

European Respiratory Society Annual Congress 2013

Abstract Number: 340

Publication Number: P3423

Abstract Group: 4.1. Clinical respiratory physiology, exercise and functional imaging

Keyword 1: Inflammation **Keyword 2:** Lung mechanics **Keyword 3:** Morphology

Title: Subchronic exposure to microcystin-LR impairs lung function and liver structure

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Body: Rationale: Microcystin-LR (MCLR) is a toxin produced by cyanobacteria and can induce lung and liver inflammation after acute exposure. Aim: To verify whether subchronic exposure to MCLR can damage lung and liver and evaluate the dose-dependency of the results. Methods: The study was approved by our Ethics Committee on Animal Use (CEUA/CCS/UFRJ) under code IBCCF142. Male Swiss mice received 10 intraperitoneal injections of distilled water (60 µL, CTRL group, n= 7) or different doses of MCLR (5, 10, 15 and 20 µg/kg in distilled water, 60 µL, TOX groups, n= 36) every other day. On the 10th injection pulmonary mechanics, FRC, lung and liver histology and liver weight were evaluated. One-way ANOVA followed by Student-Newman-Keuls test was used. $\alpha= 5\%$. Results: All mechanical parameters were significantly higher than CTRL in TOX5, 10, 15 and 20, but did not differ among them. No difference was observed in FRC. Alveolar collapse was higher in all MCLR doses [TOX5 (37.3%), TOX10 (57.9%), TOX15 (59.8%) and TOX20 (62.3%)] in relation to CTRL (10.2%), but did not differ among them. Lung inflammatory cell content (10^{-3} cells/ μm^2) increased dose-dependently in all MCLR groups: TOX5=7.5, TOX10=10.7, TOX15=11.4 and TOX20=12.7 in relation to CTRL= 3.0, being TOX20 the largest. The liver weight was significantly higher than CTRL= 1.75 g in TOX5= 2.05 g, TOX10= 2.13 g, TOX15= 2.30 g and TOX20= 2.13 g that did not differ among them. All TOX mice livers showed steatosis, necrosis, inflammatory foci and a high degree of binucleated hepatocytes. Conclusion: Subchronic exposure to MCLR impaired lung and liver in all doses but TOX20 group showed a more important lung inflammation. Supported by: CAPES, FAPERJ, CNPq, MCT.