Original Research Article

The acute effects of passive heat exposure on arterial stiffness, oxidative stress, and inflammation

Triin Kaldur [a,b,*], Eve Unt [b,c,d,e], Vahur Ööpik [a,b], Mihkel Zilmer [f], Jaan Eha [c], Kaido Paapstel [f], Jaak Kals [f,g]

[a] Institute of Exercise Biology and Physiotherapy, University of Tartu, Tartu, Estonia
[b] Estonian Centre of Behavioural and Health Sciences, University of Tartu, Tartu, Estonia
[c] Department of Cardiology, University of Tartu, Tartu, Estonia
[d] Department of Sports Medicine and Rehabilitation, University of Tartu, Tartu, Estonia
[e] Sports Medicine and Rehabilitation Clinic, Tartu University Hospital, Tartu, Estonia
[f] Institute of Biomedicine and Translational Medicine, Centre of Excellence for Translational Medicine, University of Tartu, Tartu, Estonia
[g] Department of Vascular Surgery, Tartu University Hospital, Tartu, Estonia

ARTICLE INFO

ABSTRACT

Background and objective: The aim of the study was to determine the acute effect of passive heat exposure (PHE) on arterial stiffness, oxidative stress (OxS) and inflammatory parameters.
Materials and methods: Subjects were studied in thermoneutral conditions before and after PHE in a climatic chamber. Pulse wave analysis was used for assessment of central hemodynamic and arterial stiffness parameters. Venous blood samples were obtained to measure OxS and inflammatory parameters.
Results: Rectal temperature increased after PHE exposure compared to baseline: 37.01 °C ± 0.19 °C and 36.4 °C ± 0.31 °C, respectively (P < 0.001). There was a 17% (P < 0.05) decrease in large artery elasticity index (from 24.68 ± 5.53 to 20.42 ± 2.65 mL/mmHg*10), which was predicted upon normothermic value (r = −0.878, P < 0.01). However, no significant changes were found in others arterial stiffness parameters. A 30% (P < 0.05) increase occurred in blood IL-6 concentration (from 0.43 ± 0.15 to 0.56 ± 0.23 pg/mL), but OxS parameters remained significantly unchanged.
Conclusions: This study describes for the first time acute PHE effects on arterial stiffness, inflammation and OxS. PHE significantly decreases large artery elasticity index and increases inflammatory IL-6 level. However, further larger investigations are needed for clarifying acute PHE effects on arterial function and biomarkers.

© 2016 The Lithuanian University of Health Sciences. Production and hosting by Elsevier Sp. z o.o. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

* Corresponding author at: Institute of Exercise Biology and Physiotherapy, University of Tartu, Ülikooli 18, 50090 Tartu, Estonia.
E-mail address: triin.kaldur85@gmail.com (T. Kaldur).

1. Introduction

Exercising in a hot environment is a stressful challenge for the human body. In our previous studies, we have shown the positive effects of heat acclimation on arterial stiffness [1], oxidative stress (OxS) and inflammation parameters [2]. However, the heat acclimation protocol employed in these studies [1,2] combined both exercise and heat stress. Therefore, it was not possible to evaluate the potential impact of heat exposure independently from exercise on the changes observed in arterial stiffness and the markers of OxS and inflammation.

To our knowledge, there are very few reports to date, which provide information regarding the effect of passive heat stress on arterial stiffness and the data are contradictory. It has been demonstrated in vitro that heating of isolated arteries produces thermal-induced decreases in vessel stiffness [3]. Furthermore, it has been shown in a study conducted in humans that acute local thermal therapy may result in a decrease in arterial stiffness in both healthy young and older women [4].

On the contrary, Moyen et al. [5] showed slightly increased central arterial stiffness with heating and found that baseline stiffness appears to mediate the magnitude of heating-induced changes in arterial stiffness, while peripheral arterial stiffness remained unchanged.

Furthermore, Ganio et al. [6] studied the effect of passive heat stress on arterial stiffness and concluded that an increase in core temperature induced by passive heating does not affect arterial stiffness.

However, Ganio et al. [6] showed that the magnitude by which heat stress non-significantly decreased individual arterial stiffness was predicted upon the normothermic value – individuals who had stiffer arteries were more responsive to heat exposure induced improvements.

