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Drugs and Driving: Analytical Strategy

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Abstract: Consumption of psychoactive substances may impair driving performance. Because of the diversity of the substances, toxicologists have to develop analytical strategies which allow the detection and the quantification of drugs in biological samples. The analytical strategy described here is composed of three steps: screening, confirmation, and quantification. For screening, immunological tests and chromatography techniques (GC and HPLC) are often used. For confirmation, identification by means of mass spectrometry is required, and quantification is often realized through chromatographic techniques.

Keywords: Driving under the influence of drugs (DUID) · Forensics · Gas chromatography · Immunoassays · Liquid chromatography · Mass spectrometry

Introduction

Consumption of legal or illegal psychoactive substances has become very common in our society, and an increase in the consumption of these substances can be observed. On the other hand, road traffic is increasing continuously. Because of the extent of these two social phenomena, it is not surprising that driving under the influence of drugs is gaining in significance for the health, political, juridical, and administrative authorities. It is well known that the effects of alcohol can impair driving. Therefore, it seems justified to wonder if some crashes or aberrant attitudes could be explained by impairment due to consumption of psychoactive substances such as cannabis, opiates, cocaine, amphetamines, benzodiazepines, LSD, or tranquilizers.

In most surveys reported in different European countries cannabinoids are the most frequently detected illicit drugs [1]. In general the use of opiates is less frequently observed in driver populations than the use of cannabis. The most frequently detected licit drugs in all driver populations are the benzodiazepines. In a survey concerning the nature of the drugs used among drivers suspected of driving under the influence of drugs in the Canton of Vaud, the same results were observed [2]. Moreover, methadone, which is frequently used as a heroin substitute in Switzerland for narcotic maintenance treatment of former opiate addicts, was never found as the sole drug present. The high incidence of interaction for methadone cases suggests that driving impairment of patients under methadone-substitution treatment should be evaluated carefully considering that methadone side effects could be increased by interaction with other drugs. The prevalence of drug use in combination with alcohol is frequently reported in the different studies included in the overall survey of the Council of Europe [1]. This survey emphasized also that higher accident risk in the event of multiple drug use is a reflection of the clear synergistic interaction of alcohol and drugs, if mortality is taken as the outcome variable. Consequently, the analytical strategy set up for the evaluation of the driving impairment due to the consumption of drugs must screen a wide variety of drugs which are suspected of decreasing driving performance.

Impairment due to drug consumption can be observed in two different situations. On the one hand, impairment is due to a single dose of drug. The effects of the drug consumption involve transitional impairment of driving performance (incapacity). On the other hand, impairment can also be due to chronic consumption of a drug, involving drug dependence. In this case, driving performance is impaired on a long-term basis (inaptitude). The analytical strategy is different in these two situations. In order to help the judge to demonstrate driving incapacity , forensic analysis has to determine whether the subject was under the influence of drugs which could impair driving capacity at the time of the event (police control, crash, ...). The only possibility to find an answer through forensic analysis is to quantify the drugs in the blood. In case of inaptitude, forensic analysis has to help the administration to evaluate the dependence on certain drugs. In this context, urine and hair are the matrices of choice for the analysis because of their large window of detection. However, for alcohol, blood is widely used for laboratory diagnosis of chronic alcohol abuse by the determination of carbohydrate-deficient transferrin (CDT) or other markers [3].

Substances

As suggested by one group of the Council of Europe (Pompidou group) [1], it seems unacceptable to base a reasoned argument about drugs and road safety on an over-simplified distinction between licit and illicit drugs. It is not the classification which matters, but the use to which such substances are put. A lot of psychopharmacological studies have revealed the adverse effects of many drugs on driving performance. On the basis of current knowledge, the psychotropic drugs which are capable of producing driving impairment are: anesthetics, antidepressants, antihistamines, cannabinoids, cardiovasculars, hallucinogens,

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hypnotics, narcotics, psychomimetics, sedatives, solvents, stimulants, and volatiles. The challenge for the analytical toxicologist is to develop a sensitive screening which can be used for the detection of the majority of these psychotropic drugs.

