DRY TEST VERSUS WET TEST FOR DRUG TESTING/SCREENING

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EXECUTIVE SUMMARY

Introduction

Drug testing, commonly used in health care, workplace, and criminal settings, has become widespread during the past decade. Urine drug screens have been the most common method for analysis because of ease of sampling. The simplicity of use and access to rapid results has increased demand for and use of immunoassays. However, these assays are not perfect. False positive results of immunoassays can lead to serious medical or social consequences if results are not confirmed by secondary analysis, such as gas chromatography–mass spectrometry. This technology review was conducted following a request from a clinician who wants to consider the use of dry test for drug of abuse screening.

Objective/Aim

To determine the effectiveness and cost effectiveness of dry test for drug of abuse screening in comparison to wet test.

Results and conclusion

There was evidence on the effectiveness of dry test for drug of abuse screening comparable with that obtained from wet test done in central laboratory. However, there are limitations due to inconsistencies in accuracy and cross-reactivity of these devices. There is no single dry test device suitable for screening all drug of abuse. As for cost-effectiveness there is no retrievable evidence.

Recommendation

Dry test for screening drug of abuse using urine specimen can be recommended provided the following criteria are adhered to:

a) Before using the dry test device in the selected facility, performance assessment of the device must be conducted in a controlled laboratory.
b) The users of the devices must be trained to understand limitations of devices including the statistical and analytical sensitivity, specificity and nomenclature of devices, and interferences from drugs or metabolites which could affect interpretation of test results.
c) On-site dry testing using urine specimen is only for screening purpose in clinical settings where central laboratory (wet test) testing is not available. Confirmation of screening test results by central laboratory is mandatory especially if penal or legal actions are to be taken.

Methods

Scientific electronic databases searched include Pubmed, Proquest, EBSCO Host, Medline, CINAHL, Science Direct, Cochrane database of systematic reviews, HTA databases, Horizon scanning databases and FDA website were searched.

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1. INTRODUCTION

Drug testing, commonly used in health care, workplace, and criminal settings, has become widespread during the past decade. Urine, blood, hair, saliva, sweat, and nails (toenails and fingernails) are some biological specimens used to perform laboratory drug testing, and they provide different levels of specificity, sensitivity, and accuracy. Urine is most often the preferred test substance because of ease of collection. Concentrations of drugs and metabolites also tend to be high in the urine, allowing longer detection times than concentrations in the serum allow.[1]

Urinary screening for drugs of abuse can have an important role in both the diagnosis and management of drug misuse. This service needs to be inexpensive, comprehensive and reliable, yet able to provide a rapid turn-around of results. It has been suggested that an efficient and cost-effective analytical service for drugs of abuse can only be achieved by a combination of sophisticated laboratory-based chromatographic and immunoassay techniques. However, the initial screening of urine specimens by immunoassay is a recognized technique that allows the rapid screening of many specimens, and the separation of negative from presumptive positive urine samples. Several commercial immunoassay techniques are available for drugs of abuse screening; for example, radioimmunoassay (RIA: Euro/DPC), enzyme multiplied immunoassay (Syva: EMIT) and fluorescence polarization immunoassay (Abbott:FPIA). These techniques rely on major items of laboratory equipment, such as general clinical chemistry analyzers or dedicated equipment, to be used to perform the work. In addition, the cost per test using these techniques in the clinic or near-patient situation can be high unless there is a sufficient work-load throughput to offset the reagent, consumables and maintenance costs that are required to process the urine specimens. The main disadvantage of immunoassays is obtaining false-positive results when detection of a drug in the same class requires a second test for confirmation. Gas chromatography-mass spectrometry (GC-MS) is the criterion standard for confirmatory testing. It is the most accurate, sensitive and reliable method. However, the test is time consuming, requires high level of expertise to perform and is costly. Therefore, GC-MS is usually performed after positive result is obtained from immunoassay[1, 2]

Recently, several rapid detection kits for drugs of abuse screening have been marketed whereby no laboratory equipment are required and allow on-site testing. Multiple factors have contributed to the implementation of drug-of-abuse testing at on-site, including turnaround time (TAT), convenience, and clinical benefits. On-site dry testing offers the advantage of a rapid TAT and, consequently, the ability to manage the patient, employee, or defendant in a timely manner. Common settings for on-site drug-of-abuse testing include the emergency department, drug treatment and detoxification clinics, maternal fetal medicine, pain management, workplace, law enforcement, sports franchises, and criminal justice centers. Several manufacturers have developed drugs-of-abuse assays that offer similar sensitivity and specificity to the methodologies used by central

laboratories. However, the population type, location, TAT, instrument maintenance (including calibration and controls), training, competency, results interpretation, results reporting, cost, and accuracy of billing should all be considered when implementing drugs-of-abuse testing at the point-of-care.[2,3,4]

2. OBJECTIVE/AIM

The objective of this review was to determine the effectiveness and cost effectiveness of dry test for drug of abuse screening in comparison to wet test.

