Driving Under the Influence of Opiates: Concentration Relationships Between Morphine, Codeine, 6-Acetyl Morphine, and Ethyl Morphine in Blood

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Abstract

Morphine and codeine are frequently identified in blood samples from impaired drivers. But whether these opiates reflect the use of prescription analgesics or abuse of the illicit drug heroin (diacetyl morphine) is not always obvious. Opiates, either alone or together with other drugs, were determined in 2573 blood specimens from impaired drivers by sensitive and specific methods of analysis. The specific metabolite of heroin 6-acetyl morphine (6-AM) was quantifiable in only 52 cases (2%) at mean, median, and highest concentrations of 0.015, 0.010, and 0.10 mg/L, respectively. The mean, median, and highest concentrations of morphine were 0.046, 0.03, and 1.13 mg/L, respectively (N = 2029). The corresponding concentrations of codeine (N = 1391) were 0.047, 0.01, and 2.40 mg/L. Ethyl morphine was identified in 63 cases at a mean concentration of 0.055 mg/L (median 0.03 mg/L). When 6-AM was present in urine (N = 324), the mean morphine/codeine ratio in blood was 7.5 (median 6.7), and this important ratio was less than unity in only two cases. This study finds compelling evidence that ~90% of apprehended drivers in Sweden with morphine and codeine in their blood had used heroin.

Introduction

Heroin (diacetyl morphine) is arguably the most dangerous recreational drug (1,2). Abuse of heroin has a high dependence liability and causes considerable physical and social harm to the individual and society (2). Moreover, the acute toxicity of heroin, especially after intravenous administration, is alarmingly high compared with other drugs of abuse, such as amphetamines or cocaine (3–5). Heroin overdose deaths are highly prevalent in various surveys of drug-related fatalities (6–8).

The metabolism of intravenously administered heroin occurs already in the bloodstream through the action of esterases producing the unique metabolite 6-acetyl morphine (6-AM). The 6-AM undergoes further rapid metabolism to produce morphine, which is eliminated from the blood more slowly by phase II conjugation reactions yielding morphine 3- and 6-glucuronides (9–16). Identifying 6-AM in blood or urine provides unequivocal proof that a person has used heroin. However, the short plasma elimination half-life of this metabolite (~15 min) means that it is seldom quantifiable in blood for more than 1½–2 h after a dose of heroin, although the window of

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therefore arises whether these opiates reflect use of heroin or samples from impaired drivers are analyzed. The question drugs codeine and ethyl morphine are therefore interrelated scheduled drugs in Sweden and are prescribed for relief of metabolism of acetyl codeine contained in clandestine heroin exceeded unity (1.0) gives compelling evidence that heroin morphine/codeine (Mo/Co) concentration ratio in blood from our laboratory suggested that when the medication with codeine or morphine. An earlier publication the police for toxicological analysis (24). This dramatic rise in urine samples (23).

A zero-concentration law for driving under the influence of scheduled drugs in Sweden (July 1, 1999) led to an appreciable increase in the number of blood samples submitted by the police for toxicological analysis (24). This dramatic rise in caseload prompted us to re-examine the concentrations of opiates in forensic blood samples and how these might best be interpreted to prove the driver had used heroin. Knowledge about the drug concentration in blood or serum is indispensable to allow reaching any conclusions about the effects on the individual, such as impairment of cognitive and psychomotor functioning.

This article deals with interrelationships between the concentrations of morphine, codeine, 6-AM, and ethyl morphine in blood samples from people arrested in Sweden for DUID over a five-year period (2000–2004). An attempt was made to evaluate whether the finding of morphine and codeine in blood is more a reflection of abuse of heroin or medication with codeine or morphine.

**Materials and Methods**

**Apprehending drug-impaired drivers**

Drivers are stopped and questioned by the police if they are involved in a crash, commit a moving traffic offense, are stopped in connection with routine sobriety controls, or are reported by other road users. The investigation begins with a roadside breath-alcohol screening test. If this test is positive (blood-alcohol concentration > 0.2 mg/dL or 0.02 g%) an evidential breath-alcohol test is conducted or a specimen of venous blood is taken. If the roadside breath-alcohol test is negative and the police decide that the driver shows signs of drug influence or impairment, a specimen of venous blood is taken for toxicological analysis (24).

When the zero-tolerance DUID law (July 1, 1999) was introduced the police were also allowed to examine a suspect's eyes with a flashlight to record reaction to light, and size of the pupils was measured with the aid of a pupillometer. The existence of gaze nystagmus was also noted along with other indications that might suggest use or abuse of drugs other than alcohol. The results of these simple observational tests are recorded on the arrest forms that are sent along with the blood and urine samples for toxicological analysis.

