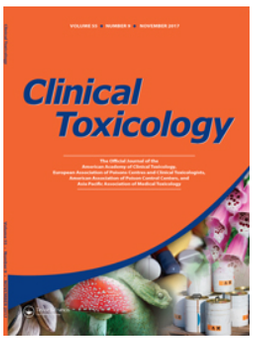

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CLINICAL RESEARCH

Do rapid comprehensive urine drug screens change clinical management in children?

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ABSTRACT

Context: Multiple studies have concluded that urine drug screens rarely change clinical management. The rapid comprehensive urine drug screen (RCUDS) at our institution detects over 300 substances using a combination of EIA and GC/MS and typically takes 2–5 h for completion.

Objective: We sought to determine whether this RCUDS altered management in the pediatric population.

Methods: All patients >1 month and <18 years of age in which a RCUDS was completed from 1 January 2012 to 31 December 2012 were eligible for the study. Assuming that clinical management would not be altered in at least 90% of cases with a confidence interval of 95%, an alpha error of 5%, we calculated a sample size of 122 cases to ensure adequate study power. Four board-certified medical toxicologists reviewed 160 cases. Cases were assigned to the toxicologists based on a random-number generator. In addition, each toxicologist reviewed 12 random cases from the other three toxicologist's cases to determine inter-rater reliability. All four toxicologists reviewed any case in which a RCUDS was believed to have changed management.

Results: A total of 908 RCUDS were performed during the study period, and 160 were selected for study. Mean age was 10.5 years; male = 83, female = 77. Most were ordered from the ED (101/160 = 63%), followed by the inpatient unit (36/160 = 23%), outpatient (14/160 = 9%), and ICU (9/160 = 6%). 111/160 (69%) had a history of ingestion. Of the 160 randomly chosen cases, only three cases were found in which overall clinical management was altered based on the results of the RCUDS. All three cases were children <3 years old with a RCUDS positive for amfetamines. In all the three cases, police, Division of Family Services (DFS), and social work were involved. In no case did the acute clinical management change occurred due to the results of the RCUDS.

Conclusions: The RCUDS rarely changed management in patients at our institution. Further study is warranted.

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Urine drug screen; pediatric; GC/MS

Introduction

The urine drug screen (UDS) is a commonly ordered test with questionable clinical utility in the vast majority of cases. Multiple studies in the adult and pediatric populations confirm that the results of a UDS rarely change clinical management [1–6]. However, UDSs may have a role in cases of child abuse and neglect [7]. Due to the speed and relative cost, most institutions utilize rapid immunoassays for urine drug screening. These immunoassays are fraught with false negative and false positive results [8–20]. Furthermore, immunoassays screen for only few drugs, and are becoming even less relevant in light of the increased use of novel psychoactive substances and the inability for these screens to detect them. Advanced laboratory methods such as gas chromatography/mass spectrometry (GC/MS) are considered the "gold standard" in confirming the results of a urine drug screening immunoassay and broad spectrum drug screening. Our institution utilizes a rapid comprehensive urine drug screen (RCUDS) that detects over 300 xenobiotics using a combination of enzyme immunoassay (EIA) and GC/MS. All xenobiotics that are detected by EIA are then rapidly confirmed by GC/MS. We sought to determine whether this expansive UDS altered clinical management in the pediatric population.

Methods

This study was a retrospective chart review performed by four board-certified medical toxicologists (authors 1–4). All patients between the age of >1 month of age and <18 years of age in which a comprehensive UDS was ordered and completed at a single urban, academic tertiary care pediatric hospital from 1 January 2012 to 31 December 2012 were eligible for the study. All clinical data were prospectively entered in real time into a structured database. Variables and outcomes

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were determined *a priori* and data abstraction was performed in a systematic manner according to the guidelines of Gilbert [21] with the exception of blinding the case abstractors to the purpose of the study. This study was approved by our Institutional Review Board.

Assuming that clinical management would not be altered in at least 90% of cases with a confidence interval of 95%, an alpha error of 5%, we calculated a sample size of 122 cases to ensure adequate study power. Allowing for some additional error, four board-certified medical toxicologists reviewed a total of 160 cases. Cases were assigned to the toxicologists by a random-number generator. In addition, each toxicologist reviewed 12 random cases from the other three toxicologist's cases to determine inter-rater reliability. All four toxicologists reviewed any case in which a comprehensive UDS was believed to have changed clinical management.

