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Utility of sweat patch testing for drug use monitoring in outpatient treatment for opiate dependence

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Abstract

We evaluated the utility of sweat testing for monitoring of drug use in outpatient clinical settings and compared sweat toxicology with urine toxicology and self-reported drug use during a randomized clinical trial of the efficacy of buprenorphine for treatment of opioid dependence in primary care settings. All study participants (N=63) were opiate dependent, treatment seeking volunteers. The results based on toxicology tests obtained from 188 properly worn and unadulterated patches (out of 536 applied) show that the level of agreement between positive sweat test results and positive urine results was 33% for opiates and 92% for cocaine. The findings of this study, that there is a low acceptability of sweat patch testing by patients (only 54.3% were brought back attached to the skin) and that weekly sweat testing is less sensitive than weekly urine testing in detecting opiate use, suggest limited utility of sweat patch testing in outpatient clinical settings.

1. Introduction

Although urine testing remains the standard for drug use monitoring, sweat testing could provide a convenient, less invasive method with a longer detection window. Urine toxicology testing has been the most commonly practiced method of drug screening in the workplace, criminal justice, and drug treatment settings for the past two decades (Caplan & Goldberger, 2001). While this method has good sensitivity and specificity for detection of recent drug use, its limitations include the difficulty of obtaining a spontaneous sample, patient complaints that it is invasive and embarrassing (Taylor et al., 1998), and its relatively short window for detection of recent drug use (2 to 3 days for opiates or cocaine). The short detection window is particularly problematic when there is weekly or less frequent contact with patients, as is often the case in office-based and outpatient treatment. For this reason, other methods have been developed to enhance accuracy and practicality. One of these methods is the analysis of sweat for traces of drug use.

Sweat and sebaceous glands are housed in the dermis and are distributed throughout the body disproportionately. The highest concentration of sweat glands resides in the hands, while the forehead contains the densest population of sebaceous glands (Levisky et al., 2000). Both, however, are capable of delivering remnants of drug use to the skin's surface through either sweat or sebum (Joseph Jr. et al., 1998; Willis, Harris, & Moretz, 1973).

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Drugs are thought to enter into sweat by passive diffusion from the blood stream to the sweat gland (Cone, 1997). Drugs are also dissolved in sweat on the skin's surface after they diffuse through the stratum corneum (Cone, 1997).

Despite variation between individuals in sweat production, researchers have successfully used sweat to test for cocaine (Burns & Baselt, 1995; Cone et al., 1995; Spiehler et al., 1996; Kintz, Edel, Tracqui, & Mangin, 1996), opiates (Cone et al., 1995; Kintz, Edel, Tracqui, & Mangin, 1996; Kintz, Tracqui, Jamey, & Mangin, 1996), benzodiazepines (Kintz, Edel, Tracqui, & Mangin, 1996; Kintz, Tracqui, & Mangin, 1996), barbiturates (Kintz, Tracqui, Jamey, & Mangey, 1996), cannabis, buprenorphine, and methylenedioxyethylaamphetamine (Kintz, Edel, Tracqui, and Mangin, 1996).

The variation between individuals in the amount of sweat they excrete has caused difficulty for those attempting to construct a universal sweat collection device. Earlier attempts to test for the presence of specific substances in sweat have used patches that occlude the skin causing numerous problems, such as skin irritation, alteration of both the steady-state pH of the skin, and the skin's colonizing bacteria (Kintz et al., 1997). Newer, nonocclusive patches, such as those used in the current study (Pharm-Chek™ patches), use a transparent film that allows oxygen, carbon dioxide, and water vapor to escape, while trapping the necessary traces of drug use excreted in sweat.

Cone (1997) found many benefits in using this type of patch, including high subject acceptability, low incidence of allergic reactions to the patch adhesive, and ability to monitor drug intake for a period of several weeks with a single patch. Several studies have also found that the patch is resistant to inconspicuous tampering (Caplan & Goldberger, 2001; Cone, 1997; Kintz et al., 1997). Kintz et al. (1997) also reported that no special precautions were needed to wear the patch for several days, except to avoid excessive towel rubbing after bathing. Discussed disadvantages have included high intersubject variability, possibility of environmental contamination of the patch before application or after removal, and accidental removal during the monitoring period (Caplan & Goldberger, 2001; Cone, 1997). In addition, Taylor et al. (1998) reported that the cost of patch testing, based on their panel of drugs tested, was five times that of urine tests.

Validation of results from sweat patches, most of which use urine testing as the criterion standard, have been mixed. Taylor et al. (1998) reported good inter-patch reliability and concurrent validity with urine tests when testing for methadone, opiates, and morphine, while tests for cocaine revealed only a moderate level of agreement. In a study specifically designed to find possible sources of contamination, Kidwell and Smith (2001) found that precautionary methods, including cleansing the skin before patch application, are not completely reliable in preventing contamination from a patient's immediate environment.

