VASCULAR DYSFUNCTION AND INCREASED BLOOD PRESSURE AFTER ALUMINUM EXPOSURE ARE PREVENTED BY THE EGG WHITE HYDROLYSATE IN RATS

Natalia Santos [1]

Caroline Silveira Martinez [2]

Janaina Trindade Piagette [3]

Franck Maciel Pecanha [4]

Marta Miguel [5]

Giulia Alessandra Wiggers Pecanha [6]

Resumo:

1. INTRODUCTION Aluminum (Al) is a non-essential metal and a significant environmental contaminant and is associated with a number of human diseases including cardiovascular disease (EXLEY, 2013). The aim of our study is to investigate the effects of egg white protein hydrolysate (EWH), obtained after enzymatic hydrolysis with Pepsin, with known antioxidant and anti-inflammatory properties, on vascular effects after by Al exposure. 2. METHODS For that, 32 three-month-old male Wistar rats were divided into four groups and treated orally for 42 days: a) Control - ultrapure water; b) AlCl3 - 100 mg/kg bw (PRAKASH & KUMAR, 2009); c) Hydrolysate - 1 g/kg/day of EWH (MIGUEL et al., 2006); d) Hydrolysate plus Aluminum. Systolic blood pressure (SBP) was measured by plethysmography. Vascular function was studied in aortic and mesenteric resistance arteries (MRA) in isolated organ bath. Concentration-response curves to acetylcholine and sodium nitroprusside were performed. Vasoconstrictor response to phenylephrine (PHE) in presence and absence of endothelium and in presence of NOS inhibitor (L-NAME), potassium channels blocker (TEA), NAD(P)H oxidase inhibitor (apocynin), superoxide dismutase (SOD), non-selective COX inhibitor (indomethacin), selective COX-2 inhibitor (NS 398), and AT1 selective receptor blocker (losartan), were analyzed. Systemic and vascular reactive oxygen species (ROS), lipid peroxidation and antioxidant capacity were measured. Results were expressed as mean and SEM, compared by t-test and ANOVA followed by Bonferroni test (P0.05). Ethics Committee Approval 028/2014 - Unipampa. 3. RESULTS AND DISCUSSION EWH prevented: a) the increased SBP observed after Al exposure (Ct: 117. 2 ± 1.09; Al: 132.4 ± 5.20*; Hydrolysate: 117.6 ± 3.12#; Hydrolysate + Al: 118.4 ± 1.93# mmHg, n=8 * vs Ct; #vs Al); b) the endothelial relaxation dysfunction; c) the increased vasoconstrictor response to PHE; d) restored the endothelium vasoconstrictor - modulation, nitric oxide bioavailability and potassium channels involvement; e) prevented the increased ROS production from NAD(P)H oxidase and contractile prostanoids from COX-2; f) inhibited the increased plasmatic and aortic ROS production and lipid peroxidation as well as the imbalance on antioxidant capacity after Al exposure. Al3+ toxicity has been related with its pro-oxidant activity in different target organs and systems in experimental animals (PRAKASH & KUMAR, 2009; YU et al. 2016). The pro-oxidant effects of Al are well documented and are possible due to formation of superoxide radical ion or by promoting the Fenton reaction by reducing Fe(III) to Fe(II) (EXLEY, 2004). It is well known that oxidative stress alters vascular reactivity through several ways such as its effects on the NO pathway, by counteracting NO effects or by reducing its bioavailability (HERNANZ et al., 2014). Here we show that EWH seems to be able to counteract the vascular toxic effects of Al and, based on our results, probably acting through inflammatory and oxidative stress pathways. 4. FINAL CONSIDERATIONS Our findings provide a better understanding of the cardiovascular risk of human exposure to Al and, suggest that the EWH seems to be able to counteract the vascular toxic effects of Al.

Palavras-chave: Metal; vascular dysfunction; functional food.

Modalidade de Participação: Iniciação Científica

VASCULAR DYSFUNCTION AND INCREASED BLOOD PRESSURE AFTER ALUMINUM EXPOSURE ARE PREVENTED BY THE EGG WHITE HYDROLYSATE IN RATS

[1] Aluno de graduação. nataliacasanova31@gmail.com. Autor principal

[2] Aluno de pós-graduação. caroline.s.martinez@gmail.com. Co-autor

[3] Aluno de pós-graduação. janainapiagette@gmail.com. Co-autor

[4] Docente. franckpecanha72@gmail.com. Co-autor

[5] Outro. marta.miguel@csic.es. Co-autor

[6] Docente. giuliapecanha@unipampa.edu.br. Orientador

9º SIEPE SALÃO INTERNACIONAL DE ENSINO, PESQUISA E EXTENSÃO
o conhecimento vai além das fronteiras
21 a 23 de novembro de 2017
Fronteira da Paz
Universidade Federal do Pampa
Campus Santana do Livramento

VASCULAR DYSFUNCTION AND INCREASED BLOOD PRESSURE AFTER ALUMINUM EXPOSURE ARE PREVENTED BY THE EGG WHITE HYDROLYSATE IN RATS

1. INTRODUCTION

Aluminum (Al) is a non-essential metal and a significant environmental contaminant and is associated with a number of human diseases including cardiovascular disease (EXLEY, 2013). Al adverse effects have been related with increased oxidative stress and inflammation (EXLEY, 2013; MARTINEZ *et al*., 2017). The aim of our study is to investigate the effects of egg white protein hydrolysate (EWH), obtained after enzymatic hydrolysis with Pepsin, with known antioxidant and anti-inflammatory properties, on vascular effects after by Al exposure.

