A comparison of medicinal drugs detected in blood of suspected impaired drivers with data on the use of driving impairing medicines in The Netherlands

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Abstract

This study presents the analytical results of blood samples of suspected impaired drivers during a four year period and compares the medicinal drugs detected in the blood samples with the use of these driving impairing medicines in The Netherlands. In 2009-2012, the blood alcohol concentrations of 9047 samples have been determined and 82% of the samples tested positive. In addition, 3038 blood samples have been analyzed for drugs and in 94% of the cases drugs were detected. Medicinal drugs were detected in 33% (1010/3038) of the drug cases, including poly-medicinal drug use in 37% (370/1010) of the positive medicinal drug cases. Anxiolytics have the highest prevalence of 19% (573/3038) in the population of suspected impaired drivers. Followed by hypnotics and sedatives (13%), medicinal opiates (6.9%), antidepressants (4.5%) and antiepileptics (1.1%). The prevalences of these medicinal drug groups in the general Dutch population are about two or three times lower for anxiolytics (6.9%), hypnotics and sedatives (5.5%), and antiepileptics (0.34%), compared to suspected impaired drivers. Medicinal opiates have about the same prevalence in both populations, which could be a result of the criteria used for the categorization of these substances. Antidepressants have a higher prevalence in the general Dutch population possibly due to differences in characteristics of the study populations (e.g. tolerance development and age). Overall, the results show that the prevalence of the selected medicinal drugs in suspected impaired drivers is higher than the prevalence of medicinal drugs in the general population. More research is needed to study the prevalence of all medicines that affect the driving performance.

Background

In the Netherlands, it is forbidden to drive under the influence of a substance of which a driver should be aware that it can negatively affect the driving performance, as stated in the Road Traffic Act [1]. This legislation includes alcohol, illicit and medicinal drugs. For alcohol, legal limits are 0.5 mg ethanol/ml blood and 0.2 mg/ml in novice drivers. For illicit drugs, there is a proposed law under consideration to adopt legal limits for nine frequently detected illicit drugs related to impairment. No legal limits are laid down for medicinal drugs. For information about side effects which could affect driving performance, drivers have to rely on medicine leaflets and information provided by pharmacists or physicians. Despite these warnings, there are still many road accidents due to impaired driving. In the year 2011, a total of 661 people were killed in road accidents in the Netherlands and an estimated 33 to 66 road fatalities are related to the use of medicinal drugs that affect the driving performance [2]. However, literature about the prevalence of medicinal drugs in suspected impaired drivers is limited.

Aims

Aim of this study is to present the analytical results of blood samples of drivers suspected of driving under the influence of alcohol, illicit drugs or medicinal drugs in The Netherlands and to compare the medicinal drugs detected in drivers with the medicinal drug use in the general Dutch population in order to get more insight in the role of medicinal drugs in road safety.

Methods

Generally, the detection of driving under the influence of alcohol is performed by breath tests. The moment drivers are not able to complete the breath test or the police-officer observes suspicious behavior which could indicate drug use, blood samples are collected. The blood samples of these suspected impaired drivers are sent to the Netherlands Forensic Institute (NFI) for alcohol and/or drugs analysis.

Alcohol concentrations were determined using the enzymatic "alcohol dehydrogenase (ADH)" method. Drugs analysis was performed by using two analytical methods LC-MS/MS and GC-MS (Liquid chromatography-tandem mass spectrometry and Gas chromatography-mass spectrometry), which gives both a qualitative and quantitative determination of a standard list of drugs (both medicinal and illicit). Table 1 gives an overview of the standard measured medicinal drugs categorized corresponding to the Anatomical Therapeutic Chemical (ATC) Classification System [3]. The illicit drug groups amphetamines, cocaine, cannabinoids, illicit opiates and GHB (*gamma*-Hydroxybutyric acid) were also included in the analytical methods. Additional targeted drugs analysis was performed on special requests or when there was a specific suspicion.