**Quantitative analysis of opiates in blood and urine**

One central laboratory (Department of Forensic Genetics and Forensic Toxicology, National Board of Forensic Medicine, Linköping, Sweden) is responsible for the toxicological analysis of blood and urine samples for the whole country (population 9 million). Two specimens of venous blood in 10-ml grey-stopper evacuated tubes that containing 100 mg sodium fluoride and 25 mg potassium oxalate as preservatives (TERUMO Europe N.V., Leuven, Belgium) are available for analysis. Whenever possible, a specimen of urine (10 mL) is also sent for toxicological analysis in a tube containing 1% NaF as preservative.

Enzyme immunoassay methods (EMIT-CEDIA) were used to screen for five classes of abused drugs, amphetamines, opiates, cannabis, cocaine metabolite, and major benzodiazepines, using an ADVIA 1650 instrument. The screening analysis was done on urine if available, otherwise on an aliquot of blood after precipitation of proteins with acetone. All positive results from the drug screening were verified by more selective and sensitive methods, such as gas chromatography–mass spectrometry (GC–MS) as described here.

**Determination of opiates in blood**

The analysis of morphine, codeine, 6-AM, and ethyl morphine in blood and urine was done by solid-phase extraction (Bond Elut Certify) and GC–MS with deuterium-labeled opiates as the internal standards (25). The GC–MS equipment was purchased from Agilent technologies GC model 6890N and MS 5973N with MS ChemStation and a quartz capillary column with DB5 as the stationary phase. Note that no prior hydrolysis step was included in the analytical procedure so the free-drug concentrations of opiates are being reported in this article.

Deuterium-labeled internal standards were added to 1 g or ~1 mL of whole blood and extracted on a solid phase after activation with methanol and washing through with water before applying the biological specimen (26,27). Any drugs retained on the solid phase were eluted by adding a mixture of dichloromethane, 2-propanol, and ammonium hydroxide. The solvent extract was concentrated under nitrogen before preparing the trimethylsilyl derivatives with BSTFA reagent.

For qualitative and quantitative analysis of opiates in blood the following mass fragments were used: m/z 414/417 (qualifier ions 361 and 577) for morphine, m/z 445/448 (qualifier ion 282) for codeine, m/z 414/417 (qualifying ions 361 and 473) for 6-AM, and m/z 459/448 (qualifier 296 and 430) for ethyl morphine. When 6-AM was determined in urine, m/z 399/402 was used for quantitative analysis, and the qualifier ions were m/z
The calibration plots for each of the opiates were linear, and the highest concentration on the plot was 0.4 mg/L for morphine, codeine, and ethyl morphine and 0.1 mg/L for 6-AM. If the opiate concentrations after an initial analysis exceeded the highest concentration on the standard curves, the specimens were re-analyzed starting with a small volume of blood and dilution to 1 mL with drug-free blood. The LOQ for reporting codeine, morphine, and 6-AM in blood was 0.005 mg/L, and for 6-AM in urine, the LOQ was 0.02 mg/L.

Statistical analysis

The frequency distributions of the concentrations of opiates in blood were skewed to the right so mean, median, and 2.5 and 97.5 percentiles were used as descriptive statistics. Differences between two means were compared by Student's t-test and two medians by the non-parametric Mann-Whitney test. Two proportions were compared by the chi-squared test.

Results

Origin of morphine and codeine in blood samples from impaired drivers

Figure 1 is a scheme showing the metabolism of illicitly produced heroin into morphine and codeine, which are the opiates mainly identified in forensic blood samples. Street heroin contains acetyl codeine as an impurity because codeine, which is a prominent alkaloid in raw opium, also undergoes acetylation (see Figure 1). Ethyl morphine is a constituent of cough medications available in Sweden and this opiate undergoes O-deethylation to produce small amounts of morphine.

Age and gender of DUID offenders with opiates in blood

The apprehended drivers with opiates in their blood (N = 2573) were mainly men (89%) with a mean age (± SD) of 33 ± 8.6 years. The women (11%) were aged 35 ± 8.9 years, and this mean difference of 2 years was statistically highly significant (t = 4.06, p < 0.001) as was the proportion of male offenders (chi-square = 873, p < 0.001). A relative frequency distribution of age of all DUID offenders with opiates in blood is shown in Figure 2.

