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A Study of Drug Detection in a Postmortem Pediatric Population

ABSTRACT: At The Office of the Cuyahoga County Coroner (CCCO), Cleveland, Ohio, it is customary to perform an autopsy and conduct toxicological testing on decedents less than 19 years of age. This study provides a retrospective evaluation of drugs detected in a pediatric postmortem population between the years 1998 and 2002 (n = 730). Demographic information, cause and manner of death, and toxicological results were examined. Blacks comprised 54% of cases, males 59%, and 48% were less than one year of age or stillborn. Forty-two percent of deaths were ruled natural, 27% accident, 13% undetermined, 5% suicide, and 2% homicide. Of the 640 cases subjected to comprehensive testing, 38% of the cases were positive for at least one compound. Resuscitative/treatment drugs were detected most frequently (56% of positive results), followed by illicit drugs (26%), ethanol (11%), carbon monoxide (8%), and antihistamines (6%). Eighty-seven cases contained more than one drug. The deaths of 47 individuals were drug related (6%). In this population, it is recommended that illicit drugs and ethanol are targeted for testing, especially when limited specimens are available for analysis.

KEYWORDS: forensic science, postmortem, forensic toxicology, pediatric

In the United States (U.S.) pediatric deaths contribute to only a small percentage of the total number of deaths reported each year. In 2002, there were a total of 2,443,387 deaths reported in the U.S. with children under the age of 19 contributing 12% (n = 53,854) (1). The low mortality rate in the pediatric population indicates that these cases make up a small percentage of a medicolegal investigators' workload. Many of the children who die in the U.S. are not autopsied, and for the cases that are, full toxicological analyses are not performed (2). Therefore, the possible contribution of drugs to these deaths is unknown.

Since 1975, the National Institute on Drug Abuse (NIDA) has studied drug use in high school seniors by providing a sample population with the Monitoring the Future (MTF) survey. In recent years NIDA has reported levels of drug use in children that have remained stable or declined for many drugs. However, the frequency of teen drug abuse remains high (3). In 2002, 53% of high-school seniors had experimented with some form of illicit drug in their lifetime and 74% had consumed ethanol (4).

The MTF survey indicated that the youth of America are using a variety of drugs including illicit drugs, prescription drugs, inhalants, and ethanol. The frequency of drug use among the young suggests drugs may play a role in their deaths. However, in most cases, unless there is suspicion of drug involvement little or no toxicological testing is performed (2). In addition, there have been several recent cases of deaths in children related to over-the-counter medication, which would not have been detected without comprehensive toxicological testing. A study conducted by Marinetti et al. in Montgomery County, Ohio found 10 infant deaths over an 8-month period in which over-the-counter cold medications were a contributing factor (5). These findings suggest the necessity of considering testing in the young. Adequate history and circumstances surrounding the death should provide the basic information to make informed decisions.

In 1985, the National Association of Medical Examiners (N.A.M.E.) established a Pediatric Toxicology (PedTox) registry. N.A.M.E. invited coroners, medical examiners, and toxicologists to voluntarily report positive toxicology results from pediatric cases. The purpose of this registry was to provide information on drug concentrations in fetuses, infants, and children 15 years and younger. The PedTox registry contains more than 1000 reported cases and mentions more than 100 drugs (6). Besides the PedTox registry, there is very little literature on drug concentrations in children postmortem.

The present study was performed to provide supplementary information on postmortem toxicology in a pediatric population, defined as children up to and including the age of 18. By providing data on drug use in this population, testing recommendations may be provided to enable those jurisdictions with limited resources to conduct targeted testing.

Methods

Medicolegal deaths in Cuyahoga County, Ohio, are investigated by The Office of the Cuyahoga County Coroner located in Cleveland, Ohio. In 2002, the estimated population for Cuyahoga County was approximately 1,373,997 (7). All deaths accepted at CCCO between the years 1998 and 2002 were evaluated. Demographic information, including age, race, and gender were collected for children between the age of 0 and 18 years.

The cases were divided into six age categories: unknown, stillborn, 0–1 day, >1 day–2 years, >2–12 years, and >12–18 years. The cause and manner (Homicide, Suicide, Natural, Accident, or Undetermined) of death were obtained from the Coroner's verdict. In addition, toxicological results were compiled.

If an autopsy was performed (complete external and internal examination), typical specimens submitted for testing included heart and femoral blood, urine, bile, gastric contents, and vitreous humor. In children <6 months tissues were often provided in addition to

