

Project Review

“The impact of gender, race and hydration status on the ergogenic and pharmacokinetic impact of short acting β 2-Agonists”

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In 2002 The International Olympic Committee (IOC) established the requirement for athletes to present evidence of current asthma, exercise induced asthma (EIA), exercise-induced bronchoconstriction (EIB) or airway hyperresponsiveness (AHR) through the therapeutic use exemptions (TUE) process. The World Anti-Doping Agency (WADA) introduced the IOC policy on inhaled short acting 2-agonists in January, 2009. The inclusion of inhaled short acting 2-agonists is based upon health concerns rather than anti-doping concerns; however, evidence is only available for the performance enhancing effect of inhaled short acting 2-agonists in endurance sports at low doses.

The initial aim of this study is to examine the impact of inhaled short acting 2-agonists on team game performance and examine higher doses that remain within The WADA anti-doping upper limit. Hydration status has recently been used in the defence of a positive anti-doping test. This has highlighted the lack of knowledge associated with potential confounding factors affecting urine analysis for short acting 2-agonists.

The second aim of this study is to examine the impact of gender, race and hydration status on urine concentrations of short acting 2-agonists at varying doses. The results of these studies will improve our understanding of the impact of inhaled short acting 2-agonists on performance, support The WADA in the implementation of regulations on the use of inhaled short acting 2-agonist and assist in the resolution of contested doping violations.

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Results and Conclusion:

Part A: Seven male runners (mean \pm SD; age 22.4 \pm 4.3 years; height 179.7 \pm 7.0 cm; body mass 76.6 \pm 8.6 kg) completed 6, 5 km running time-trials (3 in a temperate environment: 20°C, 40% RH; and 3 in a hot environment: 30°C, 40% RH) following the inhalation of 800 μ g or 1600 μ g of Salbutamol, or a placebo.

This is the first study to examine the impact of inhaled salbutamol at a dose 1600 μ g versus 800 μ g and placebo on time-trial endurance running performance. Furthermore, this study is the first to examine the pharmacokinetics of inhaled salbutamol at a dose of 1600 μ g and 800 μ g following a competitive endurance performance in temperate (20°C; 40% RH) and hot (30°C; 40% RH) environments. Results demonstrate no significant effect of Salbutamol on 5 km running time-trial performance in temperate or hot environments. Urine concentration of Salbutamol was below the WADA upper limit (1000 μ g.ml⁻¹) in all participants across all trials with the exception of one participant in the 1600 μ g, hot trial (below the decision limit). The results of this study suggest that the current WADA guidelines, which allows athletes to inhale up to 1600 μ g of Salbutamol is sufficient to avoid pharmaceutical induced performance enhancement. However, such high doses not only suggest poor management of asthma but also mean that an athlete may be at risk of contravening the current urinary threshold, particularly in hot environments.

Part B: Eighteen male and 14 female athletes (9 Caucasian males, 9 Caucasian Females, 2 Afro-Caribbean males, 2 Afro-Caribbean females, 6 Asian [Indian sub-continent] males and 4 Asian females) were recruited for this study. Participants were required to exercise in a hot, controlled environment (35°C, 40% relative humidity) at a self-selected pace until a target weight loss (2% or 5%) was achieved in the following trials: (i) 2% reduction in in body mass (BM), following inhalation of 800 μ g short acting β 2-agonist; (ii) 2% reduction in in BM, following inhalation of 1600 μ g short acting β 2-agonist; (iii) 5% reduction in in BM, following inhalation of 800 μ g short acting β 2-agonist; (iv) 5% reduction in in BM, following inhalation of 1600 μ g short acting β 2-agonist. The results of this study demonstrate that following the inhalation of 1600 μ g it is possible to present with urine Salbutamol concentrations above the current WADA limit (1000 ng.ml⁻¹) and decision limit (1200 ng.ml⁻¹) for salbutamol resulting in an adverse analytical finding (AAF; WADA, 2010) and warrant further investigation. There were no differences according to sex or ethnic origin however; a large inter-individual variation existed. In conclusion, a BM loss greater than 2% concomitant to the acute inhalation of 1600 μ g of Salbutamol may result in a urine concentration above the current WADA upper limit and decision limit leading to a positive test finding. This finding is independent of gender or ethnic origin. Hydration status per se is a critical factor in relation to doping control. The results of this study suggest that WADA consider the role of normalising drug concentrations to urine specific

gravity in an attempt to negate the impact of hydration status on doping control tests. Data from this study will assist WADA in the implementation of regulations on the use of inhaled short acting β 2-agonist and assist in the resolution of contested doping violations.

Part C: Seven male (mean + SD; age 23.1 + 3.9 years; weight 72.9 + 4.3 kg; height 177.0 + 4.7 cm) and six female (21.3 + 1.4 years; 63.9 + 5.8 kg; height 162.3 + 4.7 cm) football players completed a 52 minute football specific running protocol followed by twelve, 17.5 m sprints on three occasions following the inhalation of 800 μ g or 1600 μ g of Salbutamol, or a placebo.

This is the first study to examine the impact of inhaled salbutamol at a dose of 1600 μ g versus 800 μ g and a placebo on simulated association football (soccer) and multiple sprint performance in male and female players. Furthermore, this study is the first to examine the pharmacokinetics of inhaled salbutamol at a dose 1600 μ g and 800 μ g following a simulated association football performance in male and female players. Results demonstrated no significant effect of high dose (up to 1600 μ g) Salbutamol on association football (soccer) specific performance or multi-sprint performance in male or female players. Following inhalation of 1600 μ g of Salbutamol, Five players (2 male; 3 female) presented with concentrations of Salbutamol in urine above the WADA upper limit (1000 ng.ml⁻¹) with three players (1 male; 2 female) attaining a concentration above the decision limit (1200 ng.ml⁻¹). The results of this study suggest that the current WADA guidelines, which allows athletes to inhale up to 1600 μ g of Salbutamol is sufficient to avoid pharmaceutical induced performance enhancement in association football (soccer) in male and female players. However, inhalation of 1600 μ g may result in a urine concentration above the current WADA upper limit and decision limit.