The medicinal drugs detected were compared with data on the users of these medicines among the general Dutch population, including all ages. The prescription-based data on the users of medicinal drugs covering 95% of the public pharmacists in the Netherlands was provided by the Dutch Foundation for Pharmaceutical Statistics (Stichting Farmaceutische Kengetallen, SFK) [4]. SFK provided data on the number of users of driving impairing medicines of category II and III (categorized by DRUID, Driving under the influence of Drugs, Alcohol and Medicines) during the years 2009-2012 [5]. In this study, only the standard list of medicinal drugs for DUID analyses is used for comparison of prevalence data.

The detection of metabolites is incorporated into the drugs prevalence. For instance, the metabolite demoxepam relates exclusively to chlordiazepoxide. In other cases, the categorization of metabolites is more complicated. Both temazepam (T) and oxazepam (O) can be metabolites of diazepam (D), but are also prescription drugs. In these cases concentrations were evaluated for categorization.

- Only T or O detected, indicates intake of T or O
- Concentration T or O higher than D, indicates intake of T or O
- Concentration T or O lower than D, indicates intake of D

For morphine (M) and codeine (C) other criteria, introduced by DRUID, were used to categorize these substances in either the illicit or medicinal opiates group. Since both morphine and codeine can also be metabolites of heroin [6].

- Only M or C detected, is categorized as medicinal opiates
- Both M and C detected and concentration M is lower than C, is categorized as medicinal opiates

- Both M and C detected and concentration M is higher or equal to C, is categorized as illicit opiates
- All combinations of M and/or C with heroin metabolite 6-monoacetylmorphine (6-MAM), are categorized as illicit opiates

Table 1: The standard list of medicinal drugs cat II and III in cases of driving under the influence

ATC pharmacological subgroup name: Medicinal drug (category)
Antiepileptics (N03A): clonazepam(II)
Anxiolytics (N05B): alprazolam(III), bromazepam(III), chlordiazepoxide(III), clobazam(II), diazepam(III), lorazepam(III), oxazepam(III)
Hypnotics and sedatives (N05C): brotizolam(III), flunitrazepam(III), flurazepam(III), lormetazepam(III), midazolam(III), nitrazepam(III), temazepam(III), zolpidem(II), zolpiclon(III)
Antidepressants (N06A): amitriptyline(III), nortriptyline(II)
Medicinal opiates (N02A): codeine(II), methadone(II), morphine(III), tramadol(III)

Results

During a four year period (2009-2012), the blood alcohol concentrations of 9047 samples have been determined. Figure 1 shows the number of cases versus the blood alcohol concentration in mg alcohol per ml of blood. Positive results were obtained in 82% (7432/9047) of the cases, of which the majority (7202/9047) had concentrations higher than 0.2 mg/ml of blood and 65% (5855/9047) had concentrations higher than 0.8 mg/ml of blood. The median alcohol concentration was 1.2 mg/ml of blood.

