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Forensic Science International 153 (2005) 11–15
Forensic Science International
www.elsevier.com/locate/forsciint

Concentration of drugs in blood of suspected impaired drivers

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Available online 31 May 2005

Abstract

Analytical records concerning 440 living drivers suspected of driving under the influence of drug (DUID) were collected and examined during a 2 years period ranging from 2002 to 2003 in canton de Vaud, Valais, Jura and Fribourg (Switzerland). This study included 400 men (91%) and 40 women (9%). The average age of the drivers was 28 ± 10 years (minimum 16 and maximum 81). One or more psychoactive drugs were found in 89% of blood samples. Half of cases (223 of 440, 50.7%) involved consumption of mixtures (from 2 to 6) of psychoactive drugs. The most commonly detected drugs in whole blood were cannabinoids (59%), ethanol (46%), benzodiazepines (13%), cocaine (13%), amphetamines (9%), opiates (9%) and methadone (7%). Among these 440 cases, 11-carboxy-THC (THCCOOH) was found in 59% (median 25 ng/ml (1–215 ng/ml)), Δ^9-tetrahydrocannabinol (THC) in 53% (median 3 ng/ml (1–35 ng/ml)), ethanol in 46% (median 1.19 g/kg (0.14–2.95 g/kg)), benzoylecgonine in 13% (median 250 ng/ml (29–2430 ng/ml)), free morphine in 7% (median 10 ng/ml (1–111 ng/ml)), methadone in 7% (median 110 ng/ml (27–850 ng/ml)), 3,4-methylenedioxymethamphetamine (MDMA) in 6% (median 218 ng/ml (10–2480 ng/ml)), nordiazepam in 5% (median 305 ng/ml (30–1560 ng/ml)), free codeine in 5% (median 5 ng/ml (1–13 ng/ml)), midazolam in 5% (median 44 ng/ml (20–250 ng/ml)), cocaine in 5% (median 50 ng/ml (15–560 ng/ml)), amphetamine in 4% (median 54 ng/ml (10–183 ng/ml)), diazepam in 2% (median 200 ng/ml (80–630 ng/ml)) and oxazepam in 2% (median 230 ng/ml (165–3830 ng/ml)). Other drugs, such as lorazepam, zolpidem, mirtazapine, methaqualone, were found in less than 1% of the cases.

Keywords: Driving under the influence of drugs (DUID); Drugs; Alcohol

1. Introduction

For several years, it has been established that psychoactive drugs may impair driving skills by affecting alertness, visual acuity, reaction time, judgment and decision making and so on [1]. Yet, several recent studies have concluded that drug use and multiple drugs use increased the risk for a road trauma accident [2,3]. Blood has been undoubtedly considered to be one of the most suitable specimens for the evaluation of driving impairment due to drug consumption [4]. In January 2005, a new zero-tolerance law involving that the presence of scheduled drugs in blood (amphetamine, methamphetamine, 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylenedioxyethylamphetamine (MDE), cocaine, free morphine and Δ^9-tetrahydrocannabinol (THC)) is sufficient for prosecution, regardless of whether the driving capacity of the person is impaired, will be introduced in Switzerland. Moreover, the legal limit for the blood alcohol concentration will be reduced from 0.8 to 0.5 g/kg.

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0379-0738/$ – see front matter
doi:10.1016/j.forsciint.2005.04.025

In order to gain more information about the type and the concentration of drugs used by drivers suspected of driving under the influence of drug (DUID) in canton de Vaud, Valais, Jura and Fribourg (Switzerland), 440 blood samples were analyzed.

2. Materials and methods

2.1. Selection of cases

All DUID cases submitted by the Justice in canton de Vaud, Valais, Fribourg and Jura (Switzerland) to our laboratories during a 2 years period ranging from 2002 to 2003 were considered. The police completed application forms for general information and the doctor for medical information. The following criteria were applied to select cases: (1) driver was still alive at least 24 h after the event; (2) DUID was supported by available documentation; (3) submitted specimens (blood and urine) were suitable for analysis.

2.2. Samples

Urine and blood samples collected by a doctor, were dispatched to the laboratory by post or by the police. Urine samples were collected into 250 ml polyethylene tubes (Semadeni AG, Ostermundigen, Switzerland) and blood samples were collected into 5 and/or 10 ml polystyrene Monovette® (Sarstedt, Geneva, Switzerland) containing potassium fluoride and EDTA as preservative and anticoagulant, respectively. Rapid analysis of blood and urine samples was completed within 1 month.

