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Identifying methamphetamine exposure in children

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Abstract

Introduction

Methamphetamine (MAMP) use, distribution and manufacture remain a serious public health and safety problem in the United States, and children environmentally exposed to MAMP face a myriad of developmental, social and health risks, including severe abuse and neglect necessitating child protection involvement. It is recommended that drug-endangered children receive medical evaluation and care with documentation of overall physical and mental conditions and have urine drug testing.[1] The primary aim of this study was to determine the best biological matrix to detect MAMP, amphetamine (AMP), methylenedioxymethamphetamine (MDMA), methylenedioxyamphetamine (MDA) and methylenedioxyethylamphetamine (MDEA) in environmentally exposed children.

Method

91 children, environmentally exposed to household MAMP intake, were medically evaluated at the Child and Adolescent Abuse Resource and Evaluation (CAARE) Diagnostic and Treatment Center at the University of California, Davis (UCD) Children's Hospital. MAMP, AMP, MDMA, MDA and

MDEA were quantified in urine and oral fluid (OF) by gas chromatography mass spectrometry (GCMS) and in hair by liquid chromatography tandem mass spectrometry (LCMSMS).

Results

Overall drug detection rates in OF, urine and hair were 6.9%, 22.1% and 77.8%, respectively. Seventy children (79%) tested positive for 1 or more drugs in 1 or more matrices. MAMP was the primary analyte detected in all 3 biological matrices. All positive OF (n=5) and 18 of 19 positive urine specimens also had a positive hair test.

Conclusion

Hair analysis offered a more sensitive tool for identifying MAMP, AMP and MDMA environmental exposure in children than urine or OF testing. A negative urine, or hair test does not exclude the possibility of drug exposure, but hair testing provided the greatest sensitivity for identifying drug-exposed children.

Keywords: hair, urine, oral fluid, drug-exposed children, methamphetamine

Introduction

Methamphetamine (MAMP), a sympathomimetic amine, is a powerful central nervous system stimulant with limited medical indications including attention deficit hyperactivity disorder and obesity.[2] MAMP is an addictive substance that produces euphoria and a sense of well-being, suppresses appetite, and increases alertness and energy.[3] It is 1 of the 5 most commonly abused illicit drugs in North America, Europe and Southeast Asia.[4] Adverse effects of MAMP intake range from mild to life-threatening symptoms such as agitation, tremor, dyspnea, tachycardia, nausea, vomiting, psychosis, hypertension, stroke, and coma.[2-3, 5]

Illicit MAMP is typically produced in clandestine laboratories that are often small and poorly-ventilated.[6] Prior to March 2006, illicit MAMP production involved inexpensive and easy-to-obtain chemicals, including the precursor pseudoephedrine, which was available over-the-counter. The Combat Methamphetamine Epidemic Act of 2005 amended the Controlled Substance Abuse act requires retail stores (and their employed pharmacists) to receive training and obtain certification prior to dispensing non-prescription drugs containing ephedrine, pseudoephedrine and phenylpropanolamine.[7] Although this provision decreased the amount of pseudoephedrine available for illicit MAMP production in the US, a new method so-called “shake and bake” or “one-pot” method was developed in recent years.[8] This method allowed chemists to manufacture the drug using a small amount of pseudoephedrine and synthesize MAMP in 10 min or less. In addition, MAMP producers found a way to bypass regulations on limited pseudoephedrine procurement by working in groups (“smurfing”), using false identifications, and traveling from one pharmacy to another.[8-9] There were 6,768 MAMP laboratory seizures in 2010, a 12% increase from the previous year (6,032).[8] The National Drug Intelligence Center predicted that small-scale laboratories will remain a substantial source of MAMP, along with “super meth labs” controlled by large drug-trafficking organizations, to provide cheap, high-purity MAMP.[8]

