Comparison of Self-Reported Drug Use With Quantitative and Qualitative Urinalysis for Assessment of Drug Use in Treatment Studies

Kenzie L. Preston, Kenneth Silverman, Charles R. Schuster, and Edward J. Cone

ABSTRACT

The effectiveness of substance abuse treatment programs can be monitored by self-reported drug use and objectively measured by qualitative and quantitative urinalysis. The advantages and disadvantages of each of these three methods of assessing drug use are reviewed. Data collected in a clinical trial of a behavioral treatment for cocaine abuse are used to evaluate the relationships among qualitative and quantitative urinalysis for cocaine metabolite and self-reported cocaine use. Qualitative and quantitative urine testing showed greater rates of drug use than that shown by self-report, though there were significant correlations between self-reported use and urine toxicology results. Benzoylecgonine concentrations in urine specimens supported the suggestions that rates of drug use as determined by qualitative urinalysis are artifically high due to carryover and were informative about subjects' patterns of use.

INTRODUCTION

In clinical trials evaluating new treatments for abuse of drugs such as cocaine, an important outcome measure is the amount and frequency of illicit drug use. Unfortunately, the incidence and frequency of drug use are difficult to measure accurately. Drug use has been monitored by self-report in interviews and objectively by urinalysis. Although some clinical trials (Gawin and Kleber 1984) have relied principally on self-reported drug use and/or craving to assess outcome, most trials have used a combination of self-report and urine toxicology to monitor drug use (Weddington et al. 1991). Urine specimens usually are analyzed by immunoassay or thin layer chromatography, and the result is reported in the qualitative mode (positive/negative). More recently, interest has grown in using quantitative testing to assess treatment outcome (Batki et al. 1993). Quantitative urinalysis has

the potential to provide information regarding the amount and frequency of use (such as is gathered with self-report) while retaining the objectivity of drug testing.

The purpose of the chapter is to discuss the advantages and disadvantages of self-reported drug use and qualitative and quantitative urinalysis. Data from an ongoing clinical trial are used to evaluate the relationships among these three measures of drug use.

SELF-REPORT AS AN OUTCOME MEASURE—ADVANTAGES AND DISADVANTAGES

Self-reported drug use is usually reported in amount of drug (for example, in grams) or in amount of money spent on drugs. This information can be collected easily and nonintrusively and can cover a wide range of time periods (for example, the past 24 hours, the past week, or the past month). A significant drawback to relying upon self-reported drug use as an outcome measure in clinical trials is that the validity of the reports is questionable (Skog 1992). Self-reported drug use may not accurately reflect drug use for a number of reasons. Responses to questionnaires can be inaccurate because subjects do not know how much drug they have used, cannot remember, or are intentionally untruthful. Information about amounts of drug used (such as grams) is problematic because subjects may be poor judges of weights. In addition, the purity of drug purchased on the street is unknown and changes frequently. Collecting data in the form of dollar value has similar pitfalls, and, in addition, drug prices change over time and differ among localities.

Another frequently encountered problem is that drugs are often obtained as gifts or in exchange for goods or services, and subjects may not include drugs obtained in these ways in their reports. Recollection of amounts of drug used may be impaired by the duration of time since the use occurred (for example, when subjects are asked to estimate use in the past month) and by concurrent use of other psychoactive drugs (such as benzodiazepines) that have effects on memory. Subjects may intention- ally inflate or underreport drug use, particularly if there is a real or perceived consequence to what is reported (Magura et al. 1987; Sherman and Bigelow 1992). Therefore, interviews or questionnaires must be carefully worded, and the circumstances of their collection must be considered in order to get reports that are as accurate as possible.

QUALITATIVE AND QUANTITATIVE URINALYSIS AS OUTCOME MEASURES—ADVANTAGES AND DISADVANTAGES

Urinalysis has grown in importance as an outcome variable in substance abuse treatment research. Urinalysis is an objective measure that is independent of problems of subject memory or veracity. Typically, urine specimens are collected on a scheduled or random basis (usually one to three times per week) and analyzed in a qualitative mode for the presence of drug or metabolite at or above designated cutoff concentrations. Test results are usually expressed as positive or negative. The cutoff concen- trations can vary from test to test, but standard values have been set by the Department of Health and Human Services (DHHS) for workplace testing (DHHS 1994). The following DHHS screening cutoff values are commonly used in clinical trials: cocaine/cocaine metabolite, 300 nanograms/milliliter (ng/mL); opiates, 300 ng/mL; amphetamines, 1000 ng/mL; marijuana, 50 ng/mL; and phencyclidine, 25 ng/mL. Such standardization is extremely useful when results from separate studies are compared or when data from multiple small studies are combined to increase statistical power in meta-analyses (Levin and Lehman 1991).

