bulletin

Clinical and medico-legal implications of drug testing for cannabis

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Key points

- Cannabis is the most prevalent illicit drug found in routine clinical and medico-legal drug testing

- The amount of cannabis metabolite found in urine cannot be correlated with time of use, amount ingested or pharmacological effect

- Urine is the easiest biological fluid for identifying recent cannabis use

- Baseline urinary Carboxy-THC levels are very useful in differentiating between infrequent, frequent and heavy users of cannabis

- Successive Carboxy-THC: creatinine ratios can establish continued use or reduction to abstinence

- Caution should be exercised in interpreting cannabis results if fluids other than urine are used for testing

In Australia, drug testing has been part and parcel of clinical management of patients on drug treatment programs since the late 1960s when methadone was introduced as a heroin substitute. Since then, the discipline has evolved into an industry encompassing public and private sector laboratories, forensic institutions and racing laboratories. The scope for drug testing has widened from clinical management to sport, the workplace, correctional institutions and the judicial system. Cannabis is one of many drug types commonly tested for in all these jurisdictions; it is paradoxically easy to detect in biological fluids but complex to interpret.

The rationale for drug testing people for cannabis is multifactorial. For patients on (essentially New South Wales) public drug treatment programs, clinicians have historically chosen not to screen for cannabinoids; the rationale being that heroin was the main drug of dependence, most clients smoked cannabis anyway and a toxicology report indicating cannabis use, could jeopardise an otherwise favourable progress report. However, for many patients, especially those in residential rehabilitation environments, a policy of "no drugs" specifically includes cannabis. In many drug treatment centres throughout NSW, concurrent use of cannabis can adversely affect client management[1] and there is now a need for the monitoring of cannabis dependence. Australian defence forces and many heavy industries maintain a strict drug policy and may dismiss personnel for continued cannabis use.

Since the implementation of Occupational Health and Safety Acts in various States,[2,3] although drug testing is not specifically mentioned, there are clauses mandating managerial responsibility for a safe working environment. Although there is a paucity of data as to the extent of substance use within the Australian workforce, the need to ensure the (mainly blue collar) workforce remains drug-free, appears to comply with the relevant sections of the Act by eliminating the possible risks to health and safety of employees and visitors by persons using drugs that have the potential for impairing the user whilst in the workplace.

Metabolism of tetrahydrocannabinol

Tetrahydrocannabinol (THC) is the psychoactive ingredient in cannabis. It is extensively metabolised to a number of substances including the active metabolite, 11-hydroxy-THC and the principal inactive metabolite, 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (Carboxy-THC).[4-6] Urine testing for cannabis involves firstly, the detection of one or more cross-reacting cannabinoids using immunoassay.[7-9] Confirmation of cannabis use involves the identification and often quantification of Carboxy-THC using gas chromatography-mass spectrometry.[10-12]

Excretion of cannabinoids

Following cannabis use via smoking, orally or by injection, THC is rapidly absorbed and distributed into body fat. Drummer[5] reported that approximately 20% of THC is excreted in urine and 40% in the faeces. THC is found in blood, oral fluid, hair and sweat; 11-hydroxy-THC is also found in blood, while Carboxy-THC is the main urinary metabolite. Testing for cannabis use involves identification of either THC or Carboxy-THC, depending on the matrix. The active metabolite, 11-hydroxy-THC, is often cited as a marker of very recent cannabis ingestion, as it is found at a higher concentration in blood when cannabis is consumed than if smoked.[5] Although very small amounts of THC are excreted in urine, there is little value in attempting to identify it, as it is only present for a short period following cannabis use and testing requires a separate procedure.[10]

The question most often asked by clinicians, drug counsellors, lawyers and occupational health and safety representatives is, "how long does cannabis stay in the system?" It is a reasonable question but one that cannot be answered in a few words. Firstly, most published studies on the excretion of cannabis have been conducted using cigarettes containing a known amount of THC, either 1.75% or 3.55% and there is not necessarily a correlation between such controlled doses and use of "street" cannabis. Secondly, subjects are usually abstinent prior to the study, and thirdly, there is a wide variability in excretion profiles between subjects.[13] The rate-limiting step in the metabolism of THC is the slow redistribution from body fat deposits into the blood.[14] The concentration of THC found in fatty tissue becomes a function of the amount, frequency and potency of cannabis smoked.[15] Unlike interpretation of laboratory tests for the majority of drugs of abuse, cannabis stands out as being the single substance that requires caveats before one can provide an interpretation; this being, was the person a naïve, occasional or chronic user?

