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Can we obtain information from urine about recent cannabis consumption in DUID cases?

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Abstract

Aim: The nonlinear elimination rate of THC and metabolites in blood complicates the interpretation of last cannabis use, which is an important information in DUID cases. We evaluated cannabinoids in blood and hydrolysed urine from 50 DUID cases in order to gain additional information about last cannabis use.

Methods: THC, THC-OH and THC-COOH were analysed in blood and hydrolysed urine (β-glucuronidase) by GC-MS-MS. Cannabinoid concentrations in blood and urine were compared. Mann-Whitney-U-Tests were performed to investigate differences between cannabinoid concentrations from recent and older cannabis intake. Blood/urine cannabinoid concentrations of admitted chronic users were compared to occasional users. An approach for cluster analysis is presented.

Results: Cannabinoid concentration in blood and urine were strongly correlated. Blood and urine cannabinoid concentrations from recent cannabis consumers differed significantly from the rest of the test group. No difference in blood/urine concentration was found between chronic and occasional users. Results of a cluster analysis approach were promising.

Conclusion: In individual cases, an interpretation of last cannabis use is only possible by approximation. However, multivariate data analysis of cannabinoid concentration might facilitate the detection of recent cannabis intake.

1. Introduction

Cannabis consumption is the most frequent illicit drug use in Swiss DUID (driving under the influence of drugs) cases. A legal limit of 1.5 µg/L in whole blood is set to prove incapacity of driving. However, this blood concentration does not give evidence of the interval between cannabis intake and police control. The determination of recent cannabis consumption is complicated by the nonlinear elimination rate of cannabinoids in blood.

This study focussed on the analysis of cannabinoids in urine in order to gain more information about the time of last consumption. Concerning driving ability, this question is of great importance. A short time interval between cannabis use and driving as well as chronic cannabis use is incompatible with driving ability due to the missing separation of recreational use of cannabis and driving.

2. Material and Methods

50 randomly selected cases (88% male, 12% female) from our in-house DUID routine work were set as database. THC, THC-OH and THC-COOH were analysed both in whole blood and hydrolysed urine. Hydrolysis was performed with β-glucuronidase at 37 °C for 16 h.

2.1. Exclusion of Datasets

Information about last cannabis use and consumption habits was gained from both the police report and the report of medical examination. As people controlled by the police do not necessarily tell the truth about their drug consumption habits, several data had to be excluded. First, self-incriminating statements about recent consumption (< 5 h between consumption and blood sampling) were considered as true. Data were excluded if declarations to the police and the medical staff were inconsistent. In case of observed drug symptoms specified in the police report and the report of medical examination a recent cannabis use was suggested. Here, data were excluded if the interval of last cannabis use was declared to be long time ago. If cannabis smell or joint stubs were detected by policemen, recent cannabis consumption was assumed (< 5 h interval). Furthermore, people with declared chronic cannabis use were excluded from the study due to different elimination rates and blood concentrations of cannabinoids in chronic users [2].

For most analyses, the following two subject groups were defined. Group "<5 h" contained all subjects with an admitted recent cannabis consumption of less than 5 hours between intake and blood sampling. Group "> 5 h" comprised the rest of the subjects.

2.2. Forensic Toxicological Analyses

After precipitation of 1 g of hydrolysed urine (0.5 g of whole blood respectively) with acetonitrile, THC and its metabolites THC-OH and THC-COOH were analysed with an online GC-MS/MS system (Trace GC plus, TSQ Quantum XLS, Thermo Scientific, USA) in selected reaction monitoring (SRM) mode after extraction on a fully automated SPE sample preparation system (MPS II, Gerstel, Germany) and derivatisation with MSTFA. Deuterated analogues were used as internal standards. Limit of detection (LOD) was 0.2 µg/L for THC and THC-OH, and 2 µg/L for THC-COOH. 0.3 µg/L (THC, THC-OH) and 3 µg/L (THC-COOH) were determined as limit of quantification (LOQ). This method is validated and accredited for the analysis of cannabinoids in whole blood and urine at our institute.