While having the advantage of objectivity, urinalysis also has some limitations. Unlike self-reported drug use, a drug must be present in the body in order for it to be detected; therefore, there is a relatively narrow window of time during which drug use can be detected by urinalysis. The duration of this time window is dependent on a number of factors, including the drug itself (e.g., biological half-life), dose, time of administration, amount of fluid consumed, individual differences in metabolism and excretion, and characteristics of the assay (for review see Cone and Dickerson 1992). Infrequent specimen collection can result in underrepresentation of drug use regardless of the analytic method used, though lowering cutoff concentrations can lengthen detection time. In contrast, frequent specimen collection can result in an overrepresentation of drug use. The drug or its metabolite may be detected in more than one urine specimen if the second specimen is collected before all drug or metabolite has been excreted. These multiple positives from a single use (referred to as carryover positives) artificially inflate the apparent rate of drug use by patients. Rates of carryover vary, depending upon the same factors that affect the window of detection listed above. The impact of sample collection frequency has been reviewed elsewhere (Jain 1992).

Clinical evidence suggests that qualitative urine tests may have the significant disadvantage of being insensitive to moderate changes in drug use. For example, some clinical trials of cocaine treatments (Covi et al. 1994; Kolar et al. 1992) have found significant decreases in self-reported cocaine use without concomitant significant decreases in rates of co- caine-positive urine samples. Discrepancies between self-report and qualitative urinalysis can be partially explained by numerous factors. Moderate decreases in frequency of use may not be detected if urine tests remain positive between uses due to carryover. Decreases in amount of drug per use without changes in frequency of use may similarly not be detected by qualitative tests if the amount of drug use is high enough to produce urine concentrations above the cutoff. Although the clinical significance of decreases in drug use without complete abstinence is not clear, the identification of treatments that diminish cocaine use is important, particularly because no effective treatment agent is currently known.

As noted, there is a growing interest in the use of quantitative urine testing in clinical trials. Changes in the pattern, frequency, and amount of use that are not apparent from qualitative urinalysis might be discernible from quantitative urinalysis. On the other hand, quantitative urine testing is also somewhat more expensive than qualitative testing, and urine drug/metabolite concentration can be affected by such variables as the time between drug use and urine collection, fluid intake, and interindividual metabolic differences. For example, a urine specimen collected several days after self-administration of a large amount of drug could have the same drug/metabolite concentration as a specimen collected just after self-administration of a small amount of drug. Thus, the time of specimen collection could have greater impact on concentration than the total amount of drug used. Fluid intake can also affect urine drug/metabolite concentration, though corrections can be made using a biological indicator such as creatinine to adjust for water consumption.

To date only a few clinical trials have been conducted with quantitative testing. At least one study suggests that quantitative testing may be more sensitive to decreases in drug use than qualitative tests. Batki and colleagues (1993) found that fluoxetine significantly decreased cocaine use in a group of methadone maintenance patients as determined by self-report and by quantitative analysis of urine cocaine and cocaine metabolite concentrations corrected by creatinine concentration; however, no significant effect of fluoxetine

was shown when qualitative urine toxicology data were analyzed. McCarthy (1994) has also reported on the utility of quantitative urine drug testing in the context of substance abuse treatment. At this time, however, it is unclear whether the added cost of quantitative testing in clinical trials is justified; further comparison of the uses of quantitative and qualitative urine drug monitoring is needed.

COMPARISON OF SELF-REPORTED DRUG USE AND QUALITATIVE URINE TESTING IN A CLINICAL TRIAL

To evaluate the relationship between self-reported drug use and qualita- tive and quantitative urine testing, relevant data from a clinical trial of a behavioral treatment for cocaine abuse in methadone maintenance patients were analyzed. The study consisted of a randomized controlled trial comparing a voucher-based reinforcement contingency for cocaine abstinence to noncontingent voucher presentation in the context of an otherwise standard methadone maintenance program (Silverman et al. 1995). Under the reinforcement contingency, subjects received a voucher for each cocaine-free urine; the vouchers had monetary values that increased with the number of consecutive cocaine-free urines. In contrast, subjects in the control condition received vouchers in the same value, frequency, and pattern of presentation as the experimental group, but independent of their urine screen results. The vouchers could be exchanged for goods and services that were consistent with a drug-free lifestyle and patients' treatment goals.

