-term health management. Developing a greater understanding of the mechanisms responsible for acute exercise responses for obese and asthmatic children may elucidate the benefits of exercise for children with asthma and/or obesity and assist in the development of lifestyle regimes for enhanced health management.

The present study aimed to examine the acute effects of exercise within a high-humidity environment (~65%) on HRV and salivary oxidative stress in asthmatic children with high (obese) or low (lightweight) body mass index (BMI) values. We also sought to investigate the potential relationship between HRV and oxidative markers between groups since previous studies have reported significant association between oxidative stress/anti-oxidant markers and HRV indices in various populations[13, 16, 17]. It was hypothesized that HRV and oxidative values would be lower and higher, respectively, in obese and asthmatic children in comparison to lightweight and non-asthmatic children.

Materials and methods

Study design

This study involved examination of participants during rest (Pre), a progressive aerobic, cycle test (Ex) and a brief, post-exercise (Post) period. All recordings were conducted within environmental conditions of 22±2°C and 65±5% relative humidity, both of which were maintained at desired levels using a humidifier and air-conditioning system. All exercise tests were conducted in the morning, between 8:00 and 12:00 after an overnight fast. To ensure standardized testing conditions, participants also abided by the following conditions prior to each test: 1) no participation in intense physical activity within the 4 hours before testing, 2)

no use of long-acting bronchodilator medications for the 24 hours before testing; 3) no use of short-acting bronchodilator medications for the 8 hours before testing. This study was approved by the Faculty of Physical Education and Sports Sciences Ethical Research Committee of the University of Mazandaran (IR.UMZ.REC.1398.005), with all participants and their parents providing informed written consent prior to participation. It should be noted that data reported in the manuscript were part of a larger data set[18] with the current manuscript reporting on a separate and distinct aim.

Participant's classification and inclusion and exclusion criteria

A convenient group of 42male children were recruited with the help of education department of Babolsar city and then were categorized into four groups as follows: obese asthmatic (OA, *n*=10), obese non-asthmatic (ONA, *n*=15), lightweight asthmatic (LA, *n*=10), and lightweight non-asthmatic (LNA, *n*=7). The inclusion of non-asthmatic and non-obese/lightweight children ensured that the contributions of these body types and disease conditions, alone or in combination, on acute exercise responses could be examined in the current study. The demographic characteristics of participants are shown in Table 1. The following criteria were considered for participation in this study: 1) BMI greater than 25 kg/m^2 for obese participants; 2) a BMI less than 18.5 kg/m^2 for lightweight participants; 3) no regular physical activities undertaken during the past three months; 4) no regular intake of antioxidant supplements; 5) no hospitalization within the past 2 months prior to the study; and 6) no history of lung infection or any other chronic condition or risk factor (e.g. diabetes, high blood pressure, etc) within the past month.

Please insert Table 1 about here

Body composition and HRV measurements

Body composition was assessed using a reliable and validated bioelectrical impedance analyzer (X-Scan Plus II, Jawon Medical Company, Korea). Participants rested for 10 minutes before removing their outer clothing (coats, sweaters, shoes, and socks) and then stood on the analyzer while holding the hand electrodes. Body composition (i.e. body fat percentage) was determined with the participant's arms not touching their torso. Heart rate (HR) and RR intervals were recorded via a standard 6-lead ECG (PADSY MEDSET Holter, Hamburg, Germany) at rest following a 5-minute HR stabilization period, during exercise, and immediately after exercise (all within a seated position). For HRV assessments, R-R

intervals were analyzed from 1-minute recordings with investigators (MA, KR) visually inspecting all R-R intervals for any premature beats and artifact/noise. One-minute recordings have been reported to be valid and reliable for the assessment of HRV in a range of population including children[2, 19-21]. All R-R intervals were exported from the ECG via the manufacturer's software (Medset, Hamburg, Germany) for later analysis by customized software (Kubios HRV software, version 2.1, Department of Applied Physics, University of Eastern Finland, Kuopio, Finland). Parameters examined included time domain variables (i.e. standard deviation of normal RR intervals, SDNN; root mean square of successive differences, RMSSD), and nonlinear measures (i.e. standard deviation of the instantaneous beat-to-beat RR interval variability or minor axis of the Poincare plot, SD1; the standard deviation of continuous long-term RR interval variability or major axis of the Poincare plot, SD2; short-term (α1) and long-term (α2) fractal scaling exponents) as previously described[22, 23].