For naïve users, cannabis can be eliminated within hours after use and is usually eliminated within 24 hours. In controlled studies, Huestis et al.[15] reported large intersubject variability in the elimination of Carboxy-THC, ranging from 8 hours in one subject and approximately 1 day in three subjects. In another study into occasional cannabis use, Huestis and Cone[16] studied volunteers who smoked a single THC cigarette once a week for 3 weeks. They determined an average elimination time of 2 days for cannabinoids. Unfortunately there has been a paucity of data on the excretion and detectability of cannabis in chronic users. Cone[17] had advised that following use, urinary cannabinoids rise and then fall rapidly, taking up to 2 weeks in chronic users before dropping down to levels approaching the screening cutoff. Huestis[4] also reported levels of Carboxy-THC sharply drop to 20-50 ng/mL, and then decrease at a much slower rate.

Earlier studies on the elimination of cannabis by Ellis et al.[18] found residues of cannabinoids in subjects at up to 77 days of abstinence. However, they used a 20 ng/mL cutoff; one no longer appropriate for routine urine testing. The most useful studies into the relationship between excretion patterns of cannabinoids and chronic users of cannabis were conducted by Manno et al.[19] and Huestis and Cone.[16] These studies were predicated on an earlier finding by Hawks[20] who showed that by normalising the excreted amount of urinary Carboxy-THC to the creatinine (cannabis ratio), one obtained a more useful result.

Huestis found the best predictor of new use was achieved when the ratio was ≥ 0.5 relative to the previous sample taken at least 24 hours prior. Goodwin et al.[21] determined the elimination time in heavy cannabis users correlated with the ratio in their first urination following abstinence.

Interpretation of cannabis results should always be predicated on the possibility of a negative gap, i.e. the time interval between first negative and last positive urine test. As Carboxy-THC is highly lipophilic (i.e. it is easily able to be dissolved in fats) and its reabsorption from fatty tissue is a slow process it can result in a negative urine occurring on one particular day followed by a positive test later. This negative gap is dependent on an individual's body mass index (BMI). Goodwin found a direct correlation of BMI with the day of last positive urine. He concluded that the higher the ratio at first urination, the longer the period between first negative and last positive urine. An initial low ratio implies low use and conversely, a high initial ratio confirms chronic use.

Oral administration of THC

Although the majority of users undoubtedly smoke cannabis, toxicologists are often asked whether a laboratory result from a client or employee could have arisen from a person ingesting THC in so called "cannabis cookies". Gustafson et al.[22] measured the kinetics of orally administered THC and concluded that oral absorption of THC from the gut was slow and erratic; mean elimination half-lives of Carboxy-THC for single doses were dose-dependent, but in the order of 24 hours. Using these data, one could eliminate such excuses by reviewing the time frame from alleged consumption, amount ingested and the date of the urine test.

Cannabis and the issue of impairment

Since the introduction of drug testing into the Australian workforce, there has been much resistance by unions; their claims being that, inter alia, a person smoking a joint on a weekend could not possibly be impaired when they were at work, and what they did in their own time was personal. The pharmacological effects of cannabis and the period of acute intoxication have been well documented,[5,23] providing compelling data to support both acute and long term effects of cannabis use. As there is no relationship between the results of a drug test, pharmacological effect, time of use and amount used, there exists an argument that urine drug testing per se does not identify impairment and is therefore an inappropriate means of preventing accidents within the workplace. Researchers studying the effects of long-term cannabis use have defined both acute and long term impairing effects of the drug[24-26] and thus it is too simplistic to attempt to define a time frame of use and corresponding potential effects. In the lay community, emphasis is all too often placed on the acute impairing time of cannabis i.e. up to 4-5 hours after smoking; this concept understandably being easier to comprehend than tackling a more holistic approach to drug use within the workforce. It is an uncomfortable predicament for management; on one hand recognising that 1-2 drinks on a weekend would not have any impairing effect on an employee's performance whilst in the workplace, and on the other hand having to make a judgement on someone using 1-2 cannabis joints. The issue is not necessarily one of legality, but one in which a drug test simply cannot identify the alcohol consumed but which can detect cannabis use.

