

Urine Adulteration in Drug Testing

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Abstract

Drug abusers may attempt to conceal their drug intake by interfering with the clinical specimens sent to the laboratory for toxicology screening. This report describes a 27-year-old drug abuser who repeatedly submitted urine samples with abnormally low creatinine concentrations in order to invalidate drug screening. Adulteration by addition of ammonia-containing cleanser was suspected and eventually admitted by the patient. This case illustrates common features of urine adulteration. Various strategies for the prevention and detection of adulteration are also discussed.

Key words: High pressure liquid chromatography, Immunoassay, Substance abuse testing, Substance-related disorders, Urine chemistry

Introduction

Drug abuse is a secretive drug-seeking behaviour and relapse from rehabilitation is common. Successful abstinence determines employment opportunities, financial security, and other lifestyle factors, whereas failure may invite familial or social pressure. Denial is therefore a common feature and psychiatrists are not always provided with accurate information about drug use. When clinical symptoms or signs of drug abuse are absent during rehabilitation, biochemical testing of urine or serum is an important aspect of the follow-up procedure. To avoid unwanted consequences, patients may try to interfere with the normal analytical procedure by manipulating the specimen submitted to the laboratory.

Case Report

A 27-year-old man, who had no relevant family history, presented at a psychiatric clinic with substance-induced

psychotic disorder with hallucination, which was mainly auditory. He consumed half a bottle of cough mixture prepared by a local pharmacy every day, and his consumption was limited by financial constraint. He was prescribed benzhexol, zuclopenthixol, risperidone, and propranolol. Urine drug testing was arranged and the clinician advised the patient that his disability allowance would be discontinued if the abused drug was found in his urine.

Clear, straw-yellow urine was submitted by the patient on repeated occasions during the course of treatment. Urine drug screening by high-pressure liquid chromatography coupled with ultraviolet spectral scanning (REMEDI HS analyser; Bio-Rad Laboratories, Hercules, USA), was negative. However, a very low creatinine concentration of 0.05 mmol/L was found (normal range, 7.1 to 17.7 mmol/day).¹ Urine adulteration was suspected and additional tests were therefore performed with the following results: magnesium 0.09 mmol/L (normal excretion, 3.0-5.0 mmol/day), osmolality 517 mmol/kg H₂O (normal range, 250-900 mmol/kg H₂O), urine pH of 9 (normal range, 4.5-8), urea concentration 134.3 mmol/L (normal range, 430-710 mmol/day).

The patient was required to provide another urine specimen when supervised by a male nurse. Analysis revealed a similar biochemical profile (creatinine, 0.16 mmol/L; pH 10). It was suspected that an alkaline adulterant had been added to the specimen. On further inquiry, the nurse revealed that the urine collection procedure was not directly supervised. Another sample collection was scheduled 2 months later, using a special urine collection bottle with a temperature chart and seal. The creatinine concentration was within the normal range and ephedrine/pseudoephedrine, codeine, risperidone metabolites, and promethazine were detected in the urine. The patient admitted that he was still abusing cough medicine and upon repeated questioning eventually revealed that he had added soap solution to his urine specimens. His request for a disability allowance was refused and he subsequently defaulted follow-up. He then

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attended another hospital and submitted a similarly diluted urine specimen (creatinine, 1.7 mmol/L; pH 9). Amphetamine was detectable (473 ng/mL) but at a level below the conventional cut-off concentration (1000 ng/mL).

Discussion

Urine adulteration is the manipulation of urine specimens intended for drug testing to provide false-negative, or less commonly, false-positive results.² The prevalence of adulteration can be unacceptably high. George and Braithwaite estimated that 20% of specimens were outside physiological urinary pH and that 84% of specimens submitted for drug screening would need retesting if the dilution cut-off for urine creatinine concentration recognised by the National Institute on Drug Abuse (1.8 mmol/L) was applied.³ Local data are not available but it is believed that urine adulteration may be less prevalent in Hong Kong than in some other locations because on-site workplace drug testing is not common in Hong Kong. Many practices aimed at avoiding detection have been described, including substituting a drug-free specimen and *in vivo* and *in vitro* adulteration.⁴