The study was 17 weeks long, with a 5-week baseline phase in which subjects' drug use was monitored and a 12-week voucher phase in which the treatment intervention was in place. Participants were 37 patients who used cocaine consistently during the first 5 weeks of methadone maintenance treatment. Subjects visited the clinic 7 days per week to receive methadone (50 mg orally) for up to 17 weeks. Three days per week (Monday, Wednesday, and Friday) they also answered self-report questionnaires and submitted urine samples. Three days per week subjects were asked whether they had used any cocaine, and, if so, how much (in grams) in the last 24 hours. If the subject reported the use in dollars spent, the information was converted to grams using a conversion factor of $10 per 0.1 gram of cocaine. This information was entered into a database as a dichotomous variable (yes/no) and as amount (grams).

All urine collections were observed by trained laboratory technicians. At the time of collection, a portion of each specimen was frozen for later quantitative analysis. The rest of the sample was refrigerated and sent to a commercial laboratory for qualitative testing on the day of collection. Testing was conducted with an enzyme multiplied immunoassay tech- nique (EMIT) system that gave qualitative results for the presence of cocaine metabolite (cutoff concentration 300 ng/mL, benzoylecgonine equivalents). The EMIT assay primarily detects benzoylecgonine, the principal metabolite of cocaine. Results of the qualitative urine toxicol- ogy screens were available to the subjects and to the counselors for use in their treatment plans and counseling sessions with subjects. Primary outcome measures for the original study were cocaine abstinence in each study week and the longest duration of sustained cocaine abstinence as determined by qualitative urinalysis.

Quantitative testing of cocaine metabolite was conducted with an analyzer and cocaine metabolite reagents according to the manufacturer's recommended procedure. Results are expressed as benzoylecgonine equivalents (ng/mL). The sensitivity of the assay for benzoylecgonine as reported by the manufacturer was 30 ng/mL. The assay has been shown to be highly specific and accurate for the measurement of benzoylecgonine in urine. Cone and colleagues (1988) showed that results from the assay were highly correlated with benzoylecgonine concentrations determined by gas chromatography/mass spectrometry (GC/MS) for urine specimens collected from subjects who had received cocaine in a laboratory study.

Mean self-reported drug use in the past 24 hours (yes/no), grams of cocaine used in the past 24 hours, cocaine-positive urine specimens (qualitative assay), and benzoylecgonine equivalents concentrations were calculated across time for the 37 subjects participating in the 17-week trial. Means and standard deviations across subjects are listed in table 1. On average, subjects reported use of cocaine on 29 percent of occasions but tested positive for cocaine (qualitatively) on 68.2 percent of occasions. The concentration of benzoylecgonine equivalents varied widely, both across and within subjects, ranging from less than 30 ng/mL to more than 900,000 ng/mL. Overall, the mean benzoylecgonine were equivalent was 32,368 Å 29,254 ng/mL. Within-subject correlations between self-reported use (percent of reports positive for use) and urinalysis data (percent positive in qualitative tests or mean metabolite

TABLE 1. *Means, standard deviations, and correlation coefficients for three measures of cocaine use.*

Variable	Mean	Standard deviation	Correlation coefficient to self-reported cocaine use
Self-reported use (% yes)	29.04	25.39	--
% cocaine positive*	68.20	28.40	0.6934
Benzoylecgonine equivalents (ng/mL)	32,368	29,254	0.7975

KEY: * = Specimens were tested by EMIT for cocaine metabolite with a 300 ng/mL cutoff concentration for positive results.

concentration) were in the high range: R = 0.693 for qualitative results and R = 0.798 for benzoylecgonine equivalents. These data suggest that there was general correspondence between self-report and urinalysis results within subjects, such that subjects who reported more cocaine use also tested positive for cocaine more frequently and had higher benzoyl- ecgonine concentrations.