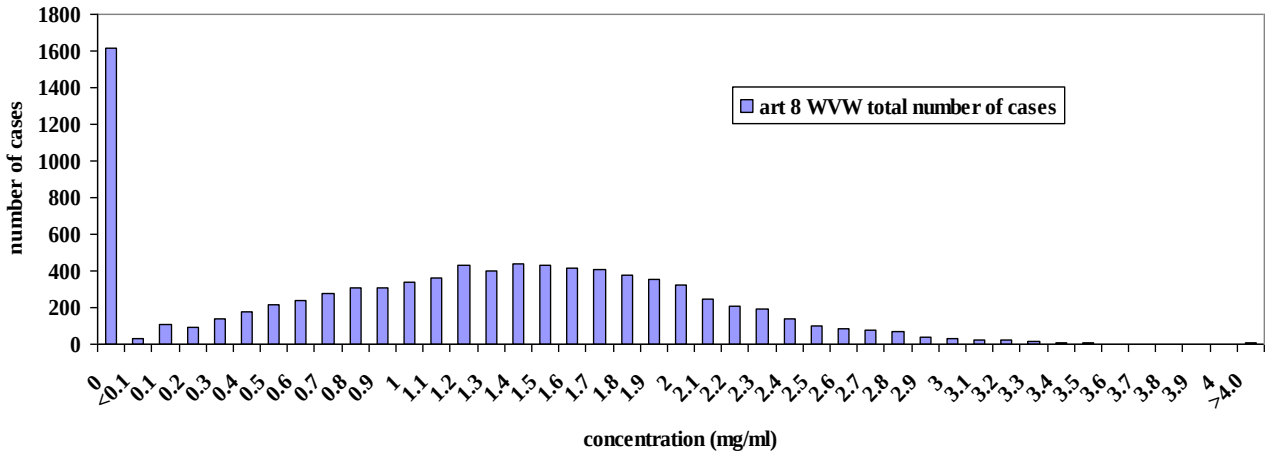

Figure 1: Blood alcohol concentrations (2009-2012). (n=9047)

In the same four year period, 3038 blood samples have been analyzed for drugs. In 94% of the cases drugs were detected. In 86% of the blood samples illicit drugs have been detected. Table 2 gives an overview of the prevalence of different illicit drug groups. The highest prevalence was found for cannabinoids, which were found in approximately half of the samples. In decreasing prevalence followed by amphetamines, cocaine, GHB and illicit opiates. The total percentage is greater than 100%, because in many cases poly-drug use is determined.

Table 2: The prevalence of illicit drugs in the analytical results. (n=3038)

Illicit drug group	*n*	*Prev. (%)*
Cannabinoids	1636	54
Amphetamines	1001	33
Cocaine	921	30
GHB	772	25
Illicit opiates	63	2.1

In addition, Figure 2 gives a global overview of the drugs analysis results, showing that 33% (1010/3038) of the samples tested positive for medicinal drugs affecting the driving performance. In 10% (306/3038) of the cases a combination of alcohol and drugs has been determined.