Chemicals such as anhydrous ammonia, sodium hydroxide, sulfuric acid, alcohols, and other solvents utilized in illicit MAMP production are toxic, hazardous, and volatile. Thus, the environment of a clandestine MAMP laboratory is inherently hazardous to inhabitants, including children living with the adult operators.[10-13] Children taken from these home-based MAMP laboratories are exposed to toxic fumes, accidental burns, and contaminated drug paraphernalia. Chronic adult MAMP use is associated

with psychosis, severely impaired judgment, agitation, hypersexuality, preoccupation with guns and violence, and frequent association with a criminal lifestyle. Thus, children of chronic MAMP users are poorly fed, improperly clothed, inadequately schooled, and lack good hygiene, as their parents (or caregivers) go through crash and binge cycles, and most often sleep through meal and school times.[6, 12-13] Children taken into custody from drug-exposed environments by Child Protection Services (CPS) are classified as drug-endangered children (DEC),regardless of the source of exposure.[1] The US Department of Justice recently established a program ("Drug Endangered Children Task Force") in response to the overwhelming need to protect children from exposure to drug environments.[1]

There are no standard guidelines for state and local agencies to act on DEC cases.[6, 11, 13-17] When a child is taken into CPS custody, drug exposure is generally evaluated with urine testing.[13-14, 16-18] Collection of urine is non-invasive, usually of adequate volume, and testing is readily available and reliable, but urine offers only a 2-3 day window of drug detection, and available cutoff concentrations are high and poorly sensitive to identify low-level MAMP environmental exposure.[19-21]

An alternative biological matrix is oral fluid (OF) that is now widely accepted in clinical, workplace and driving under the influence of drugs settings.[20] Similar to urine, drug detection times in OF are short, up to about 48 h after last exposure.[22] In contrast, drug testing in hair offers a wider window of detection than urine and OF, depending upon hair length.[23-24] Some state laws mandate that a child under CPS custody with a positive urine drug test be removed from the source of exposure until appropriate measures can be taken.[6, 13] If the drug test is negative, generally the child is returned to the home, and subject to further toxic exposures.

The goal of this study was to determine the best biological matrix for identifying children exposed to MAMP, amphetamine (AMP), 3,4-methylenedioxymethamphet-amine (MDMA), 3,4-methylenedioxyamphetamine (MDA), and/or 3,4-methylenedioxy-ethylamphetamine (MDEA) by comparing detection rates in concurrently collected urine, hair, and OF specimens from drug-exposed children.

Materials and Methods

Study Participants

The study was conducted at the Child and Adolescent Abuse Resource and Evaluation (CAARE) Diagnostic and Treatment Center at the University of California, Davis (UCD) Children's Hospital, Sacramento, CA. The Institutional Review Board of UCD and the Sacramento County Department of Health and Human Services (DHHS) approved this study. Within 2 -3 h after placement under CPS custody, drug-exposed children (1 month to 18 years old) were referred to the CAARE center for medical and forensic examinations. Specimens were de-identified after collection to protect confidentiality and ensure that results could not be traced back to a CPS custody case.

Biological Specimens

Urine specimens were collected as part of CAARE's standard operating procedures for DEC referred cases. An aliquot of urine was used for routine toxicological screening, while the remaining sample was utilized for this study. OF samples were collected via the Intercept® collection device (OraSure Technologies, Inc., Bethlehem, PA, USA).

Proximal 3.9 cm hair segments (approximately 10 mg), cut from the crown and as close to the root as possible, were collected from each child.

Urine and OF were analyzed at the Chemistry and Drug Metabolism laboratory, Intramural Research Program, National Institute on Drug Abuse (NIDA), in Baltimore, MD. Hair samples were analyzed at the Psychemedics Corporation (Culver City, CA, USA).

Reagents

AMP, AMP-d_{11}, MAMP, MAMP-d_{14}, MDA, MDA-d_5, MDMA, MDMA-d_5, MDEA, MDEA-d_6 were purchased as racemic mixtures from Cerilliant Corporation (Round Rock, TX, USA). Heptafluorobutyric acid anhydride (HFAA) was acquired from Pierce Chemical Co. (Rockford, IL, USA). HPLC grade solvents and American Chemical Society grade ammonium hydroxide, acetic acid, concentrated hydrochloric acid, potassium phosphate monobasic, and potassium phosphate dibasic were obtained from JT Baker (Phillipsburg, NJ, USA). SPEC C18AR/MP1 solid phase extraction (SPE) columns were from Agilent Technologies (Santa Clara, CA, USA).