2.3. Analytical procedures

The analytical strategy was constituted of three steps: screenings in urine sample, identification of the drugs and characterization of the consumed substances and finally quantification of drugs in blood [5]. The following groups of drugs of abuse were screened by immunological tests in urine: amphetamines (cutoff: 1000 ng equivalent D-methamphetamine/ml), barbiturates (cutoff: 200 ng equivalent secobarbital/ml), benzodiazepines (cutoff: 200 ng equivalent lormetazepam/ml), buprenorphine (cutoff: 9.7 ng equivalent buprenorphine/ml), cannabinoids (cutoff: 50 ng equivalent THCCOOH/ml), cocaine (cutoff: 300 ng equivalent benzoylecgonine/ml), LSD (cutoff: 500 pg equivalent LSD/ml), methadone (cutoff: 300 ng equivalent methadone/ml) and opiates (cutoff: 300 ng equivalent morphine/ml) (radioimmunoassay RIA®, Count-A-Count®, DPC®, USA) (Syva EMIT® II Plus, Dade Behring, USA) (COBAS® INTEGRA, Roche Diagnostic). Additional screenings and identification analyses were performed in urine by GC–MS (Hewlett Packard (HP) 5890 II plus and HP MSD 5972). Screening was performed by liquid/liquid extraction procedures, GC–MS analyses and data comparison with mass spectra drug libraries. All positive results were confirmed and drugs were quantified in blood by GC–MS (Agilent 6890 and Agilent MSD 5973 (N)), GC–NPD (Agilent 6890N), GC–ECD (Agilent 6890N) and HPLC–DAD (Agilent 1100). HPLC–MS (Perkin-Elmer Series 200 and Applied Biosystems API 150 EX) was used for determination of opiates [6]. Blood alcohol quantification was performed by head-space (HP 7694) coupled with GC–FID (HP 5890 Series II). Blood sample was considered positive for a substance when the concentration of the substance measured into blood was equal or higher than the limit of quantification (LOQ) (Table 2).

3. Results

3.1. Characteristics of the drivers

The main characteristics of the drivers suspected of DUID in canton de Vaud, Valais, Jura and Fribourg (Switzerland) are presented in Table 1. The large majority were car drivers (384 of 440, 87.3%). Other vehicle types such as motorcycle, bicycle, moped and truck were comparatively rare (13 of 440, 2.9%). In 9.8% of cases (43 of 440), the

Table 1
Incidence of vehicle type, circumstances, gender and age among 440 drivers suspected of DUID during a 2 years period ranging from 2002 to 2003

Patterns	Number of drivers
Vehicle type	
Car	384 (87.3%)
Truck	1 (0.2%)
Motorcycle	8 (1.8%)
Bicycle/moped	4 (0.9%)
Unknown	43 (9.8%)
Circumstances[a]	
Accident	225 (51.1%)
Erratic driving	74 (16.8%)
Police control	117 (26.6%)
Dizziness	4 (0.9%)
Unknown	20 (4.5%)
Gender	
Male	400 (90.9%)
Female	40 (9.1%)
Age	
Mean (±S.D.)	28 (±10 years)
Mode	21 years ($n = 49$)
Range of variation	65 (16–81 years)

[a] Accident: policemen have to be brought in after vehicle crash; erratic driving: policemen have controlled the driver after observing uncertain and irregular attitude (zigzag, irregular speed, . . .); police control: the control could be either randomly performed or occurred during a roadblock; dizziness: policemen have to be brought in after that the driver pulled over because he felt dizzy; unknown: circumstances were not indicated on the form filled in by policemen.

Table 2
Number of positive cases, median and mean concentrations and ranges for the most frequent drugs detected in blood of 440 drivers suspected of DUID

Drug	LOQ[a] (ng/ml)	*N* (positive)	Median (ng/ml)	Mean (ng/ml)	Range (ng/ml)	5 percentile (ng/ml)	95 percentile (ng/ml)	25 percentile (ng/ml)	75 percentile (ng/ml)
THCCOOH	1	261	25	35	1–215	4	104	11	49
THC	1	234	3	5	1–35	1	13	2	6
Ethanol	0.10[b]	203	1.19[b]	1.28[b]	0.14–2.95[b]	0.36[b]	2.43[b]	0.80[b]	1.72[b]
Benzoylecgonine	20	55	250	515	29–2430	50	1734	65	800
Free morphine	1	32	10	19	1–111	5	81	5	19
Methadone	20	31	110	165	27–850	30	460	70	190
MDMA	10	28	218	388	10–2480	18	1098	92	510
Nordiazepam	20	24	305	492	30–1560	55	1496	133	781
Free codeine	1	21	5	5	1–13	1	11	3	5
Midazolam	20	21	44	56	20–250	20	100	20	70
Cocaine	10	20	50	109	15–560	24	218	50	153
Amphetamine	10	16	54	63	10–183	12	128	34	89
Diazepam	50	10	200	279	80–630	107	558	164	405
Oxazepam	150	10	230	614	165–3830	181	2305	200	320
Lorazepam	10	6	41	74	10–250	13	208	21	74
Zolpidem	50	5	340	396	216–600	232	586	295	530
Mirtazapine	50	5	65	91	50–180	50	166	50	110
Paroxetine	20	5	55	68	21–120	27	114	53	90
Tramadol	100	4	425	475	100–950	139	881	295	605
Methaqualone	100	3	720	1077	150–2360	207	2196	435	1540