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the samples previously listed. If an autopsy was not performed, there may be no sample provided for testing, or a blood specimen from a cardiac "stick" may be submitted for analysis. In the latter situation typically only volatile testing was performed. Comprehensive testing was conducted on autopsied cases. This included volatile compounds by automated headspace gas chromatography using flame ionization detection (FID) with positive ethanol results confirmed using enzyme immunoassay; heart blood was analyzed for acidic neutral drugs using a liquid–liquid extraction procedure with gas chromatography (GC) with FID and confirmation by gas chromatography-mass spectrometry (GC/MS); benzodiazepines by liquid–liquid extraction with GC using an electron capture detector (ECD) and confirmation by GC/MS using selected ion monitoring (SIM); and basic drugs by liquid–liquid extraction with GC using a nitrogen–phosphorus detector (NPD) and confirmation using GC/MS operated in the full scan mode. In addition, colorimetry was used to test for acetaminophen, salicylate and ethchlorvynol. If urine was available immunoassay testing was conducted for amphetamines, benzodiazepines, cocaine and metabolites, cannabinoids, opiates, and phencyclidine. Heart blood and bile were screened for opiates using a modified immunoassay when a urine sample was not available. Positive immunoassay results were confirmed by GC/MS. When requested, clinical chemistry was performed for Na^+, Cl^-, K^+, creatinine, CO_2, urea nitrogen and glucose, on the vitreous humor using a NOVA-CRT ® analyzer (Nova Biomedical, Waltham, MA). Also, blood was screened for the presence of carboxyhemoglobin (COHb) by CO oximetry, when requested by the pathologist or indicated by case history. COHB ≥20% saturation was qualitatively confirmed by microdiffusion.

For this study, drugs were separated into seven categories: illicit drugs, ethanol, antihistamines, antidepressants, miscellaneous, resuscitative/treatment drugs, and carbon monoxide. The illicit drug category included amphetamines (amphetamine, methamphetamine, 3,4-methylenedioxymethamphetamine [MDMA], 3,4-methylenedioxyamphetamine) cannabinoids, cocaine and metabolites, 6-acetylmorphine (6-AM), morphine (when case history was indicative of illicit use or when present with 6-AM), and phencyclidine (PCP). The antihistamines group included chlorpheniramine, dextromethorphan, diphenhydramine, and doxylamine. Incorporated in the antidepressant category were amitriptyline, bupropion and metabolites, sertraline, trazodone, and venlafaxine. Acetaminophen, acetone, amantadine, carbamazepine, cyclobenzaprine, norpropoxyphene, oxycodone, phenylpropanolamine, propoxyphene, and pseudoephedrine/ephedrine were considered miscellaneous drugs. Resuscitative/treatment drugs included atropine, bupivacaine, codeine, diazepam, ketamine, laudanosine, lidocaine, lorazepam, meperidine, midazolam, morphine, nordiazepam, papaverine, pentobarbital, phenobarbital, and phenytoin.

Results

Demographics

Table 1 summarizes the demographic data for this study. A total of 730 cases were identified between 1998 and 2002. The average number of cases per year was 146. Fifteen individuals were not autopsied. The age group most represented was the >1 day–2 years (n = 271/730, 37%), followed by >12–18 years (n = 204, 28%), >2–12 years (n = 117, 16%), stillborn (n = 86, 12%), 0–1 day (n = 43, 6%), and unknown (n = 9, 1%). There were 394 (54%) black decedents, 331 (45%) white decedents, and five (1%) oriental decedents. Fifty-nine percent (n = 433) of the population was male and 41% (n = 296) was female. There was one decedent of unknown sex. The highest percentage of decedents (n = 310, 42%) died of natural causes, followed by accidents (n = 198, 27%), undetermined deaths (n = 96, 13%), homicides (n = 90, 12%), and suicides (n = 36, 5%). Forty-four percent of the children in the study died under violent circumstances (homicide, suicide, or accident). The age range for homicides in this study was 4 min–18 years. 58% of homicides were individuals over the age of 13, followed by children 1 day–2 years old (26%). For suicides the ages ranged from 10–18 years, with 92% of the suicides falling in the >12–18 year age group. Accidental deaths were represented in every age range in the study. The most common causes of death for homicide, suicide, and accident victims were gunshot wounds (Fig. 1), self-inflicted gunshot wounds (Fig. 2), and blunt force injuries caused by motor-vehicle accidents (Fig. 3), respectively.

Toxicology

Toxicological testing was performed on 655 of the 730 cases (90%). No toxicology was performed on 75 of the cases due to no testing requested by the pathologist, no sample provided by the pathologist, or the quantity of sample received by the toxicology laboratory was not sufficient for testing. For 15 of the children in the study, only volatile testing was performed. All other cases were subjected to comprehensive testing as outlined in the Methods section. Of 640 cases in which comprehensive testing was performed,

TABLE 1—*Demographic data.*

Categories	1998	1999	2000	2001	2002	Total	% (n = 730)
Unknown	4	1	1	1	2	9	1
Stillborn	13	17	17	18	21	86	12
0–1 day	4	8	11	10	10	43	6
>1 day–2 years	58	57	69	44	43	271	37
>2 –12 years	20	23	30	23	21	117	16
>12–18 years	45	34	40	53	32	204	28
Blacks	72	75	87	89	71	394	54
Whites	71	63	80	60	57	331	45
Other	1	2	1	0	1	5	1
Males	84	80	96	96	77	433	59
Females	59	60	72	53	52	296	41
Unknown	1	0	0	0	0	1	1
Undetermined	18	21	25	17	15	96	13
Accident	37	39	53	38	31	198	27
Suicide	12	3	7	6	8	36	5
Homicide	21	14	16	26	13	90	12
Natural	56	63	67	62	62	310	42