There is a lack of information regarding the impact of heat stress without exercise on OxS in humans. Heat stress is suggested to be an environmental factor responsible for stimulating reactive oxygen species production. We have previously shown that exhausting endurance exercise in the heat increases OxS level [2]. Data from an animal study by Yang et al. [7] showed that acute exposure to high temperatures may result in increased OxS and others [8] suggested that OxS should be considered a part of the stress response to heat exposure.

There is also a lack of information regarding the impact of heat stress on inflammation.

During prolonged exercise with or without heat stress, the level of inflammatory cytokines increases, heat exposure tends to stimulate the release of IL-6 [9]. Human studies have shown that heat stress increases plasma IL-6 values and plasma IL-6 concentrations have been previously shown to be positively correlated with increase in core temperature [10].

Thus, considering the paucity of relevant literature and the discrepancy in the data available, the aim of this study was to determine the acute effects of passive heat exposure (PHE) on arterial stiffness, OxS and inflammatory indices in young healthy men.

2. Materials and methods

2.1. Ethical approval

The study was approved by the Research Ethics Committee of the University of Tartu. Prior to the beginning of the study, all subjects gave their written informed consent. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. Subjects and study design

The present study constitutes one part of a complex experimental heat acclimation study [1,2].

The sample consisted of 9 physically active men (age 28.78 ± 3.35 year; height 182.33 ± 4.64 m; weight 78.88 ± 11.15 kg; peak oxygen uptake 53.58 ± 7.92 mL/kg/min; heart rate 48.83 ± 9.93 beats/min; systolic blood pressure 117.22 ± 8.69 mmHg; diastolic blood pressure 66.00 ± 7.35 mmHg).

None of the subjects took any medication, none of them were smokers nor had a history of heat illness. Two months prior to participation in this study, the subjects were instructed to avoid any use of additional food supplements, to follow a healthy diet and keep it stable. The study was conducted during the winter period in Estonia, which is situated between 57°37′ and 59°49′ of north latitude. Parameters of arterial stiffness, OxS and inflammation were measured in thermoneutral conditions (22 °C; relative humidity 35%) twice: before and after PHE in a climatic chamber.

During PHE the subjects stayed in a sitting position for 110 min in a climatic chamber. After the exposure, they walked out of the chamber (distance 10 m) after which the body mass of the subjects was measured. In thermoneutral conditions the procedures of measurement of arterial stiffness were conducted after a period of 10 min in supine position in order to ensure the standardization of physiological parameters. After the measurement of arterial stiffness, the blood samples for parameters of oxidative stress and inflammation were taken.

2.3. Passive heat exposure

The subjects stayed in a sitting position for 110 min in a climatic chamber (Design Environmental Ltd., Gwent, South Wales, UK) maintained at a high temperature (42 °C; relative humidity 18%), which was set up accordingly to the previous study where combined heat and exercise regimen was used [1,2]. It is suggested that core body temperature is a factor participating in the induction of OxS and inflammation and has an effect on arterial stiffness. Subjects' core body temperature was monitored in real time using a rectal probe (TX-2, Columbus Instruments, Columbus, OH, USA) and the values before and immediately after they entered/exited the climatic chamber were recorded by means of an electronic data logger (Iso-Thermex 256, Columbus Instruments, Columbus, OH, USA). Body mass of the subjects was measured to the nearest 0.001 kg before and after passive heat exposure, using an electronic scale (CH3G-150I Combics, Sartorius AG, Göttingen, Germany).

2.4. Measurements of arterial stiffness

The procedures of measurement of blood pressure and arterial stiffness were conducted in thermoneutral conditions twice: before and after PHE in the climatic chamber. The first arterial stiffness measurement was conducted in the morning after an overnight fast and the second measurement was conducted immediately after PHE.

Brachial blood pressure was measured supine in the left arm using an automated digital oscillometric BP monitor (OMRON M4-I; Omron Healthcare Europe, Hoofdorp, the Netherlands).

Sphygmocor apparatus (SCOR Px, 7.0; AtCor Medical®, Sydney, Australia) was used to assess the arterial stiffness. A high fidelity micromanometer (SPT-301B; Millar Instruments®, Texas, USA) was employed to record the peripheral pressure waveforms from the radial artery of the dominant arm at the wrist. The corresponding ascending aortic waveforms were then generated by using a transfer function. Central hemodynamics, augmentation index (AIx) and the travel time of the reflected wave (Tr) were calculated. The AIx was corrected for heart rate of 75 beats per minute (AIx@75). The pulse wave velocity (PWV) was measured by the foot-to-foot method, using the Sphygmocor device [11]. PWV at carotid–femoral segment (PWVc–f) and carotid–radial segment (PWVc–r) were determined by sequentially recording ECG-gated carotid and femoral or radial artery waveforms.

