

***“Long-term effects of Beta2-agonists on skeletal muscle characteristics, hypertrophy and exercise performance in healthy trained males and elite athletes”***

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**Project overview**

Elite athletes have a high prevalence of asthma and asthma-like symptoms as well as a high use of anti-asthmatic therapy. Salbutamol and salmeterol, has been removed from the prohibited list and these drugs can now be used more freely, also by athletes with asthma-like symptoms only. Performance enhancing effects of beta2-agonists are, though, to some degree contradictory, and the scientific problems concerning beta2-agonists are as follows:

1. A recent systemic review by Pluim et al (2011), they points out that the current literature concerning possible performance enhancing effects of systemic beta2-agonists is weak and calls for future studies with the use of more reliable, valid and sensitive performance protocols.
2. Furthermore, Pluim et al (2011) showed that the training level of the participants in the salbutamol studies have been low to moderate, which is not representative for elite athletes.
3. In another recent review, Collomp et al (2010), reports that no studies, has thoroughly investigated the ergogenic effects of terbutaline after oral administration, neither on exercise performance nor on metabolic parameters and body composition.

**Hypothesis:**

Beta2-agonists have acute and chronic intracellular actions on skeletal muscle in animal studies, which could take place in human skeletal muscles as well, and by that induce 1) muscle strength and performance, and 2) increase volume of the muscles.

The therapeutic doses used in most former studies might have been too low to induce performance-enhancing action, whereas multi-pharmacy with the use of maximal allowed doses of each of the beta2-agonists might have additive effect. Acute use of mixed Beta2-agonists may enhance exercise performance in elite athletes.

**Aim:**

The aim is therefore to investigate acute, as well as, chronic effects of daily Beta2-agonists use on skeletal muscle hypertrophy, muscle fiber characteristics, intracellular adaptations and exercise performance in healthy trained and elite trained athletes.

## Results and Conclusions

The primary purpose of the project was to investigate acute and chronic effects of beta2-agonists in skeletal muscle and on performance in healthy trained men. We observed that acute combined inhalation of salbutamol, salmeterol and formoterol, within the current therapeutic dosing limits, enhanced arm ergometer performance and muscle strength, but not swim endurance performance, in elite swimmers. Furthermore, we observed that acute systemic beta2-agonist treatment with terbutaline augmented ion handling of skeletal muscle, which was associated with an enhancement in knee-extensor exercise performance. We also observed that acute systemic beta2-agonist treatment with salbutamol modified expression of genes involved in growth of skeletal muscle in recovery from resistance exercise. When administered chronically, treatment with terbutaline and salbutamol augmented the hypertrophic response to 4 and 11 weeks of resistance training, respectively. However, the larger gains in muscle mass induced by these beta2-agonists did not translate into any superior improvements in muscle strength compared to resistance training with placebo. In fact, chronic beta2-agonist treatment repressed maximal oxygen consumption (VO<sub>2</sub>max) relative to lean body mass. Muscle fiber-type distribution shifted towards a fast-twitch phenotype with salbutamol treatment, while no significant change was observed for terbutaline. In conclusion, our observations support the restriction towards systemic administration of beta2-agonists on the prohibited list. Our data also suggest that a therapeutic dosing limit should be introduced for terbutaline. Combined inhalation of several beta2-agonists may also be of concern, at least during competitions of short and intense duration.