2.3. Statistical Analyses

Urine cannabinoid concentrations were normalised to creatinine concentration following equation 1 [4]:

$$\frac{\text{drug concentration in urine (µg/L)}}{\text{creatinine concentration in urine (mmol/L)}} = \frac{\text{drug (µg)}}{\text{creatinine (mmol)}}$$

The cannabinoids in the datasets "blood" and "urine" were compared by a linear regression. A nonparametric Mann-Whitney-U-Test was performed to test the independence of the subject groups "recent consumption < 5h" and "consumption > 5 h". The independence of the subject groups "chronic user" and "occasional user" was determined by a Mann-Whitney-U-Test. Here, data from recent consumers were disregarded. Finally a visual approach for multivariate data analysis was shown.

3. Results and Discussion

Datasets of 28 DUID cases were left after the exclusion of obviously unreliable statements about last consumption and exclusion of admitted chronic users. This dataset was used for all the analyses except the test of independence of chronic user vs. occasional users. The linear regression analysis showed a distinct correlation in all analytes (Fig. 1). An outlier in the

THC-OH dataset was excluded. The strongest correlation was found for THC-COOH (R^2 = 0.78), THC and THC-OH showed an R^2 of 0.57.

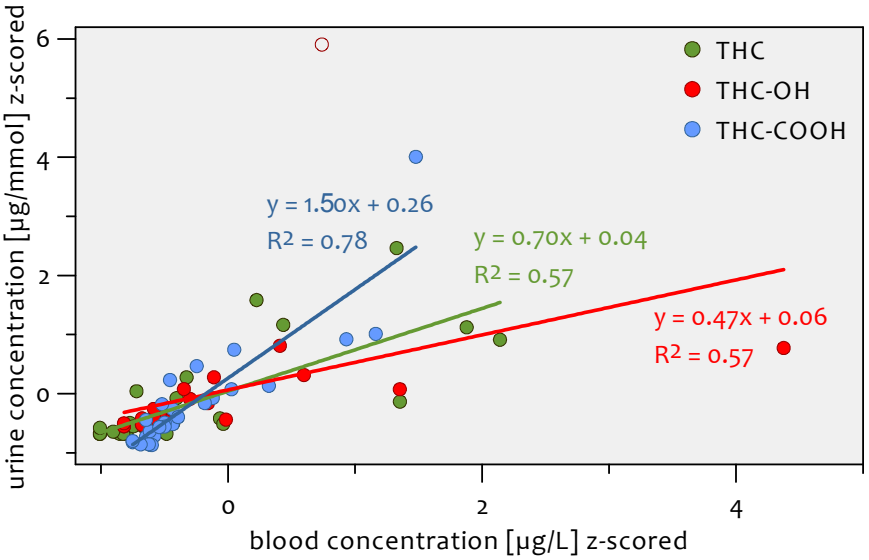

Fig. 1. Regression analysis of cannabinoids in blood and urine.

The results of a Mann-Whitney-U-Test for independence in the test groups "< 5 h" and "> 5 h" are shown in Fig. 2. For all analytes except THC in urine, the variation of cannabinoid concentrations in blood and urine is higher in group "< 5 h". Cannabinoid concentrations of recent users are significantly different from the other subject group. A significance level of 95% was applied for all analyses. For THC and THC-OH in blood the difference of the subject groups was significantly stronger.

