

URATYLATED SERUM ALBUMIN IS POSITIVELY CORRELATED WITH HEART FAILURE AND INCREASES THE ADHESION OF THP-1 MONOCYTES TO ENDOTHELIAL CELLS

Railmara Pereira da Silva^{1,2}, Flavia Carla Meotti¹, Nicholas J Magon², Anna P. Pilbrow², Bianca Dempsey¹, A. Mark Richards², Anthony J. Kettle²

¹ USP, Universidade de São Paulo, São Paulo - SP, Brasil;

² UO, University of Otago, Christchurch, New Zealand;

Urate is a reductant and may act as an antioxidant. However, its oxidation products have the potential to exacerbate oxidative stress. Here we show that modification of serum albumin by products from urate oxidation is associated with poor outcomes in patients with heart failure and it can be a player of inflammation. We developed a multiple-reaction monitoring mass spectrometry method to identify twenty tryptic peptides from human serum albumin that were modified after a reaction containing xanthine oxidase, myeloperoxidase, hypoxanthine and uric acid. All the modified peptides contained a lysine residue with a 140 Da mass addition from urate oxidation derived-product, a process we call uratylation. Uratylated peptides were significantly elevated in the plasma of patients with heart failure and diabetes ($p < 0.01$), and positively correlated with myeloperoxidase ($r = 0.3$; $p < 0.01$) and allantoin ($r = 0.4$, $p < 0.001$) – the final stable product of urate oxidation. This modification on albumin was associated with death or heart failure ($p < 0.027$). Allantoin was associated with death events or exacerbation of heart failure. Incubation of uratylated albumin with HUVECs induced higher monocytes adhesion to these endothelial cells and higher TNF- α release. In conclusion, oxidation of urate is more prone to happen in patients suffering heart failure and the presence of uratylated serum albumin could be a valuable marker in cardiovascular disease. The strong association between uratylated serum albumin and worst outcome in heart failure patients suggests that uric acid could contribute to the pathology of this disease. Taken together, uric acid oxidation products may play an important role in vascular inflammation and could contribute to the pathology of heart failure.

Agradecimentos: FAPESP, CNPq, USP, New Zealand Health Research Council, University of Otago