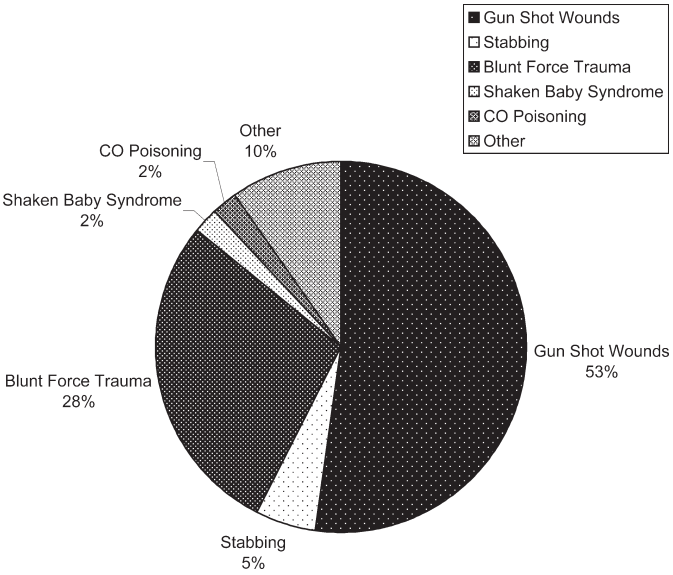

FIG. 1—*Homicides: causes of death.*

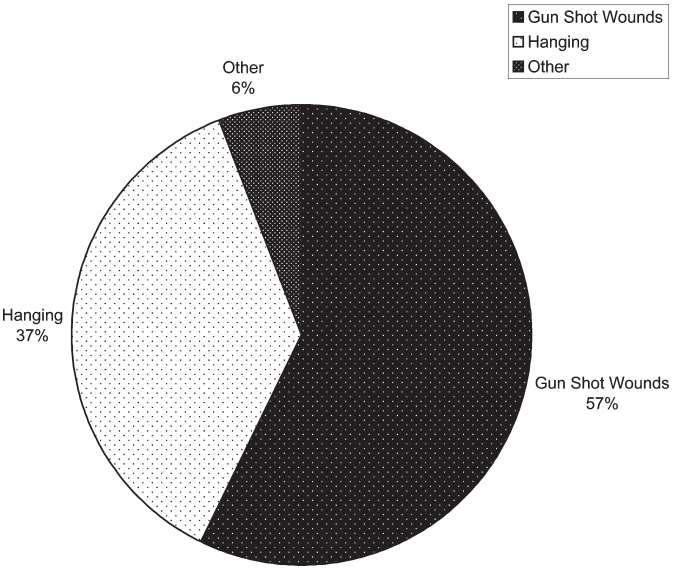

FIG. 2—*Suicide: causes of death.*

247 (38%) tested positive in any matrix for one or more drug categories (Fig. 4).

Illicit Drugs

During the 5-year study, 65 (65/730 = 10% of all cases and 65/247 = 26% of positive cases) tested positive for illicit drugs. Seventy-four percent (n = 48) of the illicit drug positives occurred in the >12–18 year age group. The youngest children in the study were the next likely to be positive for illicit drugs, 0–1 day (14%), stillborn (11%), and unknown age (1%). There were no children between the ages of >1 day and 12 years that were positive for illicit drugs. Sixty-five percent of the positive cases were black. The male population (82%) was more likely to be positive for illicit drugs than the females. Homicidal death was the most common manner when illicit drugs were detected (43%), followed by accident (35%), suicide (15%), and natural (6%). Ninety-three percent (n = 61) of the illicit drug positives were considered violent deaths.