Specimen Preparation and Analysis

Urine specimens, calibrators, and controls were analyzed with minor modifications to a previously published method.[25] Briefly, urine specimens (1 mL) fortified with internal standards were hydrolyzed with 100 µL of concentrated hydrochloric acid at 120 °C for 40 min. After hydrolysis, 100 µL 10 N sodium hydroxide and 3 mL 0.1 M phosphate buffer (pH 6.0) were added. Specimens were loaded onto preconditioned SPE columns and eluted with methylene chloride/2-isopranol/ammonium hydroxide (78:20:2 v/v). Eluates were reconstituted with 0.1M triethylamine in heptane (100 µL) and 10 µL HFAA before derivatization for 30 min at 60°C. Derivatized extracts were cooled at room temperature prior to adding 200 µL of 0.1 M phosphate buffer (pH 7.4). Samples were vortexed, centrifuged and the upper organic layer transferred to an autosampler vial and quantified by gas chromatography mass spectrometry (GCMS).

OF specimens, calibrators, and controls were analyzed by a previously published assay with minor modifications.[26] Briefly, 400 µL Orasure specimens, containing 133 µLOF and 267 µL elution buffer, were fortified with internal standards and diluted with 2 mL of 0.1 M potassium phosphate buffer (pH 6.0) prior to application onto preconditioned SPE columns. Columns were washed with 1 mL0.1 M acetic acid followed by 1 mL hexane and 2 mL methanol. Columns were dried for 2 min after acetic acid, 1 min after hexane and 2 min after methanol washes. Analytes were eluted with 1.5 mL ethyl acetate:methanol:ammonimum hydroxide (78:20:2, v/v/v) elution solvent. Eluates were reconstituted with 0.1 M triethylamine in heptane (100 µL) and 10 uL HFAA before derivatization for 20 min at 60°C. Derivatized samples were cooled to room temperature prior to adding 200 uL of 0.1M phosphate buffer (pH 7.4). Samples were vortexed and the upper organic layer transferred to an autosampler vial and quantified by GCMS.

Hair specimens were treated according to the Psychemedics Corporation hair testing protocol.[27-28] Briefly, 5 – 10 mg hair specimens were washed with 100% isopropyl alcohol for 15 min in a shaking water bath at 37°C, followed by three 0.1 M phosphate buffer washes (pH 6.0) for 1 h with each wash. Hair specimens were digested with a low pH proprietary solution containing DTT, protease K and Cholic acid solution in a shaking water bath for 6 h at 37 °C.

GCMS analysis of urine and OF specimens was performed with an Agilent 6890 GC interfaced with Agilent 5973 mass selective detector operating in electron impact (EI) selected ion monitoring (SIM) mode. A DB-35ms capillary column (15 m × 0.32 mm, internal diameter × 0.25 µm film thickness) was employed for urine testing and a HP-5ms capillary column (30 m × 0.32 mm, internal diameter × 0.25 µm film thickness) for OF analyses. GCMS parameters were based on previously published methods

[26-27]. Limits of quantification (LOQ) for all analytes were 25 ng/mL (urine) and 15 ng/mL (OF). Urine calibration curves were linear from 25-5000 ng/mL for all analytes and OF calibration curves from 15 – 1500 ng/mL. Three quality control samples with concentrations across the linear dynamic range of the assay were analyzed in triplicate in each batch.

Three ions for each analyte and two for each deuterated internal standard were monitored for urine and OF analyses. The following ions were monitored (quantitative ions are underlined): AMP 240, 91, 118; AMP-d_{11} 244, 98; MAMP 254, 118, 210; MAMP-d_{14} 261, 213; MDA 162, 135; MDA-d_5 167, 380; MDMA 254,162, 210; MDMA-d_5 258, 213; MDEA 268,162, 240; and MDEA-d_6 274, 244.

