

## **THE EFFECT OF INHALED B<sub>2</sub>-SYMPATHOMIMETICS AND GLUCOCORTICOIDS ON RESPIRATORY TRACT DEFENSE MECHANISMS**

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Combination of inhaled  $\beta_2$ -sympathomimetics and glucocorticoids represents the first line therapy in moderate and severe asthma. Our study evaluates the efficiency of combination therapy on cough reflex, airway reactivity and ciliary beat frequency during acute and chronic administration.

The experiments were performed using ovalbumin sensitized guinea pig model of allergic asthma. Animals were acutely treated by inhalation of budesonide ( $7 \times 10^{-3} \text{M}$ ), salbutamol ( $4 \times 10^{-3} \text{M}$ ) and their half-dose combination or chronically, by daily exposure to budesonide ( $10^{-3} \text{M}$ ), salmeterol ( $1,7 \times 10^{-4} \text{M}$ ) and to their half dose combination. Antitussive and bronchodilator activity were assessed in vivo, using a double chamber plethysmograph. The ciliary frequency was evaluated in vitro on tracheal brushed samples using light microscope and high speed video camera.

During the acute administration we observed that: (i) none of these therapies has shown antitussive activity; (ii) only salbutamol managed to decreased values of specific airway resistance; (iii) salbutamol increased ciliary beat frequency; (iv) budesonide and combination therapy reduced ciliary movement. Long-term therapies: (i) reduced airway responsiveness, (ii) suppressed cough reflex, (iii) stimulated ciliary frequency.

The combination of budesonide and salbutamol after a single inhalation did not increase antitussive and bronchodilator activity, neither reversed negative effect of budesonide on ciliary movement. On the contrary, chronic combination therapy was more effective than the therapy of each drug administered alone and led to additive or even synergic antitussive, bronchodilator and ciliostimulatory effect.

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