Concentrations of opiates in blood samples from DUID suspects

Table 1 gives descriptive statistics for the concentrations of morphine, codeine, 6-AM, and ethyl morphine in blood samples from DUID suspects. Note that the number of analytical findings are more than the number of suspects (N = 2573) because many of the blood samples contained several of the opiates listed.

<table>
<thead>
<tr>
<th>Opiate in Blood</th>
<th>N</th>
<th>Mean (Median)</th>
<th>2.5 and 97.5 Percentiles</th>
<th>Min and Max Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>2029</td>
<td>0.046 (0.03)</td>
<td>0.006-0.21</td>
<td>0.005-1.13</td>
</tr>
<tr>
<td>Codeine</td>
<td>1391</td>
<td>0.047 (0.01)</td>
<td>0.005-0.34</td>
<td>0.005-2.40</td>
</tr>
<tr>
<td>6-AM</td>
<td>52</td>
<td>0.016 (0.01)</td>
<td>0.005-0.09</td>
<td>0.005-0.10</td>
</tr>
<tr>
<td>Ethyl morphine</td>
<td>63</td>
<td>0.055 (0.03)</td>
<td>0.006-0.26</td>
<td>0.005-0.39</td>
</tr>
</tbody>
</table>

* Blood samples might also have contained other licit or illicit drugs besides the opiates listed.
6-AM was identified in only 52 blood samples (2% of total) at mean, median, and highest concentrations of 0.016 mg/L, 0.010 mg/L, and 0.10 mg/L, respectively. Two blood specimens contained 6-AM (0.006 and 0.02 mg/L) as well as morphine (0.06 and 0.02 mg/L), but the concentration of codeine was below the LOQ.

A relative frequency distribution of the concentration of morphine in blood (N = 2029) is plotted in Figure 3, and the corresponding distribution for codeine (N = 1391) appears in Figure 4. The skewed nature of these distributions is evident so mean, median and 2.5 and 97.5 percentiles are more appropriate to use as the descriptive statistics (Table I).

Ethyl morphine was identified in 63 blood samples at mean, median, and highest concentrations of 0.055, 0.03, and 0.39 mg/L, respectively (Table I). In two cases, 6-AM was also present, which proves that these individuals had also taken heroin. Ethyl morphine was the only opiate identified in blood in 36 cases, and in 27 others, this cough medication was present together with other drugs. The relative frequency distribution for the concentrations of ethyl morphine in blood is depicted in Figure 5.

Table II presents descriptive statistics for the concentrations of morphine in blood depending on whether they were present alone or in various combinations. The mean and median concentrations of morphine in blood alone were lower (p < 0.01) than those in Table I, whereas the corresponding concentrations of codeine as the only opiate were higher (p < 0.01). The presence of low concentrations of morphine without any other opiates present suggests that a considerable length of time had elapsed after use of heroin or that the person was medicated with morphine. Many of the codeine-only cases can be attributed to the use of prescription drugs containing this analgesic. Conversion to the morphine metabolite was insignificant or the concentration of morphine had decreased below LOQ of the method by the time blood was sampled.

When both morphine and codeine were present together in blood samples (N = 883), the concentration of morphine was significantly higher and concentration of codeine was significantly lower compared with instances when these opiates were present individually (Table II).

Analyses of 6-AM in urine

6-AM as definite proof of heroin intake was identified in 324 urine samples although the concentration was below LOQ in blood (Table III). In these cases the mean (median) concentrations of morphine in blood were 0.078 mg/L (0.060 mg/L), being much higher than the coexisting mean (median) concentrations of codeine 0.012 mg/L (0.009 mg/L) (Table III). In another 404 DUID cases, 6-AM was identified in urine whereas morphine was the only opiate identified above LOQ in blood samples (data not shown).

When 6-AM was negative in urine (N = 42) the concentration of morphine in blood was appreciably less (mean 0.0036 mg/L, median 0.003 mg/L) than that of codeine (mean 0.024 mg/L and median 0.02 mg/L), which is more in line with use of prescription drugs containing codeine.