[a] Limit of quantification.
[b] (g/kg).

vehicle type was not indicated. Accidents (225 of 440, 51.1%) and police controls (117 of 440, 26.6%) were the most frequent circumstances involving requests for toxicological analyses. Other circumstances, such as erratic driving (74 of 440, 16.8%) and dizziness (4 of 440, 0.9%) were seldom mentioned. In 4.5% of cases (20 of 440), no circumstances were indicated.

As observed in other studies, males (400 of 440, 90.9%) heavily predominated over females (40 of 440, 9.1%) [3,7]. The mean age of the drivers was 28 ± 10 (S.D.) years. Drivers younger than the mean age represented 60.9% of the population and drivers who were 21 years old included the mode age of the distribution (49 of 440, 11.1%). These results are in the same order of magnitude to those obtained some years ago in a similar study carried out in Switzerland [7].

3.2. Types of drugs

In 11.4% (50 of 440) of blood samples and 8.4% (37 of 440) of urine samples, neither drug nor alcohol was found. Among these drug-free cases, 35 (70%) and 28 (76%), respectively, were accidents, situations where the police or the judge asked routinely for toxicological analyses. Consequently, one or several groups of psychoactive drugs were found in 89% of blood samples.

In 38% (167 of 440) blood samples, one psychoactive drug group composed of the parent drug, metabolites and/or related compounds was found. Half of cases (223 of 440, 50.7%) involved consumption of mixtures (from 2 to 6) of psychoactive drugs. The most commonly detected substances in blood were cannabinoids (59%), ethanol (46%), benzodiazepines (13%), cocaine (13%), amphetamines (9%), opiates (9%) and methadone (7%) (Fig. 1). Other psychoactive substances such as zolpidem, mirtazapine, paroxetine, methaqualone or tramadol were only rarely detected (<2%).

3.3. Concentration of drugs in blood

The number of positive cases, the median, the mean, 25 and 75 percentile, 5 and 95 percentile, minimum and maximum concentrations and the range of concentration for the 20 most detected substances are presented in Table 2. The LOQ for those substances are also presented in Table 2.

4. Discussion

As observed in a previous study carried out in canton de Vaud some years ago [7], drugs and/or alcohol were found in the large majority of cases that involved police suspicion of drug or alcohol consumption. Conversely, it is not known whether many drugged drivers remained undetected. It could be reasonable to suppose that a certain number of drug-drivers were not discovered, as suggested by Lapham et al. [8].

Because cannabis and alcohol are the most common recreational drugs used in western countries among the

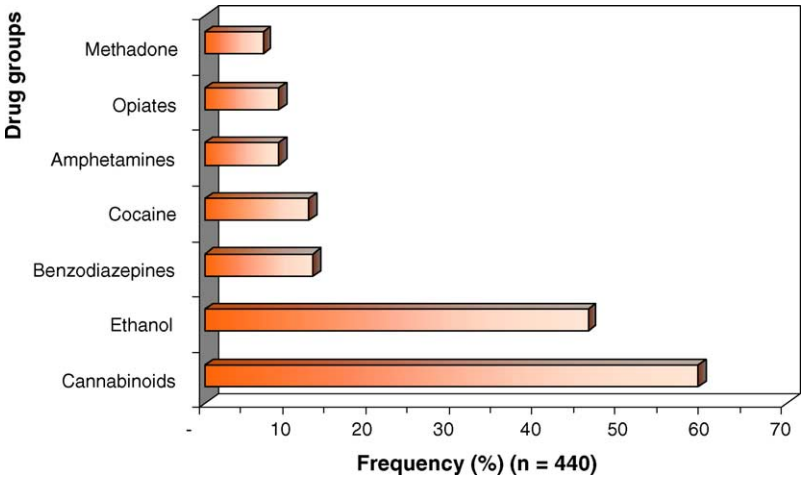

Fig. 1. Frequency of groups of psychoactive drugs detected in blood of 440 drivers suspected of driving under the influence of drugs (DUID) during a 2 years period ranging from 2002 to 2003. The most commonly detected substances in blood were cannabinoids (261 of 440, 59%), ethanol (203 of 440, 46%), benzodiazepines (57 of 440, 13%), cocaine (55 of 440, 13%), amphetamines (39 of 440, 9%), opiates (39, 9%) and methadone (31 of 440, 7%).

young population [9], it is not surprising that cannabinoids and ethanol appear to be the most frequent substances measured in the blood of drivers suspected of DUID.

