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$\beta_2$ -Agonists and physical performance: a systematic review and meta-analysis of randomized controlled trials.

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Inhaled  $\beta_2$ -agonists are commonly used as bronchodilators in the treatment of asthma. Their use in athletes, however, is restricted by anti-doping regulations. Controversies remain as to whether healthy elite athletes who use bronchodilators may gain a competitive advantage. The aim of this systematic review and meta-analysis is to assess the effects of inhaled and systemic  $\beta_2$ -agonists on physical performance in healthy, non-asthmatic subjects. To this end, MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to August 2009. Reference lists were searched for additional relevant studies. The search criteria were for randomized controlled trials examining the effect of inhaled or systemic  $\beta_2$ -agonists on physical performance in healthy, non-asthmatic subjects. Two authors independently performed the selection of studies, data extraction and risk of bias assessment. Parallel-group and crossover trials were analysed separately. Mean difference (MD) and 95% confidence intervals were calculated for continuous data and, where possible, data were pooled using a fixed effects model. Twenty-six studies involving 403 participants (age range 7-30 years) compared inhaled  $\beta_2$ -agonists with placebo. No significant effect could be detected for inhaled  $\beta_2$ -agonists on maximal oxygen consumption ( $VO_2(\max)$ ) [MD  $-0.14 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ; 95% CI  $-1.07, 0.78$ ; 16 studies], endurance time to exhaustion at 105-110%  $VO_2(\max)$  (MD  $-1.5 \text{ s}$ ; 95% CI  $-15.6, 12.6$ ; four studies), 20-km time trial duration (MD  $-4.4 \text{ s}$ ; 95% CI  $-23.5, 14.7$ ; two studies), peak power (MD  $-0.14 \text{ W} \cdot \text{kg}^{-1}$ ; 95% CI  $-0.54, 0.27$ ; four studies) and total work during a 30-second Wingate test (MD  $0.80 \text{ J} \cdot \text{kg}^{-1}$ ; 95% CI  $-2.44, 4.05$ ; five studies). Thirteen studies involving 172 participants (age range 7-22 years) compared systemic  $\beta_2$ -agonists with placebo, with 12 studies involving oral and one study involving intravenous salbutamol. A significant effect was detected for systemic  $\beta_2$ -agonists on endurance time to exhaustion at 80-85%  $VO_2(\max)$  (MD  $402 \text{ s}$ ; 95% CI  $34, 770$ ; two studies), but not for  $VO_2(\max)$  (placebo  $42.5 \pm 1.7 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ , salbutamol  $42.1 \pm 2.9 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ , one study), endurance time to exhaustion at 70%  $VO_2(\max)$  (MD  $400 \text{ s}$ ; 95% CI  $-408, 1208$ ; one study) or power output at 90%  $VO_2(\max)$  (placebo  $234.9 \pm 16 \text{ W}$ , salbutamol  $235.5 \pm 18.1 \text{ W}$ , one study). A significant effect was shown for systemic  $\beta_2$ -agonists on peak power (MD  $0.91 \text{ W} \cdot \text{kg}^{-1}$ ; 95% CI  $0.25, 1.57$ ; four studies), but not on total work (MD  $7.8 \text{ J} \cdot \text{kg}^{-1}$ ; 95% CI  $-3.3, 18.9$ ; four studies) during a 30-second Wingate test. There were no randomized controlled trials assessing the effects of systemic formoterol, salmeterol or terbutaline on physical performance. In conclusion, no significant effects were detected for inhaled  $\beta_2$ -agonists on endurance, strength or sprint performance in healthy athletes. There is some evidence indicating that systemic  $\beta_2$ -agonists may have a positive effect on physical performance in healthy subjects, but the evidence base is weak.

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