Concentration ratios of morphine to codeine in blood as evidence of heroin intake

The Mo/Co concentration ratios in blood are also shown in Table III and are arranged according to whether 6-AM was verified present in blood or urine as proof of heroin intake. The Mo/Co ratios were highest (mean 10.9, median 10.0, range 3.0 to 25) when 6-AM was still measurable
in blood, which indicates fairly recent use of heroin. When 6-AM was identified in urine \((N = 324)\) but not in blood (which also verifies use of heroin but further back in time), the mean, median, and range of Mo/Co ratios in blood were 7.5, 6.7, and 0.4–58, respectively. In only two cases \((0.6\%)\) was the Mo/Co ratio in blood less than unity. The mean \((\text{median})\) concentration ratios of morphine to codeine in blood were 2.6 and 1.5 in 42 cases when 6-AM was negative in urine. When urine specimens were not available for analysis of 6-AM \((N = 467)\) the mean and median Mo/Co ratios were 6.1 and 5.7, respectively, suggesting that many of these individuals had used heroin before driving.

Table III. Concentrations of Morphine (Mo), Codeine (Co) and Mo/Co Ratios in Blood With or Without 6-AM present in Blood or Urine as Evidence of Heroin Intake

<table>
<thead>
<tr>
<th>Presence of 6-AM</th>
<th>N*</th>
<th>Morphine (mg/L)</th>
<th>Codeine (mg/L)</th>
<th>Mo/Co Ratio Mean (Median) and Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-AM positive in blood</td>
<td>50</td>
<td>0.210 (0.16)</td>
<td>0.023 (0.02)</td>
<td>10.9 (10.0) 3–25</td>
</tr>
<tr>
<td>6-AM negative in blood</td>
<td>833</td>
<td>0.070 (0.05)</td>
<td>0.035 (0.01)</td>
<td>6.5 (6.0) 0.01–58</td>
</tr>
<tr>
<td>6-AM positive in urine</td>
<td>324</td>
<td>0.078 (0.06)</td>
<td>0.012 (0.009)</td>
<td>7.5 (6.7) 0.4–58</td>
</tr>
<tr>
<td>6-AM negative in urine</td>
<td>42</td>
<td>0.035 (0.003)</td>
<td>0.023 (0.02)</td>
<td>2.6 (1.5) 0.25–12</td>
</tr>
<tr>
<td>Urine not available for analysis of 6-AM</td>
<td>467</td>
<td>0.068 (0.05)</td>
<td>0.053 (0.01)</td>
<td>6.1 (5.7) 0.01–31</td>
</tr>
</tbody>
</table>

* Only cases with both morphine and codeine measurable in blood are considered in this table.

Figure 6 plots the Mo/Co concentration ratios in blood from 883 cases of DUID and in 90% of these the ratio exceeded unity and thus suggesting use of heroin.

Concentrations of opiates in blood from non-traffic cases

Table IV compares age, gender, and concentrations of opiates in blood of people arrested for use of illicit drugs, so-called petty drug offences (non-traffic cases). There was again a clear dominance of male offenders \((88\%)\), and they tended to be a few years younger \((30\text{ years})\) compared to DUID suspects \((33–35\text{ years})\) on average. The concentrations of morphine, codeine, ethyl morphine, and 6-AM in blood samples from non-traffic cases were similar to the apprehended drivers (see Table I). Furthermore, blood samples from only 48 of 1825 non-traffic cases \((2.6\%)\) contained quantifiable amounts of 6-AM, which also agrees well with the DUID suspects \((2\%\) had 6-AM in blood).

Discussion

Among psychoactive drugs identified in blood samples from apprehended drivers in Sweden, the opiate analgesics morphine and codeine are highly prevalent \((28\%)\). Although the presence of these substances could be explained by use of prescription medication, they might also have arisen as metabolites of heroin (see Figure 1). Morphine and codeine are prominent alkaloids in raw opium and both undergo acetylation during clandestine synthesis of heroin. After use of illicit heroin, acetyl codeine is metabolized into codeine, which tends to complicate interpretation of DUID cases when morphine and codeine are identified in blood samples \((23\%)\). Driving a motor vehicle after use of prescription medication containing

Table IV. Age, Gender, and Concentrations of Morphine, Codeine, 6-AM, and Ethyl Morphine in Blood Samples From People Arrested for Use of Illicit Drugs (Non-Traffic Cases)