Measurements were made by recording the arterial waveform in the dominant arm by the Cardiovascular Profiling Instrument (HDI/Pulse Wave CR-2000, Hypertension Diagnostics Inc®, Eagan, USA) [12]. The tonometer was applied to the subject's radial artery at the wrist overlying the radial bony prominence. The contralateral arm was used to place the cuff for blood pressure measurement and the cuff was inflated concurrently with pulse waveform recording for calibration. During the diastolic portion of the cardiac cycle (mean of 30 s recording), the elasticity indices of the arteries were quantified. A modified 2 element Windkessel model allows for the calculation of elasticity indices of large central (capacitive) arteries (LAE) and small peripheral (oscillatory) arteries (SAE) [13].

2.5. Measurement of parameters of oxidative stress and inflammation

All blood measurements were performed at the Institute of Biomedicine and Translational Medicine (University of Tartu) and the Laboratory Department of Tartu University Hospital. All manufacturers' recommendations regarding determination procedures were carefully followed.

Venous blood samples were obtained from the *antecubital fossa* twice: baseline samples were taken between 8:00 and 10:00 following an overnight fast and the second set of samples was obtained after the heating session after the measurement of arterial stiffness.

QBC Autoread Plus autoanalyzer (QBC Diagnostics, Inc., USA) was used to assess white blood cell (WBC) counts, hemoglobin and hematocrit in whole blood. 15 min after collection, the other blood samples were centrifuged at 3000 rpm for 15 min to obtain plasma or serum. Until the analysis, all the plasma/serum samples were stored at −70 °C.

The plasma high sensitive C-reactive protein (hsCRP) was measured by a validated latex particle-enhanced high-sensitivity immunoturbidimetric assay (CRP Latex HS, Roche Diagnostics Gmbh®, Mannheim, Germany), and analyzed by the Hitaci 912 analyzer (Roche Diagnostics®, Basel, Switzerland). Total peroxide concentrations of samples were determined using OXYSTAT Assay Kit Cat. No. BI-5007 (Biomedica Gruppe, Biomedica Medizinprodukte GmbH & Co Kg, Wien). Total antioxidant capacity (TAC) was measured by using an automated measurement method [14]. The percent ratio of the total peroxide concentration of plasma to the TAC of plasma was accepted as an oxidative stress index (OSI), which is an indicator of the degree of OxS.

Evidence Investigator™ Metabolic Syndrome Array1 based on the sandwich chemoluminescent immunoassay (Randox Laboratories Ltd METS1 catalog number EV 3755) was used for simultaneous quantitative detection of interleukine-6 (IL-6) from a single patient sample.

Relative changes in plasma volume after the passive heat exposure were calculated based on hemoglobin and hematocrit values [15].

2.6. Statistical analysis

Data analysis was performed using the SPSS (version 20.0) software. All data were checked for normal distribution using the Kolmogorov–Smirnov test. All data are presented as means ± standard deviation (SD). A dependent samples (paired) t test was used to compare values of parameters measured before and after PHE. The Pearson and Spearman product moment coefficient of correlation was used to determine the relationships among variables. For all statistical analyses, the 0.05 level of significance was used.

3. Results

The subjects' rectal temperature was significantly higher after PHE compared to baseline values: 37.01 °C ± 0.19 °C and 36.4 °C ± 0.31 °C, respectively ($P < 0.001$). The values of hemodynamic and arterial stiffness parameters before and after heat stress exposure are presented in Table 1. There were no statistically significant changes in HR and blood pressure or in the values of main arterial stiffness parameters measured by systolic pulse wave analysis ($P > 0.05$).

There was a 17% decrease ($P < 0.05$) in LAE (Fig. 1) after PHE, whereas other parameters of arterial stiffness did not change ($P > 0.05$). The magnitude of the decrease in LAE was negatively related to the normothermic value of this parameter measured before PHE ($r = -0.878$, $P < 0.01$) (Fig. 2). The changes in LAE were independent of changes in core body temperature ($P > 0.05$, $r = -0.432$).