3. TECHNICAL FEATURES

Wet chemistry refers to chemistry generally done in liquid phase. It is also known as bench chemistry because many tests performed are done at a laboratory bench. The techniques can be used for qualitative chemical measurements, e.g. changes in colour (colorimetry), but often involves more quantitative chemical measurements, using methods such as gravimetry and titrimetry.

Dry chemistry refers to the use of strips impregnated with dry reagents to which the specimen is added. Applications of the chemistry include health clinics (including mobile units), point-of-care testing e.g. in critical area and on-site drug testing.

The wide range of on-site dry testing devices that are currently in use for drugs of abuse are based on immunoassays. The devices are designed to detect the presence of a specific drug (methadone), drug metabolites (benzoylecgonine), or a class of compounds (opiates). They are designed to detect the presence of a single drug or groups of drugs. Results are based on specific calibrator concentration (cutoff) which is specified by the manufacturer. Positive results reflect the concentration at or above the cutoff; negative results reflect concentration below cutoff. Most on-site testing devices for drugs of abuse are competitive immunoassays which give a negative visual sign; absence of a line indicates the presence of a specific drug or class of drug. Negative results do not exclude the presence of the drug or its metabolite. A drug conjugate is impregnated on a membrane and a free antibody is coated on microparticles. If sufficient drug is present in the patient's urine, the drug binds to the free antibody. The free antibody is subsequently inhibited from binding to the drug conjugate on the membrane, and no band is formed. However, there are devices in which positive visual sign indicate presence of drug.[5, 6]

There are different types of devices based on sample application technology. The devices vary from dipsticks to cup devices, cards, or plastic cassettes. [5]

4. METHODOLOGY

4.1. Searching

Electronic databases which include Pubmed, Proquest, EBSCO Host, Medline, CINAHL, Science Direct, Cochrane Database of Systematic Reviews, HTA Databases, Horizon Scanning databases and FDA website were searched. There was no limitation in the search. The following keywords were used either singly or in combinations: Drug screening, drug of abuse, on-site, substance abuse, drug test, point of care, cost*, dry test, wet test, urine drug screening.

4.2. Selection

All published articles pertaining to urine drug screening for drug of abuse were selected for this review.

5. RESULTS AND DISCUSSION

The search strategy yielded few published articles related to effectiveness and cost effectiveness of dry test for drug of abuse screening. These articles include cross sectional diagnostics studies and narrative reviews.

5.1. EFFECTIVENESS

Several studies have addressed the analytic performance, including sensitivity, specificity, precision, and accuracy of on-site drug-of-abuse devices using urine specimen. Most studies suggest that on-site dry testing is a reliable method to screen for drugs of abuse and the results are comparable with both automated immunoassays and the gold standard: gas chromatography/mass spectrometry. However, a few inconsistencies have been noted by the studies examining each of these devices.

Leino *et al.* evaluated eight on-site drugs-of-abuse testing devices (Dip Drug Scan 6 test, OnTrak testcup, RapiTest Multidrug, Status DS, Surescreen 6 Drug Multi-test, Syva Rapid Test 4, Triage 8, Syva Rapid Cup) for detection of cannabinoids, opiates, cocaine, amphetamines, metamphetamines and benzodiazepines. All eight devices utilized a competitive binding immunoassay to detect the presence of drugs in urine. Specificity and sensitivity were tested with urine specimens confirmed by gas chromatographic/mass spectrometry (GC/MS). The specificities and sensitivities in four drug groups; amphetamine, cannabinoids, opiates and cocaine varied between 90% and 100% among the devices, while only Dip Drug Scan 6 test for amphetamine and RapiTest Multidrug for cannabinoids and opiates had sensitivities below 90%. For benzodiazepines, sensitivities varied ranging from 91 to 97% and specificities ranging from 97 to 100%. False positive results were found with cannabinoids and amphetamine. On-site devices were not able to detect extremely high drug concentrations especially with amphetamine. Pholcodine was found to give false-positive results with most of the devices. It was reported that there was marked difference between devices regarding test interpretation and ease of test performance therefore concluded that different criteria should be used for selecting dry test devices to be used in different setting.[3] Level II-2

In a study by Philips *et al.*, Signify ER Drug Screen Test and Triage Drug of Abuse Panel plus tricyclic antidepressant were compared at four laboratories for measuring phencyclidine, barbiturates, amphetamine, cocaine metabolite, metamphetamine, tricyclic antidepressants, opiates, marijuana metabolite and benzodiazepines in urine. The specificity of both devices was shown to be 100% and their sensitivities were more than 99%. The precision of Signify ER was 95.4% and for Triage was 90%, with an accuracy of 99.9% and 99.6% respectively. Eighty seven structurally related drugs and metabolites were found to cross react with at least one of the nine tests of Signify ER.[7] Level II-2