In case of licit drug prescription, there is no doubt that some medications cause drowsiness for some patients. However, drowsiness could be a desired therapeutic goal without side-effects and depend upon the situation and the indication for which a drug is prescribed. If the patient wants to sleep during the night, drowsiness is a desired effect; but during daytime it could adversely affect the alertness of a car driver. Moreover, it must be remembered that patients for whom a tranquilizer is prescribed to treat anxiety or aggressiveness, or depressed patients who take some antidepressants, are certainly safer drivers after they have received their medication.

Matrices

Analysis of blood, urine, saliva or hair gives different information (Table 1). Blood has been considered to be the only suitable specimen. This is obviously true, because available pharmacological data attempt to correlate plasma concentrations to either therapeutic or impairment effects. The detection of a drug and/or its metabolites in blood is evidence of recent use and therefore of a potentially impairing effect. However, some drugs and their metabolites can be detected for extended periods in blood after either acute or chronic dosing. Urine is probably the specimen of choice for additional information and hair analysis can represent a powerful tool to estimate the historical aspect of the situation. Urine is preferred for screening since drug concentrations are usually higher and can be detected for longer. However the use of blood samples may be more important with respect to the evaluation of driving performance related to the drug.

Screenings

(immunoassays, GC-FID/NPD/MS, HPLC-DAD)

⇩

Confirmation & identification

(GC-MS, HPLC-MS/DAD)

⇩

Quantification

(GC-FID/NPD/ECD/MS, HPLC-MS/DAD/fluorescence)

Fig. Analytical strategy for biological sample analysis for the determination of driving impairment due to drug consumption.

Saliva has been proposed as a specimen for roadside tests. However, the concentration of drug in the saliva specimen will depend on the type of saliva, whether it is true parotid saliva or not, on the pH of salivary flow, on salivary flow stimulation, and on the plasma protein binding of the drug or metabolite. Under certain conditions (*e.g.* standardized saliva collection, development of specific immunoassays for saliva) saliva will play an important role for the recognition on the road by the police of driving impairment due to drug consumption. An earlier use of saliva testing was conducted by Peel *et al.* (1984) [4]. Fifty-six saliva samples from 445 suspected drivers were analyzed for the presence of cannabinoids, volatiles and benzodiazepines using an immunoassay technique and GC/MS for confirmation. The authors concluded that the use of saliva was a potentially versatile noninvasive technique.

Although some techniques have been examined which test hair samples, the consensus of opinion indicates that they are not reliable due to the inconsistent relationship between results and recent drug ingestion. However, hair analysis is a highly effective and reliable tool for the investigation of drug abuse behavior. This is very useful for checking the physical fitness of subjects, former users of illicit drugs, to obtain a driving license [5].

For fatally injured drivers it is recommended that blood be collected from the femoral vein at autopsy, because in the case of weakly basic drugs such as the tricyclic antidepressants, concentrations in cardiac and sub-clavian blood increase after the death. Moreover, other specimens such as gastric content, vitreous humor, liver or bile are available, and may complete information.

Analytical Strategy and Analytical Tools

Laboratories have often adopted an analytical strategy composed of three steps (Fig.):

a) general unknown analysis in order to determine the presence of drugs in the samples;
b) specific identification of the drugs;
c) quantification of drugs in blood samples and urine.

Different analytical tools can be used for the first step. Methods for the determination of the presence of drugs in the samples are based on immunological tests, gas chromatography (GC) or liquid chromatography (LC). Presence or absence of a urine sample influences the first step. In the presence of a urine sample, screenings were essentially performed on the urine. In the absence of a urine sample, screenings were done an blood. Because the aim of this step is to detect the presence of substances with potential of producing driving impairment at therapeutic and toxic levels, immunoassays and GC-MS analysis are probably complementary methods. GC-MS data can be automatically compared to mass spectrum libraries, such as the

Table 1. Time period for drug detection in different matrices and relative information

Specimen	Time period for detection	Information
Blood	about 1 d	correlation with impairing effects
Saliva	about 1 d	recent consumption of drug
Urine	about 2–4 d	consumption of drug
Hair	about 1 d to 6 mon	drug consumption during a time period depending of the length of the hair

Table 2. Main toxicological results. Car crash.

