Concentrations at about 5 ng/ml or higher have crash risks comparable to alcohol at 0.15% [152].

In situations where past cannabis exposure can lead to sanctions (workplace, pre-employment testing and prisons), the major urinary metabolite 11-nor-Δ^9-tetrahydrocannabinol (cTHC) is measured following hydrolysis of the glucuronide. In most cases a cut-off of 15 ng/ml is applied, although cut-offs of 50 or even 100 ng/ml are occasionally employed.

The mean urinary excretion half-life of cTHC was about 1.4 days in both infrequent and frequent users [155]. However, frequent users have apparent terminal urinary excretion half-lives of up to 10 days. The last positive specimens were found after 4 and 17 days for cTHC with a cutoff 15 ng/ml in infrequent and frequent users, respectively [155]. Slightly longer detection times of up to 12 and 25 days have been observed in low and regular use, respectively [156–159].

Concerns have been raised over the possible contribution to death from use of cannabis in persons with compromised cardiac function (e.g. coronary artery disease). Sharp rises in blood pressures and heart rate could give rise to myocardial infarctions in susceptible persons [160]. An increased incidence of stroke should also be considered.

6.5. Heroin and other opioids

Heroin is converted within minutes to morphine through the intermediate 6-AM. All species are active pharmacologically, although both heroin and 6-AM are only present in blood and tissues for a relatively short period. Morphine is often the dominant active species in cases and is removed from the body by metabolism to 3- and 6-glucuronides and excretion in urine and bile. Morphine is rapidly excreted in urine as glucuronides, with up to 85% of the dose recovered in urine within 24 h. Only small amounts of morphine are excreted unchanged (2–10%). The presence of 6-AM in urine distinguishes heroin use from morphine. Small amounts of codeine are also present in the urine of heroin users because of the presence of acetylcodeine in the heroin.

Morphine (free) concentrations in blood in deaths attributed to heroin can typically vary from less than 0.1 to over 1 mg/l, although the median concentration in Victorian deaths is about 0.2–0.3 mg/l [161]. Total morphine concentrations range to over 2 mg/l, although the median is about 0.3–0.6 mg/l. When morphine is absent in urine or has concentrations less than 1 mg/l this suggests a death shortly after injection and importantly suggests the deceased may not have been a regular user and hence had little tolerance to the drug.

The ability of laboratories to measure the two glucuronide conjugates of morphine independently rather than collectively as total morphine using LC–MS techniques may lead to an improvement in the interpretation of heroin/morphine toxicity [162,163]. However, given the variability in response to morphine and the possibility of substantial tolerance developing it is unlikely that any morphine or metabolite concentration will ever be predictive of toxicity without a complete understanding of the pathology and the circumstances of the case. This is exacerbated by polydrug use typically seen in heroin users which will increase the inherent toxicity of the drugs used [161].

Morphine and its analogs such as diacetylmorphine (heroin), codeine, oxycodone, hydromorphone, etc. are some of the many dozen opioids that form an important class of analgesics. While there are many important and legitimate medical uses, their abuse is widespread and leads to great harm in the community.

Synthetic derivatives such as methadone, buprenorphine, meperidine (pethidine), propoxyphene and fentanyl show many significantly different physiochemical and pharmacokinetics features to the morphine analogs, although they act in a very similar way to morphine. A summary of these features are shown in Table 2 for selected opioids.

In postmortem context, the morphine analogs are water soluble and show relatively low volumes of distribution. Hence, there ability to become re-distributed after death is relatively small. There is no evidence in humans that morphine concentrations in blood change much after death in the immediate postmortem period. Hydrolysis of morphine glucuronides back to morphine in decomposing specimens or bodies is a particularly important process event and can easily lead to erroneous conclusions (see earlier).

The more lipid soluble synthetic opioids such as methadone, fentanyl and meperidine will show increases in concentration after death (see Section 6). Furthermore, with long half-life drugs such as methadone significant risks are associated with drug accumulation from one dose to the next. This has led to a substantial increase in mortality both on the street and in methadone maintenance programs [164–167].

The development of tolerance to opioids is particularly important in that it seriously limits the ability to interpret the significance of blood concentrations. For example, morphine concentrations in deaths attributed to the use of heroin or morphine can vary from trivially low concentrations to many milligrams per liter. For this reason alone, without a thorough assessment of the circumstances toxicology results provide little guidance. The ratio of morphine and morphine glucuronides can sometimes assist. Acute use can be reasonably assumed when urinary concentrations of morphine are low or even absent and morphine is present in blood.

7. Concluding comments

The analysis of postmortem specimens can provide special challenges for forensic toxicologists. The selection of specimens is large, although not all specimens are suited to the analysis of all drugs. Hence, it is necessary to identify the types of substances expected and tailor the collection of specimens accordingly. The collection of several specimens to guard against the possibility of poor specimen collection is warranted. Invariably, the use of peripheral blood, particularly femoral, is warranted to reduce the number of artifacts.

Many drugs show instability and many drugs show concentration changes even when the postmortem interval is relatively short. Cocaine and heroin are rapidly hydrolyzed to their respective metabolites. Morphine glucuronide conjugates show instability in postmortem specimens producing morphine and substantially affecting the proportion of morphine to total morphine.

Postmortem forensic toxicology provides a challenge to the scientist not only in terms of analysis but also in terms of the proper interpretation of the drug detections. Artifacts caused by poor sampling, poor condition of the body and redistribution severely limit the interpretation of any analytical results. Given the variable responses seen with the drugs of abuse and the often rapid development tolerance, toxicological results must not be interpreted without a full picture of the circumstances of the case and elimination of relevant considerations from a postmortem examination.

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