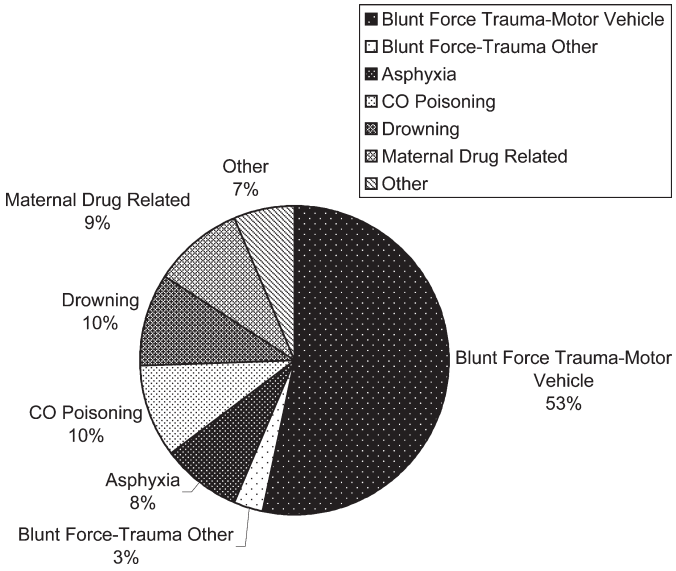

FIG. 3—*Accidental: causes of death.*

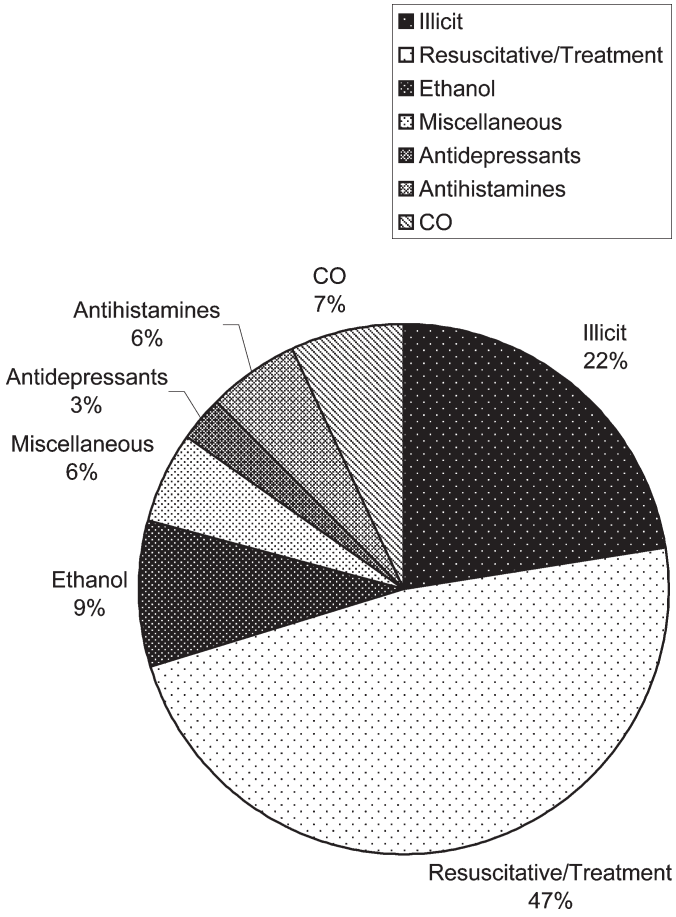

FIG. 4—*Drug-positive cases (n = 247).*

Cannabinoids were the most frequently detected illicit drug class (39/247 = 16%) occurring exclusively in the >12–18 years age group. Males comprised 92% and blacks 56% of the population positive for cannabinoids. When Δ9-tetrahydrocannabinol (THC) and/or metabolites were detected, the most common manner of death was homicide (64%, n = 25), followed by suicide (n = 9,

23%) and accidental deaths (n = 5, 13%). The concentration of THC in heart blood ranged from 5 to 75 ng/mL, with an average of 17.9 ng/mL (n = 15). The average concentration of the metabolite THC-COOH in heart blood was 19 ng/mL (n = 6), with a range of 5–29 ng/mL.

Cocaine and/or metabolites were detected in 11% (n = 27) of positive cases (4% total cases tested). All age groups were represented except for the >2 to 12 years group. The highest number of positive findings occurred in the >12 to 18 years (n = 12, 12/27 = 44% of positive cases), followed by the 0–1 day age group (22%) and stillborns (22%). There were also two (7%) decedents in the >1 day–2 years age group, and one (4%) decedent of unknown age. Seventy-four percent of the cocaine positive cases were black children and 26% were white with males predominant (70%). The majority of the deaths were accidental (52%) followed by homicide (30%), natural (15%), and suicide (4%). The mean heart blood concentration of cocaine in these cases was 280 ng/mL (n = 9) with a range of 10–1790 ng/mL. Acute cocaine intoxication was listed as the cause of death in four of the nine cases with cocaine concentrations of 10, 50, and 1790 ng/mL in heart blood, and 60 ng/g in brain. In 15 positive benzoylecgonine (BE) cases, the heart blood concentrations ranged 22–600 ng/mL with a mean = 228 ng/mL.

There were 11 cases positive for PCP in the population, comprising 4% of the positive results. All of the cases were black males between the ages >12 and 18 years. Seven decedents were homicide victims (7/11 = 64%), two were suicides, and two were accidental deaths. PCP was quantitated in the heart blood for nine cases with two cases positive only in urine. The mean heart blood PCP concentration was 410 ng/mL, with a range of 50–1060 ng/mL.

Two cases were positive for amphetamine class drugs. The decedents were white males, >12–18 years age. A heart blood concentration of 1210 ng/mL MDMA was determined in one accidental death of a young man driving a pick-up truck who collided with a public transportation bus. The decedent also had a heart blood concentration of 0.20 g/dL ethanol. In the second case, ruled a suicide by hanging, the heart blood was positive for amphetamine (120 ng/mL) and THC-COOH (7 ng/mL). The source of the amphetamine was not identified.

