The Distribution of Oxazepam and Oxazepam Glucuronide in Body Fluids After a Single Dose of Oxazepam and the Influence on Four Standardized Field Sobriety Tests

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BACKGROUND AND OBJECTIVES: In the Netherlands, oxazepam is the most frequently prescribed benzodiazepine. Driving under the influence of oxazepam may be a public health problem. Determination of the time windows of detection of oxazepam and its metabolite in blood, serum and oral fluid is needed in order to study the feasibility to establish legal limits. The aims of this study are to determine the concentration-time profile of oxazepam and its metabolite in oral fluid, to relate this to the blood and serum profiles and to explore the dose-performance relationship of oxazepam in four standardized field sobriety tests.

STUDY DESIGN: Eight healthy male volunteers completed a double blind crossover study. The subjects received in random order 15 mg and 30 mg oxazepam orally, on 2 days separated by 1 week in order to exclude carry-over effects.

METHODS: Blood (B), serum (S) and oral fluid (OF) samples were collected up to 8.5 h (blood, serum) or up to 48 h (oral fluid) after administration and assayed for concentrations of oxazepam and oxazepam glucuronide. The concentration-time profiles in serum, whole blood and oral fluid were fitted by using MwPharm® 3.50. Four standardized field sobriety tests were performed in order to study the relation between dose and performance. Before intake of oxazepam, a blood and oral fluid sample were taken and the tests were performed to establish pre-drug values.

RESULTS: Concentrations of oxazepam in blood and serum were comparable (mean ratio B/S = 0.90; range 0.83 - 0.97). Concentrations of oxazepam in oral fluid were low: the mean OF/B ratio was 0.05 (range 0.04 - 0.07) and the mean OF/S ratio was 0.04 (range 0.03 - 0.07). Concentrations of oxazepam glucuronide were higher in serum than in blood (mean ratio B/S = 0.64; range 0.46 - 0.81). Concentrations of oxazepam glucuronide in oral fluid were very low: the mean OF/B ratio was 0.004 (range 0.002 - 0.006) and the mean OF/S ratio was 0.002 (range 0.001 - 0.004). Influence of the single doses of oxazepam on the Walk and Turn Test, One Leg Stand Test, Finger to Nose Test and the Romberg Test tests was not entirely elucidated, due to possible interfering factors (e.g. practice, fatigue early in the morning) and the unknown sensitivity of the tests for oxazepam.

CONCLUSIONS: In oral fluid, both oxazepam and oxazepam glucuronide were detected. Oral fluid was tested positive for oxazepam at least 8.5 hours after intake of a single dose of 15 or 30 mg oxazepam. The window of detection of oxazepam glucuronide depended very much on the analytical detection limit and could not be established in all cases. The concentration-time profiles of oxazepam in oral fluid ran parallel to those in blood and serum. The presence of oxazepam in oral fluid is probably a good indicator of recent use and may be indicative of driving under the influence.

More research (e.g. laboratory tests, driving tests) has to be done to explore the concentration-impairment relation.

Keywords: Oxazepam, Pharmacokinetics, Performance tests