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Interviewing and Urine Drug Toxicology Screening in a Pediatric Pain Management Center:

An Analysis of Analgesic Nonadherence and Aberrant Behaviors in Adolescents and Young Adults

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Abstract

Objectives—Many adolescents and young adults report having chronic pain. Urine drug toxicology (UDT) is not routinely used in the pediatric pain management population, despite more routine use in adults with pain, particularly those prescribed opioids. As a first step toward establishing monitoring practices in pediatric and adolescent pain management, the present study evaluated the role of UDT in conjunction with a standard clinical interview in identifying the rate of adherence to an established analgesic regimen. The study also aimed to assess the use of UDT in identifying possible aberrant behaviors in this population.

Methods—Data were acquired from a convenience sample of 50 pediatric and adolescent pain management initial consultations, during which a clinical interview and UDT were conducted. Data were analyzed to determine adherence to an established analgesic prescription regimen, and for identification of aberrant behaviors including concurrent use of illicit substances and prescription medication misuse. Other pertinent demographic and clinical factors were examined as factors in adherence.

Results—Opioid medications were prescribed for 42% of the sample receiving pain medications, and 22% of the sample was nonadherent to their prescription analgesic regimen. Factors associated with a higher likelihood of nonadherence were an older age and having an opioid prescription. The majority (90%) of those nonadherent to their analgesic regimen displayed some form of aberrant behavior. Among the nonadherent patients, 50% were identified by UDT alone, and 50% were identified by self-report during the clinical encounter.

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Conclusions—These results highlight the challenges of identifying nonadherence to a prescription regimen among adolescents with chronic pain. In addition, this preliminary work suggests that UDT could be used in conjunction with careful clinical interviewing to substantiate patient report and increase the likelihood of detecting analgesic nonadherence and aberrant behaviors.

Keywords

adolescents; chronic pain; opioids; adherence; urine drug toxicology; aberrant behaviors

Urine drug toxicology (UDT) is increasingly being used as a tool to determine adherence to prescribed medications as well as to monitor for use of illicit compounds in adults with pain. Further, there is an emerging consensus among professional organizations recommending routine and random UDT in the adult patient maintained on chronic opioid therapy, with some organizations recommending use based on risk stratification (eg, presence of aberrant behaviors).^{1–5} UDT, however, is not routinely utilized by physicians treating the estimated 11% to 38% of adolescents and young adults with chronic pain.^{6–9}

UDT may offer an objective measure of adherence for certain medications. Adherence is defined by the World Health Organization (WHO) as “the extent to which a person’s behavior including taking medication, following diet plans, or executing lifestyle modifications corresponds with the agreed upon recommendations from a health care provider.”¹⁰ Adherence rates are higher by parental/youth self-reports as compared with other objective measures and while there is no gold standard for measuring adherence, a combination of methods is generally recommended.^{11–13} The use of UDT in children and adolescents with pain may also provide useful information to the clinician prescribing or considering prescribing opioids. Aberrant behaviors suggesting opioid abuse have been identified in adult pain patients.^{14,15} Thus, UDT may help to identify aberrant behaviors that may not be picked up in clinical interview, and may serve as “red flags” and assist with risk stratification when considering management of pain with opioids.

Given the lack of treatment guidelines for the pediatric pain patient, as well as for the use of UDTs in the population, the clinical combination of conducting both a UDT and a detailed clinical interview requires evaluation in the adolescent pain population as a first step toward developing generally accepted (or standard) monitoring practices. The aim of the present study, therefore, was to investigate the potential role for utilization of UDT in conjunction with a standard clinical interview in identifying the degree of adherence to an established analgesic regimen among adolescents who presented for outpatient pediatric pain management. The secondary aim included the examination of UDT as a tool to identify possible aberrant behaviors including concurrent use of illicit substances and prescription medication misuse in this population.

MATERIALS AND METHODS

Design

The study consisted of clinical interviews accompanied by UDT for subsequent data analysis conducted at the Pediatric Pain Management Center (PPMC) of Columbia University Medical Center (CUMC). The protocol for UDT collection in this sample was approved by the Institutional Review Board of CUMC.

Sample

The study aimed to recruit a convenience sample of 50 sequential patients. Participants were included if they were referred for initial pain management evaluation and were 10 to 20 years old. The data collection period was from October 2008 through July 2011; this timeframe was needed to accrue this sample size as the pediatric pain management clinic had only 1 physician with limited weekly hours for initial evaluations.