Progressive exercise protocol

The progressive exercise protocol was performed on a pre-calibrated cycle ergometer (LODE, Groningen, Netherland). Participants commenced cycling at a workload of 0 watts (cadence of 50 revolutions per minute, rpm) for 2 minutes followed by a workload of 60 watts for 2 minutes that was then increased by 10 watts every 2 minutes until volitional exhaustion. During recovery, participants cycled at 0 watts for 5 minutes. The exercise test was terminated when participants failed to maintain the target cycling frequency for 15 s [24]. No participants showed any signs of an asthama attack or respiratory discomfort during or following the exercise test. Participants were also provided with refreshments (snacks and bottled water) following all assessments to avoid any potential hypoglycemia since particpants were perfoming the exercise test after an overnight fasting.

Salivary oxidative stress

Saliva samples were collected immediately before (Pre-Ex) and after (Post-Ex) the progressive aerobic exercise protocol. After sufficient gargling with mineral water, participants chewed upon paraffin film to stimulate saliva secretion with 5 mL samples collected from each participant. Saliva samples were then centrifuged at 3,000 rpm for 10 minutes with the supernatant then placed into tubes and stored at -80 C until analysis. All samples were analysed for the oxidative stress marker, MDA. The assessment of MDA was conducted according to the thiobarbituric acid method described elsewhere[25]. The assessment

of oxidative stress via saliva samples has been reported to be reliable and comparable to blood analyses in adults and children[26].

Statistical analysis

All data are expressed as mean ± SD with missing data replaced by the calculated group mean. We analyzed the overall effect of exercise on HRV and MDA via two-way ANOVA (time x group) and Tukey's post-hoc tests. Significant relationships between HRV and MDA for each group were examined via Spearman rank correlation coefficients. Statistical significance was set at $p<0.05$. All analyses were conducted using the Statistical Package for the Social Sciences (SPSS version 22 for Windows).

Results

HRV

In all groups, α1 was lower at Ex compared with Pre and Post. In addition, α1 at Post was lower for the LNA than for the OA group ($p\leq0.05$ for time vs. group interaction, Table 2). Apart from that, there was a significant main effect of time for SDNN, RMSSD, SD1, SD2 and α2 ($p<0.05$, Table 2). SDNN and SD2 were lower at Ex compared with Pre and Post ($p<0.05$), and at Post compared with Pre ($p<0.05$). In addition, RMSSD and SD1 were lower at Ex and Post compared with Pre ($p<0.05$), and α2 was greater at Post compared with Pre and Ex ($p<0.05$). Regarding oxidative stress, a significant main effect of time was noted for MDA with greater values at Pre compared to Post ($p<0.05$, Figure 1).

Please insert Table 2 and figure 1 about here.

Correlations

For the OA group, MDA at Post-Ex was significantly correlated with RMSSD and SD1 at Post ($\rho=0.736$ and 0.736, respectively, $p<0.05$). For the LA group, MDA at Post-Ex was significantly correlated with α2 at Post ($\rho=0.676$, $p<0.05$). There were no other significant correlations between HRV and MDA.

Discussion

The purpose of the current study was to investigate the acute effect of incremental exercise within a high-humidity environment (~65%) on HRV and MDA, a salivary oxidative stress marker in obese and lightweight asthmatic children, and identify possible relationships

between variables. To our knowledge, no study to date has investigated HRV and oxidative stress responses simultaneously following exercise in a high-humidity environment among children with various conditions (i.e., obese, asthmatic, and healthy). We found a negligible difference for HRV between asthmatic and healthy children. A significant relationship, however, was observed between HRV and MDA in asthmatic children, indicating the potential role of oxidative stress status and cardiac autonomic function alike among asthmatic children.

