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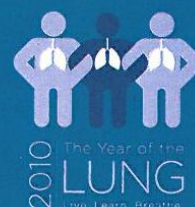
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(2mg/kg/day/animal), a specific iNOS inhibitor, daily until 15th day. Lungs were submitted to histopathology. By morphometry, we quantified macrophages, neutrophils, collagenous and elastic fibers. nNOS and iNOS-positive cells, TGF- β and MMP-12 in airway and alveolar wall.

Results: In ROFA-15d there was an increase in neutrophils and macrophage, collagen and elastic fibers, nNOS+ and iNOS+ cells, MMP-12 and TGF- β expression both in airways and lung parenchyma ($P < 0.05$ compared to Sal). The 1400W treatment reduced neutrophils and macrophage, collagen and elastic fibers and iNOS-positive cells in airways and lung tissue ($P < 0.05$ compared to ROFA). In addition, ROFA-1400W presented a reduction in MMP-12+ cells only in airways. There was no effect of 1400W on nNOS and TGF- β in airways and lung tissue.

Conclusion: iNOS is involved in the mechanisms of airway and lung tissue inflammation and remodeling induced by ambient levels of particulate matter in mice.

Supported by FAPESP, CNPq, HC-FMUSP.

P1254

Effect of SMP-028, a novel anti-inflammatory agent, on experimental allergic asthma in guinea pig model

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Rationale: SMP-028 is a novel candidate as an anti-asthmatic drug. The aim of the present study is to evaluate the effects of SMP-028 on the allergic airway response as well as inflammation in guinea pigs.

Methods: Guinea pigs were exposed to ovalbumin (OVA) aerosols once every 2 weeks. OVA-sensitized animals were challenged and then measured specific airway resistance/tidal volume (sRaw/TV) using a double-flow plethysmograph system. Bronchoalveolar lavage fluid (BALF) were collected at 6 hours after OVA challenge and infiltrated cell count, LTE₄ levels and pulmonary vascular permeability were assessed.

Results: SMP-028 (0.003 – 30 mg/kg p.o) showed marked inhibitory effect on increases of antigen-induced airway resistance in late asthmatic response with an ED₅₀ = 0.44 mg/kg. Infiltrated cell numbers of eosinophil and macrophage in SMP-028-treated animals were significantly reduced at 30 mg/kg. Moreover, SMP-028 significantly inhibited infiltration of lymphocytes at greater than 0.03 mg/kg. The increase of LTE₄ level in BALF was significantly reduced at greater than 0.03 mg/kg. OVA-induced increase in pulmonary vascular permeability was inhibited at 3 and 30 mg/kg (84% and 92%, respectively). These inhibitory activities of SMP-028 on airway inflammation were the same or more than montelukast and dexamethasone.

Conclusion: The obtained data indicate that SMP-028 was effective on various airway inflammatory responses and the anti-inflammatory effects could contribute to reduce antigen-induced airway resistance in late asthmatic response. It strongly suggests that SMP-028 improves lung function in asthmatic patients.

P1255

Effects of prednisolone and imatinib mesylate on inflammation and fibrosis in amiodarone-induced pulmonary toxicity in rats

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The experimental model of amiodarone (AM)-induced lung toxicity is one of the relevant models to study idiopathic pulmonary fibrosis (IPF). AM administered intratracheally, induces inflammatory response and activation of fibroblasts, and subsequent fibrosis. We tested the antiinflammatory and antifibrotic effect of prednisolone (PR) and imatinib mesylate (IM) against AM-induced pulmonary fibrosis in a rat model.

The study was carried out on 72 male Wistar rats weighing 220-250 g. The animals were divided into six treatment groups: control; treated intratracheally with AM; treated with AM and PR or IM from day 1 to day 10; treated with AM and PR or IM from day 10 to day 28. AM was instilled on days 0 and 2 (6.25 mg/kg with a 3.125 mg/ml water solution). PR (10 mg/kg) and IM (50 mg/kg) were given orally. Pulmonary fibrosis was assessed biochemically by measuring hydroxyproline (HP) and collagen (C) content in lung homogenate (LH) and histopathologically on 28 after AM administration.

