PROJECT REVIEW

"*Characterization and detection of prolonged Endothelin receptors antagonists administration*"

Dr. Ostojic, (Metropolitan University, Serbia)

Endothelin receptors antagonists (ERA), such as bosentan and ambrisentan, are a class of vasoactive drugs that have been developed for the treatment of pulmonary arterial hypertension. It has been anecdotally reported that ERA is frequently used among top-level athletes to counteract exercise-induced rise in pulmonary vascular pressures and increase exercise performance. Yet, the effects of ERA on exercise capacity in healthy humans are puzzling, with the drugs not included in the current Prohibited List, since the ergogenic potential is yet to be fully understood and determined. Furthermore, the urinary excretion of ERA metabolites following administration has not been studied systematically at rest and during exercise in athletes, as a way to detect its intake if performance-enhancing potential is confirmed. In the planned study ERA will be administered in newly approved doses for 8 weeks in order to assess the presumed doping potential for both male and female athletes, and to monitor serum and urinary ERA excretion dynamics after single- and multiple-dose administration. The possible effects of prolonged ERA administration in higher doses on exercise performance may be relevant, if further confirmed, in terms of their possible fraudulent utilization to influence exercise performance in sports, raising the difficult question of whether, particularly in some circumstances, the ERA might be considered as prohibited substances in athletes.

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Results and Conclusion

Endothelin receptors antagonists (ERA) are a class of vasoactive drugs that have been developed for the treatment of pulmonary arterial hypertension (PAH). The use of ERA among athletes to counteract exercise-induced rise in pulmonary vascular pressures and increase exercise performance is rather unexplored and data on efficacy and safety are limited. In particular, an increase of maximal oxygen consumption after ERA administration can be regarded as critical and should be evaluated.

The present study evaluated the effects of orally administered selective (bosentan) and non-selective ERA (ambrisentan) on aerobic and anaerobic performance, serum and urine biochemical outcomes, and the occurrence of adverse events during the intervention in healthy humans. Thirty male and female volunteers were randomized in a double-blind design to receive bosentan (250 mg daily), ambrisentan (10 mg per day) or placebo by oral administration for 8 weeks. Treatment with two different oral doses of ERA for 8 weeks had no major effect on body composition, strength, aerobic and anaerobic performance indicators and hormone profiles in physically active men and women as compared to placebo ($p > 0.05$). Serum hepatic enzymes increased significantly from before to after administration in both ERA groups ($P < 0.001$).

The proportion of participants who reported minor adverse events was similar in all intervention groups. These preliminary data suggest that 8-week oral administration of ERA is ineffective for exercise performance enhancement in healthy men and women, with significant effect on liver enzyme efflux and minimal incidence of reported side-effects.