Hair specimen extracts were analyzed based on a previously published assay with minor modifications.[27] Tandem liquid chromatography-mass spectrometry (LCMSMS) analysis of amphetamines in hair was performed on a Perkin Elmer Sciex API 2000.HPLC column: Betasil C_8 (2 mm × 50 mm, internal diameter × 5 µm particle size) with a mobile phase mixture of water and acetonitrile (86:14) with 0.1% formic acid for MAMP and AMP analysis, while a mobile phase mixture of water and acetonitrile (81:19) with 0.1% formic acid was utilized for MDMA, MDA and MDEA. HPLC was operated in isocratic mode. The mass spectrometer was operated in positive multiple reaction mode (MRM). Two independent injections were performed: the first was for MAMP and AMP and the second for MDMA, MDEA and MDA. LOQs for MAMP/MDMA/MDEA were 0.1 ng/mg, AMP 0.025 ng/mg and MDA 0.02 ng/mg in hair. Each analysis contained quality control samples (at least 10% per batch) across the dynamic range of the assay.

Two ions for each analyte and deuterated internal standard were monitored for hair analysis. The ions were (quantitative ions underlined): AMP 136, 91; AMP-d_8 144, 96; MAMP 150, 91; MAMP-d_{11} 161, 96; MDA 180, 135; MDA-d_5 185, 137; MDMA 194, 135; MDMA-d_5 199, 136; MDEA 208, 163; MDEA-d_6 214, 166.

Data Analysis

Specimens with any analyte equal to or greater than the LOQ were considered positive. Urine and OF samples were quantified by linear regression with 1/× weighting. MSD Agilent Chemstation software was utilized to calculate peak area ratios of target analytes and internal standards for GCMS analyses. A linear curve fit forced through the origin from a single point calibration per analyte was utilized for hair samples' quantification. Statistical analyses were performed with GraphPad Prism v.5 (GraphPad Software, San Diego, CA).

Results

Ninety-one children enrolled in the study and provided at least one specimen. Hair, urine, and OF specimens were collected from 89, 86, and 70 children, respectively. Participants' demographic characteristics and results for positive MAMP, AMP and MDMA in hair samples are summarized in Table 1.

Table 1

Demographics and hair confirmation results from drug-exposed children admitted to the CAARE facility. Positive methamphetamine (MAMP+), amphetamine (AMP+) and methylenedioxymethamphetamine (MDMA+) were equal or greater than limits of quantification (LOQ) of 0.1 ng/mg, 0.02 ng/mg and 0.1 ng/mg, respectively. Methylenedioxyamphetamine (MDA) and methylenedioxyethylamphetamine (MDEA) were not identified in any hair specimen.

	Total	MAMP+	AMP+	MDMA+
Demographics	**N**	**N**	**N**	**N**
Race/Ethnicity				
Caucasian	29	24	20	2
African American	22	7	2	3
Asian	7	7	7	0
Hispanic	18	18	11	1
Mixed*	11	8	6	4
No information*	3	3	3	1
Hair Color				
Black*	34	19	12	4
Brown	43	36	27	5
Blonde	10	9	7	1
No information*	3	3	3	1
Age				
Under 12 months	3	3	2	2
1 – 18 years old**	86	64	47	9

*missing 1 hair sample (not counted)
**missing 2 hair samples (not counted)

MAMP was detected in only five (7.1%) OF specimens; AMP (21.4 ng/mL) in only one (1.4%), which also contained the highest concentration of MAMP (133.6 ng/mL). MAMP OF concentrations for specimens that tested > LOQ ranged from 17.9 to 133.6 ng/mL (median 48.6; mean 58.2; SD 44.9). MDMA, MDA and MDEA were < LOQ in all OF specimens.