The values of OxS and inflammation parameters are presented in Table 2. OxS parameters remained unchanged ($P > 0.05$) after heat exposure and there were no significant associations between OxS, arterial stiffness and core body temperature ($P > 0.05$). There were no significant changes in

Table 1 – The values of hemodynamic and arterial stiffness parameters before and after passive heat exposure.

Parameters	Before heat stress	After heat stress
Aix, %	5.556E−02 (12.05)	2.50 (8.29)
AIx@75, %	−12.43 (13.01)	−8.71 (8.00)
Tr, ms	175.11 (12.97	173.33 (10.48)
PWVc–f, ms	5.91 (0.49)	5.93 (0.71)
PWVc–r, ms	8.71 (0.86)	8.41 (0.87)
SAE, mL/mmHg × 100	11.05 (1.68)	10.01 (1.90)
PSBP, mmHg	117.22 (8.69)	119.56 (7.04)
PDBP, mmHg	66.00 (7.35)	64.78 (3.80)
CSBP, mmHg	99.17 (8.86)	100.33 (7.83)
CDBP, mmHg	66.44 (7.49)	65.22 (4.12)
PPP, mmHg	51.22 (4.15)	54.67 (5.32)**
CPP, mmHg	32.83 (4.09)	35.11 (4.97)
PPP/CPP	1.57 (0.13)	1.57 (0.10)
MAP, mmHg	80.72 (8.06)	78.33 (9.29)
HR, beats/min	48.83 (9.93)	50.83 (7.28)

Values are mean (standard deviation).
Aix, augmentation index; AIx@75, augmentation index corrected for heart rate of 75 beats per minute; Tr, travel time of the reflected wave; PWVc–f, pulse wave velocity at carotid–femoral segment; PWVc–r, pulse wave velocity at carotid–radial segment; SAE, small artery elasticity index; PSBP, peripheral systolic blood pressure; PDBP, peripheral diastolic blood pressure; CSBP, central systolic blood pressure; CDBP, central diastolic blood pressure; PPP, peripheral pulse pressure; CPP, central pulse pressure; MAP, mean arterial pressure; HR, heart rate.
** $P < 0.01$ as compared to the value measured before passive heat exposure.

body weight values after passive heat exposure: 78.89 ± 11.15 and 79.06 ± 11.29, respectively ($P > 0.05$).

PHE induced a 30% increase ($P < 0.05$) in the blood IL-6 concentration but there was no significant association between the before and after PHE values of IL-6. Likewise, the before and after PHE values and the changes in the blood
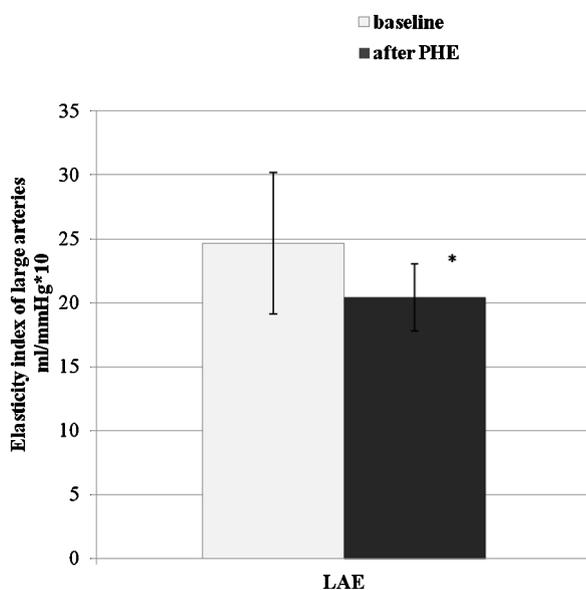

Fig. 1 – Large artery elasticity index (LAE) at baseline and after passive heat exposure (PHE). *$P < 0.05$ as compared to the baseline measurement.
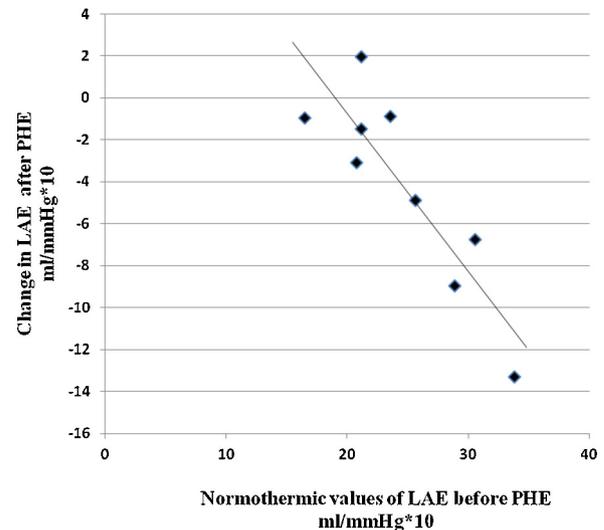

Fig. 2 – Relationship between baseline large artery elasticity index (LAE) and change in large artery stiffness after passive heat exposure (PHE) ($r = -0.878$, $P < 0.01$).