AM resulted in significantly increased HP and C content in LH on day 28 in comparison with controls. The content of HP in animals, treated with AM+IM, given after day 10 (4.76±0.36 mcg/ml LH) and AM+PR, given after day 1 (4.76±0.36 mcg/ml LH) was decreased compared to AM alone (4.79±0.18 mcg/ml LH) on day 28 ($p < 0.05$). Intratracheal AM led to moderate interstitial and perivascular fibrosis, thickening of interstitial spaces and cellular infiltration; these damages were attenuated by above-mentioned dosing regimes.

The results obtained from our study showed that IM, given from day 10, attenuated fibrosis, whereas corticosteroid PR was effective during the inflammatory phase of the model.

P1256

iNOS inhibition reduces lung vascular inflammation and remodelling induced by repeated particulate matter instillation

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Aims: Particulate matter exposure is associated to lung vascular alterations. NO, produced by iNOS, is involved in lung inflammation and remodeling. We hypothesized that repeated ROFA (residual oil fly ash) instillation induces lung vascular inflammation and remodeling in C57BL/6J mice. We investigated if iNOS inhibition by 1400W (specific iNOS inhibitor) modulates this response.

Methods: Mice received ROFA (60ug/day/animal) for 5 (ROFA-5group), 15 days (ROFA-15group) or saline (Sal-group). In 12th day, part of the animals from ROFA-15 and Sal groups received 1400W until 15th day (ROFA-W and Sal-W groups). Afterwards, animals were anesthetized and lungs removed. Using morphometry, macrophages, neutrophils, nNOS and iNOS-positive cells were quantified around vascular wall. Collagenous and elastic fibers content, TGF- β and MMP-12 expression in vascular wall were analyzed.

Results: In ROFA-5 and ROFA-15 groups there was an increase in neutrophils, macrophages, nNOS and iNOS-positive cells and TGF- β compared to Sal ($P < 0.05$). ROFA-15 group presented an increase in collagen, elastic fibers, and MMP-12 compared to Sal ($P < 0.05$). In ROFA-W, macrophages, neutrophils, iNOS-positive cells, collagen and elastic fibers, and TGF- β were lower compared to ROFA-15 ($P < 0.05$). iNOS inhibition did not modify nNOS-positive cells and MMP12.

Conclusion: ROFA induces inflammation and remodeling in lung vessels, increasing nNOS, iNOS, TGF- β and MMP-12 in vascular wall. iNOS inhibition attenuates inflammatory and structural lung vessels alterations, at least in part by controlling TGF- β expression.

Supported by: FAPESP, CNPq, HC-FMUSP.

P1257

Modulation of oxidative stress pathway by arginase inhibition: Evaluation in an animal model of chronic pulmonary inflammation

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Aims: We previously had shown that arginase inhibition is involved on lung tissue responsiveness to antigen challenge in animals with chronic pulmonary inflammation (Aristóteles et al., 2007). In the present study, we evaluated if this response was associated to alterations on the activation of oxidative stress.

Methods: GP were exposed to repeated ovalbumin or normal saline aerosols 2x/week/4 weeks (OVA and NS groups). After 72hs of the last inhalation, GP were anaesthetised and strips were cut, suspended in Krebs-Henseleith organ bath, preconditioned by sinusoidally oscillating during 1 hour, maintained at 1 Hz. Tissue resistance (Rt) and elastance (Et) were obtained at baseline. Then NOR-NOHA (10 μ M) was infused in the bath. After 40 min Rt and Et were obtained and % of maximal responses after OVA challenge (0.1%) in organ bath. Afterwards, lung strips were stained for iNOS and PGF2alpha and analysed by morphometry.

Results: There was an increase in iNOS positive cells and %PGF2alpha in OVA compared to NS ($p < 0.05$). In sensitized GP, NOR-NOHA decreased both iNOS [7.72 (4.16-10.9)] and %PGF2alpha [0.25 (0.09-0.47)] compared to OVA animals [35.42 (22.55-56.35); 0.81 (0.3-1.52), respectively, $p < 0.05$].

Conclusions: Arginase modulates the oxidative stress pathway response in this animal model of chronic pulmonary inflammation. These results may contribute to explain the mechanisms involved in the attenuation of distal lung mechanical responsiveness by arginase inhibition, as previously shown in this animal model.

Supported by: FAPESP, CNPq, LIM-20-HC-FMUSP.

115. Exhaled biomarkers: smells like disease

P1258

Methodological aspects of an electronic nose

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We studied the between-day reproducibility (study 1) and the influence of a micro-

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