MAMP was detected in 18 (20.9%) urine specimens; AMP in three (3.5%), (two with concurrent MAMP), for an overall detection rate of 22.1%. MAMP urine concentrations for specimens that tested > LOQ ranged from 25.1 – 107.8 ng/mL (median 0.0; mean 10.3; SD 22.4). One positive urine specimen only contained AMP only at 3851.1 ng/mL. MDMA, MDMA, and MDEA were < LOQ in all urine specimens.

MAMP, AMP, and MDMA were detected in 67 (75.3%), 49 (55.1%), and 11 (12.4%) hair specimens, respectively, for an overall detection rate of 77.8%. For specimens that tested > LOQ, MAMP hair concentrations ranged from 0.1– 22.0ng/mg (median 1.4; mean 3.3; SD 4.3), AMP concentrations were 0.025 - 1.2ng/mg (median 0.1; mean 0.20; SD 0.25). AMP was always present at a lower concentration than MAMP, with the exception of 1 hair specimen that only contained AMP at 0.05 ng/mg. Hair AMP/MAMP ratios ranged from 0.017 to 0.115. MDMA was detected in 9 of 11 hair samples with concurrent MAMP. MDMA hair concentrations for specimens that tested >LOQ ranged from 0.10 – 2.3 ng/mg (median 0.25; mean 0.56; 0.66 SD). Among the 3 infants (< 12 months), MAMP was detected in all, and AMP or MDMA in two of three infants. MDA or MDEA were not detected in any hair specimens.

Seventy children tested positive for at least one analyte in at least one matrix. All matrices were available from 67 children: 12 (17.9%) were drug negative in all matrices, 41 (61.2%) were positive in one matrix, 12 (17.9%) in two matrices and 2 (3.0%) in all 3 matrices. All positive OF (n = 5) and 18 of 19 positive urine specimens also had positive hair tests. AMP was detected alone in hair (0.05 ng/mg) and urine (3851.1 ng/mL) from the same child. Results are summarized in Table 2 and Figure 1 .

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Figure 1

(A) Confirmed positive specimens for methamphetamine (MAMP), amphetamine (AMP), methylenedioxymetamphetamine (MDMA) in urine, oral fluid, and head hair concurrently collected specimens from 91 children. Specimens with concentrations equal to or greater than the limit of quantification (LOQ) were considered positive. Methylenedioxyamphetamine (MDA) and methylenedioxyethylamphetamine (MDEA) were not identified in any biological matrix, thus excluded from this figure.(B) Concentrations of methamphetamine (MAMP), amphetamine (AMP), methylenedioxymethampethamine (MDMA) that quantified equal or greater than the limit of quantification (LOQ) in 89 hair samples. MAMP concentrations (ng/mg) were plotted on the left y-axis; AMP and MDMA concentrations (ng/mg) were plotted on the right y-axis.

Table 2

Amphetamine (AMP), methamphetamine (MAMP), and methylenedioxymeth-amphetamine (MDMA) concentrations in head hair (ng/mg), urine (ng/mL) and oral fluid (ng/mL) of drug-exposed children.