IL-6 level did not correlate with the pre- and postvalues or changes in core body temperature and LAE ($P > 0.05$).

4. Discussion

The aim of this study was to determine the acute effects of PHE on arterial stiffness, OxS and inflammatory indices in young healthy men. The use of the PHE study protocol (42 °C; relative humidity 18%) was in accordance with the study protocol in which a 10-days heat and exercise acclimation program was applied [1,2]. However, a question arose about the independent effect of heat exposure on arterial stiffness and other related parameters. Furthermore, there are only few studies available regarding the role of passive heat on arterial stiffness, which show contradictory results [3–6].

Table 2 – The values of oxidative stress and inflammation parameters before and after passive heat exposure.

Parameters	Before heat stress	After heat stress
WBC, ×10⁹/L	4.64 (1.14)	4.93 (1.20)
Hgb, g/L	142.33 (14.12)	140.67 (10.56)
HCT, %	42.83 (5.77)	41.83 (4.43)
hsCRP, mg/L	0.74 (0.35)	0.72 (0.34)
Total peroxide concentration, μmol/L	282.67 (114.37)	305.90 (156.49)
TAC, mmol Trolox equivalent/L	1.54 (0.22)	1.44 (0.20)
OSI, %	19.02 (7.94)	22.13 (11.07)
IL-6, pg/mL	0.44 (0.16)	0.59 (0.27)*

Values are mean (standard deviation).
WBC, white blood cells; Hgb, hemoglobin; HCT, hematocrit; hsCRP, high-sensitive C-reactive protein; TAC, total antioxidant capacity; OSI, oxidative stress index; IL-6, interleukin-6.
* $P < 0.05$ as compared to the value measured before passive heat exposure.

The main finding of this study is that acute PHE induced a significant 17% decrease in LAE. Furthermore, the observed decrease in LAE inversely correlated with the normothermic values of this parameter, i.e. the greatest PHE induced decrements in LAE occurred in individuals exhibiting the highest values of LAE before heat exposure. There was a 30% ($P < 0.05$) increase in the value of IL-6 after acute heat exposure in a climatic chamber. We demonstrated that acute PHE (42 °C; relative humidity 18%) does not have an effect on OxS parameters.

The results of studies trying to demonstrate the effect of heat stress on arterial stiffness are contradictory. Mitchel et al. [3] showed in vitro that heating vessels to a non-physiological temperature (60 °C) decreased the stiffness of these vessels. In addition, it has been found that acute local thermal therapy decreases the stiffness of arteries [4]. Moyen et al. [5] showed slightly increased central arterial stiffness with heating, while peripheral arterial stiffness remained unchanged.

Ganio et al. [6] studied the effect of passive heat stress on carotid–femoral pulse wave velocity as a parameter of arterial stiffness and according to their experimental protocol, the core temperature increased from baseline to 0.5 °C, 1.0 °C and 1.5 °C but they did not reveal statistically significant changes in pulse wave velocity. However, Ganio et al. [6] showed that the magnitude by which heat stress non-significantly decreased individual arterial stiffness was predicted upon the normo-thermic value. Nevertheless, it has been shown that as core temperature increased from baseline to 1.5 °C, the arterial stiffness increased compared to the baseline value ($P > 0.05$). Furthermore, in this experimental study by Ganio et al. [6] the changes detected were independent of core temperature.

In our study, we registered a rise in rectal temperature after exposure to heat stress: from 36.4 °C ± 0.31 °C at baseline to 37.01 °C ± 0.19 °C at the end of heat exposure ($P < 0.001$). According to our results, this 0.61 °C rise in rectal temperature was not sufficient to change the values of most arterial stiffness parameters but our study revealed a decrease in the value of LAE: from 24.68 ± 5.53 to 20.42 ± 2.65 mL/mmHg*10 ($P < 0.05$). Our data showed that changes observed in arterial stiffness were independent of changes in core temperature, which has also been shown in earlier studies [6].