The patient's own urine collected during drug abstinence, urine from other people, or commercial drug-free urine preparations have been used for substitution. Since all measurable urinary parameters are similar to normal values in such cases, it is difficult to prove dishonesty. A special collection cup that indicates sample temperature has been used. However, this does not prevent possible prewarming of the specimen to an acceptable temperature by placing it in the axilla or vaginal cavity, for example.⁵ Direct observation of sample collection by same-gender health personnel is unpleasant and occasionally fails because, in extreme cases, the patient may use a urinary catheter to transfer the substitute sample to the urinary bladder before sample collection.⁴ The potential use of oral polyethylene glycol as an enteral dilution marker has recently been highlighted by Gauchel et al.⁶ Detection of polyethylene glycol by reversed-phase high-performance liquid chromatography in post-ingestion urine virtually excludes the possibility that substitution of specimens will escape detection.

In vivo adulteration refers to the use of diuretics and/or the drinking of massive amounts of water before sample collection so that very diluted urine is provided. This is done in the hope that the drug concentration will be reduced to less than the cut-off value for detection. All laboratory assessments are affected by this practice. However, it is not necessarily an effective way to prevent detection since conventional cut-off values for most abused drugs are well above the detection limit and, in most circumstances, lowering the cut-off level will ensure that the abused drug is still detected.

In vitro adulteration refers to the manipulation of the sample after collection. It occurs more commonly in cases of unanticipated drug testing, when preparation of a substitute specimen or ingestion of water and/or diuretics is not possible. A great variety of offending agents, have been described, including Visine eyedrops,⁷ hand soap, Dettol or

vinegar,⁸ table salt or bleach,⁹ and lemon juice,¹⁰ but the agents most commonly used are those that are easily accessible in the toilet, such as fresh or toilet water, cleansing agents, and soap.

The various adulterants may interfere differently with each of the detection methods. Most of the adulterants will not pose a problem in a modern laboratory because more than one analytical method is used for routine toxicology analysis. A common combination is immunoassay and high-pressure liquid chromatography. A deviation in results obtained using different methods should raise suspicion of urine adulteration and indicate that confirmation by a more definitive method is required. However, only 1 method is available for detection of some drugs. These would escape detection if that method were to be invalidated by adulteration.

Another strategy for detecting urine adulteration is to measure various urinary parameters. It has been suggested that samples intended for drug screening should routinely be assessed with respect to pH, relative density, and urine appearance.¹¹ In the authors' laboratory, creatinine is the only analyte measured routinely for detection of urine adulteration. This is adequate in most cases since the majority of the toxicology requests to an acute hospital are emergent intoxication and urine adulteration is not commonly encountered in this group of patients. In the reported patient, the abnormally low creatinine concentration suggested the possibility of adulteration and further investigations were initiated. Low creatinine concentration indicates inappropriate dilution by fresh or toilet water after collection. In the latter case, depending on water quality, the magnesium content may be very high. Other electrolytes are not useful indicators because of wide fluctuations in their concentrations. The pH of normal urine ranges from 4.5 to 8.0.¹ It is likely that an alkaline adulterant has been added if urine pH is greater than 8, although the presence of urea-catabolising organisms (in improperly stored urine) may increase the pH to 9. The concentration of urea must be interpreted carefully in the context of abnormal dilution. For example, in the reported patient, the seemingly normal urinary urea concentration was inconsistent with the low creatinine concentration; changes in urea concentration should parallel changes in creatinine concentration. Urea is measured by a method that employs urease, in which ammonia is generated as an intermediate. Falsely elevated values will therefore arise if ammonia is present in the adulterant. In the reported patient, the alkaline pH and high concentration of urea relative to creatinine suggested that the adulterant might be an ammonia-containing agent.

The most effective way to avoid *in vitro* adulteration is to adhere strictly to an appropriate urine collection protocol. Individual drug-abuse clinics should devise their own collection protocol based on patient type, staffing, and other resources available. Direct observation of urine collection should be mandatory for high-risk patients, for example, those with unexpected laboratory results in a previous study or whose eligibility to receive financial benefit is conditional

upon the result. However, urine collection in a room without a sink, water-flush toilet, detergents, or other potential adulterants may be suitable for low-risk patients. Documentation of the temperature of the specimen is also recommended, if possible. It is also important to maintain good communication between clinicians and testing laboratories. In laboratories where drug testing is being carried out to monitor abstinence in drug abusers, the panel of tests could be extended and interpretative criteria could be modified appropriately to ensure that adulteration is detected.

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