To evaluate the correspondence between the cocaine use measures at individual data-collection points, data from the 37 study participants were combined, and 1,678 sets of concomitantly collected urine specimens and self-reports were examined (table 2). Overall, 1,124 (67 percent) of the specimens tested positive (yes/no) for cocaine, and 470 (28 percent) of the self-reports were positive for cocaine use. Chi-square analysis comparing cocaine-positive urine specimens and self-reports of cocaine use was highly significant ($p < 0.001$). When self-report was positive for cocaine use, correspondence between self-report and positive results by urinalysis was quite high: Of 470 occasions of self-reported use, 463 (98.5 percent) were also positive by qualitative urinalysis. In contrast, there was a lack of correspondence when qualitative urinalysis results were positive: Subjects reported using cocaine on only 41 percent of the 1,124 occasions that urine tested positive for cocaine. There was agreement between urinalysis and self-report (both positive or both negative for cocaine use) on 60.19 percent of occasions. A Kappa value of 0.307, in the moderate range, was computed from these data. Kappa (Cohen 1960) assesses the degree

TABLE 2. *Relationship between qualitative urinalysis and self-reported drug use in data analyzed as individual occasions.*

	Self-reported cocaine use		
Urinalysis*	No	Yes	Total
Negative	547	7	554 (33%)
Positive	661	463	1,124 (67%)
Total	1,208 (72%)	470 (28%)	1,678 (100%)

KEY: * = Specimens were tested by EMIT for cocaine metabolite with a 300 ng/mL cutoff concentration for positive results.

of validity between the self-reports of drug use and urinalysis beyond that expected by chance alone. Thus, self-report of cocaine use predicted a positive result on qualitative urinalysis, but positive urinalysis was not predictive of self-report because subjects reported using cocaine on only about half of these occasions.

CAN QUANTITATIVE URINALYSIS RESOLVE THE DISCREPANCY BETWEEN SELF-REPORT AND QUALITATIVE URINALYSIS?

Close inspection of individual data suggests that benzoylecgonine concentration (as determined by quantitative urinalysis) does provide a basis for examining the relationship between self-reported drug use and qualitative urinalysis. Data for the three measures of cocaine use (self- report, quantitative urinalysis results, and benzoylecgonine concentrations) of two representative subjects are shown in figures 1 and 2. Benzoy- lecgonine concentrations are indicated by open circles graphed on a log scale. Urine specimens were collected and analyzed three times per week over a period of 17 weeks for a total of 51 occasions; sequential urine specimens numbers 1 through 15 were collected during baseline; urine specimens numbers 16 through 51 were collected during the experimental treatment phase. The cutoff for the quantitative testing (300 ng/mL) is indicated by the horizontal dashed line. The subject in figure 1 showed a cyclical pattern of drug use (based on benzoylecgonine