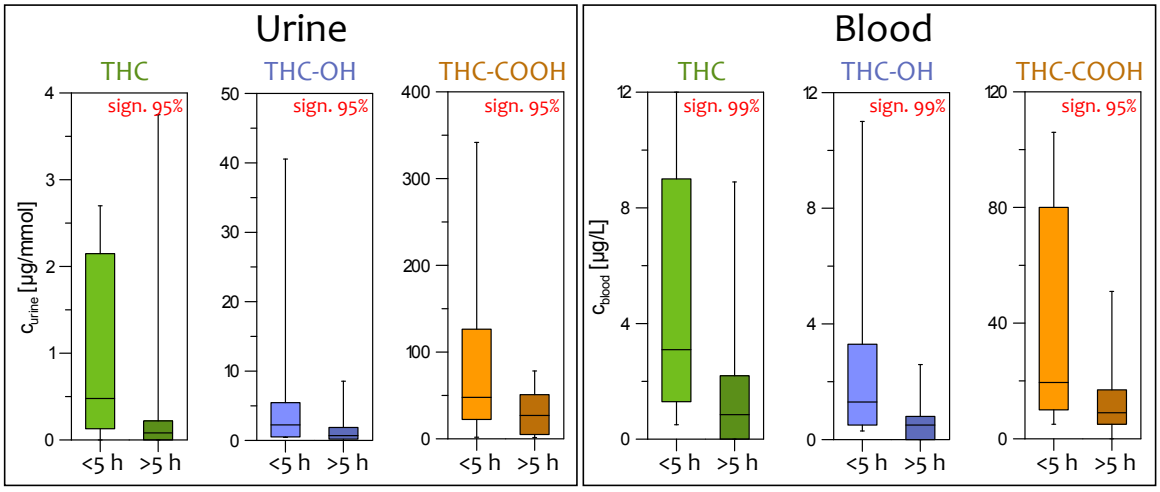

Fig. 2. Mann-Whitney-U-Test for independence of subject groups "<5 h" and "> 5 h".

A second independence test investigated the difference between cannabinoid concentrations in chronic and occasional users. Self admitted chronic users (consumption several times per week) with an interval of minimum 5 hours between cannabis intake and blood sampling were compared to the occasional cannabis users (interval > 5 h). Tab. 1 summarises the results from the independence test. Surprisingly, the subject groups do not differ significantly. A marginal significance is found for THC-OH in urine. These findings are contradicting the literature and can be explained by the experiment set-up. The occurrence of chronic users in the dataset with no admitted chronic cannabis use is reasonable.

Tab. 1. Test for independence between chronic and occasional users

p-value	THC	THC-OH	THC-COOH
Blood	0.16	0.16	0.07
Urine	0.16	**0.02**	0.20

Finally, a visual multivariate approach showed some interesting results. Plotting cannabinoid urine concentrations in a 3D coordinate system resulted in a delimitable cluster comprising only recent cannabis users. In the present study, 50% of the recent cannabis users fall into this cluster. For a statistical investigation a larger database would be needed. However, the verification of this hypothesis could ease the detection of recent cannabis consumption in parts of DUID cases.

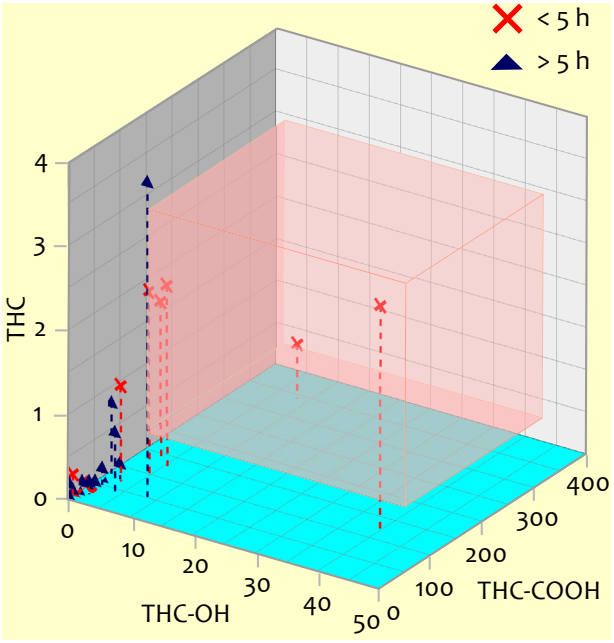

Figure 3: Multivariate approach with cannabinoid urine concentrations (mmol/L).

4. Conclusions

We found a distinct correlation between cannabinoids in blood and urine. Cannabinoid concentrations in blood and urine of recent cannabis users differ significantly from the rest of the subject group. Unfortunately, these findings can not be applied to individual cases and interpretation of the toxicological results has to be based on known controlled studies such as [1] or [3]. A multivariate approach with a larger subject group could give evidence on a clustering of urine and blood concentrations of recent users. Within this study no additional information in urine cannabinoid concentration was found to determine last cannabis use.

5. References

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