EFFECTS OF SIMVASTATIN, ROSUVASTATIN AND ATORVASTATIN DURING LUNG REPAIR IN EMPHYSEMATOUS MICE

Pinho-Ribeiro, V.¹, Lanzetti, M.¹, Kennedy-Feitosa, E.L.¹; Carvalho, G.².; Gitirana, L.B.¹, Zin, W.²; Samuel Santos Valenca¹.

¹Laboratory of Integrative Histology, Instituto de Ciências Biomédicas – Universidade Federal do Rio de Janeiro. ²Laboratory of Respiratory Phisiology, Instituto de Biofísica Carlos Chagas Filho – Universidade Federal do Rio de Janeiro.

Introduction: The lung is particularly willing to oxidative stress because the airways are the first point of contact with multiple inhaled oxidants from cigarette smoke, which contribute for development of Emphysema. Recent papers have showed pleiotropic properties of statins that go beyond their known lipid-lowering abilities.

Objective: On this study was evaluate the therapeutic potential of statins during lung repair on mouse emphysema.

Materials and Methods: After approval by the UFRJ Ethics Committee (DFBCICB046), C57BL/6 mice were exposed to cigarette smoke (CS) during 60 days, and separated into groups: AIR; CS+ vehicle (CS+V), CS+simvastatin (CS+S), CS+rosuvastatina (CS+R); CS + atorvastatin (CS+A). From there, group CS received vehicle or statins (1mg/mL) by inhalation with a jet nebulizer during more 60 days.

Results: Simvastatin and Rosuvastatin have an antioxidant effect better than atorvastatin, once these two statins presented CAT activity (U/mg protein) (CS+S= 5,20 ± 0,80; CS+R= 5,31±1,16; CS+A= 8,53±0,86); GSH/GSSG ratio (CS+S= 1,63 ± 0,16; CS+R= 1,46±0,27; CS+A= 1,33±0,18); NO₂ levels (mM/mg ptn) (CS+S= 2,99 ± 0,20; CS+R=3,27± 0,26; CS+A=3,54±0,37); and malondialdehyde levels (MDA, nmol/mg ptn) (CS+S=0,24±0,06; CS+R=0,26±0,01; CS+A =0,54±0,06) similar to AIR group (CAT= 6,15±1,01; GSH/GSSG= 1,41±0,10; NO₂= 3,03±0,10; MDA=0,26±0,01). Already the atorvastatin was more efficient in containing the inflammation once population of total leukocytes (0,52 ± 0,06 x10⁶ cells) and cytokine levels (IL-6= 44,00±5,20; KC =11,90±2,35; TNF-α=1,67±3,28) were similar to AIR group (0,45± 0,07x10⁶ cells; IL-6= 52,50±6,93; KC=8,66 ±1,86; TNF-α= 31,97±7,18). The length of air spaces (Lm) demonstrate that all statin groups have dimensions similar to AIR group. Lung static elastance (cmH₂O/mL) of CS+V group was significantly higher (26,29±1,31) than AIR (20,42±1,01) (p<0,05).

Conclusions: The data suggest that atorvastatin provides a predominantly anti-inflammatory action, while simvastatin and rosuvastain are more effective regarding the oxidative stress, during lung repair after cigarette smoke-induced emphysema.