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Post-mortem cases involving amphetamine-based drugs in the Netherlands
Comparison with driving under the influence cases

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Abstract

In this study we reviewed the post-mortem cases in the years 1999–2004 that were presented at the Netherlands Forensic Institute. The concentrations of amphetamine-based drugs in femoral blood from cases of suspected unnatural death were compared with concentrations in whole blood from non-fatal cases of driving under the influence (DUI cases) and with literature. Furthermore, the combinations with other drugs and/or alcohol were investigated. Amphetamine-based drugs were present in 70 post-mortem cases and 467 DUI cases. The most detected amphetamine-based drug was MDMA, followed by amphetamine. The presence of MDA could usually be explained by metabolism of MDMA. Methamphetamine and MDEA were rarely present. Frequently, the amphetamine-based drugs were taken in combination with alcohol and/or other non-amphetamine-based drugs such as cocaine or cannabinoids. The 70 post-mortem cases were divided into 38 amphetamine-based drug caused (i.e. the amphetamine-based drug directly caused or contributed to the death) and 32 amphetamine-based drug related deaths (i.e. death was not directly caused by the amphetamine-based drug). In the latter category, other (poly)drug intoxications and death by violence or drowning were the most frequent causes of death.

In 30 cases, MDMA caused death directly. The range in blood concentrations of MDMA in these cases was substantial, i.e. 0.41–84 mg/L with a median concentration of 3.7 mg/L ($n = 30$). MDMA blood concentrations in the MDMA related deaths ($n = 20$) and in the DUI cases ($n = 360$) varied up to 3.7 and 4.0 mg/L, respectively. Seven victims died from the direct effects of amphetamine; the blood concentration of amphetamine ranged from 0.24 to 11.3 mg/L, with a median concentration of 1.7 mg/L ($n = 7$). The median concentrations of amphetamine in the amphetamine related deaths ($n = 13$) and the DUI cases ($n = 208$) were much lower, i.e. 0.28 and 0.22 mg/L, respectively. Amphetamine blood concentrations up to 6.0 and 2.3 mg/L were seen in the drug related deaths and DUI cases, respectively. The most frequently encountered amphetamine-based drugs in the investigated deaths were MDMA and amphetamine. The majority of MDMA- and amphetamine-caused deaths, i.e. 90% of these deaths, occurred with blood concentrations above 1.5 and 0.80 mg/L, respectively. MDMA and amphetamine blood concentrations in drug related deaths and DUI cases, however, overlap the range of fatal concentrations. Therefore, MDMA or amphetamine concentrations should never be used alone to establish the cause of death.

Keywords: Amphetamines; Post-mortem; Driving under the influence; Blood concentrations; Interpretation

1. Introduction

Amphetamine, methamphetamine and the amphetamine-derivates 3,4-methylenedioxymethamphetamine (MDMA, also known as Ecstasy and XTC), 3,4 methylenedioxyamphetamine (MDA) and 3,4-methylenedioxyethylamphetamine (MDEA) are widely abused recreational drugs. These drugs are very popular among young clubbers in the Netherlands [1],

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because they enhance energy, endurance, sociability and sexual arousal [2]. Compared to a number of other European member states, the percentage of ever and recent ecstasy users in the Netherlands are rather high, 3.6 and 1.5%, respectively [1].

The amphetamine-based designer drugs tablets in the Netherlands usually contain MDMA. The amount of MDMA per tablet has increased during the years; in 1997–1999 approximately 1% of the tested tablets contained more than 140 mg MDMA per tablet, whereas in 2003 approximately 6% and in 2004 approximately 10% contained such high amounts of MDMA [1].

Although the acute health risks from amphetamine-based drugs can be considerable, it is not known how frequently serious or fatal intoxications occur in the Netherlands. The interpretation of post-mortem toxicology data is a crucial factor in the determination of the cause of death. This study was performed to obtain more insight in the number and classification of fatalities with amphetamine-based drugs in the Netherlands, as well as blood concentrations and combinations with other drugs and alcohol. The post-mortem results were compared with the results from non-fatal driving under the influence cases and previously published fatal and therapeutic concentrations.

2. Methods

2.1. Selection of cases

From the archives of the years 1999–2004 post-mortem cases were selected for which an autopsy was performed by the pathologists of the Netherlands Forensic Institute (NFI) and in which the presence of (meth)amphetamine or an (meth)amphetamine-derivative (MDA, MDEA, MDMA) in whole blood (femoral blood) was demonstrated at a concentration of 0.01 mg/L or higher. These cases were divided into *drug caused* and *drug related* cases using the autopsy and toxicology results and the circumstances of death; in the *drug caused* cases the amphetamine-based drug directly caused or contributed to the death, in the *drug related* cases the death was not directly caused by the amphetamine-based drug. The concentrations of amphetamine-based drugs in the post-mortem cases were compared with the recreational concentrations obtained from non-fatal drivers. These non-fatal drivers were suspected of driving under the influence of alcohol and/or drugs in the Netherlands between January 1999 and December 2004 (DUI cases).

