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**Title:** Acute dose- and time-dependent effects of budesonide on airway blood flow in asthma

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**Body:** Inhaled corticosteroids (ICS) have been shown to decrease airway blood flow (Qaw) via a non-genomic action on airway vascular smooth muscle contraction. We have previously shown a dose-dependent decrease in Qaw with a single inhalation of 360, 720 and 1440 µg budesonide (BUD) in moderate-to-severe asthmatics where Qaw decreased transiently from 12 to 21% after all doses (p<0.05 vs baseline and placebo). Objective: Here, we have investigated the effects of repetitive BUD inhalations on Qaw in moderate-to-severe asthma patients on regular ICS use. Methods: The 18 subjects enrolled were told to abstain from ICS for at least 36 h before the experiment. Inhalation of 720 µg BUD was given 4 times, separated by 30 min. Qaw, FEV1, blood pressure, heart rate and oxygen saturation were measured before each inhalation and 30, 90, 150, 210 and 270 min after the last dose. A soluble, inert gas-uptake method was used to measure Qaw. Results: Baseline mean Qaw was 61.33 ± 3.15 µL/min (per mL of lung anatomical dead space) and FEV1 2.3 ± 0.3 L. Numerically, mean Qaw progressively decreased after each BUD inhalation. At 30 min after the last dose, mean Qaw was 28% below baseline (p<0.05) and remained 11% below baseline after 270 min. There were no statistically significant changes in FEV1, FEF 25-75%, PEF, oxygen saturation and mean blood pressure. Conclusions: In moderate-to-severe asthma patients on regular ICS use, repeated inhalations of high BUD dose have a cumulative acute vasoconstrictive effect in the airway suggesting an acute non-genomic action that increases vasomotor tone. This effect could decrease airway obstruction and the vascular clearance of concomitantly inhaled bronchodilators from the airway.