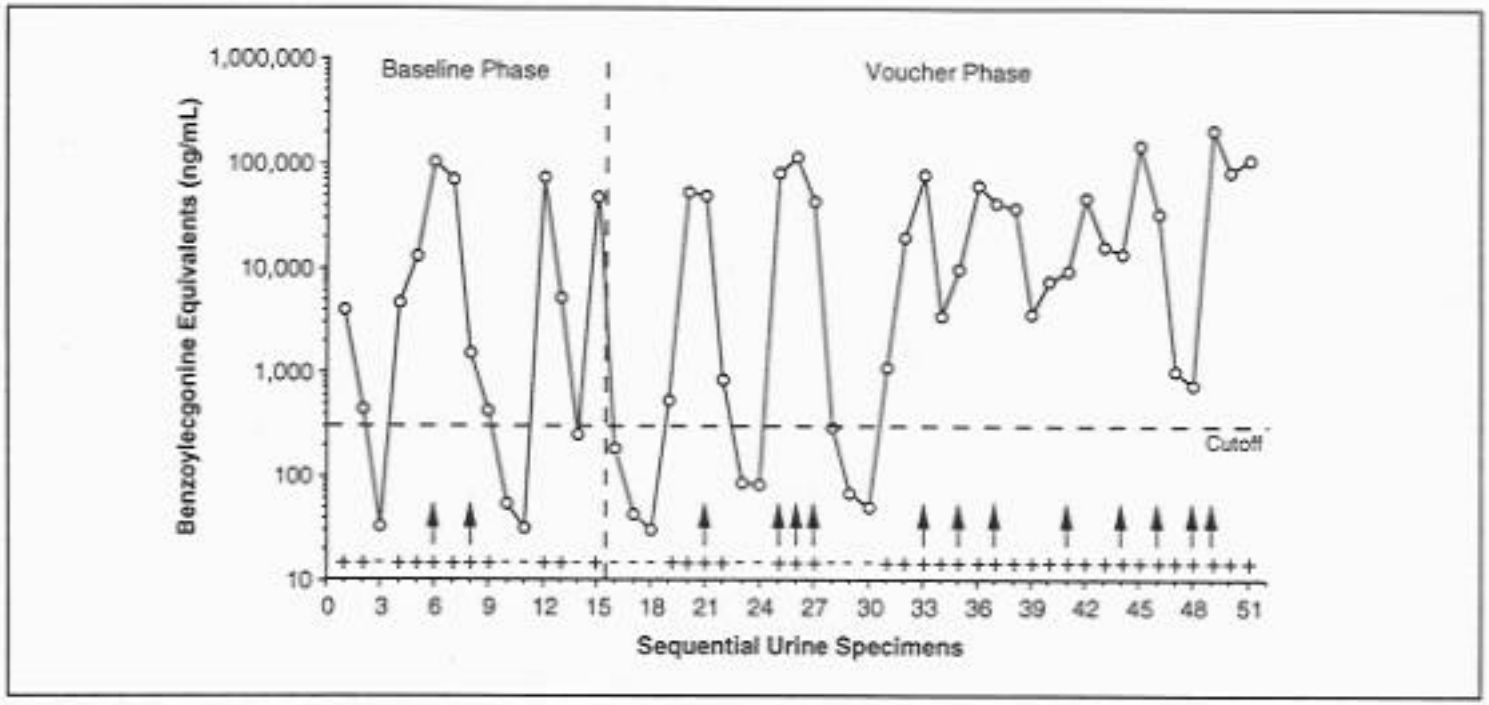

FIGURE 1. *Urinalysis results and self-reported cocaine use across time from a subject in the control group. Plus signs (+) above the X axis indicate urine samples testing positive for cocaine metabolites at concentrations of 300 n/mL or greater, and minus signs (-) indicate negative urine samples. Arrows indicate days on which the subject reported using cocaine within the previous 24 hours. Horizontal dashed line indicates 300 ng/mL; vertical dashed line indicates end of baseline phase.*