	Hair			Urine			OF		
Subject	MAMP	AMP	MDMA	MAMP	AMP	MDMA	MAMP	AMP	MDMA
23	16.8	0.8	N	107.8	N	N	58.1	N	N
4	16.5	1.0	N	N	N	N	133.6	21.4	N
58	15.0	0.3	0.1	94.5	26.0	N	N	N	N
40	14.0	0.4	N	N	N	N	N	N	N
13	12.3	1.2	N	42.9	N	N	N	N	N
48	11.9	0.1	N	32.1	N	N	N	N	N
74	10.2	0.3	N	35.4	N	N	MS	MS	MS
28	9.5	0.4	N	N	N	N	N	N	N
84	8.0	0.2	0.2	N	N	N	MS	MS	MS
85	7.9	0.2	0.1	35.6	N	N	MS	MS	MS
59	7.6	0.3	N	45.8	N	N	N	N	N
53	6.7	0.2	N	MS	N	MS	48.6	MS	N
75	6.6	0.1	N	27.0	N	N	MS	MS	MS
90	6.5	0.3	N	MS	MS	N	MS	MS	MS
8	6.1	0.3	0.1	N	N	N	N	N	N
38	6.0	0.2	N	N	N	N	N	N	N
54	5.7	0.1	N	72.0	N	N	32.6	N	N
66	4.5	0.1	0.1	17.9	N	N	N	N	N
10	3.1	0.2	N	N	N	N	N	N	N
14	2.9	0.2	N	31.4	N	N	N	N	N
29	2.8	0.1	N	N	N	N	N	N	N
33	2.7	0.1	N	N	N	N	N	N	N
83	2.6	0.1	N	57.8	25.2	N	MS	MS	MS
63	2.6	0.1	N	N	N	N	N	N	N
37	2.5	0.2	N	61.9	N	N	N	N	N
36	1.8	0.1	N	41.3	N	N	N	N	N
9	1.7	0.1	0.4	N	N	N	N	N	N
62	1.6	0.1	N	N	N	N	N	N	N

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Limits of quantification (LOQ) were 0.1 ng/mg (MAMP and MDMA), 0.02 ng/mg (AMP) in hair; 25 ng/mL (all analytes) in urine; and 15 ng/mL (all analytes) in oral fluid (OF). Methylenedioxyamphetamine (MDA) and Methylenedioxyethylamphetamine (MDEA) were not identified in any biological matrix. Specimens tested <

LOQ were annotated with “N” while subjects with incomplete set (missing matrix) were annotated with “MS.”

Discussion

Our results suggest that hair is the most suitable biological matrix for evaluating systemic exposure of children to sympathomimetic amine stimulants, such as MAMP, AMP, and MDMA. More than 60% of children with all 3 biological matrices had a positive hair result for at least one analyte. In contrast, only 18% and 6% had positive urine and OF tests, respectively. Low detection rates in OF and urine with positive hair tests in our study suggest drug exposure more than 1 week prior to specimen collection, or environmental exposure. In a retrospective analysis by Farst et al., 2011, the MAMP detection rate (82.2%) was higher in hair than urine (2.2%) in samples from 45 children.[15] Our study is the first to simultaneously compare drug concentrations in hair, urine and OF from drug-exposed children.

Typical immunoassay screening cutoffs are too high to detect low drug concentrations in exposed children's urine and oral fluid specimens.[20-22] Testing, therefore, must be performed with lower cutoffs available with mass spectrometric methods or high sensitivity ELISA assays. In addition, it is highly recommended that urine and/or OF samples are collected immediately after the child is removed from the site of exposure.[29] This is to minimize false negative results due to a narrow window of detection for MAMP, AMP and MDMA in urine and OF.

All three infants in our study tested positive for MAMP (0.27 – 4.5 ng/mg) with AMP (0.1 ng/mg) or MDMA (0.1 – 0.25 ng/mg) in hair; 1 also was positive for MAMP in OF (17.9 ng/mL) but had a negative urine test. This suggests more recent drug exposure. A source of MAMP exposure in young children (infants and toddlers) could be from crawling on floors and placing contaminated objects in their mouths. This also was observed by Farst et al, who noted that children under 3 years of age were more likely than older children (3 – 12 years old) to have a positive MAMP hair test, regardless of hair color.[15] Based on our results, there is no significant difference in the likelihood of testing positive for MAMP between a child with black or brown hair and a child with blonde hair color (odds ratio 0.29, p-value 0.255). In another study, 52 hair samples were analyzed from children 2 months to 15 years old recently removed from MAMP clandestine laboratories. Similarly, 73% of samples quantified >LOQ (0.1 ng/mg) for MAMP, with children <5 years old having the highest mean MAMP concentration (13.8ng/mg) compared to the group mean (7.0ng/mg). No other biological specimens were analyzed from these children.[30] Our lower mean MAMP concentration (3.3ng/mg)could be attributed to the fact that children referred to CAARE were not all from MAMP clandestine laboratories, but from homes where the drug was allegedly consumed. Nonetheless, finding drugs in our subjects'hair samples after the incorporation of wash procedures in the analysis suggests environmental exposure. Another limitation we encountered was the anonymity of the children's age enrolled in the study due to active CPS custody cases during sample collection. Hence, we are not able to fully evaluate whether MAMP level in hair could come from accidental and environmental exposure or self-administration (adolescent MAMP consumption).

