Fast beneficial systemic anti-inflammatory effects of inhaled budesonide and formoterol on circulating lymphocytes in asthma

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BACKGROUND AND OBJECTIVE
Inhaled glucocorticoids and long acting β2-agonists reduce airway inflammation. It is unclear if this effect is based on the local action of the drugs or is due to a systemic effect on circulating peripheral blood lymphocytes. We assessed whether inhaled budesonide and/or formoterol modify the activity of circulating peripheral blood lymphocytes.

METHODS
Placebo controlled crossover design, including healthy (n = 10) or mild asthmatic males (n = 8). Blood was collected in the morning at 08:00 before drug inhalation, and drugs (placebo, budesonide 400 μg, formoterol 12 μg) were inhaled alone or in combination at 08:30. Four more blood samples were collected after inhalation at 09:00, 09:30, 12:30 and at 09:30 am on the following day. The activity of the glucocorticoid receptor, NFκB and IκB was determined in isolated lymphocytes. Lymphocytes were stimulated with lipopolysaccharide (LPS 10 μg/mL) for 24 h and interleukin (IL)-1β, IL-6, IL-8, tumor necrosis factor (TNF)-α, eotaxin level were determined. Lymphocyte proliferation was induced by phytohaemagglutinin (PHA 10 μg/mL) over 24 h.

RESULTS
When combined, the drugs synergistically activated the glucocorticoid receptor within 30 min but did not modify NFκB or IκB activity. Inhaled budesonide significantly reduced LPS-induced IL-1β, IL-6, IL-8 and TNF-α secretion, while inhaled formoterol had no such effect; however when combined, the inhibitory effect of budesonide was significantly increased by formoterol. PHA-induced proliferation was reduced by both drugs alone and in combination.

CONCLUSIONS
Combined budesonide and formoterol may reduce airway inflammation and immune reactivity of circulating lymphocytes through its local and systemic effects.
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