Cutoffs in cannabis testing

Cutoffs are simply reporting levels and a means of deeming whether a drug is present or not. Cutoffs were originally determined empirically, based on available technology. Today there is less of a relationship between the ability to detect a drug in a biological fluid and the cutoff. Originally, the screening cutoff for cannabis was 20 ng/mL;[27] however laboratories were being challenged by claims of passive absorption, forcing the cutoff to be raised to 100 ng/mL. This resulted in fewer false positives but allowed many recent users to escape detection. The screening cutoff is now accepted as 50 ng/mL (ug/L) and 15 ng/mL for the confirmatory analysis of Carboxy-THC. Liu et al.[28] showed that using a combination of 50 ng/mL screening cutoff followed by 15 ng/mL confirmatory cutoff, one obtained a confirmation rate of around 99%. Importantly, use of this combination eliminates any claims of passive inhalation.

On-site testing

At one time, drug testing was the domain of the laboratory. In recent years, following the trend in the United States, the development of on-site screening devices has become popular in the workplace and in some clinical settings. These devices, using either a few drops of urine placed onto an absorbent pad, or having the pad integrated into a collection cup, allow organizations to perform screening tests for specified drug groups. Although not always as accurate as laboratory-based screening tests, they do provide the opportunity of a result within a few minutes and allow workers with a "negative" test to return to work immediately. Due to cost and the inability to provide any indication of cannabis increase or reduction, such devices have little value in a clinical setting.

Cannabis testing in saliva

Although THC is found in saliva (or more correctly, oral fluid), levels are very low and there are often difficulties in recovery from collection pads. Essentially, THC comes from debris within the oral cavity after smoking, rather than diffusion from plasma. Studies by Cone et al.[29] concluded that for reliable identification of THC in oral fluid (fewest false negatives), the most appropriate screening cutoff should be set at 4 ng/mL, followed by a confirmatory cutoff of 2 ng/mL. The ROSITA study[30] concluded that no existing on-site device for THC was sensitive enough to be used for workplace drug testing.

The issue at stake is one of duty of care. Studies such as ROSITA have been available for a number of years, yet many industries, wishing to avoid the often confrontational issues of mandating for urine tests, have opted for oral fluid testing.

Urine testing has the ability to identify infrequent as well as chronic cannabis users, and this may be perceived as either unfortunate, unfair or an invasion of their personal life outside the work environment. Conversely, current use of relatively insensitive on-site devices for saliva may be viewed as ineffective and to a degree, a failure to comply with a duty of care in eliminating risk of cannabis-induced impairment in the workplace. Furthermore, the now established knowledge of the relative insensitivity of oral fluid screening might well encourage people to smoke cannabis before or whilst at the workplace.

Conclusion

Cannabis has been the most studied drug of abuse and is the most prevalent illicit substance found in the workplace. Laboratory-based testing is a mature discipline with a high degree of accuracy. Interpretation of results remains contentious and as further studies evolve on the excretion by long-term users, it may be possible to use algorithms to accurately predict time of last use. To date, the high individual variability in metabolism and excretion of cannabinoids

precludes this approach, despite a number of research studies reporting various terminal elimination half-lives of Carboxy-THC. Individual laboratory reports cannot be correlated with usage; however as more tests are conducted on individual patients or employees, the changing pattern of corrected metabolite becomes easier to interpret. In Australia, oral fluid testing for THC continues despite amendments to U.S. workplace testing guidelines, recommending a moratorium on its use until the sensitivity of procedures becomes more robust.

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