Elimination Half-Lives of Benzoylecgonine and MDMA in an Apprehended Driver

To the Editor:

After a zero-tolerance law was introduced in Sweden for driving under the influence of drugs (DUID), the number of blood samples sent by the police for toxicological analysis increased more than 10-fold (1). Central stimulant amines, as exemplified by amphetamine and methamphetamine are highly prominent in DUID suspects and are identified in 50–60% of all cases (2). Other stimulants encountered in blood from impaired drivers, although much less frequently, are cocaine and ecstasy (MDMA) (2).

This report concerns a 27-year-old man apprehended by the police on suspicion of impaired driving on three separate occasions during a 24-h period. Blood samples for forensic analysis were obtained with the aid of evacuated tubes containing 100 mg sodium fluoride and 25 mg potassium oxalate as preservatives. The times of sampling blood were 2:03 p.m., 10:27 p.m., and 3:30 a.m. the next day. Table I gives the sampling times and the concentrations of benzoylecgonine (BZE), amphetamine, MDMA, and MDA in the blood samples.

After an initial screening analysis of blood by immunoassay methods all positive results were verified by more specific methods involving gas chromatography–mass spectrometry (GC–MS) and deuterium-labeled internal standards. The limit of quantitation (LOQ) for amphetamine in blood was 30 ng/mL, compared with 20 ng/mL for MDA and MDMA. The corresponding LOQ for cocaine and BZE in blood analyzed by GC–MS was 20 ng/mL.

The concentrations of BZE and MDMA at the three sampling times were used to calculate the elimination rate constants for these substances, assuming first-order kinetics, by fitting a least-squares regression equation of the form:

\[ \ln(C_t) = \ln(C_0) - k_e t \]

In this equation, \( C_t \) is drug-concentration at time \( t \), \( C_0 \) is the y-intercept, and \( k_e \) is the first order elimination rate constant. The elimination half-life (\( t_{1/2} \)) is calculated from the following relationship:

\[ t_{1/2} = \ln 2/k_e = 0.693/k_e \]

The values of \( t_{1/2} \), derived mathematically and reported in Table I, agreed well with graphical estimates obtained using a semi-logarithm plot and extrapolation.

A search of the scientific literature showed that the elimination half-life of BZE is much longer than that of the parent drug cocaine (3,4). In the present traffic case, BZE was measurable over a 13.5-h period when the concentrations of cocaine in blood were below LOQ (20 ng/mL) at all three sampling times (Table I). The elimination half-life of cocaine shows large individual variations depending on dose and route of administration, whether intravenous, intranasal, or by smoking (3–5). The half-life of BZE in this DUID case was 6.4 h, which agrees well with information from controlled dosing studies (3–5).

Amphetamine has a long elimination half-life (7–34 h), and the drug might be measurable in plasma and urine for several days.
days after abuse-level doses (6). The plasma half-life depends to some extent on urinary pH, with alkaline urine leading to retention in the blood (\( t_{1/2} = 18-34 \) h) and acidic urine promoting renal clearance and resulting in a shorter plasma half-life of 7–14 h (6). Table I indicates that the concentration of amphetamine in blood increased slightly between the time of obtaining the second and third samples. This suggests that the DUID suspect might have taken a fresh dose of the drug, which precludes calculating an elimination half-life for amphetamine.

The half-life of MDMA in this individual was 10.3 h (Table I), which agrees well with results from a few controlled dosing studies with this designer drug (mean \( t_{1/2} 9 \) h, standard deviation 2.3, \( n = 8 \)) (7–10). The concentrations of MDMA's metabolite MDA were below LOQ in all but the first blood sample, which precludes estimating the elimination half-life of MDA.

Human pharmacokinetic studies with illicit drugs are not feasible to undertake in most countries because of ethical constraints as well as various legal restrictions. Such studies are usually done at hospital or prison environments with strict control of all participants and administration of a single moderate dose of the drug. Moreover, drugs and their metabolites are usually analyzed in plasma or serum and not in whole blood, which is the biological matrix available for forensic toxicology (1,2,11). The \( C_{max} \) after dosing, the elimination half-life and the volume of distribution might also depend on the dose of drug, the route of administration and the biological matrix analyzed (11).

Caution is warranted whenever half-lives of illicit drugs are cited in forensic casework because the number of human dosing studies are relatively few and participants are limited (usually \( n = 6 \) to 8). In some publications it is not always made perfectly clear whether \( t_{1/2} \) was derived from concentration-time plots for individual subjects or from an average curve for all subjects. The biological matrix analyzed, whether plasma, serum, or whole blood can impact on the elimination half-life as well as other pharmacokinetics parameters (11). The pharmacokinetics of a drug after therapeutic doses is not necessarily the same as after abuse doses because of enzyme induction and metabolic tolerance, which is often the situation in forensic toxicology casework. Instead of citing a definitive half-life for a particular drug, it would be more prudent to give a range of values or simply classify drugs as having short half-lives (e.g., GHB, 6-acetylmorphine, and cocaine), intermediate half-lives (e.g., morphine, codeine, and ethyl morphine), or long half-lives (e.g., diazepam, methamphetamine, and methadone).

Three successive blood samples are not ideal for a pharmacokinetic evaluation and the calculation of an elimination half-life. However, opportunities to perform such calculations in actual cases of impaired driving are rare, which motivates this short communication. The half-lives found for BZE (6.4 h) and MDMA (10.3 h) in this impaired driver are consistent with those published in the scientific literature.

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References