The study by Ganio et al. [6] showed that the magnitude by which heat stress non-significantly decreased individual arterial stiffness was predicted upon the normothermic value – individuals who had stiffer arteries were more responsive to heat exposure induced improvements. This finding about correlations is in agreement with the study by Moyen et al. [5], who found that baseline stiffness appears to mediate the magnitude of heating-induced changes in arterial stiffness.

The suggestion by Ganio et al. [6] and Moyen et al. [5] that heat stress affects vessels differently depending on the baseline tone is supported by our study results. We found that the magnitude by which heat stress increased arterial stiffness was negatively related to the normothermic value – the decrease in LAE was higher in individuals with a higher baseline value of LAE. In addition, the role of the baseline value of arterial stiffness is also outlined in our previous heat acclimation study, in which individuals with the biggest heat-acclimation-induced decrease in arterial stiffness had the highest baseline stiffness value [1].

As discussed in the study by Ganio et al. [6], it is unknown how heat stress affects arterial stiffness differently depending on the baseline tone of the arteries. We agree with Ganio and his colleagues that this may partially be explained by the possibility that in the vessel with low arterial stiffness during normothermia, the amount of arterial tone changing factors released in response to heat stress were not adequate or these arteries were not sufficiently sensitive to these factors.

In addition, it has also been found that an increase in sympathetic activity occurs with heat stress [16] and that an increase in activity is associated with the increase in arterial stiffness [17]. Although this has not been evaluated in our study, we can speculate that individuals with lower normo-thermic arterial stiffness had higher sympathetic activity in response to heat stress and this is part of the reason they were more responsive to heat stress induced changes in arterial stiffness.

The response of arterial stiffness on heat stress may also have been attenuated by increased low-grade inflammation. It has been found that heat exposure tends to stimulate the release of inflammatory cytokine IL-6 [9] and that a higher value of IL-6 is associated with higher carotid–femoral PWV [18]. We found a 30% ($P < 0.05$) increase in the value of IL-6 after heat stress exposure in a climatic chamber. Nevertheless, our study did not reveal associations between the values or changes in core temperatures, IL-6, and LAE ($P > 0.05$).

According to in vitro evidence, heat stress may induce an increased OxS level and OxS is part of the stress response to heat exposure [7,8]. In addition, it has been demonstrated that environmental temperature can influence exercise-induced OxS [19] and it is suggested that the core body temperature is a participating factor in the induction of OxS [20]. In our previous studies, we have demonstrated that heat acclima-tion through combined concurrence of exercise and heat stress increases the OxS level in young healthy men [2]. We and others have also demonstrated that OxS is directly linked to increased arterial stiffness [21,22]. In the present study, we did not reveal any significant changes in OxS parameters ($P > 0.05$) after heat stress exposure nor were there any associations between OxS, arterial stiffness and core temper-ature values ($P > 0.05$).

Our study has some limitations. Firstly, according to our study design, subjects' core body temperature values were recorded before and immediately after the passive heat exposure, but the arterial stiffness values were measured 10 min later in order to ensure the standardization of physiological parameters. Bearing this in mind, it is possible that lower heat stress occurred at the time of measurements of arterial stiffness.

Secondly, from the methodological point of view, the existence of a control group would have been appropriate and further research is warranted in order to assess the effect of PHE.

5. Conclusions

In conclusion, the data of this study suggest that acute PHE induces a normothermic value dependent decrease in LAE. Acute passive PHE also induces an increase in inflammatory

IL-6 level but does not influence OxS. However, despite some PHE effects on functional and biochemical indices further larger investigations are needed to clarify mechanisms responsible for PHE effects on vascular functional and biochemical parameters.

Conflict of interest

The authors state no conflict of interest.

Acknowledgments

REFERENCES

[1] Kaldur T, Kals J, Ööpik V, Burk A, Kampus P, Zagura M, et al. Heat acclimation increases arterial elasticity in young men. Appl Physiol Nutr Metabol 2013;38:922–7.

[2] Kaldur T, Kals J, Ööpik V, Zilmer M, Zilmer K, Eha J, et al. Effects of heat acclimation on changes in oxidative stress and inflammation caused by endurance capacity test in the heat. Oxid Med Cell Longev 2014. http://dx.doi.org/10.1155/2014/107137

[3] Mitchel JF, Fram DB, Aretz TA, Gillam LD, Woronick C, Waters DD, et al. Effect of low-grade conductive heating on vascular compliance during in vitro balloon angioplasty. Am Heart J 1994;128(1):21–7.

