Área: FAR 06

# ADJUVANT-INDUCED ARTHRITIS MODIFIES RESPONSES OF ANGIOTENSIN II AND NOREPINEPHRINE IN VEINS

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#### **INTRODUCTION**

Cytokines released by joints affected by arthritis may promote vascular changes that may differ as to vascular territory and the stage of development of the disease. These changes are known in several arterial beds but are poorly understood in the venous beds. The present study aimed to identify the influence of adjuvant induced arthritis (AIA) on norepinephrine (NOR) and angiotensin II (ANGII) responses in rat central veins, including the role of nitric oxide in this process.

## **MATERIAL AND METHODS**

Male Wistar rats at 12 weeks of age, distributed in Control (not immunized) and (immunized groups Mycobacterium tuberculosis (50mg / mL), injected into the right hind paw). These animals were killed on the 4th, 15th or 40th day post immunization/false immunization to obtain cava, femoral, mesenteric and portal vein rings. These preparations were mounted on organ baths containing Krebs-Henseleit solution. The preparations were then challenged with cumulative concentrations of NOR and ANGII in the absence and presence of L-NAME. The contractions were recorded by isometric transducers and expressed as concentration-response curves. From these curves pD2 was obtained (negative logarithm of the concentration that promotes 50% of the maximum effect). The maximum response values (Rmax) also determined. Data expressed as mean ± standard deviation with significance when P <0.05. Study approved by CEUA / FAMEMA no 092/17.

### **RESULTS**

We didn't observe modifications of the parameters evaluated for both agonists, in any of the beds studied, at the 40th day after induction. At the other moments of the study, we didn't observe modifications of pD2. AIA reduced Rmax to NOR in mesenteric on day 4 (0,45±0,16 to 0,29±0,15) and femoral on day 15 postinduction (1.00±0,27 to 0,54±0,16). AIA reduced Rmax to ANGII in the cava on the 4th day  $(0.11\pm0.09 \text{ to } 0.04\pm0.12)$  and on the 15th day (0,14±0,17 to 0,14±0,39) in the mesenteric vein on the 4th day  $(0,36\pm0,21 \text{ to } 0,14\pm0,09)$  and on the 15th day (0,42±0,28 to 0,19±0,21) and in the portal vein on the 15th day post-induction  $(0.553\pm0.265 \text{ to } 0.251\pm0.320)$ . In the presence of L-NAME, the differences from Rmax to Ang II were no longer observed.

### **CONCLUSIONS**

AIA reduces vein responses to NOR and ANGII at the earliest stage of the disease, around the 4th and 15th post-induction days. These response modifications, which differ depending on the venous bed, are probably due to the increased participation of nitric oxide in the modulation of these responses.

### **ACKNOWLEGMENTS**

Coordination of Improvement of Higher Education Personnel - Brazil (CAPES) - Financing Code 001.