Results

A total of 908 rapid comprehensive UDS were performed during the study period. Based on our sample size calculation, of these 908 cases, we reviewed 160 leaving some margin for error. Mean age was 10.5 years (range: 1 month to 18 years) and 52% ($N = 82$) were male. A majority of RCUDS were ordered from the ED (101/160 = 63%), followed by the inpatient unit (36/160 = 23%), outpatient (14/160 = 9%), and ICU (9/160 = 6%). In 69% of cases ($N = 111$), there was a documented history of ingestion. In 75% of cases ($N = 121$), the RCUDS detected at least one xenobiotic. Only three cases were found in which overall clinical management was altered based on the results of the comprehensive UDS. In all the three cases, some combination of social services, Division of Family Services (DFS), police, and the Medical Toxicology service were involved as a result of the RCUDS. In no case did the acute clinical management change due to the results of the RCUDS. We found no case in which an antidote was given or withheld based upon the results of the RCUDS. In addition, each toxicologist reviewed 12 random cases from the other three toxicologist's cases to determine inter-rater reliability. There was no disagreement between reviewers. On average, the clinical turnaround time of the RCUDS was 2.5 h during weekdays and 5 h on the weekend. Patients were charged approximately $450 for the RCUDS.

Discussion

While previous studies have demonstrated that immunoassay UDS rarely, if ever, change acute clinical management, this is the first study to demonstrate that more advanced drug screens, such as RCUDS utilized at our institution, also rarely alter clinical management. Despite the fact that the RCUDS at our institution tests for >300 substances, has significantly fewer false positives and false negatives and has a turnaround time similar to a standard immunoassay UDS, it was still unlikely that the clinical management was altered after the results of the test returned. Specifically, we found no case in which an antidote was administered or withheld due to the results of a RCUDS. Multiple factors may explain our finding. First, many toxins with specific antidotes have quantitative drug assays that guide management (i.e., acetaminophen, iron, digoxin, heavy metals, toxic alcohols, etc.). Similarly, other toxins that require treatment with an arsenal of "supportive care" drugs (benzodiazepines, dextrose, sodium bicarbonate, etc.) are administered based on history of exposure and clinical symptomatology as opposed to the results of a UDS. Furthermore, despite the rapid turnaround of our RCUDS, patients often required treatment with a drug (i.e., benzodiazepine for agitation) before the results of the RCUDS were available. Finally, there are xenobiotics not detected by our institution's RCUDS that do occasionally warrant treatment with antidotal therapy. These include sulfonylureas, buprenorphine, and cyanide, most calcium channel blockers, and most beta blockers.

In three cases, the overall clinical management did change based on the results of our RCUDS. All three cases involved young children exposed to amfetamines. In all the three cases, some combination of social services, DFS, police, and the Medical Toxicology service were involved based on the results of the RCUDS.

Case 1

A previously healthy 2 month-old male was presented to the ED with acute onset of bilateral upper "shaking" and "crossed eyes". Patient's initial vital signs were temperature of 36.2 (rectal), heart rate of 144 bpm, and respiratory rate of 36 bpm. Physical exam revealed nasal deviation of both eyes, rhythmic motions of mouth and lips, increased tone of bilateral upper extremities, and the infant cried when stimulated. Initial work-up including complete blood count, chemistry panel, hepatic panel, urinalysis, non-contrast CT head, and cerebrospinal fluid analysis were negative. A rapid comprehensive UDS was positive for amfetamine and methamfetamine. The patient returned to baseline over the course of the day. No medications were given. A skeletal survey was negative. Social services, DFS, police, and the Medical Toxicology service were involved due to the results of the UDS. Ultimately, the patient was discharged home with his parents. Reflexive confirmatory quantitative testing was performed. Quantitative urine methamfetamine concentration was 13,184 ng/mL and urine amfetamine concentration was 1393 ng/mL. While the source of the exposure was not clearly identified, the patient's paternal grandfather had been recently incarcerated for selling methamfetamine. The paternal grandfather had been in contact with the patient shortly before the onset of symptoms.