There were four accidental illicit morphine related deaths (4/247 = 2% of positive results). Three of the decedents were white males in the >12–18 years age group. The fourth decedent was a white male in the 0–1 day age group. One case was ruled an acute morphine and oxycodone intoxication with a heart blood level of 3024 ng/mL morphine and 1278 ng/mL oxycodone. Another case was ruled an acute intoxication by morphine and cocaine, with heart blood concentrations of 56 ng/mL morphine and 220 ng/mL BE. A third death was heroin related, with a heart blood concentration of 118 ng/mL morphine and 6 ng/mL 6-AM. The fourth case involved maternal cocaine and heroin abuse which resulted in a morphine concentration of 64 ng/mL in the 11-hour-old decedent. The presence of illicit drugs was listed as the primary cause or other condition for 26 (26/730 = 4%) cases. The most common drug used as a cause of death was cocaine and/or metabolites.

Ethanol

In this study, there were 26 cases (26/247 = 11% of positive results, 26/640 = 4% cases tested for ethanol) positive for ethanol (lower reporting limit 0.01 g/dL). Seventy-three percent of the cases occurred in the >12–18 years age group. Fifteen percent (n = 4) of the ethanol positive results were stillborn, one decedent in the 0–1 day group, one in the >1 day–2 years group, and one in the unknown age group. The majority (69%) were white males. There was one ethanol positive where the gender of the decedent was undetermined. This decedent was stillborn and presumed to be male. The most common manner of death in ethanol positive cases was accident (38%), followed by homicide (23%). Ethanol was quantitated in heart blood in 21 cases, the remaining five cases were qualitative results detected in blood, urine, or tissue samples. Individual cases ranged from 0.01 g/dL to 0.29 g/dL in heart blood, the average concentration was 0.07 g/dL. In urine, the average concentration was 0.11 g/dL, with a range of 0.01 to 0.39 g/dL. Thirty-five percent (n = 9) of the cases positive for ethanol had concentrations ≥0.08 g/dL. Four (44%) of these cases were ruled as suicides. There were five (19%) cases with ethanol concentrations >0.10 g/dL. At concentrations >0.10 g/dL there were two natural deaths, one suicide, one accident, and one homicide. Ethanol was not included in the cause of death for any of the cases.

Antihistamines

Antihistamine positive cases accounted for 6% (n = 16) of the positive results in the population. Thirty-eight percent of the positive findings occurred in the >1 day–2 years and 38% in the >2–12 years age group. Eight decedents (50%) were female and 56% were white. Most of the deaths (38%) were classified as accidental, followed by natural deaths (25%), homicides (19%), and undetermined deaths (19%). The most common antihistamine detected was diphenhydramine (DPH), followed by dextromethorphan, chlorpheniramine, and doxylamine. In six positive cases for DPH, heart blood concentrations ranged from 120 ng/mL to 1020 ng/mL, with an average of 380 ng/mL. The presence of antihistamines was included in the cause of death for one case. This case, ruled a homicide, involved a 1-year-old white female with a heart blood diphenhydramine concentration of 490 ng/mL (Femoral: 270 ng/mL).

Antidepressant Drugs

Antidepressants were detected in 3% of the positive cases (n = 8). The >12–18 year age group dominated (n = 5, 63%), followed by one decedent each in the stillborn, 0–1 day, and >2–12 years age groups. By race, whites were more likely to be positive for antidepressants (n = 6, 6/8 = 75%) compared with blacks (n = 2, 25%). The males in this population contributed 75% (n = 6) of the positive results. The most common manner of death for these decedents was accident (n = 5, 63%), followed by suicide (n = 2, 25%) and natural (n = 1, 13%). Bupropion and metabolites, and venlafaxine were each detected in two cases. Amitriptyline, sertraline, and trazodone were each detected in one case. The presence of an antidepressant was related to the cause of death in one case, with cocaine and venlafaxine (5900 ng/mL) in a stillborn child, due to maternal drug use.

Miscellaneous Drugs

In this study there were 16 cases positive for drugs classified as miscellaneous drugs. The most common age group positive for miscellaneous drugs was the >1 day–2 years (n = 6), followed by the >2–12 and >12–18 year groups (each n = 5). Whites (56%) had slightly more positive cases than blacks. Again, males dominated by a margin of 3:1. The most common drugs detected in this

category were pseudo/ephedrine and oxycodone, each with three positive results. There were six undetermined deaths, six accidental deaths, and four natural deaths associated with this drug group. The presence of oxycodone was the cause of death in two separate cases. The first case was a 2-year-old black female with a heart blood concentration of 1360 ng/mL oxycodone, the manner of death was undetermined. The second case was previously mentioned in the illicit drug category as an acute morphine and oxycodone intoxication, with heart blood concentrations of 3024 ng/mL and 1280 ng/mL, respectively. Propoxyphene was also listed as a cause of death in a 4-year-old white male with a heart blood concentration of 4100 ng/mL propoxyphene and 16,000 ng/mL norpropoxyphene. The manner of death in this case was undetermined.

