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Title: Novel experimental model of maintained acute lung injury

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Body: Rationale: Several animal models have been developed to study acute lung injury (ALI); however the majority of these studies are focused on different mechanisms within the acute phase. These models do not allow studying the mechanisms in the later phases or testing any possible long-term treatment. The aim of this study was to develop an experimental ALI model simulating bronchial aspiration of gastric contents with bacterial superinfection with alveolar epithelial damage persisting over time. Methods: Sprague-Dawley rats (200-250g) were anesthetized with isoflurane. ALI was induced by intratracheal instillation of HCl (1 µl/g, 0.1 mol/L pH=1.4) followed by instillation of LPS from Escherichia coli O55:B5 (0, 10, 20, 30 or 40µg/g b.w.) two hours later. Control rats were treated with intratracheal instillations of saline. After 72h, the animals were sacrificed and bronchoalveolar lavage fluid (BALF) was sampled for further analysis of total protein concentration by bicinchoninic acid method. Results: At 72 h, rats suffered a significant loss of weight proportional to the administered dose of LPS (5.6% with 10µg/g b.w, 12.6% with 20µg/g b.w, 14.2% with 30µg/g b.w and 17.7% with 40µg/g b.w). Control rats gained in weight at 72h. LPS at 10, 20, 30 and 40µg/g b.w induced a 1.7, 2.5, 2.9 and 3.4 fold increase in total protein concentration in BAL fluid, respectively, reflecting a substantial increase proportional to the LPS dose. Conclusion: The degree of weight loss and the increase of total protein concentration in BAL fluid in the current model may reflect disease severity and progression. This model would be useful in future for new therapeutical options. Grant acknowledgements: FIS-PI12/02548 and Fundació Parc Taulí.