2.2. Samples

The post-mortem samples (heart blood, femoral blood, urine (or kidney), vitreous humor, bile, gastric content, small intestine content, brain, liver) were obtained by the pathologists of the NFI and stored at −20 °C until analysis. The femoral blood, urine and vitreous humor samples for alcohol analysis contained sodium fluoride as preservative and sodium heparin as anticoagulant, whereas all other samples contained no preservative or anticoagulant. Urine or heart blood were used for screening purposes, whereas the confirmation and determination of concentrations occurred in femoral blood.

The samples from the suspected impaired drivers, urine and blood, were collected by physicians and stored in containers with sodium fluoride as preservative. The blood containers also contained sodium heparin as anticoagulant. Samples were sent to the NFI by mail or special delivery and stored at 4 °C during the process of analysis. In general, alcohol tests were performed at the police office using a breath alcohol analyzer. A blood and/or urine sample was sent to the NFI only if the driver was not able to perform the test or to finish the breath test properly or if there was a suspicion of drug use.

2.3. Analytical procedures

2.3.1. Drugs screening

Routine systematic toxicological analysis was performed on all blood and/or urine samples to investigate for drugs of abuse, prescription drugs or alcohol. Until 2002, drug screening in urine or whole blood samples (heart blood if present in post-mortem cases) was performed by fluorescence polarization immunoassay (FPIA) using Abbott ADx. The classes of drugs screened for included amphetamines, benzodiazepines, cannabinoids, cocaine-metabolite, methadone and opiates (threshold concentrations in urine: 0.30, 0.20, 0.025, 0.30, 0.25 and 0.20 mg/L, respectively; threshold concentrations in blood: 0.010, 0.050, 0.025, 0.030, 0.010 and 0.050 mg/L, respectively). From 2002, whole blood samples (heart blood if present in post-mortem cases) were screened for the following classes of drugs: amphetamines, benzodiazepines, cannabinoids, cocaine-metabolite, methadone, methamphetamines and opiates by using Enzyme-Linked Immuno Sorbent Assay (ELISA, Cozart reagents; threshold concentrations in blood: 0.025, 0.010, 0.010, 0.050, 0.010, 0.025 and 0.010 mg/L, respectively).

In most post-mortem cases and in some DUI cases, additional screening for drugs of abuse and prescription drugs was performed in whole blood (heart blood) after solid phase extraction (SPE) by using high performance liquid chromatography with diode array detection (HPLC–DAD) and/or gas chromatography with mass spectrometric detection (GC–MS) after derivitization with BSTFA (bis(trimethylsilyl)trifluoroacetamide) [3].

The presence of the various compounds was confirmed in whole blood (femoral blood in post-mortem cases), by using the methods described below.

2.3.2. Specific drugs and alcohol analysis

Amphetamine derivatives (amphetamine, methamphetamine, MDEA, MDA and MDMA) were identified and quantified after SPE and derivitization with hexafluorobutyric acid anhydride by using GC–MS [4].

The benzodiazepines diazepam, oxazepam, temazepam, desmethyldiazepam and lormetazepam were identified and quantified after liquid–liquid extraction by using HPLC–DAD.

The confirmation of the presence of cocaine, benzoylecgonine and methylecgonine and the determination of the concentrations of these analytes was done by using GC–MS after SPE and derivitization with HFIP/PFPA (hexafluoro-isopropanol/pentafluoro propionic acid anhydride) [5].

Methadone was identified and quantified after liquid–liquid extraction, by HPLC–DAD alone or in combination with gas chromatography with nitrogen–phosphorus detection.

Opiates were identified and quantified using GC–MS after SPE and derivitization with BSTFA.

The cannabinoids delta-9-THC (THC), 11-hydroxy-delta-9-THC (11-OH-THC) and 9-carboxy-11-nor-delta-9-THC (THC-COOH) were determined by GC–MS/MS after protein precipitation, SPE and derivitization [6].

In some cases, initiated by specific information from the police, GHB was identified and quantified in whole blood (femoral blood) and urine using GC–MS after lactone-formation and liquid–liquid extraction [7] or after liquid–liquid extraction and derivitization with BSTFA [8]. As reported in literature [9–11], GHB can be formed in post-mortem blood during storage up to peripheral blood concentrations of 76 mg/L. Therefore, only a GHB concentration in femoral blood higher than approximately 80 mg/L in combination with a GHB concentration in urine of higher than 20 mg/L was considered indicative for an exogenous origin of GHB. In antemortem blood, GHB concentrations in blood higher than 5 mg/L were indicative for administration or consumption of GHB [9–11].

Concentrations of alcohol (i.e. ethanol) in post-mortem cases were determined in whole blood and urine by head-space GC with flame ionization detection. In the DUI cases, the alcohol concentrations were determined by using the enzymatic alcohol-dehydrogenase method, after vapor micro-diffusion [12].

3. Results

3.1. General

Amphetamine, methamphetamine, MDMA, MDA and MDEA were present in a total of 70 post-mortem cases in