Our findings demonstrated that HRV parameters (SDNN, RMSSD, SD1, SD2, and α1) significantly declined during and after exercise compared to Pre-Ex, except for α2, which significantly increased at Post-Ex compared to Pre-Ex and Ex. These findings are in line with a previous study that reported a significant decrease in HRV during and following various exercise bouts (i.e. aerobic and resistance)[27]. This HRV reduction during progressive exercise and immediate recovery represents the well-known withdrawal of parasympathetic activity, which is regulated by central (i.e., central command) and peripheral (cardiac and arterial baroreflexes, muscle afferents) mechanisms; and also by a likely increase in sympathetic activity which is usually observed during exercise of moderate to high intensities[28].

While typical acute, exercise-induced changes in HRV were identified, significant differences in post-exercise HRV were noted between groups with α1 values significantly greater for OA compared to LNA. The association of obesity with HRV has not been consistently reported with studies predominantly looking at various subgroups and different obesity parameters [29]. Recent studies have reported decreased HRV during stressful conditions with the greatest HRV attenuation observed in obese participants [29]. One previous study also reported that both resting sympathetic and parasympathetic activities were reduced in obese compared to healthy children[30]. More specifically, Vanderlei et al reported that obese children exhibited a reduced α1 that was associated with a reduction in both sympathetic and parasympathetic modulations [31]. The higher values of α1 within the current study were inconsistent with previous studies of obese children (i.e., decreased)[29, 31]. Further, the α1 values were only greater for OA compared to LNA, indicating the potential modulatory effect of asthma on obesity-induced reduction in ANS activity. Gupta et al reported greater central vagal outflow with a concomitant lower central sympathetic efferent for asymptomatic asthmatic patients compared to a healthy group[32]. This parasympathetic dominance was suggested as a potential mechanism for airway constriction, the hallmark of bronchial asthma[32]. Widdicombe reported that the cholinergic motor component of the parasympathetic nervous system supplied several structures which may be important in determining the resistance of normal

and diseased airways including 1) lower airway smooth muscle, 2) mucus secretion, (3) sub-mucosal tissues, (4) the larynx, and (5) the nose[33]. However, we are cautious in stating that asthma per se was responsible for the higher values of α1 and higher parasympathetic activity and/or lower sympathetic activity in the current study, since there was no similar α1 increase for LA participants. Potentially the combination of obesity and asthma conditions may have triggered unknown mechanisms for the HRV changes that require further investigation of ANS activity in obese asthmatic patients.

It is worth mentioning that α1 values below 0.85 have been associated with an increase in mortality rate[34], especially in those with cardiovascular disease[35]. Although there were no values below 0.85 for α1 at rest and following exercise for all groups, we found lower values during exercise (Table 2), suggesting a significant loss of fractal dynamics during exercise in high-humidity. This loss exemplifies a potential cardiac risk for children performing incremental exercise in high-humidity. However, all groups had similar responses highlighting the minimal impact of obesity and asthma presence on exercise autonomic modulation response. The significance of a loss of fractal scaling in children during exercise remains to be investigated especially in those that may be more susceptible to cardiovascular events (i.e., obese and asthmatic)[31].

Our findings showed that MDA levels were significantly decreased at Post-Ex compared to Pre-Ex in all groups. This finding was supported by previous human and animal studies. A reduction in MDA levels have been reported following acute walking and combined exercise (i.e., walking and resistance training)[36] and after acute exhaustive swimming exercise[37]. The lower MDA levels following acute exercise could be a result of increased lipid lipoperoxidation during exercise, which in turn elicits a greater production of antioxidant enzymes[38]. It is, therefore, plausible that this greater antioxidant production may shift the oxidative balance towards greater antioxidation after acute exercise[38]. Moreover, it has been reported that the reduced MDA levels post-exercise may be associated with detoxification of reactive oxygen species, resulting in a reduction of nitric oxide degradation and subsequent augmentation of plasma nitrite levels[39]. This explanation, however, could not be substantiated within the presented study as nitrite oxide production was not assessed. Consequently, future studies should consider this potential relationship (i.e., lower MDA level and higher nitrite oxide) when examining the MDA response to acute exercise.