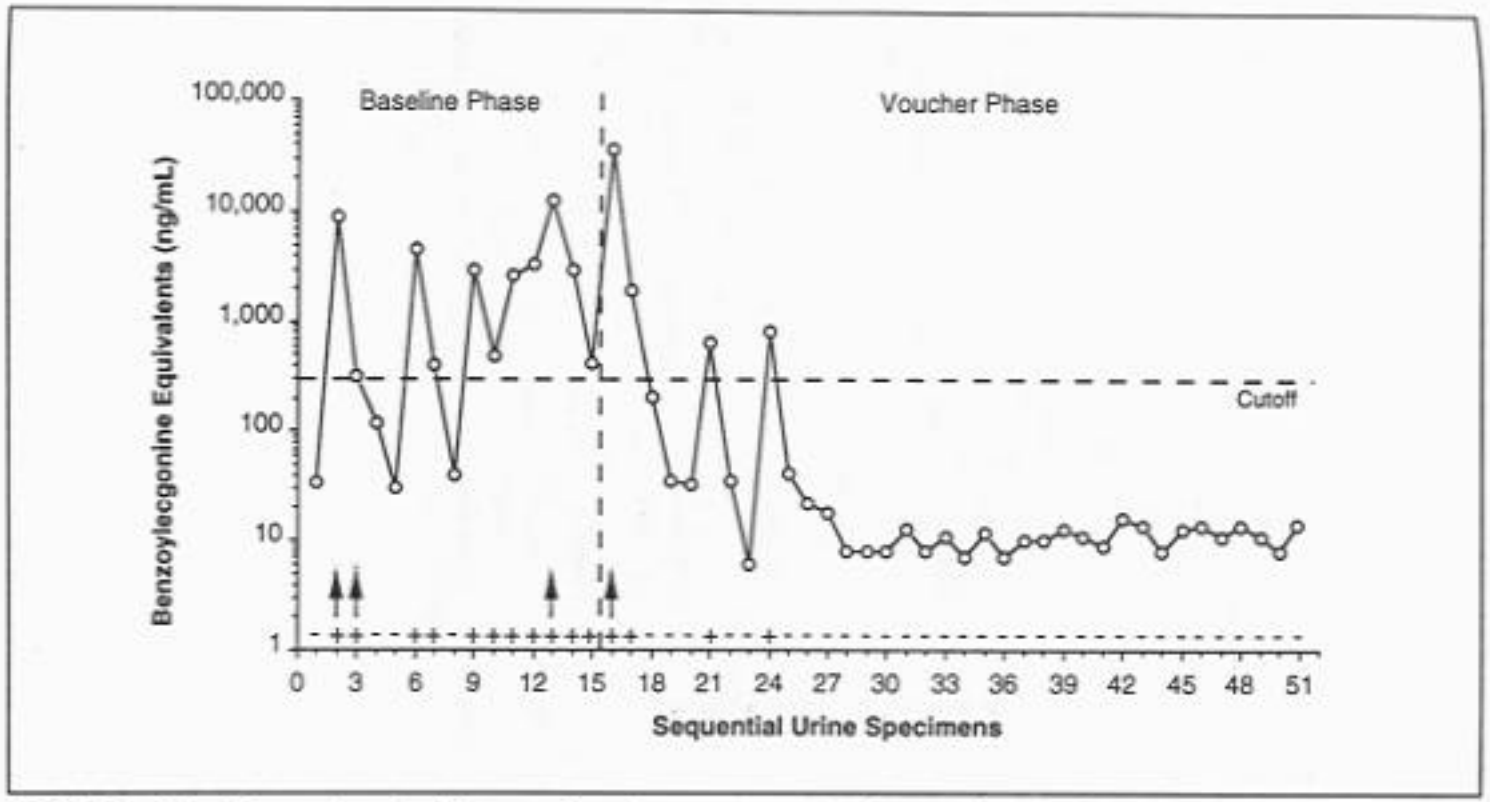

FIGURE 2. *Urinalysis results and self-reported cocaine use across time from a subject in the voucher-based reinforcement group. Details are the same as described for figure 1.*

concentrations), with episodes of varying length separated by periods of no use. The results for this subject are typical of other subjects in the control group, which showed no significant decrease in cocaine use during the voucher phase of the study. Benzoylecgonine equivalent concentrations varied over a wide range from 31 to 216,500 ng/mL.

In contrast, the participant whose results are illustrated in figure 2 had a cyclical pattern of drug use early in treatment, followed by sustained cocaine abstinence. During the first 5 weeks of methadone maintenance (baseline), benzoylecgonine equivalent concentrations varied from approximately 30 to 36,000 ng/mL. This subject decreased cocaine use with the initiation of the experimental treatment in the sixth week of treatment, and after two short relapses, stopped using cocaine completely; benzoylecgonine equivalent concentrations decreased to less than 30 ng/mL, the limit of detection of the assay.

Qualitative urinalysis results and self-reported cocaine use are also indicated in figures 1 and 2. Results of qualitative urinalysis are shown as plus signs (+) indicating urine samples testing positive for cocaine metabolites at concentrations of 300 ng/mL or greater; minus signs (-) indicate negative urine screens. Arrows indicate days on which the subject reported using cocaine within the previous 24 hours. Clearly, there is a lack of concordance between self-reported uses and cocaine-positive urine specimens for both subjects. In figure 1, 39 of 51 samples (76.5 percent) were above the 300 ng/mL cutoff, while the subject reported cocaine use within the previous 24 hours on only 14 occasions. Self-reports of use tended to coincide with the longer periods of cocaine-positive urine specimen, and multiple self-reported uses were associated with longer periods during which consecutive urine specimens were above the 300 ng/mL positive/negative cutoff. Early in treatment, the subject infrequently reported using cocaine in the previous 24 hours and had numerous negative qualitative urinalysis results. Beginning with the 33rd sequential urine specimen, the subject began reporting use more frequently, and qualitative urinalysis were continuously positive. Quantitative urinalysis, however, suggests a continuing cyclical pattern of use, even though the urine benzoylecgonine concentration never decreased to below the 300 ng/mL cutoff.

For the subject whose data are illustrated in figure 2, 15 (29.4 percent) out of 51 urine specimens tested above the 300 ng/mL cutoff; all of the positive urine specimens occurred during the first half of treatment. The subject reported using cocaine in the past 24 hours on four occasions; on each occasion the subject also tested positive on the qualitative urinalysis. As with the subject described in figure 1, quantitative urinalysis suggests a continuing cyclical pattern of use, even during the period of sustained cocaine-positive urinalysis results

from sequential urine numbers 9 through 17. Thus, quantitative urinalysis results provided additional information on patterns of drug use and documented the subject's response to treatment.