Resuscitative/Treatment Drugs

The resuscitative/treatment drugs were determined to have been administered by emergency medical or hospital personnel for treatment or during life saving procedures. These drugs resulted in the majority of positive findings in this study accounting for 138 cases (138/247 = 56%). By age, the most represented group was the >12–18 years (n = 54, 39%), followed by >2–12 years (n = 39, 28%), >1 day–2 years (n = 34, 25%), 0–1 day (n = 6, 4%), and stillborn (n = 5, 4%). There were 76 (55%) white decedents and 61 (44%) black decedents. Males (n = 74, 54%) and females (n = 64, 46%) were nearly equally represented in this category. Forty-one percent (n = 56) of the cases were classified as accidental, 35% (n = 48) natural deaths, 14% (n = 19) homicides, 6% (n = 8) undetermined, and 5% (n = 7) suicides. Lidocaine was the most prevalent resuscitative/treatment drug (n = 64, heart blood concentration range 70 ng/mL to 15,590 ng/mL). Phenytoin was the second most common drug detected from this group. There were 27 cases positive for phenytoin with heart blood concentrations ranging from 5400 to 30,300 ng/mL. The presence of resuscitative/treatment drugs were not related to the cause of death in any cases.

Carbon Monoxide

In this study, there were 20 cases positive (20/247 = 8% of positives) for carbon monoxide (CO). The highest number of deaths positive for CO occurred in the >2–12 year age group (n = 11, 55%), followed by >1 day–2 years (n = 5, 25%) and >12 –18 years (n = 4, 20%). There were 10 white and 10 black decedents with 60% (n = 12) male. In 17 (85%) of the cases, the ruling was accidental death and occurred due to fires in the home. There were also two homicides and one suicide. The homicides were due to a house fire and the suicide was an intentional automobile collision. During the 5-year study, there were four separate fires that each took the lives of two children. Three of the fires were ruled accidental and the fourth was ruled arson, resulting in a ruling of homicide. The two homicide victims were 2- and 3-year-old black females who were living with relatives. The percentage saturation of COHb ranged from 9% to 87% (57% ± 26%).

Multiple Drugs

Multiple drugs were found in 87 cases (comprising 35% of positive cases). A majority of these cases were male (n = 57, 66%) and 60% white. Multiple drugs were detected most often (59%) in decedents who were >12–18 years old, followed by >2–12 years (18%), and 1 day–2 years (15%). Accidental deaths were the most common, contributing 50% of the cases. Twenty-four percent were classified as homicide, 18% natural, 2% undetermined, and 1% suicide. Resuscitative/treatment drugs were present in 72% of the cases that were positive for multiple drugs. Illicit drugs were detected in 46% of the cases, ethanol 22%, antihistamines 11%, miscellaneous drugs 11%, antidepressants 7%, and carbon monoxide 4%.

The most common combination was resuscitative/treatment drugs with other resuscitative/treatment drugs (n = 44, 51%). Thereafter, illicit drugs with other illicit drugs (n = 16, 18%), followed by illicit drugs with ethanol (n = 12, 14%), resuscitative/treatment drugs with illicit drugs (n = 8, 9%), resuscitative/treatment drugs with ethanol (n = 5, 6%). Other combinations contributed less than 5% of the multi-drug cases.

Drug-Related Deaths

Forty-seven cases in this study listed the presence of a drug to be the primary (acute intoxication) or secondary (maternal intoxication) cause of death. The >2–12 years age group provided 26% (n = 12) of these deaths followed by both the 0–1 day and the >1 day–2 years with 21% (n = 10) each, >12–18 years 17% (n = 8), and stillborn 15% (n = 7). The significant drug deaths were mostly black (62%) and male (57%). Eighty-five percent of these deaths were ruled accidental, followed by 6% homicide, with undetermined and natural each at 4%. There were no suicidal drug overdoses in this study.

Discussion

This retrospective study evaluated the prevalence of drugs found in a pediatric postmortem population from 1998 to 2002. During the 5-year period, 730 cases were identified for inclusion. This represented 4% of cases reported to the Cuyahoga County Coroner. The age group with the highest representation was children >1 day–2 years old (n = 271, 37%) followed by >12–18 years (n = 204, 28%). These findings are similar to those of Garg et al. who reported frequencies of 40%, 16%, and 44% in age groups <6 years, 6–12 years, and 12–<18 years, respectively (8).

When reviewing all cases received at CCCO during the 5-year study, males predominated (57%) (9). The pediatric population followed the same trend with 59% male decedents (n = 433) and 41% females (n = 296). Out of all decedents received at CCCO 70% were white and 30% were classified as non-white (9). According to the U.S. Census Bureau, Cuyahoga County is 68% white and 29% black (10). In the pediatric population, the races were evenly distributed with 394 (54%) black decedents and 331 (45%) white decedents. In addition, there were five decedents in the current study that were classified by race as other, who were oriental. Therefore, the pediatric epidemiological data on race do not follow the overall county trend. The statistics pertaining to all of the decedents received at CCCO are nearly identical to the county's race demographics. Even though the number of pediatric cases represented only 4% (730/18066) of the total CCCO population, the data suggest that black children are at higher risk of death than black adults while their white counterparts have lower risk.

