Urinary elimination of 11-nor-9-carboxy-delta 9-tetrahydro-cannabinol (CTHC) after its intravenous application

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AIMS: Urinary excretion profiles of free and conjugated (glucuronidated) 11-nor-9-carboxy-delta-9-tetrahydrocannabinol (CTHC), a major metabolite of delta-9-tetrahydrocannabinol (THC) in urine are commonly used for estimation of marihuana consumption behaviour. But the pharmacokinetic knowledge about this metabolic compound is still inadequate. The focus of this study was to investigate the "pure" renal excretion of free and conjugated CTHC without the involvement of the parent compound THC.

METHODS: Urinary excretion of CTHC in absence of the precursor delta-9-tetrahydrocannabinol (THC) was studied after intravenous (i.v.) application of 5 mg CTHC to 10 healthy, male non-users. Urine specimens were collected over a period of 96 hours. All samples were extracted before and after alkaline deglucuronidation and were analysed using gaschromatography-mass-spectrometry (GC/MS).

RESULTS: Expectedly, excretion rate of unconjugated CTHC in urine was below 0.5 %. Surprisingly, summated excretion rate of free and conjugated (glucuronidated) CTHC recovered in urine was variable and only between 3 and 11 % (mean: 339.1 ± 122.6 µg, range: 151.8 µg – 569.3 µg), with no correlation between serum AUC and totally excreted amounts. No relevant individual variations were seen in distribution and elimination of CTHC in serum in the present study. Similar AUCs of CTHC-Glucuronide (CTHC-Glu) indicate that, after glucuronidation of administered CTHC, a relatively constant portion of CTHC-Glu reaches the bloodstream. But only a small and variable portion of injected dose was excreted in urine until 96 hours.

CONCLUSIONS: Therefore renal excretion profiles of CTHC may have less significance in estimation of marihuana abuse than expected. Hence faecal excretion and possible further metabolic breakdown seem to determine the elimination of CTHC. As a consequence the metabolic splitting ratio between renal and faecal excretion including possible deconjugation of CTHC-Glu in faeces and entero-hepatic circulation might have relevant influences on the individually cumulated CTHC concentrations in serum and urine. Differences in ratio between excretion pathways could possibly explain inter individual variations in CTHC concentration profiles of previous studies and of practical cases. The preferred excretion pathway (renal or faecal) might be even diet-related.

KEYWORDS: *Pharmacokinetic, Renal excretion, CTHC*

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