2. METHODS

For that, 32 three-month-old male Wistar rats were divided into four groups and treated orally for 42 days: a) Control - ultrapure water; b) AlCl3 - 100 mg/kg bw (PRAKASH & KUMAR, 2009); c) Hydrolysate - 1 g/kg/day of EWH (MIGUEL *et al*., 2006); d) Hydrolysate plus Aluminum. Systolic blood pressure (SBP) was measured by plethysmography. Vascular function was studied in aortic and mesenteric resistance arteries (MRA) in isolated organ bath. Concentration-response curves to acetylcholine and sodium nitroprusside were performed. Vasoconstrictor response to phenylephrine (PHE) in presence and absence of endothelium and in presence of NOS inhibitor (L-NAME), potassium channels blocker (TEA), NAD(P)H oxidase inhibitor (apocynin), superoxide dismutase (SOD), non-selective COX inhibitor (indomethacin), selective COX-2 inhibitor (NS 398), and AT1 selective receptor blocker (losartan), were analyzed. Systemic and vascular reactive oxygen species (ROS), lipid peroxidation and antioxidant capacity were measured. Results were expressed as mean and SEM, compared by t–test and ANOVA followed by Bonferroni test ($P<0.05$). Ethics Committee Approval 028/2014 - Unipampa.

3. RESULTS AND DISCUSSION

EWH prevented: a) the increased SBP observed after Al exposure (Ct: 117. 2 ± 1.09; Al: 132.4 ± 5.20*; Hydrolysate: 117.6 ± 3.12#; Hydrolysate + Al: 118.4 ± 1.93# mmHg, n=8 * vs Ct; #vs Al); b) the endothelial relaxation dysfunction; c) the increased vasoconstrictor response to PHE; d) restored the endothelium vasoconstrictor – modulation, nitric oxide bioavailability and potassium channels involvement; e) prevented the increased ROS production from NAD(P)H oxidase and contractile prostanoids from COX-2; f) inhibited the increased plasmatic and aortic ROS production and lipid peroxidation as well as the imbalance on antioxidant capacity after Al exposure.

Al^{3+} toxicity has been related with its pro-oxidant activity in different target organs and systems in experimental animals (PRAKASH & KUMAR, 2009; YU et al. 2016). The pro-oxidant effects of Al are well documented and are possible due to formation of superoxide radical ion or by promoting the Fenton reaction by reducing Fe(III) to Fe(II) (EXLEY, 2004). It is well known that oxidative stress alters vascular reactivity through several ways such as its effects on the NO pathway, by counteracting NO effects or by reducing its bioavailability (HERNANZ *et al*., 2014).

Here we show that EWH seems to be able to counteract the vascular toxic effects of Al and, based on our results, probably acting through inflammatory and oxidative stress pathways.

4. FINAL CONSIDERATIONS

Our findings provide a better understanding of the cardiovascular risk of human exposure to Al and, suggest that the EWH seems to be able to counteract the vascular toxic effects of Al.

5. REFERENCES

EXLEY, C. The pro-oxidant activity of aluminum. Free Radic Biol Med, v.3, p. 380-387, 2004.

EXLEY, C. Human exposure to aluminium. Environ Sci Process Impacts, v. 10, p. 1807-16, 2013.

HERNANZ, R.; BRIONES, A.M.; SALAICES, M.; ALONSO. M.J. New roles for old pathways? A circuitous relationship between reactive oxygen species and cyclo-oxygenase in hypertension. Clin Sci (Lond), v. 126, n.2, p. 111-21, 2014.

MARTINEZ, C.S.; ALTERMAN, C.D.; PEÇANHA, F.M.; VASSALLO, D.V.; MELLO-CARPES, P.B.; MIGUEL, M. et al. Aluminum Exposure at Human Dietary Levels for 60 Days Reaches a Threshold Sufficient to Promote Memory Impairment in Rats. Neurotox Res, v. 31, n.1, p. 20-30, 2017.

MIGUEL, M.; LOPEZ-FANDINO, R.; RAMOS, M.; ALEIXANDRE, A. Long-term intake of egg white hydrolysate attenuates the development of hypertension in spontaneously hypertensive rats. Life Sci, v. 78, n. 25, p. 2960e2966, 2006.

PRAKASH, A.; KUMAR, A. Effect of N-acetyl cysteine against aluminium-induced cognitive dysfunction and oxidative damage in rats. Basic Clin Pharmacol Toxicol, v. 2, p. 98-104, 2009.

YU, L.; ZHAI, Q.; YIN, R.; LI, P.; TIAN, F.; LIU, X.; *et al.*, Lactobacillus plantarum CCFM639 Alleviate Trace Element Imbalance-Related Oxidative Stress in Liver and Kidney of Chronic Aluminum Exposure Mice. Biol Trace Elem Res, v. 176, n.2, p. 342-349, 2016.