Title: Effects of long and short acting $\beta_2$-agonists on respiratory muscles during hypercapnia

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Body: Both short acting Salbutamol (Salb) and long acting Sameterol (Salm) $\beta_2$-agonists are widely used bronchodilators. Both significantly increase sniff nasal inspiratory pressure and inspiratory muscle EMG in humans (ERJ P2965,2003, P358s,2005). Do these $\beta_2$-agonists exert similar effects on expiratory muscles as on inspiratory muscles, during breathing? In 8 normal subjects, we inserted electrodes into parasternal intercostals (PARA) and transversus abdominis (TA) muscles using ultrasound. After baseline measurement, 20µg/min of Salb was administrated continuously in Salb group (n=4):, or 100µg of Salm was inhaled Salm group (n=4). Then, ventilation, as well as PARA and TA EMG were measured during resting and CO$_2$ stimulated breathing in both groups. Data was analyzed with and without $\beta_2$-agonist in four conditions (room air, Etco$_2$=50 Torr (CO$_2$Mild), 55 Torr (CO$_2$Mod) and 60 Torr (CO$_2$Hi)). Tidal EMG was expressed as percent maximum tidal EMG (%EMG$_{max}$). Compared to baseline, A) with Salb, 1) $V_T$ increased significantly in all conditions, and $V_t$ and $f$ increased significantly in CO$_2$Mod and CO$_2$Hi. 2) PARA EMG increased significantly in CO$_2$Mod and CO$_2$Hi, 3) TA EMG decreased significantly in CO$_2$Hi. B) with Salm, 1) $f$ and $V_t$ increased significantly in CO$_2$Hi, but $V_T$ did not increase in all conditions, 2) PARA EMG increased significantly in all conditions, 3) TA EMG did not change in all conditions. We conclude that during resting and CO$_2$ stimulated breathing $\beta_2$-agonists do affect both inspiratory and expiratory muscles, but there is a different effect on breathing pattern and muscle activation for short versus long acting $\beta_2$-agonists. This study was approved by Kitasato university human ethics committee.