According to the official Coroner's verdict, 42% of the cases in the study were classified as natural (n = 310) compared with 64% of all cases at CCCO during this period. Deaths in this study classified as violent (n = 324) included accidents (27%, n = 198), homicides (12%, n = 90), and suicides (5%, n = 36). Undetermined deaths contributed 13% (n = 96). The statistics regarding manner for all cases reported to CCCO indicated 28% were accidental, 4% suicide, 3% homicide, and <1% undetermined (9). Therefore, the

pediatric population contained fewer natural deaths, more homicides and more undetermined deaths than the general CCCO population. One possible explanation for the greater number of deaths ruled undetermined is that since there is typically less information (toxicological and other testing, autopsy, medical history) available in pediatric deaths it may be more difficult for an accurate official ruling on cause of death, resulting in a higher percentage of undetermined deaths than the total population. In addition, this data adds support to national statistics demonstrating high rates of homicide in the young. According to the U.S. Center for Disease Control and Prevention (CDC) young adults aged 15–24 years old account for 33% of homicide victims (1). In 2001, homicide was ranked fourth or higher as a leading cause of death in each age group in the present study according to the National Center for Statistics and Analysis (11). Violent deaths occurred most often in the >12–18 years age group with 58% homicides, suicides (92%), and accidents (41%). Gunshot wounds were the most prevalent cause of death for homicides (52%, $n = 48$), followed by blunt force trauma (28%, $n = 26$), stabbings (5%, $n = 5$), shaken baby syndrome (2%, $n = 2$), and homicide by other means (10%, $n = 9$). In this study, self-inflicted gunshot wounds were the most common cause of death in pediatric suicides (57%, $n = 20$), followed by hangings (37%, $n = 13$). Most of the accidental deaths in this study were caused by blunt force trauma (57%, $n = 104$), 98 being motor-vehicle related (94%). The remainder of the accidents were caused by carbon monoxide poisoning (10%, $n = 18$), drowning (10%, $n = 18$), maternal drug use (9%, $n = 17$), asphyxia (8%, $n = 15$), and other causes (7%, $n = 12$).

For young children, >1 day–2 years and >2–12 years there were 68 and 78 violent deaths (accident, homicide, suicide), respectively. The causes included blunt force trauma, shaken baby, asphyxia, hanging, maternal drug abuse, carbon monoxide poisoning, drowning, motor-vehicle accidents, and a number of other miscellaneous causes. At CCCO drug-related deaths in the newborn due to maternal drug abuse were ruled accident not homicide and there were 21 cases in this category. All 21 of these cases involved cocaine, including one patient positive for both venlafaxine and cocaine, and another positive for diazepam and cocaine.

Of the 730 total cases reviewed for this study, toxicology was performed on 655 of the cases. There were 15 cases in which only the volatile assay was performed. There were 247 decedents in this study who were positive for *at least* one type of drug. Resuscitative/treatment drugs account for 138 (56%) of the positive findings. This data suggests that regardless of injury or disease exhaustive efforts are frequently made to save these lives.

Illicit drugs were the second most common type of drugs detected. There were 65 cases (26% of positives) in which illicit drugs were detected. Of these 65 cases, 93% were considered violent deaths. Males were far more likely to be positive for illicit drugs (82%). The oldest age group provided 74% of the illicit drug positives, while 26% were provided by children under the age of 2. The latter statistic reflected maternal use. The most common illicit drug class detected was cannabinoids, specifically the THCOOH metabolite. Detection of THC and/or metabolites was found predominately in males (92%) and children over the age of 12 (100%). The manner of death linked most closely to the detection of THC and/or metabolites was found to be homicide (64%). THC was detected in 15 cases. Given the rapid elimination of THC from blood and the average concentration of 17.9 ng/mL, these findings are indicative of acute ingestion. A study conducted in 2002 and 2003 by Garg et al. complimented the THC results compiled in this study. Garg et al. found that 98% of their THC positives were children over the age of 12 years (8).

Cocaine and metabolites were the next most common illicit drugs detected in the population (11%). The cocaine positive results followed the same trend as the cannabinoid statistics: males (70%) over the age of 12 years (45%) were most likely to be positive for cocaine and/or metabolites. One notable difference was that children under the age of 2 years old contributed 51% of the cocaine positive results. Research has established that cocaine readily passes through the placenta by diffusion (12). It has been demonstrated that neonates metabolize cocaine differently than adults. In meconium samples from newborns the most common metabolite detected is m-hydroxy benzoylecgonine compared with BE (13). Studies have shown that it takes longer for cocaine to be eliminated from a fetus than an adult. Slower elimination causes the drug to be present in the fetus for longer periods of time than in the mother's body and therefore endangers the baby (14). When faced with investigating the death of a decedent who is less than a few days old and there is a history of maternal cocaine use, the brain and meconium are suitable alternate specimens for detection of cocaine and metabolites. Cocaine has been found to be very stable in brain tissue (13). One disadvantage with using brain as a sample is the high lipid content which renders drug extraction more difficult. In this study, there were five cases in which drugs were detected in tissue. A 3-h-old black female decedent had a BE concentration of 217 ng/g in the liver. A concentration of 540 ng/g BE and 60 ng/g cocaine was found in the brain of a 15-min-old black male, and 228 ng/g cocaine and 1516 ng/g BE were detected in the liver tissue of a 1-min-old black female. A stillborn black male was found to have a concentration of 290 ng/g BE and 67 ng/g cocaine in the liver. The final case in this category was a stillborn black female with a brain concentration of 200 ng/g BE.