<table>
<thead>
<tr>
<th>Opiates in Blood (Non-traffic cases)*</th>
<th>Gender</th>
<th>N (%)</th>
<th>Age of Suspects Mean (Median) and Range</th>
<th>Blood Conc. (mg/L) Mean (Median) and Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>Men</td>
<td>1415 (88)</td>
<td>29 (27) 15–62</td>
<td>0.043 (0.03) 0.38</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>190 (12)</td>
<td>26 (24) 15–50</td>
<td>0.037 (0.03) 0.22</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>1605 (100)</td>
<td>29 (27) 15–62</td>
<td>0.043 (0.03) 0.38</td>
</tr>
<tr>
<td>Codeine</td>
<td>Men</td>
<td>783 (88)</td>
<td>31 (29) 15–55</td>
<td>0.026 (0.01) 1.0</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>108 (12)</td>
<td>27 (24) 16–53</td>
<td>0.021 (0.01) 0.30</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>891 (100)</td>
<td>30 (28) 15–55</td>
<td>0.026 (0.009) 1.0</td>
</tr>
<tr>
<td>6-Acetyl morphine</td>
<td>Men</td>
<td>42 (88)</td>
<td>31 (29) 19–50</td>
<td>0.0134 (0.0095) 0.05</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>6 (12)</td>
<td>23 (23) 19–28</td>
<td>0.0095 (0.008) 0.02</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>48 (100)</td>
<td>30 (28) 19–50</td>
<td>0.0129 (0.009) 0.05</td>
</tr>
<tr>
<td>Ethyl morphine</td>
<td>Men</td>
<td>28</td>
<td>30 (29) 16–44</td>
<td>0.15 (0.04) 0.79</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
</tbody>
</table>

* N = 1825 cases.
opiates is exempt from the zero-tolerance law provided the drugs were taken in accordance with a physician’s ordination (24).

In the present study, the concentrations of free morphine and free codeine in blood covered a wide range (Tables I and II), and the frequency distributions were skewed to the right as shown by the large discrepancies between mean and median values. The median and 2.5 and 97.5 percentiles are more appropriate as descriptive statistics to characterise these distributions. The concentrations of morphine and codeine in DUID blood samples were mostly within the therapeutic range expected for legitimate use of prescription analgesics for relief of moderate to severe pain, namely 0.01 to 0.07 mg/L for morphine and 0.01 to 0.25 mg/L for codeine (29). The plasma elimination half-lives of morphine and codeine are fairly similar, being in the range of 2 to 4 h, albeit with large interindividual variations (30).

Less than 10% of codeine is converted to morphine, which means that the $C_{\text{max}}$ of codeine is considerably higher than $C_{\text{max}}$ of morphine. Because these two opiates have similar plasma elimination half-lives (2–4 h), the concentration of morphine in blood drops below LOQ much sooner than that of codeine (31). When 100 mg of codeine phosphate was given to nine healthy volunteers, the $C_{\text{max}}$ in blood was 0.183 mg/L (range 0.114–0.326 mg/L) (32). The concentration ratios of morphine-to-codeine in blood were less than unity for up to 24 h post-dosing. In another study, 12 volunteers received 60 mg codeine phosphate, and the mean plasma $C_{\text{max}}$ for codeine (± standard deviation) was 0.115 ± 0.041 mg/L (33). The administration of a second 60-mg dose increased $C_{\text{max}}$ to 0.136 ± 0.037 mg/L and after seven daily doses $C_{\text{max}}$ was 0.149 ± 0.060 mg/L. The coexisting $C_{\text{max}}$ concentrations of morphine in this study were 40–50 times lower than those of codeine: mean plasma morphine concentrations were 0.0024 mg/L (first dose), 0.0027 mg/L (second dose), and 0.0038 mg/L (seventh dose). These studies verify that after therapeutic doses of codeine, it is virtually impossible to find a Mo/Co concentration ratio in blood less than 1.0 (34).

The concentrations of codeine in blood of DUID suspects in this study were fairly low and within the therapeutic interval: mean 0.047 mg/L and median 0.010 mg/L. In a study of impaired drivers in Norway, when codeine was the only drug present in blood, the mean and median concentrations were 0.175 and 0.127 mg/L, respectively (35). A concentration of codeine exceeding 0.221 mg/L was considered above the therapeutic range. In this Swedish material, 27 individuals had a codeine concentration above 0.221 mg/L and had probably overdosed with codeine medication before driving.

A key question arising during prosecution of DUID suspects is whether the concentrations of morphine and codeine in blood might reflect use of prescription drugs (opioid analgesics) or abuse of heroin (23). Many blood specimens in this study ($N = 499$) contained codeine without any measurable amounts of morphine (Table II), which probably reflects medication with codeine and the fact that the concentration of the morphine metabolite had dropped below LOQ by the time that blood was taken. Morphine was the only opiate identified in 1146 cases of DUID, which either means the person was medicated with morphine or an appreciable time had elapsed after the last use of heroin. In 9% of these morphine-only cases, the concentration in blood was above 0.05 mg/L and at this level might have resulted in impairment of cognitive and psychomotor functioning (36).

