III SIMPÓSIO INTERNACIONAL EM INVESTIGAÇÕES QUÍMICO-FARMACÊUTICAS
I ENCONTRO IBERO-AMERICANO DE PLANTAS MEDICINAIS DR. MAHABIR GUPTA
I CONGRESSO LUSO-BRASILEIRO DE CIÊNCIAS E TECNOLOGIAS EM SAÚDE

Área: FAR 26

AMELIORATION OF PULMONARY INFLAMMATION BY PPAR GAMMA AGONIST A1 IN LPS-EXPOSED MICE

Roberta Nunes[1]*, Larissa Benvenutti[1], Fernanda C. Goldoni[1], Fellippe R. Wolff[1], Carlos R. Vaz[1], Rita C. V. Silva[1], Maria E. S. Pereira[1], Fátima de C. Buzzi[1], Priscila de Souza[1], Nara L. M. Quintão[1], José R. Santin[1].

[1]*Universidade do Vale do Itajaí, Brasil.* *robertaa_nunes@hotmail.com.

INTRODUCTION

Respiratory infections have gained repercussion after the COVID-19 pandemic (WANG et al. 2022). Peroxisome proliferator-activated receptor (PPAR) agonists are of great importance in anti-inflammatory action, as they inhibit numerous components of the inflammatory cascade (KORBECKI et al. 2019). The present work investigated the effects of the PPARγ A1 agonist on LPS-induced lung inflammation and tracheal reactivity in an isolated trachea model in mice.

MATERIAL AND METHODS

To reproduce the lung damage, the LPS-induced acute respiratory distress syndrome (ARDS) model was performed. Mice received intranasal instillation of LPS (4 mg/kg) and oral treatment (A1 3, 10 or 30 mg/kg) 1 hour before induction. Dexamethasone (0.5 mg/kg) was used as a positive control. Tracheal reactivity was evaluated using the isolated organ model using isolated mouse tracheas stimulated with 10 µM Carbachol (CCh) and incubated with A1 (10, 30 or 100 µM). To investigate the possible mechanisms of action of compound A1, it was then pretreated with the following drugs: Indomethacin 1 µM (COX inhibitor); 1 µM propranolol (β-adrenergic antagonist); L-NAME 100 µM (nitric oxide synthases inhibitor); quinoxalin-1-one (ODQ) 10 µM (selective inhibitor of guanylate cyclase); $BaCl_2$ 10 µM (KIR: K^+ channel internal rectifier inhibitor), Glibenclamide 10 µM (ATP-sensitive K+ channel inhibitor); 1 and 10 µM Tetraethylammonium (TEA) (non-selective K^+ channel inhibitor) and Nifedipine 1 µM (L-type Ca^{2+} channel inhibitor) for 15 min before adding CCh. CEUA: 015/22.

RESULTS

The results showed a decrease in leukocytes in bronchoalveolar lavage (BAL) at doses of 10 and 30 mg/kg. Treatment with A1 (10 mg/kg) promoted a lower secretion of TNF, IL-1β, IL-6 and CXCL1 in BAL and lung tissue. The PPARγ A1 agonist was also evaluated for its relaxing effect. In addition to inhibiting CCh-induced contraction, the results shows a concentration-dependent relaxation effect on CCh-contracted tracheal smooth muscle. A1 relaxation mechanism pathways were evaluated. A1 does not act on the COX, β-adrenergic and nitric oxide pathways, however, when previously incubating the trachea with the K channel blocker TEA 1 and 10 µM, a longer time interval was observed for get 100% relaxation. In addition, A1 seems to act on Ca^{2+} channels, mainly on intracellular Ca^{2+}.The PPAR antagonist GW9662 was used to evaluate the participation of the PPAR receptor in relaxation, however, the relaxation promoted by A1 was independent of PPAR receptors.

CONCLUSIONS

The data obtained showed that compound A1 has anti-inflammatory activity in the respiratory tract, decreasing migration of

leukocytes and secretion of pro-inflammatory cytokines. In addition, a participation of K and Ca^{2+} channels in the relaxing effect promoted by compound A1 in the trachea is suggested.

ACKNOWLEDGMENTS: UNIVALI, CAPES