Case 2

A previously healthy 16 month-old female was presented to the ED as "inconsolable". Patient had been crying for nine hours. Patient's initial vital signs were temperature of 36.8 (rectal), heart rate of 160 bpm, and respiratory rate of 40 bpm. Physical exam revealed an irritable, hyperactive patient. Exam was negative for corneal abrasion and hair tourniquets.

Patient was given 20 mcg of intranasal fentanyl followed by lorazepam 1 mg IV with improvement of agitation prior to return of any diagnostic studies with the exception of a normal point of care blood sugar determination. Initial labs including a CBC and BMP were unremarkable. A rapid comprehensive UDS was positive for amfetamines and phenylpropanolamine. Social services and Medical Toxicology service were involved due to the UDS. Confirmatory quantitative testing was performed. Quantitative urine amfetamine concentration was >50,000 ng/mL. Quantitative urine methamfetamine concentration was <100 ng/mL. It was discovered that the patient's 12 year-old maternal uncle was on Adderall (amfetamine/dextroamfetamine) and was the likely source of the exposure.

Case 3

A previously healthy 23 month-old male was presented to the ED as agitated and hyperactive for the past 19 h. Patient's mother stated that he became agitated shortly after receiving 5 mL of ibuprofen suspension the night before for a fever. Mother was concerned that the patient was allergic to the purple dye in the ibuprofen suspension. Initial vital signs were temperature of 37.3 (rectal), heart rate of 128 bpm, and respiratory rate of 32 bpm. Physical exam revealed an irritable toddler. Initial labs including a CBC, BMP, and LFTs were unremarkable. A rapid comprehensive UDS was positive for amfetamine and methamfetamine. The patient returned to baseline over the course of the day. No medications were given. Social services, DFS, police, and Medical Toxicology service were involved due to the results of the UDS. Ultimately, the patient was discharged home with his parents. Quantitative urine methamfetamine concentration was 12,108 ng/mL and urine amfetamine concentration was 2780 ng/mL. While the source of the exposure was not clearly identified, the parents admitted taking the patient to a "party hall" shortly before the onset of symptoms.

One potential argument for the clinical utility of a RCUDS is the detection of novel psychoactive substances, such as synthetic cannabinoids or cathinones, which are not detected by standard immunoassay UDS. Our institution's RCUDS does screen for a number of novel psychoactive substances. None were detected in this study. However, as use of these substances continues to rise, more young children may potentially be exposed to these drugs raising the possibility that there may be a role for a more expanded UDS in cases of child abuse and neglect. Furthermore, as our diagnostic testing becomes more sophisticated (i.e., time of flight analysis coupled with EIA and/or GC/MS), faster, and, hopefully, more economic, there may be a role for more advanced testing. This may be particularly useful in cases of exposure to novel psychoactive substances.

This study has several limitations. First, this was a retrospective review of randomly chosen cases. The review of these cases was based upon expert opinion, and it is impossible to truly know whether the RCUDS changed the clinical management for a given patient in real time. It is also important to mention that the four medical toxicologists reviewing these cases also provided bedside consultation for multiple patients included in this study. Although unavoidable, we realize that this may have introduced some bias into the study. In addition, based on our power analysis, only 160 of 908 RCUDS sent over the course of the year were reviewed. Thus, cases in which the treating physicians felt that the RCUDS changed the clinical management of the patient may have been missed. In addition, our study population is heterogeneous and there are important differences between an unintentional exposure in a toddler and an intentional ingestion in a teenager. Although we did not observe outcome differences between age groups, the study was not powered to determine this. Since, there were no outcome differences seen, the data from these groups were combined but it is possible that in a larger study, differences might be found that would affect the analysis. Finally, this was a study of pediatric patients and applicability to adult patients is unknown.

Conclusions

In this study, the RCUDS rarely changed the clinical management in pediatric patients at our institution. There were rare instances in which the RCUDS initiated the involvement of social services and law enforcement due to concern for child abuse and neglect. Further studies are warranted to define the role of the RCUDS in cases of suspected exposure to a novel psychoactive substances in the pediatric population.

Disclosure statement

The authors report no declarations of interest.

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