Diagnoses and Medications

Pain diagnoses were divided into 2 categories: chronic noncancer pain (CNP) and subacute postoperative pain (SAPOP). We defined chronic pain as pain lasting ≥ 6 months and SAPOP as pain following surgery, lasting >7 days but <1 month.¹⁶ Self-reported current or past psychiatric history (eg, anxiety, depression) was noted as present or not. Medication reported by patients and their parents were divided into the following categories: opioid, nonsteroidal anti-inflammatory drug (NSAID), benzodiazepine, nonbenzodiazepine muscle relaxant, neuropathic pain agent, psychostimulant, or antidepressant; we attempted to include a wide range of medications that included psychotropic medications that may affect pain threshold.

Interview Procedures and Specimen Collection

All interviews and UDT were done at the initial pain management consultation, and were conducted by the same physician (author J.M.S.). Individuals with SAPOP were referred at the time of hospital discharge following surgical procedure, and seen in consultation at the time of discharge or immediately thereafter; those with CNP waited 2 weeks to 2 months for an appointment following receipt of referral documentation. A 90- to 120-minute structured interview consisted of an initial meeting with the patient alone, in which self-report was obtained, followed by an interview with the family caregiver, with the patient present. Guardians/patients provided the pain history, past medical, developmental, and psychosocial history, psychiatric history, past medication-based and nonmedication-based therapies. Prescription and nonprescription analgesic medication usage was elicited with and without parents present. Questions routinely asked to identify potential opioid misuse followed the format listed in Table 1.

Assurance of confidentiality was given, and the purpose of UDT (ie, to assess for prescribed, nonprescribed, and illicit drugs) was specified.¹⁷ Following consent (and assent if patient was a minor) for UDT collection, patients provided an unobserved, temperature-tested urine sample. All samples were sent to Calloway Labs (<http://www.callowaylabs.com>). All collected urine samples had to conform to temperature requirements ($> 90^{\circ}\text{F}$ within 4 min of voiding). Specimen validity testing, which included integrity testing (temperature,

creatinine, specific gravity, and pH), adulterant testing (oxidant screen), and aldehyde screen, was completed by Calloway Labs. Urine samples testing positive on initial immunoassay screen were further evaluated using gas chromatography/mass spectrometry, which is widely regarded as the highest standard for UDT.¹⁸ Gas chromatography/mass spectrometry is a particularly useful tool for detecting and distinguishing between different types of opioids.¹⁹ Drugs included in this commercially available panel were: amphetamines, barbiturates, benzodiazepines, buprenorphine, cocaine, ethyl glucuronide, ethanol, fentanyl, methadone, opioids (both synthetic and opium based), phencyclidine, tetrahydrocannabinol, propoxyphene, and tramadol. Results were uploaded by Calloway Labs onto a secure Web site. Unexpected results that suggested nonadherence resulted in telephone contact to the parent or patient. Treatment or referral recommendations were offered, depending on age and as deemed clinically indicated.

Adherence Monitoring

All patients were classified as either adherent or nonadherent with respect to both UDT and reported use of prescribed medications. For the purposes of this analysis, “adherence” represents adherence to the analgesic medication regimen, which may include opioids or nonopioid analgesics (eg, muscle relaxants, benzodiazepines, and psychotropic medications which affect pain threshold). An “adherent” classification indicated that a patient’s UDT and self-reported drug use were consistent with the patient’s medical and prescription analgesic history. We have reported nonadherence defined as either (1) noncompliance with the analgesic medication regimen (which would include unauthorized dose escalation) or (2) the presence of aberrant behaviors (eg, illicit substance use by self-report and/or urine toxicology, continued opioid seeking despite adverse consequences). Patients were classified as “nonadherent” if either the UDT or self-report was inconsistent with the prescribed medication history. This designation could also result from an absence of prescribed analgesic medications in the UDT or by self-report.

Statistical Analyses

Age of the patients ranged from 10 to 20 years old and were grouped into 3 age categories (10 to 12, 13 to 17, and 18+) consistent with published stages of adolescence.^{20,21} The primary aim of this study was to determine the rate of adherence to an already-established prescription analgesic regimen among adolescents who presented for pain evaluation. Demographic variables representing possible predictors of nonadherence were identified from the literature review, and included: sex,²² race,²³ history of opioids prescribed for pain,²⁴ number of classes of medications prescribed,²⁵ and psychiatric diagnosis.^{26,27} The secondary aim was to identify possible aberrant behaviors including concurrent use of illicit substances and prescription medication misuse in this population. These data were obtained from considering the UDT together with the patient interview, and were descriptively summarized. IBM SPSS (v.9.0) was used in the present analyses.

