
“Is tramadol a Performance Enhancing Drug?”

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PROJECT OVERVIEW

Tramadol is potent narcotic analgesic that acts on the opioid system. Data from the WADA Monitoring Programme and from athlete testimonies suggest that this drug is used across multiple sports in order to reduce exertional pain and allow the athlete to work even harder. In doing so, it is likely that tramadol is being used to provide the athlete with a performance advantage. However, there is currently no convincing research evidence to support or reject whether tramadol is performance enhancing in highly trained, healthy athletes. This project will employ an experimental design that focuses purely on the question of whether tramadol allows athletes to work harder by reducing pain, and thus allow for a better performance. Therefore, the main outcome of this project will be to provide robust experimental evidence to inform whether the use of tramadol in competition should be regulated. Thirty highly trained road racing cyclists will be recruited for this study, as the efficacy of performance enhancing interventions vary according to athletic ability. In a randomized, controlled, double-blinded crossover design, these cyclists will complete a laboratory cycling task that replicates the time/intensity demands of professional road cycling following the ingestion of tramadol or a placebo. The cycling task will involve fixed intensity and self-paced time trial cycling, amounting to approximately 1.5 hours of hard cycling. The intensity/time of the task is critical, as the ergogenic effects of tramadol are likely to be reduced in shorter duration exercise that induces less fatigue, and is therefore not representative of the context in which it is purportedly taken. Exercise performance (completion time) and perceptual responses (perceived pain and effort) will be compared between conditions, with results used to inform consultation with WADA regarding the S7 Narcotics category of the Prohibited List.

RESULTS AND CONCLUSIONS

Tramadol is a potent narcotic analgesic that acts on the opioid system. Data from the World Anti-Doping Agency (WADA) Monitoring Programme suggest tramadol use in sport is highly prevalent, and several other sources suggest it is used to reduce exertional pain and confer a performance advantage. However, it is not included in WADA's Prohibited List. This study sought to identify whether tramadol enhances performance in time trial cycling.

The funding decision for the current study was made in October 2019, and the project started in March 2020. The Covid-19 pandemic started in the UK some 2-weeks after the project started and had a significant impact on the project duration and the ability to recruit and retain participants. As a result, the study was extended beyond its original time scale.

Twenty-seven highly trained cyclists (Age = 33 ± 10 years; stature = 180 ± 7 cm; mass = 77.9 ± 11.3 kg; $VO_2\max$ = 4.5 ± 0.5 L/min; Peak power output = 439 ± 56 W) were screened for tramadol sensitivity through an online interview, and then attended the

laboratory across three visits. The first visit identified VO_{2max} , Peak Power Output and Gas Exchange Threshold through a Graded Exercise Test. Following this visit, participants returned to the laboratory on two further occasions to undertake cycling performance tests following the ingestion of either 100 mg of soluble tramadol (as 2x50 mg Zydol® tablets) or a taste-matched placebo control in a double-blind, randomised, and cross-over design. The performance tests required participants to complete a 30 min non-exhaustive fixed intensity cycling task at a Heavy exercise intensity, immediately followed by a competitive self-paced 25-mile time trial (TT). Data from two participants were not included in the analysis as they were classified as outliers (i.e. difference in completion time between the two conditions was greater than 2 standard deviations outside of the mean of the group). Participants completed the TT significantly faster ($t_{24} = 2.71$, $p=0.012$, $95\%CI_{diff} = 12.11 - 89.23$, $d = 0.54$) in the tramadol condition (3758 s \pm 232 s) compared to the placebo condition (3808 s \pm 248 s). Twenty of the twenty-five participants produced faster TT completion times in the tramadol condition.

In the current group of cyclists, the 1.3% faster time in the tramadol condition could confer a performance advantage sufficient to change the medalling positions. The data from this study suggests that tramadol is a performance enhancing drug in time trial cycling. Given the prevalence of use of tramadol in sport, and that there is data to suggest it is frequently being taken with the intention of improving performance, there is now strong evidence to warrant tramadol being placed on the Prohibited Substance List.

PUBLICATIONS/PROCEEDINGS

Data from the interim analysis of this study (n=21) was presented at the British Association of Sport and Exercise Medicine (BASEM) Conference in May 2022 (https://basem.co.uk/wp-content/uploads/2022/08/Mauger_BASEM-Abstract.pdf).

The conference abstract will be published in the British Journal of Sports Medicine in 2023.

- Mauger A.R, Thomas T, Smith S, Fennell C. (2022). Is tramadol a performance enhancing drug? A randomised controlled trial. *British Association of Sport and Exercise Medicine Conference*, Brighton, UK.