Prevalence of medicinal drugs in suspected impaired drivers and a comparison with the use in the general Dutch population

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A B S T R A C T

The aim of this study was to investigate the prevalence of psychotropic medicines in drivers suspected of driving under the influence of medicinal and illicit drugs in The Netherlands and to compare the prevalence of selected impairing medicines with the use of these medicines in the general Dutch population. In total, 3038 blood samples of suspected impaired drivers in The Netherlands have been analyzed for the presence of medicinal and illicit drugs between January 2009 and December 2012. In 94% (2842/3038) of the cases medicinal and/or illicit drugs were detected. Medicinal drugs were found in 33% of the blood samples, with the highest prevalence for anxiolytics. In 86% of the cases illicit drug-positive results were obtained, with the highest prevalence for cannabis. At least in 56% of the blood samples poly-drug use was determined, including medicinal and/or illicit drugs. The highest prevalence of poly-medicine use was found for combinations including anxiolytic and hypnotic drugs. In general, the prevalence of driving impairing medicines in suspected impaired drivers is higher than the use of these medicines in the general Dutch population, due to a positive selection bias in the first population. Differences between both populations may be explained by the used methodological approach (e.g., classification criteria of analytical findings, sample selection bias) and abuse of certain medicinal drugs (e.g., diazepam). Negative effects of medicinal drugs on driving performance determine largely the prevalence in the population of suspected impaired drivers. The degree of impairment depends on different factors, including pharmacokinetic properties of the drug and pharmacodynamic aspects. More research is needed to study the prevalence of all prescribed driving impairing medicines and to investigate if providing additional information to medicinal drug users on driving impairing medicines would lower the prevalence of medicinal drug positive drivers.

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1. Introduction

Drug use is an important risk factor for traffic accidents due to the possibility of driving impairment, especially in case of poly-drug use and drug–alcohol combinations [1–3]. Many different studies have been performed to investigate driving under the influence of alcohol, illicit and medicinal drugs in The Netherlands [4,5] and in other countries [6–14]. In addition, some studies also include the prevalence of individual prescription drugs [15–21]. In the year 2011, a total of 661 people were killed in road accidents in The Netherlands and an estimated 33–66 road fatalities were associated with the use of medicinal drugs [22]. Recently, an extensive integrated European research project has been completed that investigated driving under the influence of drugs, alcohol and medicines (DRUID), and studied the prevalence of psychoactive substances in European traffic by using a general design. The Netherlands was one of the thirteen countries participating is this project [23].

The Dutch Road Traffic Act states that is it forbidden to drive under the influence of a substance of which a driver should be aware that it can negatively affect the driving performance. For alcohol, legal limits are laid down of 0.5 mg ethanol/ml blood and 0.2 mg ethanol/ml blood for novice drivers [24]. For illicit drugs, there is a proposed law under consideration to adopt legal limits for nine frequently detected illicit drugs [25]. No legal limits are proposed for prescription drugs. Package information leaflets, pharmacists and/or physicians provide information about a medicine's side effects and possible driving impairment.

Possible driving impairment caused by medicinal drugs and their role in traffic safety are difficult to predict due to influencing

factors such as type of drug, dosage, individual variations and tolerance development. Different types of studies are applied to test the effects of medicinal drugs on driving performance and risk potential. Experimental studies, using driving simulators and on-the-road tests, focus on measuring the driving performance in a controlled environment and epidemiological studies investigate existing driver populations to get insight in prevalence of drugs and their effects on traffic safety. Studies on the effects of medicinal drugs, e.g., antidepressants, anxiolytics and/or hypnotics, have shown that supratherapeutic levels and even therapeutic levels of these medicines can cause impaired driving and increase the risk of road traffic accidents [26–33].

Although extensive research is available for driving under the influence of alcohol and illicit drugs, literature on the prevalence of medicinal drugs in road traffic is limited. This paper presents the analytical results of blood samples collected from drivers suspected of driving under the influence of medicinal and/or illicit drugs in The Netherlands between 2009 and 2012. The prevalence of impairing medicines will be compared with the use of these medicines in the general Dutch population to get more insight in the role of medicinal drugs in road traffic.

2. Materials and methods

2.1. Case selection

In The Netherlands, the first step in a suspected impaired driving case is usually an alcohol breath test. When drivers are not able to complete this alcohol breath analysis or the police-officer observes suspicious behavior which could indicate drug use, blood samples are collected by physicians. The blood samples of these suspected impaired drivers are sent to The Netherlands Forensic Institute (NFI) for drug analysis. Data were collected of the different alcohol, medicinal and illicit drug concentrations detected in blood samples of suspected impaired drivers between the years 2009 and 2012.