RESULTS

Participants

Fifty-eight patients were consented for UDT, and 50 were able to provide a specimen. Forty-five patients were included in the final sample because they were maintained on medications regimens for which adherence could be assessed; 3 participants were not prescribed any medications at the time of initial consultation, and 2 additional participants were prescribed only nonanalgesic medications (loestrin, melatonin). Table 2 presents a summary of the demographic characteristics of the sample. Adolescents were primarily white females with an average age of 14.7 years (SD = 2.26; range, 10 to 20). The sample was largely comprised of adolescents with CNP (96%, N = 43); 6% (N = 3) had SAPOP, 1 participant with SAPOP was also classified as CNP as she had both chronic low back pain and postoperative back pain. Opioid medications were prescribed for 42% (n = 19) of the sample of patients receiving pain medications, with the remaining 58% (n = 26) of those prescribed analgesics receiving nonopioid analgesic medications. A self-reported history of psychiatric illness was present in 33% of the sample, and psychiatric comorbidities were present across all age groups and pain categories, with depression and anxiety disorders being the most common.

Medication Adherence

Adherence to the established analgesic medication regimen was assessed by interview for noncompliance, aberrant behaviors, or signs of substance abuse, as well as by UDT. None of the 45 urine samples failed specimen validity testing. Of the 45 participants included in the adherence analyses, 78% were deemed adherent to their medication regimen (n = 35), whereas 22% were nonadherent (n = 10).

Table 3 depicts characteristics of the 10 nonadherent participants, and whether the nonadherence distinction was identified based upon clinical interview or UDT. Five of the 10 nonadherent (NA) patients were identified through UDT (UDT NA), and the remaining 5 through clinical interview (Interview NA). Of the 10 that were identified as nonadherent, 7 were nonadherent based upon the traditional WHO definition, and labeled “medication nonadherent” (rows shaded in Table 3): 3 of these 7 participants were “medication nonadherent” due to the absence in UDT of a prescribed medication (Subject A: psychostimulant; D and E: opioids). The remaining 4 participants were identified by clinical interview as they reported unauthorized dose escalation of their prescribed opioid (Subjects F, G, H, J). Unauthorized dose escalations were also considered aberrant behaviors, and are additionally labeled as “behavioral nonadherent” in Table 3. Of note, Subject G described managing his own medications, reporting unauthorized dose escalations and taking opioids as he felt he needed for pain, not as prescribed. His referring physicians noted concerns that his report of pain did not correlate with objective measures of illness severity. Subject H reported intentionally skipping opioid doses in attempt to reduce tolerance and subsequently doubling his dose stating, “it’s not as much fun if I take it daily.” In addition to the aforementioned, 9 of the 10 nonadherent patients were also classified as “behaviorally nonadherent” due to the presence of aberrant behaviors. As noted above, 4 patients were classified due to unauthorized dose escalation; 4 patients had nonprescribed controlled or

illicit substances on UDT testing (B, C: opioids; D: cocaine and alcohol metabolites; E: tetrahydrocannabinol), and 1 patient (Subject I) reported continued opioid use despite adverse consequences. Subjects D and E were both medication nonadherent and behavior nonadherent.

We were able to obtain follow-up information from some, but not all, of those patients classified as “nonadherent.” Two participants (Subjects B and C) reported taking leftover opioid medication from prior prescribers when they experienced pain, but reported they did not reveal this to the interviewer as it was not one of their standing medications. One additional participant who was excluded from the analyses as she was not prescribed any medication at the time of initial consultation, was UDT positive for benzodiazepines; the participant’s mother told investigators that she had been giving her daughter her own medication (diazepam) in an attempt to treat her daughter’s ongoing pain.

This study was not sufficiently powered to determine differences in sex, race, pain diagnosis, or medication history, and no nonstatistical trends were observed. We did see differences in adherence as a function of age. Patients 18 years and older were significantly more nonadherent (75% of this age group was nonadherent) than 10- to 12-year-olds (11%) and 13- to 17-year-olds (19%) ($\chi^2=7.31$, $P=0.026$). However, as previously noted, this analysis should be treated cautiously due to the small cell sizes.

The likelihood of a discrepancy between UDT and clinical interview was higher in those patients who were prescribed an opioid: 37% versus 12% ($\chi^2=4.07$, $P=0.04$). It should be noted that patients classified as opioid prescribed were, in some cases, also prescribed concomitant nonopioid medications.

DISCUSSION

This pilot study of adherence in a PPMC represents, to our knowledge, the first attempt to evaluate the use of UDT in an adolescent chronic pain population. We examined adherence first narrowly, with respect to the analgesic regimen, and second defined in a more expanded manner to include aberrant behaviors such as prescription analgesic misuse and illicit substance abuse. We found that 22% of the total sample of adolescent patients was nonadherent with this expanded definition of adherence (vs. 16% with the narrower definition), and that 50% of those nonadherent were identified by UDT, and not by clinical interview.