The current study evaluated the utility of sweat patch monitoring for drug use during office-based agonist treatment of opiate dependence and compared sweat test results with urine toxicology tests and self-reports. No studies to date have examined the use of sweat patches in a clinical setting. Conducting an outpatient study in a setting approximating the real-life clinical environment provides valuable data on the viability of sweat patch testing as an alternative to urine toxicology testing in clinical practice. Because urine testing once a week can miss some of drug use due to the limited detection window (3 to 4 days), we expected to obtain higher rates of opiate positive patches than urines in the sample of opiate dependent individuals.

2. Materials and methods

2.1. Subjects

A subset of 63 patients enrolled in a randomized clinical trial of the efficacy of buprenorphine maintenance (Fiellin, et. al., 2006) received Pharm-Chek™ sweat patches in addition to weekly urine toxicology screens and weekly self-reports. Treatment seeking volunteers meeting DSM-IV criteria for opioid dependence, as assessed by SCID interview and documented by opioid positive urine toxicology testing, were enrolled in the study after providing informed, voluntary consent. Potential subjects were excluded if they were currently dependent on alcohol, benzodiazepines or sedatives; currently psychotic or experiencing major depression; at high risk for suicide or violence; had an unstable medical problem; or were unable to understand the protocol or assessment questions. The study protocol was approved by the Human Investigation Committee for the Yale University School of Medicine. There were 48 males and 15 females in the sample, the average (standard deviation) age of all subjects was 39.1 (7.7) years. Study participants received an average of 8.5 patches each (range from 1 to 26).

2.2. Study materials and methods

A total of 536 patches were applied and scheduled for removal one week later. During patch application and removal, a trained research assistant followed the procedures outlined by the patch manufacturer (see Liberty, et al., 2004 for details). During patch application study participants were instructed not to tamper with the patches and to return for patch removal with the patch fully attached. During removal, patches were inspected for tampering signs (e.g., punctures, partial detachment from the skin). The research assistant also asked the patients about their subjective experience with the patch. If the patch was either removed completely or missing, the RA interviewed the patient to obtain a more detailed report about the exact circumstances of patch removal. All collected patches were sent to the manufacturer and tested for opiates and cocaine metabolites (see Liberty, et al., 2004, for description of laboratory procedures).

Urine samples were collected at least once per week by the research assistants and tested immediately for temperature. Urine samples were sent to a commercial laboratory and tested for presence of opiate and cocaine metabolites by radioimmunoassay method. We obtained a total of 575 valid urine toxicology screens during the study. Drug use self-reports were collected weekly, using a daily timeline follow back methodology, in which study participants reported daily amounts and routes, if any, of use for heroin, other opiates and cocaine. 436 weekly self reports of drug use were obtained during the study.

2.4. Data and statistical analyses

For each removed patch, we identified a corresponding urine toxicology result collected and a corresponding week of self-reported drug use. Self-reported drug use was coded as positive (separately for opiates and for cocaine) if the subject reported opiate or cocaine use during the preceding week and coded as negative if the patient reported no use. An indicator of documented use was created by coding a week as positive if either the urine test or self-report was positive. Due to methodological limitations of the study (see discussion section) patch toxicology results, urine tests, and self-reports were compared using raw agreement indices (a simple concordance of results). The data used in the computation of concordance values among patch, urine, and self-report results was further limited to the records where the patch was removed on the same day when a urine sample was obtained (184/188 patches) and there was a complete overlap of the patch wear period and self-report (109/188 patches). Estimated values of sensitivity and specificity of sweat patches in detecting both

opiate and cocaine use were also computed (Kraemer, H.C., 1992), but caution should be used when interpreting these values.

3. Results

3.1 Sweat patch results

Of the total of 536 patches that were applied, 291 (54.3%) completely attached patches were removed by the research personnel. Of the 291 patches, 188 (64.6%) were removed as planned, 7 days after the application; 85 (29.2%) were obtained within 2 days of the planned one week wear period, and the remaining 18 (6.2%) were obtained from 2 to 14 days after the application. Toxicology results obtained from analyzing the 188 patches that were removed as planned are included in the subsequent analyses. An additional 47 patches were brought in by study participants detached from the skin. They were either removed by the study participants themselves or fell off before completing the one week wear period. The results obtained from analyzing these patches were not included in the subsequent analyses due to the possibility of environmental contamination or tampering. The remaining 198 patches were never received. In most such cases, study participants reported that they fell off. Of the 188 patches analyzed, 31 (16.5%) were positive for at least one opiate or opiate metabolite (morphine, codeine, heroin, or 6 mono acetyl morphine) and 46 (24.5%) were positive for either cocaine or benzoylecgonine.

