Inhaled terbutaline attenuates hyperpnoea-induced bronchoconstriction and mast cell activation in athletes.

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Background: Anderson *et al.*[1,2] proposed that β_2-adrenoceptor agonists taken by inhalation were superior to tablets for inhibiting exercise-induced bronchoconstriction (EIB) because sufficiently high concentration of drug was delivered directly to the airway to prevent mediator release from mast cells.
Aim: The aim of this study was to investigate the effect of a clinically recommended dose of β_2-adrenoceptor agonist on mast cell activation in response to dry air hyperpnoea in athletes with EIB.
Methods: A randomized, double blind, placebo controlled, cross over design in 18 subjects. Terbutaline (0.5 mg) or placebo was inhaled 15 min before 8 min of eucapnic voluntary hyperpnoea (EVH) with dry air at ~80% predicted maximum ventilation. The response to EVH was measured as the maximum % fall in FEV_1 from baseline after EVH. Mast cell activation was measured by urinary 11β-prostaglandin(PG)$F_{2\alpha}$ concentrations at baseline and 30, 60 min post-EVH.
Results: The ventilation achieved was 100±18 (SD) & 101±18 $L \cdot min^{-1}$ ($p>0.07$) & the % fall in FEV_1 after EVH was of 17±9 and 8±6% after the placebo & terbutaline, respectively ($p<0.001$). Terbutaline afforded 54±35% bronchoprotection & 14 of the 18 subjects had <10% fall in FEV_1 after EVH. There was a significant increase in 11β-$PGF_{2\alpha}$ ng.mmol creatinine $^{-1}$ from baseline to after EVH following placebo (37±17 to 51 ±23 $p<0.001$), but not following terbutaline (36±14 to 40±18, $p=0.103$). The rise in 11β-$PGF_{2\alpha}$ post-EVH (14±14 vs 4±11) was significantly attenuated with terbutaline ($p<0.01$)
Conclusion: These data provide novel *in vivo* evidence of a mast cell stabilising effect of a single, therapeutic dose of terbutaline following bronchial provocation with EVH in athletes with EIB. The findings support the earlier proposal[1,2] that the concentration of β_2-adrenoceptor agonist achieved in the airway from a clinically recommended dose is sufficient to prevent the release of mast cell mediators and associated bronchoconstriction.
References: [1]Anderson et al., ANZ J Med, 1975, 5, 544-550. [2]Anderson et al., Am Rev Respir Dis, 1976, 114, 493-500.
Key Words: mast cell, prostaglandin, terbutaline, eucapnic hyperpnoea