Specimen	Results
Blood	free morphine (260 ng/ml), total morphine (2900 ng/ml), free codeine (80 ng/ml), total codeine (100 ng/ml), flunitrazepam (9 ng/ml), midazolam (65 ng/ml), methaqualone (280 ng/ml)
Urine	free morphine, total morphine, free codeine, total codeine, 6-monoacetyl-morphine, normorphine, norcodeine, cocaine, benzoylecgonine, ecgonine methylester, ethylcocaine, ethylecgonine, THCCOOH, methaqualone, metabolites of methaqualone, flunitrazepam, 7-aminoflunitrazepam, hydroxymidazolam, trimipramine, diphenhydramine, papaverine, metabolites of papaverine, paracetamol, metabolite of paracetamol, nicotine, cotinine, caffeine

PMW database. During the second step, the use of mass spectrometry (MS) is undoubtedly needed. Immunoassays cannot be used to confirm immunoassays. MS is an important technique in the forensic laboratory. Because it is possible to differentiate and identify substances, the use of GC-MS has become the method of choice for confirming the presence of drugs and their metabolites in blood. LC with diode array UV detection is sometimes also appropriate. Recently, the use of LC-MS as a method for the screening of drugs in biological samples has been proposed. LC- or GC-MS are also appropriate procedures for determining the concentrations of drugs and their metabolites, in particular when deuterated internal standards are available. Other methods are also suitable for quantifying drugs in biological samples. Depending on the drugs and their metabolites, LC with UV or fluorescence detection and GC with a nitrogen phosphorus detector (NPD), electron capture detection (ECD) or a flame ionization detector (FID) represent appropriate techniques. Each of these procedures requires either sample preparation, extraction, or optimization of chromatographic conditions. Therefore, these types of analysis should only be performed in laboratories with experience in analytical toxicology.

The introduction in the last twenty years of many different immunoassays and mass spectrometric procedures has permitted the detection, specific identification, and measurement of very low concentrations of drugs (ng/ml). Unfortunately, as underlined by Peat and Finkle [6], the ability to interpret these concentrations in terms of cause and effect relationships and risk in the context of highway safety lags far behind. An adequate pharmacodynamic or pharmacokinetic database does not exist for most drugs to allow for such an interpretation or prediction of effects in the context of all known factors. Therefore, each case must be evaluated individually. Moreover, numerous studies support the disturbing fact that most drivers who test positive have more than one drug in their blood. A drug-and-alcohol combination is the most frequent, but the use of multiple drugs is very common. This further complicates the task of the analytical laboratory, because procedures must be selective enough to identify each drug and metabolite separately.

Example

On Sunday at 7 a.m. in a city, a 24-year-old man lost control of his vehicle. The car struck a lamp post. Police noticed that the man did not walk straight and had coordination problems, although the breathalyzer indicated no alcohol consumption. The physician who took samples observed that the driver was clearly under the influence of drugs. The patient declared that he had drunk champagne and that he had taken some pills of Rohypnol® (flunitrazepam). Analytical results (GC-MS/NPD/ECD) are given in Table 2.

Toxicological findings confirmed the consumption of flunitrazepam and alcohol. The alcohol consumption was indirectly confirmed through the presence of ethylcocaine and ethylecgonine, two metabolites of cocaine. When cocaine and alcohol are taken together, cocaine is partially converted by a liver enzyme to its ethyl homologue called ethylcocaine [7]. The analysis also indicated the consumption of other psychoactive substances such as heroin (confirmed by the presence of 6-monoacetyl-morphine [8]), cocaine, cannabis, methaqualone, midazolam, and trimipramine. Quantitative analysis of the blood indicated that the driver was most probably under the influence of opiates, flunitrazepam, and midazolam. These substances presented the risk of driving impairment. Pharmacological interactions between these substances have to be considered, resulting in higher driving impairment.

Conclusion

Driving is a task which can be impaired by psychoactive substances. When judges want to know whether a driver was under the influence of drug, the analytical strategy must include screening of a huge diversity of psychoactive drugs. It is not sufficient to look for only a few substances. Blood has been considered to be the only suitable specimen for identifying cases of driving under the influence of drugs, even though no concentration threshold beyond which driving performance becomes impaired is given, as is the case for alcohol. The analytical strategy developed for the evaluation of driving impairment due to the consumption of drugs is based on three steps: screening, confirmation, and quantification. For a precise identification of substances, mass spectrometry is recommended and for quantification, different chromatographic techniques can be used depending on the drug.

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