Han et al. reported that MAMP and AMP were detected in hair samples (6 – 20 cm) from chronic adult MAMP users with concentration ranges of 0.39 - 35.2 ng/mg and 0.45 – 2.7 ng/mg for MAMP and AMP, respectively.[23] Participants self-reported insufflating (“snorting”) or smoking 0.25 – 4 g/day MAMP. AMP/MAMP ratios of 0.08 - 0.32 were found in hair. When we orally administered four low (10 mg) and high (20 mg) doses S-(+)-MAMP HCl over 1 week, incorporation of MAMP and AMP was dose-dependent.[31] MAMP concentrations ranged from 0.6 - 3.5 ng/mg after the low and 1.2 - 5.3

ng/mg after the high dose. The study reported that the overall AMP/MAMP ratios ranged from 0.07 - 0.37 with a mean value of 0.15 ± 0.07. The median MAMP hair concentration in the drug-exposed children in our study was 1.4ng/mg with AMP/MAMP ratios of 0.02 - 0.12.This would suggest a systemic ingestion of the drug.

The average hair growth in adults is 1 cm/month[32-33], while hair growth in children varies more and is proportional to the duration of the growing anagen stage.[34] Biological factors such as diet, illness, metabolic disorders or stages in a child's development can also influence hair growth.[34] Assessment of the magnitude and duration of a child's drug exposure through hair analysis should be done cautiously for these reasons.

Children are uniquely susceptible to a myriad of harmful effects from their MAMP-using caregivers. These include the possibility of direct MAMP exposure through contaminated surfaces [35], direct ingestion, physical abuse and neglect by caregivers (or their associates). There also is an increased risk of exposure to crime, hypersexuality, intimate partner and interpersonal violence in the home.

Cases of children exposed to acutely high MAMP levels via direct ingestion involved CNS excitation, tachycardia, rhabdomyolysis, and hyperthermia.[16, 36-37] Infants and toddlers living in MAMP homes are at higher risks due to their smaller size, faster metabolism, prolonged indoor exposure, and propensity to crawl and place objects in their mouths. Direct skin exposure and contact with MAMP was documented[38], although, effects of chronic low dose MAMP exposure in children are not well described. Serious detrimental effects on children's health and welfare from such living environments are well-documented.[13, 17, 39-40]

Parents preoccupied with drug use (or abuse) have significant difficulties forming healthy emotional attachments with their children that are critical for normal childhood development. Early interventions such as immediate removal from contaminated areas, medical treatment and counseling are necessary to help drug-endangered children from short- and long-term effects of MAMP exposure.

Conclusion

These are the first data of which we are aware comparing concurrently collected hair, OF, and urine specimens from children with MAMP environmental exposures. Drug exposure from possible environmental contamination in children is typically evaluated with conventional urine drug testing. Hair analysis was shown to be a more sensitive method than urine in evaluating environmental drug exposure in children.[15, 30, 41] However, other sources of MAMP exposure could be self-administration in adolescents, and ingestion in toddlers exposed to MAMP from solid material on floors or surfaces. Higher MAMP detection rates in hair than OF and urine in our data suggest that hair testing is a valuable tool for identifying drug-exposed children. Hair testing offers a wider window of detection for identifying MAMP-, AMP-, and MDMA-exposed children than OF or urine. A negative drug test in urine, OF or hair does not ensure the absence of drug exposure, but hair testing provides the best opportunity for identifying children exposed to MAMP, AMP and MDMA in their environment.

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Footnotes

The authors declared no conflict of interest.

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