It should be noted that notwithstanding the reduction in MDA Post-Ex, no significant difference was noted between groups at either Pre or Post-Ex. This finding is inconsistent with previous studies that reported the presence of greater oxidative stress markers in obese[40]

and asthmatic[41] children compared to heathy counterparts. This discrepancy could be attributed to different samples used for measuring oxidative stress markers (i.e., blood vs. saliva). All of the aforementioned studies measured oxidative stress markers in blood samples whilst in the present study, salivary samples were examined. Previous studies have reported different oxidative stress results within saliva and blood samples[41]. In the present study, the MDA level was not assessed in blood with future studuies encouraged to assess oxidative strees markers in both blood and plasma to confirm the current results in obese asthamitc and healthy children.

We found significant positive correlations between salivary levels of MDA at Post-Ex with Post HRV components (i.e., RMSSD, SD1, and α2) in asthmatic groups, highlighting the inter-relationship between oxidative stress markers and autonomic function in asthmatic children. These findings, however, were inconsistent with previous studies that reported a significant negative correlation between cardiac autonomic function and oxidative/inflammatory markers[17]. An explanation for the discrepancy was not apparent with future studies encouraged to consider further the relationships between oxidative stress and HRV in response to various exercise modalities within high-humidity environments and confirm the current results among asthmatic children.

Conclusions

Our findings suggest that exercise in high-humidity may induce minor differences among asthmatic and healthy children regarding their cardiac autonomic function (HRV), with no difference between groups for oxidative stress activity (i.e., MDA). Furthermore, our findings showed significant relationships between oxidative stress and cardiac autonomic function following exercise in asthmatic groups, indicating the potential role of asthma on the relationship between cardiac autonomic function and oxidative stress production following exercise.

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Declaration of interest

The authors have no conflicts of interest.

References

1. Carreiro-Martins P, Gomes-Belo J, Papoila AL, Caires I, Palmeiro T, Gaspar-Marques J, et al. Chronic respiratory diseases and quality of life in elderly nursing home residents. Chronic respiratory disease. 2016;13:211-9.
2. Zużewicz K, Roman-Liu D, Konarska M, Bartuzi P, Matusiak K, Korczak D, et al. Heart rate variability (HRV) and muscular system activity (EMG) in cases of crash threat during simulated driving of a passenger car. International Journal of Occupational Medicine and Environmental Health. 2013;26(5):710-23.
3. Maslan J, Mims JW. What is asthma? Pathophysiology, demographics, and health care costs. Otolaryngologic Clinics of North America. 2014;47:13-22.
4. Castro-Rodriguez JA, Custovic A, Ducharme FM. Treatment of asthma in young children: evidence-based recommendations. Asthma research and practice. 2016;2:5.
5. Lang JE. Obesity, nutrition, and asthma in children. Pediatric Allergy, Immunology, and Pulmonology. 2012;25:64-75.
6. Lang JE. Obesity and asthma in children: current and future therapeutic options. Pediatric Drugs. 2014;16:179-88.
7. Eijkemans M, Mommers M, Draaisma JMT, Thijs C, Prins MH. Physical activity and asthma: a systematic review and meta-analysis. PloS One. 2012;7(12):e50775-e.
8. Billen A, Dupont L. Exercise induced bronchoconstriction and sports. Postgraduate Medical Journal. 2008;84:512-7.
9. Hayes JD, Jhaveri MA, Mannino DM, Strawbridge H, Temprano J. The effect of mold sensitization and humidity upon allergic asthma. The Clinical Respiratory Journal. 2013;7(2):135-44.
10. Silva A, Appell, H.J., Duarte, J.A. Influence of environmental temperature and humidity on the acute ventilatory response to exercise of asthmatic adolescents. Archives of Exercise in Health and Disease. 2011;2(1):69-75.
11. Pingitore A, Lima GPP, Mastorci F, Quinones A, Iervasi G, Vassalle C. Exercise and oxidative stress: Potential effects of antioxidant dietary strategies in sports. Nutrition. 2015;31:916-22.
12. Freitas PD, Ferreira PG, da Silva A, Trecco S, Stelmach R, Cukier A, et al. The effects of exercise training in a weight loss lifestyle intervention on asthma control, quality of life and psychosocial symptoms in adult obese asthmatics: protocol of a randomized controlled trial. BMC Pulmonary Medicine. 2015;15:124. eng.
13. Thiyagarajan R, Subramanian SK, Sampath N, Madanmohan T, Pal P, Bobby Z, et al. Association between cardiac autonomic function, oxidative stress and inflammatory response in impaired fasting glucose subjects: cross-sectional study. PloS One. 2012;7(7):e41889-e.
14. Oztasan N, Taysi S, Gumustekin K, Altinkaynak K, Aktas O, Timur H, et al. Endurance training attenuates exercise-induced oxidative stress in erythrocytes in rat. European Journal of Applied Physiology. 2004;91:622-7.
15. Niewiadomski W, Gąsiorowska A, Krauss B, Mróz A, Cybulski G. Suppression of heart rate variability after supramaximal exertion. Clinical Physiology and Functional Imaging. 2007;27:309-19.
16. Pavithran P, Nandeesha H, Sathiyapriya V, Bobby Z, Madanmohan T. Short-term heart variability and oxidative stress in newly diagnosed essential hypertension. Clinical and Experimental Hypertension. 2008;30:486-96.

