

Vasoconstriction after inhalation of budesonide: a study in the isolated and perfused rat lung.

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Abstract

Clinical studies have shown that inhaled corticosteroids can induce rapid vasoconstriction in the airways, leading to decreased mucosal blood flow. The aim of this study was to investigate whether vasoconstriction of the pulmonary circulation after short inhalation of a corticosteroid can be detected in the isolated and perfused rat lung (IPL) - a model which could serve as a substitute or a complement to clinical models.

IPLs were briefly exposed to dry powder aerosol of budesonide. The pulmonary perfusate flow rate was assessed during 100min post-exposure. A reduction in perfusion flow rate was interpreted as vasoconstriction.

Vasoconstriction was more pronounced after brief inhalation of 10 and 50microg budesonide than 2microg. The onset of vasoconstriction became statistically significant within 10-40min after inhalation. Co-administration of a selective alpha(1)-adrenoceptor antagonist (prazosin 50nM added to the perfusate) reduced vasoconstriction by approximately 50% during 100min of perfusion (p=0.003).

Inhaled budesonide rapidly induces pulmonary vasoconstriction suggesting a nongenomic mechanism probably related to disposition of noradrenaline at the neuro-muscular junction. This ex vivo model could serve as a substitute or a complement to clinical models for investigating rapid effects of glucocorticoid receptor agonists on the pulmonary/bronchial circulation.