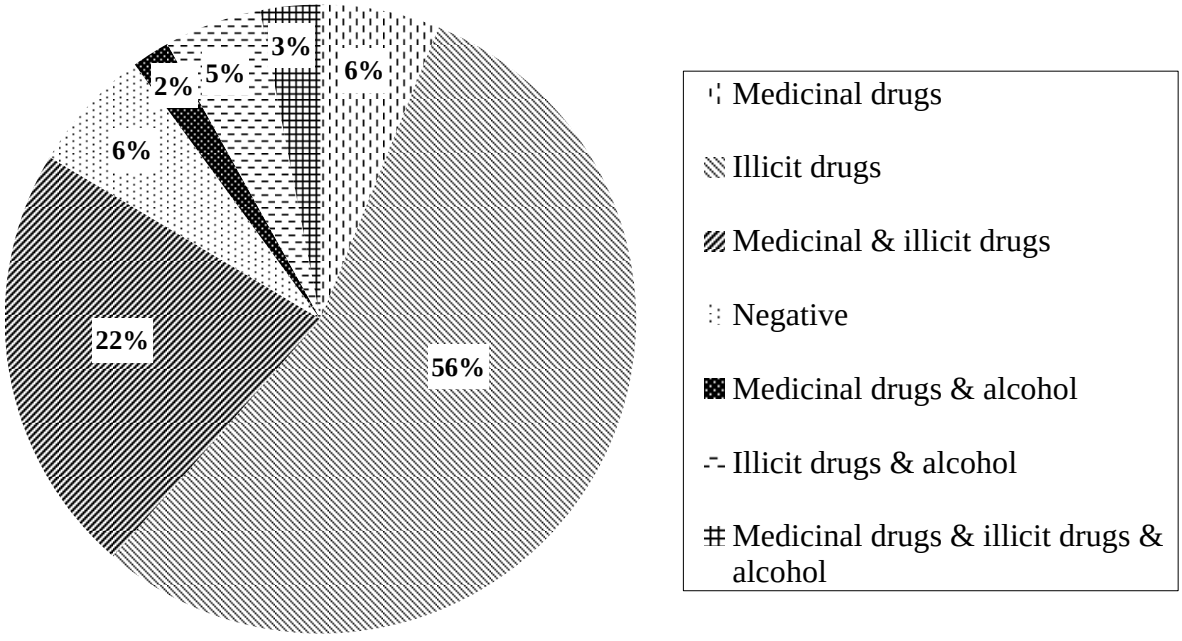

Figure 2: Results of the blood samples analyzed for drugs between 2009-2012. (n=3038)

The medicinal drugs are categorized according to the Anatomical Therapeutic Chemical (ATC) Classification System. Table 3 gives the prevalence of medicinal drugs in blood of suspected impaired drivers compared with the prevalence of medicinal drug use in the general Dutch population (SFK database). These results only include the substances which are standard tested in cases of driving under the influence (see Table 1). The total percentage in Table 3 is not equal to 100% because of the exclusion of the additional measured substances and because in many cases poly-drug use is detected. Anxiolytics have the highest prevalence (19%) in the blood samples, followed by hypnotics and sedatives (13%), medicinal opiates (6.9%), antiepileptics (1.1%) and antidepressants (0.89%).

The use of axiolytics (6.9%) is the highest in the general Dutch population, followed by medicinal opiates (6.8%), hynotics and sedatives (5.5%), antidepressants (1.4%) and antiepileptics (0.34%).

Table 3: The prevalence of "standard list of medicinal drugs"for analyzing blood of suspected impaired drivers (n=3038) and medicinal drug users in the general Dutch population (n=16.647.367*)

	Blood samples		*SFK database*	
Medicinal drug group	*n*	*Prev. (%)*	*n*	*Prev. (%)*
Antiepileptics (N03A)	34	1.1	56320	0.34
Anxiolytics (N05B*)*	573	19	1152275	6.9
Hypnotics and sedatives (N05C)	408	13	910170	5.5
Antidepressants (N06A)	27	0.89	233465	1.4
Medicinal opiates (N02A)	209	6.9	1130923	6.8

* The total population of The Netherlands, averaged between 2009-2012 [7].

Overall, the prevalence of selected medicinal drugs detected in the blood samples of suspected impaired drivers is higher than the prevalence in the general Dutch population, except for antidepressants. The prevalence of anxiolytics, hypnotics and sedatives, and antiepileptics are approximately three times lower in the general Dutch population than detected in the blood samples of suspected impaired drivers.

Figure 3 presents the number of combinations of different medicinal drug groups. In 37% (370/1010) of the positive medicinal drugs cases poly-medicine use was observed. Poly-medicine use of anxiolytics combined with hypnotics or sedatives has the highest prevalence of 7.8%. Another frequent combination of anxiolytics and medicinal opiates has a prevalence of 5.5%.