17. Fadaee SB, Beetham KS, Howden EJ, Stanton T, Isbel NM, Coombes JS. Oxidative stress is associated with decreased heart rate variability in patients with chronic kidney disease. Redox Report. 2017;22:197-204.
18. Rezvan K, Dabidi VR, Mahmudi SA. Short-term heart rate variability in asthmatic obese children: effect of exhaustive exercise and different humidity conditions. The Journal of Sports Medicine and Physical Fitness. 2015;55(11):1390-6.
19. Finley JP, Nugent ST, Hellenbrand W, Craig M, Gillis DA. Sinus arrhythmia in children with atrial septal defect: an analysis of heart rate variability before and after surgical repair. Heart. 1989;61(3):280-4.
20. Hautala AJ, Karppinen J, Seppänen T, editors. Short-term assessment of autonomic nervous system as a potential tool to quantify pain experience. 2016 2016: IEEE.
21. Lehavi A, Golomb N, Leiba R, Katz Y, Raz A. One-minute heart rate variability-an adjunct for airway obstruction identification. Physiological reports. 2019;7(1):e13948.
22. Ahmadian M, Roshan VD, Hosseinzadeh M. Parasympathetic reactivation in children: influence of two various modes of exercise. Clinical Autonomic Research. 2015;25:207-12.
23. Leicht AS, Crowther RG, Golledge J. Influence of peripheral arterial disease and supervised walking on heart rate variability. Journal of Vascular Surgery. 2011;54(5):1352-9.
24. Ahmadian M, Ghorbani S, Roshan VD, Leicht AS. Influence of waterpipe smoking on cardiac autonomic function at rest and following high-intensity anaerobic exercise. Acta Gymnica. 2018;48:36-43.
25. Draper HH, Hadley M. [43] Malondialdehyde determination as index of lipid Peroxidation. Methods in Enzymology: Academic Press; 1990. p. 421-31.
26. Wang J, Schipper HM, Velly AM, Mohit S, Gornitsky M. Salivary biomarkers of oxidative stress: A critical review. Free Radical Biology and Medicine. 2015;85:95-104.
27. Kingsley JD, Figueroa A. Acute and training effects of resistance exercise on heart rate variability. Clinical Physiology and Functional Imaging. 2014;36(3):179-87.
28. White DW, Raven PB. Autonomic neural control of heart rate during dynamic exercise: revisited. The Journal of Physiology. 2014;592(12):2491-500.
29. Adam M, Imboden M, Schaffner E, Boes E, Kronenberg F, Pons M, et al. The adverse impact of obesity on heart rate variability is modified by a NFE2L2 gene variant: The SAPALDIA cohort. International journal of cardiology. 2017;228:341-6.
30. Nagai N, Matsumoto T, Kita H, Moritani T. Autonomic Nervous System Activity and the State and Development of Obesity in Japanese School Children. Obesity Research. 2003 2019/05/10;11(1):25-32.
31. Vanderlei LCM, Pastre CM, Junior IFF, de Godoy MF. Fractal correlation of heart rate variability in obese children. Autonomic Neuroscience. 2010;155(1):125-9.
32. Gupta J, Dube A, Singh V, Gupta RC. Spectral analysis of heart rate variability in bronchial asthma patients. Indian J Physiol Pharmacol. 2012;56:330-6.
33. Gupta J, Dube A, Singh V, Gupta RC. Spectral analysis of heart rate variability in bronchial asthma patients. Indian J Physiol Pharmacol. 2012;56(4):330–6.
34. Widdicombe J. Role of the parasympathetic cholinergic system in normal and obstructed airways. Respiration. 1986;50(2):1-8.
35. Mäkikallio TH, Høiber S, Køber L, Torp-Pedersen C, Peng C-K, Goldberger AL, et al. Fractal analysis of heart rate dynamics as a predictor of mortality in patients with depressed left ventricular function after acute myocardial infarction. American Journal of Cardiology. 1999;83(6):836-9.