Taylor *et al*. evaluated five commercially available dry test devices (Roche OnTrak TestCup, Pharmscreen, Accusign DOA 2, the American Bio Medica Rapid Drug Screen, and the LifeSign Status DS). Each device was challenged with 10 replicate analyses of quality control specimens of known drug and metabolite concentration and known positive and negative clinical specimens previously analyzed by immunoassay and GC-MS. The results indicated discrepancies between the manufacturer's claims and the performance of the product particularly with amphetamines.[8]

Biosite Diagnostics launched the Triage 7 NPT device, which could be used to monitor amphetamines, barbiturates, benzodiazepines, cocaine, opiates, phencyclidine, and tetrahydrocannabinol. In 1993, Wu et al. compared the results obtained by the Syva enzyme-multiplied immunoassay (Emit) to the Triage system for 606 positive and 325 negative specimens. They concluded that the Triage NPT device produced results identical to those produced by the Syva Emit commercial comparison method. The Triage system had a sensitivity of 93–100% with a specificity of 95–100% depending on the drug being tested. The Triage system was also found to be better suited for the analysis of benzodiazepines than the Abbott Diagnostic fluorescence polarization immunoassay and the Syva Emit. The test was found to be reliable and reproducible, with no dependence on the analyst performing the work. [2]

Mastrovitch *et al*. conducted a study in 170 subjects to evaluate the on-site dry testing for illicit substance screening in the emergency department (ED) of a tertiary-care, urban medical center. Urine specimens were tested simultaneously by a dry test device (OnTrak) and by a laboratory-based screening system (Triage). There was significant reductions ($p<0.001$) in turnaround time (both the time to completion and time to physician). Concordance between the results obtained by the two analytical methods was excellent ($p< 0.001$ for all categories).[9]

A multiple-site laboratory evaluation was conducted by Crouch *et al*. to compare EZ-Screen, OnTrak and Triage against Syva Emit immunoassay and GC-MS. The results showed that EZ-Screen did not appear to adhere to a cutoff concentration, giving positive results at concentrations below the stated cutoff. Furthermore, comparing on-site test device results with those obtained form EMIT was very complex for samples with drug concentrations near the reporting cutoff. Ensuring accuracy required a thorough knowledge of the performance of each device, EMIT cross reactivity, and GC-MS findings.[10] Kranzler *et al.* found that EZ-Screen might not be suitable for use in a busy clinical setting unless specific measures are taken to ensure the accuracy of the test.[11]

Five different rapid detection systems for urinary drugs of abuse screening have been evaluated against the in-house techniques of the Regional Laboratory for Toxicology. This study concluded that rapid tests are unreliable and unsuitable for clinical use unless the test kit is available with a distinctive, consistent and reproducible reaction response to denote positive findings.[12]

5.2. COST / COST- EFFECTIVENESS

Cost analysis in a study by Mastrovitch *et al.* showed at least 37.5% decrease in cost per analyte when urine samples were tested by on-site dry test device, compared to laboratory-based screening system.[9]

There is no retrievable evidence on cost-effectiveness of using dry test for drug of abuse screening.

5.3 TRAINING

There is evidence indicating training of all personnel involved in the entire process of dry test use is the key to successful use of the on-site devices. Results determined using on-site dry test devices are comparable to those generated by central laboratories with operator training.[13 Level I]

6. CONCLUSION

a) Effectiveness:
There is evidence to show that analytic performance of most dry test devices is comparable with that obtained from wet test done in central laboratory. However, there are limitations due to inconsistencies in accuracy and cross-reactivity of these devices. There is no single dry test device suitable for screening all drug of abuse.

b) Cost-effectiveness
There is no retrievable evidence on cost-effectiveness of dry test for drug of abuse screening. However, there is a study showing that dry test may be cheaper than wet test for screening drug of abuse using urine specimen.

7. RECOMMENDATION

Based on the above review, dry test for screening drug of abuse using urine specimen can be recommended provided the following criteria are adhered to:

a) Before using the dry test device in the selected facility, performance assessment of the device must be conducted in a controlled laboratory.
b) The users of the devices must be trained to understand limitations of devices including the statistical and analytical sensitivity, specificity and nomenclature of devices, and interferences from drugs or metabolites which could affect interpretation of test results.
c) On-site dry testing using urine specimen is only for screening purpose in clinical settings where central laboratory (wet test) testing is not available. Confirmation of screening test results by central laboratory is mandatory especially if penal or legal actions are to be taken.
d) The cost/economic impact must be considered and evaluated at the institutional setting before introduction of the devices. This is due to the fact that different dry test devices are suitable for different types of drug of abuse.

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