The enzyme responsible for converting codeine into morphine (CYP2D6) exhibits polymorphism and rapid and slow metabolizers have been identified in the population (20). The particular genotype a person inherits has relevance when codeine and morphine concentrations in blood are interpreted or if a person shows an unusual reaction after repetitive therapeutic use of codeine (19,37). Depending on the person’s ability to metabolize codeine into morphine, the concentration of one or both opiates might have dropped below the LOQ by the time the blood was drawn. Morphine is sometimes administered to victims of a road-traffic crash to relieve pain from any injuries sustained. This treatment, which is usually well documented in hospital records and police reports, obviously needs to be considered when toxicological results of opiates are interpreted.

Two pharmaceutical products registered in Sweden contain ethyl morphine as the active ingredient (Cocilanna-Etyfin® and Lepheton®) and these are normally prescribed as cough medication. The pharmacokinetics of ethyl morphine was investigated in eight subjects after a dose of 1.5 mg/kg body weight was administered (38). The median $C_{\text{max}}$ was 0.341 mg/L (range 0.140–0.532 mg/L) and the drug was eliminated with a terminal half-life of ~2 h (range 1.7 to 2.4 h). In DUID suspects ($N = 63$), the mean and (median) concentration of ethyl morphine was 0.055 mg/L (0.030 mg/L) and the range was 0.005 to 0.39 mg/L being in good agreement with values expected after therapeutic use of cough medication.

The unique metabolite of heroin (6-AM) was verified in only 52 of 2573 opiate-positive blood samples (2%). In two cases, 6-AM and morphine were present in blood without there being any measurable amounts of codeine, which suggests that these individuals had taken pharmacologically pure heroin. In a large number of non-traffic cases (Table IV), representing mainly people arrested for use of illicit drugs, $N = 48$ (2.6%) had 6-AM in blood. These non-traffic cases also showed a high predominance of men who on average were a few years younger than the impaired drivers. The mean, median, and maximum concentrations of morphine and codeine in blood of non-traffic cases were remarkably similar to the findings for DUID suspects.

The short elimination half-life of 6-AM (10–15 min) makes it clear that this metabolite of heroin is rarely identified in blood samples from impaired drivers. When 6-AM was above the LOQ in blood, the concentration of morphine (mean 0.210 mg/L) was considerably higher than that of codeine (mean 0.023 mg/L). The 10-fold higher concentration of morphine compared with codeine and the similar elimination half-lives of the two opiates means that codeine will not always be measurable in blood after abuse of heroin. This supports the conclusion that many DUID cases in which morphine was the only drug present in blood had been abusing the illicit drug heroin. Batch to batch variations in the amounts of acetyl codeine in the heroin preparations purchased also impacts on the relative
concentrations of morphine and codeine in blood in this study of DUID suspects.

The time between arrest and sampling blood for toxicologic analysis varies in any individual impaired driving case, but it is mostly between 30 and 90 min after arrest, and thus an even longer time has elapsed after the last use of heroin (9,12). Unequivocal proof of heroin intake is easier to obtain if specimens of urine are available for toxicologic analysis because this extends the window of detection by several hours compared with blood samples (10). When 6-AM was identified in blood or in urine (N = 374), the Mo/Co concentration ratio in blood averaged 7.9 (median 7.0) and was less than unity in only two instances. In DUID investigations when urine is not available for analysis, finding a Mo/Co concentration ratio in blood exceeding unity gives compelling evidence for abuse of heroin. Applying this standard to the entire sample of opiate positive blood specimens with both morphine and codeine above LOQ (N = 883) showed that about 90% of suspects (N = 795) had used heroin before driving.

Conclusions

This study verifies that opiates such as morphine and codeine are common analytical findings in blood samples from DUID suspects either alone or together with other drugs. Evidence of heroin use is easier to obtain if urine is available for analysis because the window of detection for the specific metabolite 6-AM is then much longer (8–10 h) compared to blood (1½–2 h). When urine is not available, compelling evidence of heroin use is obtained if the Mo/Co concentration ratio in blood exceeds unity. With codeine as the only opiate present in blood or a Mo/Co concentration ratio less than unity makes it more likely that prescription medication containing codeine had been taken before driving.

This large-scale investigation of DUID suspects apprehended in Sweden where a zero-tolerance law operates provides a comprehensive picture of the concentrations of morphine, codeine, 6-AM, and ethyl morphine likely to be found in forensic blood samples.

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