Aberrant UDT results have been reported to be significantly more frequent in younger rather than older adult patients.²² While our sample is small, and therefore analysis should be interpreted cautiously, our findings suggest that older adolescents are may be more likely to exhibit nonadherent tendencies than younger patients ($P<0.03$). This finding highlights the need for future studies to determine if, in fact, late adolescence and young adulthood may be a time of heightened risk for opioid abuse. An analysis conducted in a similarly aged cohort found that for every year that onset of illicit substance use is delayed, the odds were reduced for developing lifetime prescription drug abuse (5%) or drug dependence (2%).²⁵ Given this association between earlier age of use and development of abuse or dependence, and that

rates of nonadherence appear to increase as patients approach young adulthood, routine implementation of UDT may permit early detection of aberrant behaviors and timely clinical interventions for adolescent patients before the onset of prescription opioid abuse.

While this small study was not designed to identify risk factors for nonadherence, we believe it is worth noting that 50% of those nonadherent per the WHO definition had a self-reported psychiatric diagnosis, and conversely 33% of those in the sample with a psychiatric diagnosis were nonadherent. Among adult chronic pain patients, there is an association between psychiatric comorbidities and likelihood of progressing to abuse of opioids.^{28–31} Future studies to better characterize risk factors and reasons for analgesic nonadherence in the pediatric pain population may be helpful in identifying those for whom increased monitoring may be useful.

It is important to note that while rates of adherence to analgesic regimens in the pediatric pain population have not yet been characterized, reported adherence rates for other pediatric chronic medical conditions average approximately 50% to 55%, with a wide range, depending upon how adherence is defined and measured.¹¹ One explanation for the higher adherence rates found in this study among pain patients is that adherence rates are generally higher by parental/youth self-reports as compared with other objective measures^{11–13}; self-report may overestimate adherence by >50%.¹⁰ Our findings are in fact similar to other adherence data based solely on self-report of the pediatric patient or parent.^{11,12,32}

We included UDT as an objective measure in this study in attempt to increase detection of analgesic nonadherence. UDT, however, does not test for the full range of analgesic classes prescribed to this population (eg, non-NSAID, nonbenzodiazepine muscle relaxant, neuropathic pain agent, or antidepressant). Less than half of the participants in our sample were prescribed a medication detected by UDT (eg, opioid, benzodiazepine, stimulant). Even for those prescribed opioids, the UDT only reflects the qualitative presence or absence of the opioid, and does not provide a more nuanced view of adherence.

Despite the restricted scope of analgesic testing provided by UDT in this population, its inclusion afforded us detection of nonadherence and aberrant behaviors that otherwise were not picked up by clinical interview. While the present study is limited in ability to identify clinical reasons for discrepant results between UDT and clinical interview, the identification of discordance may provide an important signal to the provider to obtain more clinical information to better understand the discrepancy. This preliminary work suggests that UDT could potentially be used in combination with careful clinical interviewing to corroborate patient self-report and increase the likelihood of detecting analgesic nonadherence. Thus aberrant behaviors may serve as “red flags” to assist with risk stratification when considering opioid prescribing for pain management.

LIMITATIONS

The primary limitations of this study are that it was a convenience sample, and retrospective in nature. The retrospective nature of this study hindered our ability to investigate the potential range of reasons for nonadherence and aberrant behaviors. For example, it may be

possible that individuals “appropriately” stopped medication, either due to side effects or resolved pain; however, in our sample, we would have classified them as “nonadherent.” Similarly, unauthorized dose escalations may have been the result of undertreated pain. Despite the possibility that UDT may detect nonadherence which is clinically appropriate, its use provides important clinical information which should be discussed in the clinical encounter. Another limitation of this study is that a standard clinical interview was not designed and implemented for this data collection. The set of questions (Table 1) posed in each clinical interview did not represent a validated questionnaire. The presence or absence of past alcohol/substance abuse, or psychiatric diagnoses, is subject to underdetection because of unconfirmed patient and parental report. Self-report on substance use is subject to recall and social desirability bias even during the administration of anonymous questionnaires. A pain management setting may be expected to increase the likelihood of underreporting. Even though participants were interviewed without the parent(s) in the room, proximity to the consenting parent may have interfered with divulging history of misuse. In addition, review of primary care and subspecialty inpatient and outpatient provider documentation was not always available. And finally, the requirement for UDT may have excluded those who were either unable or unwilling to void.