2.2. Analytical methods

Routinely, blood samples were analyzed for 58 compounds. The identification and quantification of 57 substances in blood, including both medicinal and illicit drugs, was performed using a validated UPLC–MS/MS (ultra performance liquid chromatography-tandem mass spectrometry) method [34]. The presence and concentration of GHB in blood was determined separately by using GC–MS (gas chromatography mass spectrometry) [35]. The limits of quantification (LOQ) are 0.001 or 0.005 mg/l for all drugs using the UPLC–MS/MS method and 5 mg/l for GHB. In total, 3038 blood samples have been analyzed between 2009 and 2012 using the above descripted methods. In 47% (1420/3038) of the cases alcohol concentrations were determined in addition, using the enzymatic alcohol-dehydrogenase method after vapor micro-diffusion with a LOQ of 0.2 mg ethanol (alcohol)/ml blood [36]. In 7% (206/3038) of the cases additional specific analysis for one or more compounds was performed mainly by UPLC–MS/MS and GC–MS.

2.3. Categorization criteria

The detected medicinal and illicit drugs have been divided in twelve different drug groups. Medicinal drugs were categorized corresponding to the Anatomical Therapeutic Chemical (ATC) Classification System, using the third level pharmacological subgroup names [37]. Fig. 1 gives an overview of the drugs and metabolites which are routinely tested in all suspected impaired driving cases at the NFI. Additional targeted drug analysis was performed on special request of the prosecutor or if there was a specific suspicion, i.e., confession of suspect.

Detection of metabolites is incorporated into the drugs prevalence. For instance, the metabolite demoxepam relates exclusively to the parent compound chlordiazepoxide [38]. In other cases, the categorization of metabolites is more complicated. Temazepam and oxazepam can be metabolites of diazepam [39], but are also parent compounds. In these cases concentrations were evaluated for categorization. For morphine and codeine criteria introduced by DRUID (EU-project driving under the influence of drugs, alcohol and medicines) were used to categorize these cases in either medicinal or illicit opiates, since morphine could be a prescription medicine or a metabolite of either codeine or heroin [40]. Detection of the metabolite 6-monoacetylmorphine (6-MAM) gives exclusive evidence of heroin use. In practice, this definite distinction cannot always be made, because the half-life time of 6-MAM is very short and can only be detected in blood up to a few hours [41]. The antidepressant nortriptyline can be prescribed, but can also be a metabolite of amitriptyline [42]. Analytical findings of both substances indicates metabolism of amitriptyline, since
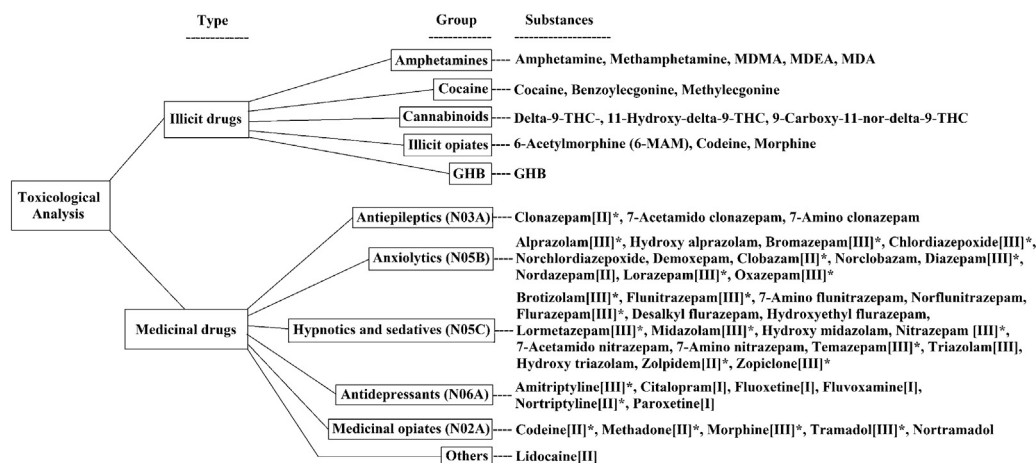

Fig. 1. Overview of the drugs and metabolites routinely tested for in suspected impaired driving cases, and their categorization into pharmacological (ATC) groups (for medicines only).

*Indicate the selected impairing medicines used for comparison with the general Dutch population.vvvvvv

[] gives the ICADTS category (I, II or III) for driving safety of medicinal drugs.

Note: Codeine and morphine cases are categorized in either illicit or medicinal opiates.