As described above, one of the potential reasons for discrepancies between self-reported drug use and qualitative urinalysis in clinical trials with frequent urine specimen collections is from carryover positives. Benzoylecgonine can usually be detected in the urine for about 48 hours after cocaine administration (Saxon et al. 1988), though even longer detection times are possible depending on the amount of cocaine taken and individual rates of excretion. Benzoylecgonine concentration data may provide a basis for evaluating the discrepancy between self-report and qualitative urinalysis and the impact of carryover. As noted above, self-reported cocaine use occurred at a much lower rate than cocaine- positive urine specimens for the study as a whole: 470 (28 percent) versus 1,124 (67 percent) out of 1,678 occasions (table 2). A similar pattern was seen in the data of the individual subjects illustrated in figures 1 and 2. Examination of the quantitative data supports the suggestion that at least part of the differential rates of self-report and qualitative cocaine-positive urine specimens was due to carryover. In figure 1, for example, benzoylecgonine concentration dropped substantially between sequential urine specimens numbers 21 and 22, but remained above 300 ng/mL. Possible carryover positives are also seen in figure 2 for sequential urine specimens numbers 7, 15, and 17. Further research may lead to a more systematic approach to estimating rates of cocaine use from urine benzoylecgonine concentrations.

SUMMARY

The effectiveness of substance abuse treatment programs can be monitored by self-reported drug use and objectively measured by urinalysis. Self-reported drug use is usually reported as amount of drug (for example, in grams) or amount of money spent on drugs. While this information can be collected easily and nonintrusively, the validity of the self-reported drug use is often questionable, particularly if there is a real or perceived conse-quence to what is reported. Therefore, urinalysis is a critical variable in treatment research. Typically, urine specimens are collected on a scheduled or random basis and analyzed in a qualitative mode for the presence of drug or metabolite at or above a designated cutoff concentration, with testing results usually expressed as positive or negative. Qualitative urine testing may be insensitive to decreases in drug use because of carryover positives (more than one drug-positive test from a single use). Rates of carryover vary depending upon a number of factors including dose, time of drug administration, individual factors such as rates of metabolism and excretion, water consumption, and

characteristics of the assay. Urine samples can also be tested with quantitative measures to determine urine drug/metabolite concentrations. Quantitative testing may be more sensitive to decreases in drug use, though many of the factors affecting qualitative tests also affect quantitative testing.

The relationships among qualitative and quantitative urinalysis for cocaine metabolite and self-reported drug use were assessed with data collected in a clinical trial of a voucher-based reinforcement contingency treatment intervention. There was significant correlation between self-reported use and urine toxicology results, although qualitative and quantitative urine testing showed greater rates of drug use than that shown by self-report. Benzoylecgonine concentrations in urine specimens were informative about subjects' patterns of use and the relationship between patterns of self-report and qualitative urinalysis. Benzoylecgonine concentrations also supported the suggestion that rates of drug use as determined by qualitative urinalysis are artificially high due to carryover. Quantitative urinalysis may be a useful measure of drug use in clinical trials of cocaine abuse treatments.

The value of quantitative testing in the context of community substance abuse treatment is unclear. In general, community treatment programs conduct relatively infrequent urine testing. Concentrations of drugs in urine specimens collected at intervals that are too long cannot give information about patterns of use. They may also not be particularly useful indicators of amount of drug use because urine concentrations can fluctuate dramatically even over relatively short periods of time (e.g., 48 hours, as in the current study). The problem of carryover positives is much less likely under current treatment practices when specimens are collected at wide intervals. In addition, the costs of testing may be prohibitive. However, in those settings where urine testing is frequent (for example, some programs associated with the justice system), quantitative testing could decrease the number of occasions when negative consequences are applied to individuals who test positive more than once because of carryover. If future research demonstrates that rates and patterns of drug use are helpful for predicting treatment outcome or for identifying appropriate treatments for individual patients, increased funding and changes in standards of care that would permit frequent quantitative urinalysis might be justified.

REFERENCES

Batki, S.L.; Manfredi, L.B.; Jacob, P.; and Jones, R.T. Fluoxetine for cocaine dependence in methadone maintenance: Quantitative plasma and urine cocaine/benzoylecgonine concentrations. *J Clin Psychopharmacol* 13:243-250, 1993.

Cohen, J. A coefficient of agreement for nominal scales. *Educ Psychol Measure* 20:37-46, 1960.

Cone, E.J., and Dickerson, S.L. Efficacy of urinalysis in monitoring heroin and cocaine abuse patterns: Implications in clinical trials for treatment of drug dependence. In: Jain, R.B., ed. *Statistical Issues in Clinical Trials for Treatment of Opiate Dependence*. National Institute on Drug Abuse Research Monograph 128. DHHS Pub. No. (ADM)92-1947. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1992. pp. 46-58.