36. Seo Y-G, Choi M-K, Kang J-H, Lee H-J, Jang HB, Park SI, et al. Cardiovascular disease risk factor clustering in children and adolescents: a prospective cohort study. Archives of Disease in Childhood. 2018:archdischild-2017.
37. Sun Y, Cui D, Zhang Z, Zhang T, Shi J, Jin H, et al. Attenuated oxidative stress following acute exhaustive swimming exercise was accompanied with modified gene expression profiles of apoptosis in the skeletal muscle of mice. Oxidative Medicine and Cellular Longevity. 2016;2016.
38. Ji LL. Exercise-induced modulation of antioxidant defense. Annals of the New York Academy of Sciences. 2002;959:82-92.
39. Lima AHRA, Correia MA, Soares AHG, Farah BQ, Forjaz CLM, Silva AS, et al. Acute effects of walking and combined exercise on oxidative stress and vascular function in peripheral artery disease. Clinical Physiology and functional Imaging. 2018;38:69-75.
40. Lechuga-Sancho AM, Gallego-Andujar D, Ruiz-Ocaña P, Visiedo FM, Saez-Benito A, Schwarz Mn, et al. Obesity induced alterations in redox homeostasis and oxidative stress are present from an early age. PloS One. 2018;13(1):e0191547-e.
41. Dundaroz R, Erenberk U, Turel O, Demir AD, Ozkaya E, Erel O. Oxidative and antioxidative status of children with acute bronchiolitis. Jornal de Pediatria (Versão em Português). 2013;89:407-11.

Table 1. Demographic characteristics of participants.

Groups	**OA** (n=10)	**ONA** (n=15)	**LA** (n=10)	**LNA** (n=7)
Age (yrs)	11.4 ± 0.7	11.2 ± 0.7	12.8 ± 0.8	12.5 ± 1.2
Height (cm)	158.0 ± 7.5	158.6 ± 6.6	145.0 ± 5.6	148.6 ± 5.9
Weight (kg)	63.4 ± 11.3	68.1± 10.3	35.5 ± 4.4*†	37.1 ± 8.8*†
Body Fat (%)	29.9 ± 3.0	31.5 ± 2.7	16.2 ± 5.9*†	13.4 ± 5.4*†
BMI (kg/m^2)	25.1 ± 2.4	26.8 ± 2.3	16.7 ± 1.7*†	16.9 ± 2*†

Data are expressed as mean ± SD. BMI – body mass index, OA – obese asthmatic, ONA – obese non-asthmatic, LA – lightweight asthmatic, LNA – lightweight non-asthmatic; $^{*}p<0.05$ vs. OA; $^{\dagger}p<0.05$ vs. ONA

Table 2. Heart rate variability for all groups at baseline, during, and after exercise.