THCCOOH was detected in 272 urine (62%) and in 261 blood samples (59%). THC was detected in 234 blood samples (53%). Taking into account the slow excretion of THCCOOH in urine, the small number of cases in which blood analysis did not confirm urine analysis is remarkable. One could probably find an explanation in the selection of cases made by the policemen. The police requested toxicological investigations when impairment due to drug consumption was suspected. Past consumption of drugs exemplified by the presence of cannabinoids in urine only remained undetected. Yet, the rapid decrease of THC concentrations in blood after cannabis smoking [10] are a real challenge for forensic experts in case of DUID, in particular when biological specimens were collected several hours after the event. Rapid elimination of THC in blood and the length of time between the event and specimen collection (mean: 2.7 h) are probably the reason why the 75 percentile of the whole blood THC concentration was only 6 ng/ml. In comparison, Ramaekers et al. indicated in a recent review [11] that maximal performance impairment would be achieved at THC concentrations >7 ng/ml in whole blood. It must also be emphasized that THC and alcohol were observed together in 28% of cases (122 of 440), situations where driving performance are severely diminished [12].

The fact that 203 drivers (46%) suspected of DUID presented blood alcohol concentration (BAC) higher than 0.10 g/kg points out to the high incidence of drug ethanol interaction and the high risk of increased impairment. Moreover, it shows that symptoms of ethanol consumption could easily be mistaken with drug intoxication. Ethanol is always a dominant problem, even when policemen suspect drug consumption. Interestingly, mean BAC value (1.28 g/kg) appeared to be lower than the mean BAC value (1.52 g/kg, $n = 1044$) obtained in a previous study among drunken drivers [13].

Benzodiazepines were the most represented legal drugs in this study (57 of 440, 13%). Nine types of benzodiazepines were detected, assuming that some substances were the result of metabolism, direct consumption or combination of drugs. In these 57 cases, some are positive for more than 1 benzodiazepines, leading to 79 benzodiazepine confirmations. Nordiazepam was the most frequent benzodiazepine detected in blood. Nordiazepam concentrations measured in whole blood (30–1560 ng/ml) were in the range of therapeutic levels [14] taking into account a plasma/whole blood ration of 1.7 [15]. Similar results were obtained with the other benzodiazepines. Only one driver presented an oxazepam concentration of 3830 ng/ml in whole blood, which can be considered as toxic. Moreover, THC (5.4 ng/ml) and ethanol (1.74 g/kg) were also measured in this case in whole blood. This driver was involved in a car crash.

Comparatively to a previous study [7], the slight increase of the frequency of cocaine (from 11 to 13%) and amphetamine (from 4 to 9%) and the decrease of the frequency of opiates (from 36 to 9%) reflect very likely the evolution of the illegal drug market and the changes of the habits of consumption. Concerning opiates, only one case was a consequence of codeine consumption. The other 38 cases involved heroin consumption, demonstrated by the presence of 6-mono-acetyl-morphine, and/or a codeine to morphine ratio in urine. Consequently, codeine concentrations in blood were very low (1–13 ng/ml).

Methadone is currently used in Switzerland in substitution therapy. As observed previously [7], methadone was never found alone in blood. Even if concentrations of

methadone measured in whole blood (27–850 ng/ml) could be considered as therapeutic [14], driving impairment of patients under substitution treatment should be evaluated carefully considering that methadone side-effects could be increased by interaction with other drugs.

5. Conclusion

As observed some years ago, it was possible to conclude that police suspicion concerning impaired drivers highly correlates with positive results for drug analysis in blood. Young males predominated over females and old drivers. The drug concentrations presented in this paper as well as medical and police reports have to be considered as an important basis for discussion concerning the question whether a per se limit could be proposed in different countries. Accordingly, except benzodiazepines and methadone, the most commonly detected substances in this study are scheduled in the new zero-tolerance law, which will be introduced in January 2005 in Switzerland.

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