As collection was cross-sectional, UDT testing may have missed nonadherence, partial nonadherence, or episodic use of illicit drugs, especially for substances with short half-lives (eg, cocaine, amphetamines). As shown by Subjects F to J, who were categorized as adherent based on UDT testing but nonadherent based on interview, UDT alone does not serve as an adequate means of drug screening. Similarly, there is a possibility for both false positives and false negative with UDT. Thus, while UDT may provide important clinical information, it has limitations and should be used in conjunction with clinical interview. Age groupings were a limitation; the number of patients in the 18+ category was only 4 (8%), which may not represent other PPMCs in this age range. Grade level would have been more easily compared with national data on drug abuse in adolescence. Future studies should collect both age ranges and grade levels for participants. However, even when taking the limitations into account, this study demonstrates the feasibility and necessity of larger studies to address opioid prescribing and monitoring in this population.

CONCLUSIONS

In conclusion, this preliminary work suggests that UDT could potentially be used in conjunction with careful clinical interviewing to substantiate patient report and increase the likelihood of identifying analgesic nonadherence, and aberrant behaviors that may serve as “red flags,” in this population that may be at greater risk for opioid abuse. Larger studies looking at the role of UDT in this population are needed, as is the development of standard accepted monitoring practices in the pediatric pain population. Longitudinal studies are needed in this population to examine the scope of nonadherence and relevant risk factors. Early identification of opioid misuse may permit entry into substance abuse treatment for adolescent patients with pain.

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TABLE 1

Suggested Questions for Identifying Potential Opioid Misuse

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1. How does your pain change with Drug X? Does the pain intensity decrease?
 2. Does the medication help you to feel more relaxed?
 3. Does Drug X give you energy or make you feel more organized?
 4. Have you ever taken more X than prescribed?
 5. Have you ever taken X for anxiety, sleep, or “the feeling”?
 6. Have you ever taken MORE strong medication for PAIN than what your doctor prescribed?
 7. Have you taken any strong medications for PAIN other than what your doctor prescribes?

If YES, where did you get the medication? (Circle all that apply)

Family Member

Friend

Other _____

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TABLE 2

Demographic Summary of Patients Prescribed Analgesics at the Pediatric Pain Management Center (N = 45)

Variables	n (%)
Sex	
Male	13 (29)
Female	32 (71)
Ethnicity	
White	35 (78)
Hispanic	9 (20)
African American	1 (2)
Age	
10–12	9 (20)
13–17	32 (71)
18+	4 (9)
Condition (diagnosis)	
CNP (all)	43 (96)
SAPOP	3 (7)
Medication prescribed	
Opioids	19 (42)
No opioid	26 (58)
NSAID	24 (53)
Neuropathic pain agent	19 (42)
Antidepressant	7 (16)
Psychostimulant	5 (11)
Muscle relaxant	1 (2)
Psychiatric history	
Present	15 (33)
Not present	30 (67)

TABLE 3

Descriptive Characteristics of Nonadherent (NA) Participants

ID	Age	Sex	Ethnicity	Psych History	Pain	Opioid Prescribed	Medication NA		UDT NA	Interview NA	Behavioral NA
							Opioid	Nonopioid			
A	11	F	C	X	CNP			X	X		
B	16	F	H		CNP			X			X
C	17	F	C		CNP			X			X
D	18	F	C	X	CNP	X	X	X			X
E	20	M	AA		CNP	X	X	X			X
F	13	F	C		CNP	X	X		X		X
G	16	M	C		CNP	X	X		X		X
H	16	M	C	X	CNP	X	X		X		X
I	16	F	C	X	CNP	X			X		X
J	18	F	C	X	CNP, SAPOP	X	X		X		X

Shaded rows have been used to identify nonadherent participants per the WHO definition of nonadherence.

Ethnicity: AA, African American; C, Caucasian; H, Hispanic.

Opioid Prescribed: X indicates an opioid was prescribed to the patient.

Medication NA, Opioid: X indicates a patient was nonadherent with the prescribed opioid medication regimen.

Medication NA, Nonopioid: X indicates the patient was nonadherent with the prescribed nonopioid medication regimen.

UDT NA: X indicates nonadherent patients identified through UDT. Bolded Xs in the UDT NA column identify participants whose urine did not contain a prescribed substance (and should have).

Interview NA: X indicates nonadherent patients identified through clinical interview. Bolded Xs in the Interview NA column identify participants who reported dose escalation of prescribed opioids.

Behavioral NA: X indicates participants with aberrant behaviors.

UDT indicates urine drug toxicology.