3.2 Urine toxicology and self-report results

We obtained a total of 575 urine toxicology screens during the study and 184 opiate and cocaine urine toxicology screens matching the wear time periods of 188 sweat patches worn exactly for 7 days were identified. Overall, 81 of 184 (44.0%) urine toxicology results were positive for opiates, and 36 of 184 (19.6%) were positive for cocaine. Additionally, 436 weekly self reports of drug use were obtained during the study and 109 of these reports were identified as completely overlapping with the patch wear period. Overall, 59 out of 109 (54.1%) self-reports indicated opiate use and 23 out of 109 (21.1%) cocaine use during the 7 days of wearing the sweat patch.

3.3 Concordance of sweat patch, urine toxicology, and self reports

Of the 81 opiate positive urine toxicology screens only 27 (33.3%) had a corresponding opiate positive patch result. Four of 31 (12.9%) opiate positive patch results had a corresponding opiate negative urine toxicology screen. Of the 36 cocaine positive urine toxicology screens, 33 (91.7%) were matched with a corresponding cocaine positive patch result, and 13 of the 46 (28.3%) cocaine positive patch results were matched with cocaine negative urine toxicology screens (see table 1 for complete tabulation of results). When compared to self reports, opiate patch tests were positive in 19 of 59 (32.2%) cases reporting recent opiate use. Cocaine patch tests were positive for 21 of the 23 (91.3%) cases reporting recent cocaine use (see table 2). Comparisons of urine toxicology screens and patient self-reports show that self-reports indicate heroin or other opiate use in 88% of cases when the corresponding urine toxicology screen was also positive for opiates, and cocaine use in 77.8% of cases when the corresponding urine toxicology screen was also positive for cocaine.

3.4 Estimated sensitivity and specificity of patch results when compared to an index of documented drug use

For each study participant we calculated opiate and cocaine use indexes by combining urine toxicology results with self reports. We assigned a positive value to the opiate use index if both urine toxicology result and self-reported data indicated opiate use during the patch wear period and a negative value when both urine toxicology and self-report indicated no opiate

use during the patch wear period. The cocaine use index was calculated following the same rules. These computed drug use indexes were then used as reference values in estimating sensitivity and specificity of sweat patches in detecting both opiate and cocaine use. The estimated values of opiate sensitivity and specificity of the tested sweat patches were 36.5% and 95.0% respectively. Similarly, the estimated sensitivity and specificity of sweat patches in detecting recent cocaine use were 95.0% and 92.6% (see table 3).

4. Discussion

The results of the study indicate some important limitations to the use of sweat patch testing in clinical settings, including a low overall acceptability of patch testing by patients and a low sensitivity for detecting illicit opiate use. Only 54.3% of the applied patches remained attached and were removed by the research personnel, and only 35.1% were obtained exactly 7 days after their application. Additionally, sweat patches detected only one third of the instances of illicit opioid use detected by weekly urine toxicology testing. However, the concordance between sweat patch and urine toxicology testing for cocaine was substantially better. Sweat patches tested positive for cocaine in 90.2% of instances where the corresponding urine test was positive for cocaine. These results suggest that there may be some marginal utility of incorporating sweat patch testing in evaluating cocaine use, if the acceptability of sweat patches can be improved.

Study limitations include an outpatient setting enrolling a convenience sample (a subsample from a population of a large, randomized clinical trial) and substantial variability in the number of patches obtained from each study participant. In this context, it is also reasonable to assume that the results of this study could be biased, such that more patches from the time periods during which study participants were using drugs were “lost” and more of the valid patches came from the time periods of lighter use or no use.

5. Conclusions

The results of this study suggest that it would be premature to replace urine toxicology testing with sweat patch testing in both research and clinical settings, despite some limitations and inconveniences associated with urine collection and testing, and some apparent benefits of sweat patch applications. Continuing improvements in sweat collection and testing methods may result in availability of substantially improved sweat testing devise in the near future.

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Table 1

Concordance of urine toxicology screens and patch data.

	Patch opiate negative	**Patch opiate positive**	**Total**
Utox opiate negative	99	4	103
Utox opiate positive	54	27	81
Total	153	31	184
	Patch cocaine negative	Patch cocaine positive	Total
Utox cocaine negative	135	13	148
Utox cocaine positive	3	33	36
Total	138	46	184

Table 2

Concordance of self-report and patch data.

	Patch opiate negative	**Patch opiate positive**	**Total**
Self-report opiate negative	47	3	50
Self-report opiate positive	40	19	59
Total	87	22	109
	Patch cocaine negative	Patch cocaine positive	Total
Self-report cocaine negative	65	11	76
Self-report cocaine positive	2	21	23
Total	67	32	99

Table 3

Comparison of opiate patch results with opiate and cocaine use indexes.

	Opiate use index negative	**Opiate use index positive**	**Total**
Patch result opiate negative	38	33	71
Patch result opiate positive	2	19	21
Total	40	52	92
	Cocaine use index negative	Cocaine use index positive	Total
Patch result cocaine negative	63	1	64
Patch result cocaine positive	5	19	24
Total	68	20	88