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Title: Comparison of two immunosuppressant triple therapies on airway mucociliary clearance in rats

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Body: The vast majority of lung transplant patients receive a maintenance immunosuppressive therapy consisting of a triple-drug regimen. However, these drugs are related with important side effects and toxicities that limit their clinical use. We hypothesized that different triple therapies could have different effects upon airway mucociliary clearance. Wistar rats were randomly assigned in three groups (n=10 each): Control = saline solution; T1 = tacrolimus + mycophenolate + prednisone; and T2 = cyclosporine + azathioprine + prednisone. After 7 days of treatment by gavage, animals were killed, lungs excised and in situ mucociliary transport velocity (MCTV) and ciliary beating frequency (CBF) measured by microscopic direct view of airway ciliated epithelium. Mucus production by goblet cells was quantified in tracheobronchial tissue. All animals from T1 and T2 groups showed a significant decrease in MCTV in comparison with Control group (0.51±0.08, 0.98±0.13, and 1.34±0.23mm/min, respectively; $p<0.001$). The MCTV in T1 was worse than in T2 ($p<0.001$). Indeed, CBF was slower in T1 and T2 versus Control (9.82±0.71, 12.38±1.09, and 13.68±0.60 Hertz, respectively; $p<0.005$). Mucus production was higher in T1 and T2 groups than in Control group (7.30±1.03, 5.92±0.75, and 4.27±1.29 %, respectively, $p<0.05$). We conclude that both triple therapies, mainly T1, caused an important impairment in airway mucociliary clearance by reducing MCTV and CBF and increasing mucus production. These data must be considered by clinicians at the best immunosuppressant therapy choice. This study was support by São Paulo Research Foundation.