Cone, E.J.; Menchen, S.L.; and Mitchell, J. Validity testing of the TDx® cocaine metabolite assay with human specimens obtained after intravenous cocaine administration. *Forensic Sci Int* 37:265-275, 1988.

Covi, L.; Hess, J.M.; Kreiter, N.A.; and Haertzen, C.A. Three models for the analysis of a fluoxetine placebo controlled treatment in cocaine abuse. In: Harris, L.S., ed. *Problems of Drug Dependence, 1993*. National Institute on Drug Abuse Research Monograph 141. DHHS Pub. No. (ADM)94-3749. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1994. p. 138.

Department of Health and Human Services. "Mandatory Guidelines for Federal Workplace Drug Testing Programs." *Federal Register*, June 9, 1994.

Gawin, F.H., and Kleber, H.D. Cocaine abuse treatment. Open pilot trial with desipramine and lithium carbonate. *Arch Gen Psychiatry* 41:903-909, 1984.

Jain, R.B. Design of clinical trials for treatment of opiate dependence: What is missing? In: Jain, R.B., ed. *Statistical Issues in Clinical Trials for Treatment of Opiate Dependence*. National Institute on Drug Abuse Research Monograph 128. DHHS Pub. No. (ADM)92-1947. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1992. pp. 46-58.

Kolar, A.F.; Brown, B.S.; Weddington, W.W.; Haertzen, C.C.; Michaelson, B.S.; and Jaffe, J.H. Treatment of cocaine dependence in methadone maintenance clients: A pilot study comparing the efficacy of desipramine and amantadine. *Int J Addict* 27:849-868, 1992.

Levin, F.R., and Lehman, A.F. Meta-analysis of desipramine as an adjunct in the treatment of cocaine addiction. *J Clin Psychopharmacol* 11:374-378, 1991.

Magura, S.; Goldsmith, D.; Casriel, C.; Goldstein, P.J.; and Lipton, D.S. The validity of methadone clients' self-reported drug use. *Int J Addict* 22:727-749, 1987.

McCarthy, J. Quantitative urine drug monitoring in methadone programs: Potential clinical uses. *J Psychoactive Drugs* 26:199-206, 1994.

Saxon, A.J.; Calsyn, D.A.; Haver, V.M.; and Delaney, C.J. Clinical evaluation of urine screening for drug abuse. *West J Med* 149:296-303, 1988.

Sherman, M.F., and Bigelow, G.E. Validity of patients' self-reported drug use as a function of treatment status. *Drug Alcohol Depend* 30:1-11, 1992.

Silverman, K.; Higgins, S.T.; Brooner, R.K.; Montoya, I.D.; Schuster, C.R.; and Preston, K.L. Differential reinforcement of sustained cocaine abstinence in intravenous polydrug abusers. In: Harris, L.S., ed. *Problems of Drug Dependence, 1994.* National Institute on Drug Abuse Research Monograph 153. DHHS Pub. No. (NIH) 95-3883. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1995.

Skog, O.-J. The validity of self-reported drug use. *Br J Addict* 87:539-548, 1992.

Weddington, W.W.; Brown, B.S.; Haertzen, C.A.; Hess, J.M.; Mahaffey, J.R.; Kolar, A.F.; and Jaffe, J.H. Comparison of amantadine and desipramine combined with psychotherapy for treatment of cocaine dependence. *Am J Drug Alcohol Abuse* 17:137-152, 1991.

ACKNOWLEDGMENTS

This research was funded by the National Institute on Drug Abuse Intramural Research Program. Quantitative assays were performed by Christopher Sheppard and Rosalind Jones; data were analyzed by Chris Johnson and Nancy Kreiter.

AUTHORS

Kenzie L. Preston, Ph.D.
Chief, Clinical Trials Section

Edward J. Cone, Ph.D.
Chief, Chemistry and Drug Metabolism Section

Intramural Research Program
National Institute on Drug Abuse
Addiction Research Center
P.O. Box 5180
Baltimore, MD 21224

Kenneth Silverman, Ph.D.
Assistant Professor
Department of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine
5510 Nathan Shock Drive
Baltimore, MD 21224

Charles R. Schuster, Ph.D.
Professor
Department of Psychiatry and Behavioral Neurosciences
Director
Clinical Research Division on Substance Abuse
Wayne State University
2751 East Jefferson
Detroit, MI 48207

Click here to go to page 146