[4] Hu Q, Zhu W, Zhu Y, Zheng L, Hughson RL. Acute effects of warm footbath on arterial stiffness in healthy young and older women. Eur J Appl Physiol 2012;112(4):1261–8.

[5] Moyen NE, Ganio MS, Burchfield JM, Tucker MA, Gonzalez MA, Dougherty EK, et al. Effect of passive heat stress on arterial stiffness in smokers versus non-smokers. Int J Biometeorol 2015. http://dx.doi.org/10.1007/s00484-015-1046-2

[6] Ganio MS, Brothers RM, Shibata S, Hastings JL, Crandall CG. Effect of passive heat stress on arterial stiffness. Exp Physiol 2011;96(9):919–26.

[7] Yang L, Tan GY, Fu YQ, Feng JH, Zhang MH. Effects of acute heat stress and subsequent stress removal on function of hepatic mitochondrial respiration, ROS production and lipid peroxidation in broiler chickens. Comp Biochem Physiol Part C: Pharmacol Toxicol Endocrinol 2010;151:204–8.

[8] Lin H, Decuypere E, Buyse J. Acute heat stress induces oxidative stress in broiler chickens. Comp Biochem Physiol Part A: Mol Integr Physiol 2006;144:11–7.

[9] Cosio-Lima LM, Desai BV, Schuler PB, Keck L, Scheeler L. A comparison of cytokine responses during prolonged cycling in normal and hot environmental conditions. Open Access J Sports Med 2011;2:7–11.

[10] Hammami MM, Bouchama A, Al-Sedairy S, Shail E, AlOhaly Y, Mohamed GE. Concentrations of soluble tumor necrosis factor and interleukin-6 receptors in heatstroke and heatstress. Crit Care Med 1997;25(8):1314–9.

[11] Wilkinson IB, Fuchs SA, Jansen IM, Spratt JC, Murray GD, Cockcroft JR, et al. Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. J Hypertens 1998;16:2079–84.

[12] Gardner AW, Parker DE. Predictors of large and small artery elasticity in healthy subjects from 9 to 89 years old. Am J Hypertens 2011;24(5):599–605.

[13] Beltran A, McVeigh G, Morgan D, Glasser SP, Neutel JM, Weber M, et al. Arterial compliance abnormalities in isolated systolic hypertension. Am J Hypertens 2001;14:1007–11.

[14] Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Clin Biochem 2004;37:112–9.

[15] Dill DB, Costill DL. Calculation of percentage changes in volume of blood, plasma, and red cells in dehydration. J Appl Physiol 1974;37:247–8.

[16] Low DA, Keller DM, Wingo JE, Brothers RM, Crandall CG. Sympathetic nerve activity and whole body heat stress in humans. J Appl Physiol 2011;111:1329–34.

[17] Swierblewska E, Hering D, Kara T, Kunicka K, Kruszewski P, Bieniaszewski L, et al. An independent relationship between muscle sympathetic nerve activity and pulse wave velocity in normal humans. J Hypertens 2010;28(5):979–84.

[18] Schnabel R, Larson MG, Dupuis J, Lunetta KL, Lipinska I, Meigs JB, et al. Relations of inflammatory biomarkers and common genetic variants with arterial stiffness and wave reflection. Hypertension 2008;51:1651–7.

[19] Quindry J, Miller L, McGinnis G, Kliszczewiscz B, Slivka D, Dumke C, et al. Environmental temperature and exercise-induced blood oxidative stress. Int J Sport Nutr Exerc Metab 2013;23:128–36.

[20] Mestre-Alfaro A, Ferrer MD, Banquells M, Riera J, Drobnic F, Sureda A, et al. Body temperature modulates the antioxidant and acute immune responses to exercise. Free Radic Res 2012;46:799–808.

[21] Kals J, Kampus P, Kals M, Zilmer K, Kullisaar T, Teesalu R, et al. Impact of oxidative stress on arterial elasticity in patients with atherosclerosis. Am J Hypertens 2006;19:902–8.

[22] Patel RS, Al Mheid I, Morris AA, Ahmed Y, Kavtaradze N, Ali S, et al. Oxidative stress is associated with impaired arterial elasticity. Atherosclerosis 2011;218(1):90–5.