POSTER 14

Associations between biochemical parameters and metabolites of kynureninergic pathway in heart failure patients

Ana Sousa[1*], Cláudia Ribeiro[1,2], Virgínia M.F. Gonçalves[1,3], Joana Barbosa[1], Bruno Peixoto[1,4], Sandra Leal[1,4]

[1]OXRUN – Toxicology Research Unit, University Institute of Health Sciences, CESPU, CRL, 4585-116 Gandra, Portugal.

[2]Centro Interdisciplinar de Investigação Marinha e Ambiental (CIIMAR), Universidade do Porto, 4050-123 Porto, Portugal.

[3]UNIPRO – Oral Pathology and Rehabilitation Research Unit, University Institute of Health Sciences (IUCS), CESPU, 4585-116 Gandra, Portugal.

[4]Center for Health Technology and Services Research (CINTESIS), Associate Laboratory RISE-Health Research Network, University of Porto, 4200-450 Porto, Portugal.

**✉A23452@alunos.cespu.pt*

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Resumo

Introduction: Heart failure (HF) is associated with chronic inflammation and oxidative stress, characterized by an increase in brain-type natriuretic peptide (BNP), a biomarker predictor of adverse cardiovascular events [1]. Tryptophan (TRP) metabolism through kynurenine pathway is an emerging field, emphasizing the role of its metabolites in the modulation of 'classical' cardiovascular risk factos [2], such as hypertension, obesity and diabetes mellitus [3]. Therefore, kynurenine pathway can be a useful tool to elucidate the disease mechanisms. **Objectives:** Finding correlations between concentration of TRP and its metabolites and biochemical parameters in HF patients. **Material and Methods:** Study enrolled 22 HF patients, recruited from the Centro Hospitalar do Tâmega e Sousa, EPE. TRP and its metabolites (KYN, kynurenine; KA, kynurenic acid) were measured in urine samples collected from patients and controls (n=5), using a liquid chromatography with ultraviolet and fluorescence detection (LC-UV/FD) according to a previously published method [4]. Plasma BNP levels were measured by enzyme-linked immunosorbent assay (ELISA). Urinary creatinine and serum glucose levels were measured with a Prestige 24i automated analyzer (Cormay, Tokyo Boeki). HF patients with were stratified: diabetic (DM) and non-diabetic (NonDM) groups. Statistical analyses were conducted using JASP 0.16.1.0. p-values reported for Mann-Whitney or Welch test. **Results:** Higher urinary TRP and metabolites levels (mmol/mol cr) were measured in HF compared to controls (TRP, KYN p=0.04; KA p=0.03). KYN levels tend to be higher in DM than NonDM (p<0.07). DM patients had a higher KYN/TRP ratio (p=0.02), while KA/KYN ratio tend to be lower (p=0.09) compared to NonDM patients. BNP concentrations (pg/mL) were higher in NonDM [(mean±SD) 239±51; p=0.04] than in DM (203±38). Glucose levels (mg/mL) were higher in DM patients (196±77; p=0.003). Partial correlation analysis showed that BNP had a positive correlation with KYN levels (r=0.74; p=0.002) and KYN/TRP ratio (r=0.53; p=0.04) in NonDM patients, but not in DM subgroup. However, in DM patients was found a negative correlation between glucose levels and KYN/TRP ratio (r=0.69; p=0.04). **Conclusions:** TRP metabolites in urine were significantly higher in HF compared with controls. The positive correlation between BNP and KYN in NonDM patients, suggests a shift of the kynurenine pathway, potentially due to systemic inflammation.

Keywords: heart failure 1; diabetes 2; tryptophan metabolites 3; BNP 4; kynurenine 5.

References:

[1] Bibbins-Domingo K, Gupta R, Na B, Wu AH, Schiller NB, Whooley MA. N-terminal fragment of the prohormone brain-type natriuretic peptide (NT-proBNP), cardiovascular events, and mortality in patients with stable coronary heart disease. JAMA, 297: 169-176, 2007.

[2] Dschietzig TB, Kellner KH, Sasse K, Boschann F, Klüsener R, Ruppert, J, Armbruster FP, Bankovic D, Meinitzer A, Mitrovic V, Melzer C. Plasma kynurenine predicts severity and complications of heart failure and associates with established biochemical and clinical markers of disease. Kidney Blood Press Res 44: 765-776, 2019.

[3] Braunwald E. Diabetes, heart failure, and renal dysfunction: the vicious circles. Prog Cardiovasc Dis 62: 298-302, 2019.

[4] Sousa A, Ribeiro C, Gonçalves VMF, Barbosa J, Peixoto B, Andrade A, Silva P, Andrade JP, Leal S. Development and validation of a liquid chromatography method using UV/fluorescence detection for the quantitative determination of metabolites of the kynurenine pathway in human urine: Application to patients with heart failure. J Pharm Biomed Anal 198:113997, 2021.