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Title: Treatment with proteinase inhibitor, BbCI, modulates inflammatory response, mechanic alterations, and remodeling on elastase-induced emphysema in mice

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Body: Bauhinia bauhinioides Cruzipain Inhibitor (BbCI) is a proteinase inhibitor that neutralizes neutrophil elastase and cathepsin G. The present study evaluated the capacity of BbCI in the treatment of elastase-induced emphysema. Methods: Mice received elastase intratracheally (ELA group) or saline (SAL group). Afterwards, mice were treated with BbCI (2 mg/kg) at days 1, 15 and 21 after elastase (ELABI group) or saline instillation (SALBI group). At day 28, mice were ventilated and respiratory resistance (Rrs), elastance (Ers), tissue elastance (Htis), tissue damping (Gtis), airway resistance (Raw), and exhaled nitric oxide (ENO) were analyzed, and BALF was obtained. We also quantified, mean linear intercept (Lm), elastic and collagen fibers. Results: In ELA group, there was a significant increase in the Ers, Rrs, Raw, Htis, Lm, ENO, total cells, macrophages, neutrophils and lymphocytes in BALF, elastic and collagen fibres compared to controls ($p<0.05$). In ELABI group, we observed a decrease in Ers (37.08± 1.6 cmH2O.mL.-1), Rrs (0.76± 0.1 cmH2O/mL.-1.s), Raw (0.27 ± 0.1 cmH2O/mL/s), Htis (39.47 ± 1.7 cmH2O/mL/s(1-α)), Lm (58.2 ± 2.7 µm), elastic content (0.34 ± 0.02 %), total cells (1.17 ± 0.1 104 cells/mL) and neutrophils (0.00 ± 0.0 104 cells/mL) in BALF compared to ELA group ($p<0.05$). Conclusions: The treatment with BbCI reduced inflammatory, mechanics and extracellular matrix remodeling alterations induced by elastase. Although more studies need to be performed to elucidate the mechanisms involved in this process, but we may considerate BbCI as a therapeutic tool for COPD management. Supported by: FAPESP, CNPq, LIM-20 HCFMUSP.