		OA (n=10)	ONA (n=15)	LA (n=10)	LNA (n=7)	Main effect for time
SDNN (ms)						
	Pre	49.7 ± 19.6	44.1 ± 32.2	41.9 ± 18.6	48.6 ± 15.7	Pre-Ex > Post-Ex > Ex***
	Ex	8.3 ± 1.9	7.0 ± 2.6	16.0 ± 14.2	12.0 ± 7.3	
	Post	29.2 ± 16.3	25.1 ± 13.2	26.7 ± 12.1	17.4 ± 6.5	
RMSSD (ms)						
	Pre	41.3 ± 25.1	31.8 ± 31.3	28.9 ± 18.1	32.6 ± 9.1	Pre-Ex > Post-Ex, Ex***
	Ex	10.3 ± 3.9	8.2 ± 3.6	17.3 ± 10.0	17.2 ± 12.7	
	Post	15.0 ± 6.1	12.4 ± 6.9	11.5 ± 5.3	14.6 ± 8.4	
SD1 (ms)						
	Pre	30.3 ± 17.8	22.6 ± 22.3	20.6 ± 12.9	23.2 ± 6.5	Pre-Ex > Post-Ex, Ex***
	Ex	7.8 ± 2.6	5.8 ± 2.6	12.2 ± 7.1	10.8 ± 6.4	
	Post	10.6 ± 4.3	10.2 ± 8.2	10.3 ± 7.8	10.4 ± 5.9	
SD2 (ms)						
	Pre	63.3 ± 22.5	55.1 ± 41.5	55.3 ± 23.9	63.1 ± 20.2	Pre-Ex > Post-Ex > Ex***
	Ex	8.8 ± 1.9	7.8 ± 3.2	18.8 ± 19.5	11.5 ± 5.9	
	Post	43.8 ± 22.2	33.1 ± 18.5	35.6 ± 16.8	23.9 ± 7.4	
α1						
	Pre	1.13 ± 0.26	1.32 ± 0.28	1.26 ± 0.27	1.39 ± 0.27	Pre-Ex, Post-Ex > Ex***
	Ex	0.43 ± 0.12^{a}	0.44 ± 0.13^{a}	0.50 ± 0.26^{a}	0.44 ± 0.30^{a}	
	Post	1.29 ± 0.34^{b}	1.25 ± 0.43^{b}	1.11 ± 0.31^{b}	0.82 ± 0.50^{a‡}	
α2						
	Pre	0.74 ± 0.32	0.70 ± 0.22	0.92 ± 0.32	0.80 ± 0.32	Pre-Ex, Ex < Post-Ex***
	Ex	0.99 ± 0.34	1.01 ± 0.30	0.88 ± 0.29	0.68 ± 0.22	
	Post	1.21 ± 0.30	1.08 ± 0.30	1.11 ± 0.35	1.03 ± 0.36	

Data are expressed as mean ± SD. OA – obese asthmatic, ONA – obese non-asthmatic, LA – lightweight asthmatic, LNA – lightweight non-asthmatic, SDNN – standard deviation of normal RR intervals, RMSSD – root mean square of successive RR intervals differences, SD1 – standard deviation of the instantaneous beat-to-beat RR interval variability or minor axis of the Poincare plot, SD2 – the standard deviation of continuous long-term RR interval variability or major axis of the Poincare plot, MDA – malondialdehyde; Pre-Ex – pre exercise; Post-Ex – post exercise; Ex – exercise. $^{***}p<0.001$; $^{a}p<0.05$ vs. Pre; $^{b}p<0.05$ vs Ex; $^{†}p<0.05$ vs. Pre-Ex; $^{‡}p<0.05$ vs. OA.

Figure captions

Figure 1. Malondialdehyde values for all groups at baseline, during, and after exercise. *MDA*, Malondialdehyde. *p<0.05 main effect for time vs. Pre-exercise.