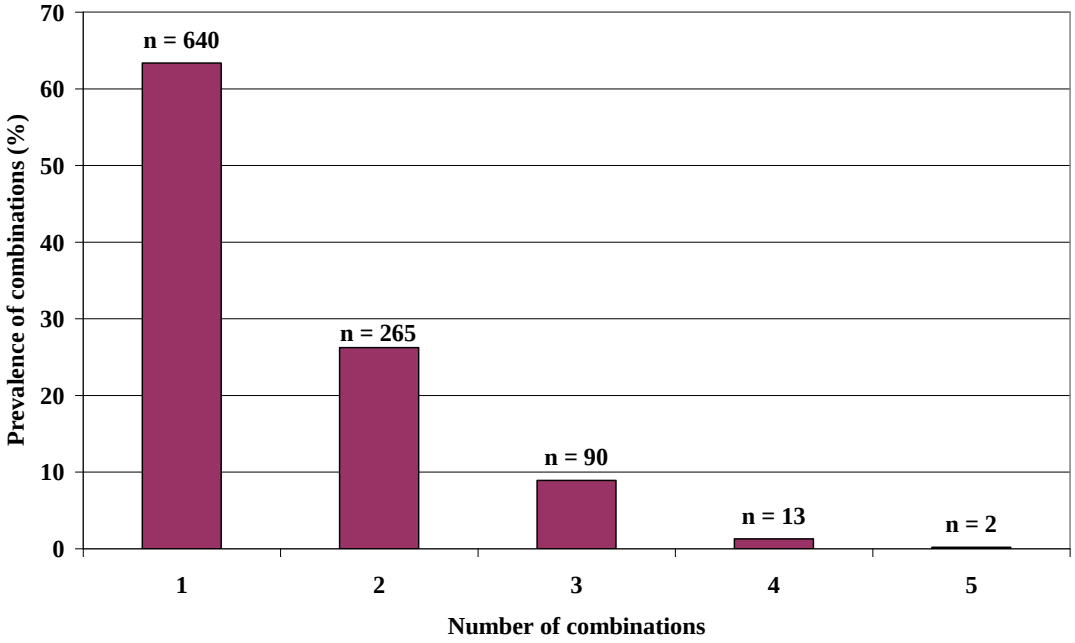

Figure 3: Poly-medicine use: combinations of different medicinal drug groups. (n=1010)

Discussion and conclusions

The results show that in 33% of the drug cases blood samples tested positive for medicinal drugs affecting the driving performance. In general, the prevalence of medicinal drugs in the blood samples is higher than the prevalence in the general Dutch population. This difference is due to the fact that blood samples are only collected from suspected impaired drivers, thereby creating a positively biased sample population. The prevalences of the medicinal

drug groups anxiolytics, hypnotics and sedatives, and antiepileptics are about 3 times higher in the blood samples than in the general Dutch population, but maintain approximately the same ratio relative to each other.

The prevalence of antidepressants is higher in the general Dutch population compared to the prevalence in the blood samples. Differences between both populations in tolerance development and age could have contributed to this finding. Due to tolerance development driving impairing effects could become less noticeable to the police, leading to a lower prevalence in the population of suspected impaired drivers. In addition, the age distribution varies between both populations. The suspected impaired drivers population only includes people of sixteen years and older, while the data representing the general Dutch population includes all ages.

About the same prevalence is observed for medicinal opiates in both the general Dutch population and the suspected impaired drivers population. Categorization of morphine and codeine into either illicit or medicinal opiates drug use is difficult based on the toxicological results. Often, the analytical results cannot make a definite distinction, because the half-life time of the heroin metabolite 6-monoacetylmorphine is very short and can only be detected in blood up to a few hours. Therefore, additional criteria, introduced by DRUID (Driving under the influence of Drugs, Alcohol and Medicines), have been used and this could have lowered the prevalence of medicinal opiates in the suspected impaired drivers population.

In 37% of the positive medicinal drug cases poly-medicinal drug use is detected. In general, the prevalence of poly-medicinal drug use in the blood samples of impaired drivers may be underestimated. The same holds for the prevalence of combinations of alcohol and drugs. The first reason is that the moment a frequently used drug is detected there will be no further investigation into other drugs, except on special requests. The second reason is that in The Netherlands, blood samples containing alcohol concentrations higher than 0.8 mg/ml of blood are not screened for drugs, unless on special request of the public prosecutor. In this study, 5855 samples had a blood alcohol concentration over 0.8 mg/ml of blood of which some extend could have had an indication for drugs use. Finally, not all blood samples analyzed for drugs have also been tested for alcohol.

In conclusion, the results show that the medicinal drug positive drivers in this study population of suspected impaired drivers represent only a minor part of the users of the selected medicinal drugs affecting the driving performance in the general Dutch population. More research is needed to study the prevalence of all prescribed driving impairing medicines in the Dutch driving population and to investigate if providing additional information to medicinal drug users on driving impairing medicines would lower the number of medicinal drug positive drivers.

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