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EFFECTS OF SELECTIVE INHIBITION OF PDE4 AND PDE7 ON AIRWAY REACTIVITY AND COUGH IN HEALTHY AND OVALBUMIN-SENSITIZED GUINEA PIGS

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Introduction: Phosphodiesterases (PDEs) are enzymes responsible for degradation of cAMP and cGMP in many cells, leading to several effects, like contraction of smooth muscle or stimulation of inflammation. Thus, PDE inhibitors may have significant clinical benefit in respiratory diseases associated with inflammation. **The aim** was to evaluate the effects of selective PDE4 (rolipram) and PDE7 inhibitors (BRL50481) on citric acid induced cough, as well as *in vivo* and *in vitro* airway smooth muscle reactivity in both healthy and ovalbumin sensitized guinea pigs. **Methods:** Healthy and sensitized male guinea pigs were used divided in 8 groups. After 1% ovalbumin sensitization (4 groups), tested drugs were administered once daily for 7 days i.p.: 10% DMSO (as vehicle) 3 ml/kg, rolipram (ROL) 1 mg/kg, BRL50481 (BRL) 1 mg/kg, and ROL + BRL 0.5 mg/kg each. Double chamber whole body plethysmograph was used for evaluation of citric acid induced cough (2 minutes during and 2 minutes after nebulization, 0.6 M). Organ bath method was used for measurement of tracheal and lung tissue strips contractions evoked by cumulative doses (10^{-8} - 10^{-3} mol/l) of acetylcholine (ACH) and histamine (HIS). **Results:** In healthy guinea pigs the only significant *in vitro* relaxation was observed after ROL in ACH induced contractions. This was in concordance with the results of *in vivo* airway reactivity to histamine nebulization. The effect on cough was in healthy animals negligible. In ovalbumin sensitized animals, more pronounced *in vitro* relaxing effect of BRL in HIS induced contractions and of combination (ROL and BRL) in ACH induced contractions were observed, with similar result after nebulization with histamine in *in vivo* conditions. Nevertheless, there was no significant change in number of cough efforts observed in any of tested groups. **Conclusions:** Our results suggest that PDE4 and PDE7 inhibitors have stronger anti-inflammatory effects compared to direct effect on smooth muscle and cough, with potential benefit of their simultaneous administration.

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