Phencyclidine (PCP) was detected in 4% of the positive cases in this study. The CCCO statistic reports indicated that over the 5-year study period only 1% (69/6486) of the total CCCO population was positive for PCP (9). Decedents positive for PCP in this study were black males over the age of 12 years ($n = 11$). With PCP use, there is a high tendency for violent actions, also a schizophrenic-like state can occur after use that could potentially last for weeks (15). All of the deaths positive for PCP in this study were considered violent in nature: there were seven homicides, two suicides, and two accidental deaths. A report published in 2004 by the Drug Abuse Warning Network (DAWN) indicated that between 1999 and 2002 emergency room visits involving PCP doubled. By 2002, PCP was the hallucinogen detected most frequently in emergency room visits. The results of the DAWN report support the findings in the present study. According to the report there were more black (43%) males (64%) positive for PCP admitted to emergency rooms in the United States during 2002 (16). These results indicate that it is beneficial to screen for illicit drugs when there is a violent death in an individual 13–18 years old, especially when the decedent is male. Since maternal drug use was causative in 21 children deaths as noted on the verdict, children under the age of 2 should also be screened for illicit drugs. In practice, this may be problematic since often low sample volumes are collected for testing, and urine, useful for screening, is not available. According to the 2002–2003 National Survey on Drug Use and Health, 4.3% of the pregnant women who took the survey admitted to taking illicit drugs while pregnant (17). Three percent of all pediatric deaths reported to CCCO during the 5-year study were due to maternal use of illicit drugs.

In 2002, the National Institute on Drug Abuse (NIDA) conducted a survey of eighth, tenth, and twelfth graders about their lifetime drug use. Forty-seven percent of eighth graders, 67% of tenth

graders, and 78% of twelfth graders admitted to consuming ethanol at some point in their lifetime (4). Ethanol was detected in 11% of the positive cases in this study. This number is consistent with the number of cases in which ethanol was reported (10%) in all coroner cases received at CCCO during the 5-year study period (9). Seventy-three percent of ethanol positive cases in the pediatric population were reported in decedents over the age of 12 years. Decedents positive for ethanol were more likely to be white males who died as a result of an accident. In this study, five of the decedents positive for ethanol were involved in an automobile accident immediately prior to death. Three of the decedents were driving the automobile at the time of the accident and had blood alcohol concentrations of 0.20, 0.09, and 0.01 g/dL. The other two decedents were passengers with ethanol concentrations of 0.06 and 0.02 g/dL. There was one alcohol related accident in which there were multiple fatalities. Due to the prevalence of underage drinking and the detection rate of ethanol in pediatric deaths in the current study, the authors recommend volatile analysis on all medicolegal deaths in children, especially teenagers.

In this study, the antihistamines detected were over-the-counter medications. Six percent of positive cases (n = 16) included antihistamines. These drugs were overwhelmingly present in children between the ages of 1 day and 12 years (75%). This is an interesting statistic because this category of drug was one of only three (miscellaneous and CO) where the oldest children in the study did not contribute the majority of positive results. Possible explanations include ease of access to the drugs, and parental ignorance about proper dosing of over-the-counter medications in the young. Several of the drugs are contraindicated in children less than 2 years of age. Children's cold medications containing diphenhydramine are not recommended for children under 6 years old, adult formulations are inadvisable for those under 12 years of age (18). In recent years, the National Institute of Child Health and Human Development (NICHD) has been working with the FDA to establish appropriate labeling on over-the-counter medicines for neonates and infants to clarify dosing for these individuals (19). For the 271 cases occurring in the age category 1 day–2 years, one death was determined to be related to antihistamine use. This death was ruled a homicide. In this particular case there was a heart blood concentration of 0.49 mg/L diphenhydramine. A study conducted by Marinetti et al. in Montgomery County, Ohio, found 10 infant deaths over an 8-month period in which over-the-counter cold medications contributed to the cause of death. In the Marinetti et al. study ephedrine and pseudoephedrine were detected in nine out of the 10 infant deaths (5). Therefore, medicolegal investigators should consider testing for antihistamines and other over-the-counter drugs when presented with a case of a young child under the age of 2 years.

Since the 1990s, prescribing of antidepressants, especially the selective serotonin reuptake inhibitors (SSRIs), to juveniles has increased. In 2002, it was estimated that 10.8 million prescriptions were dispensed to children under the age of 18 (20). In this study, 3% of positive cases included antidepressants. Children over the age of 12 years (63%), white (75%) males (75%) were most likely to be positive. Several studies in recent years investigated antidepressant use and suicide in adolescents. In a 10-year retrospective study completed in Kentucky comprehensive toxicology was performed on 466 suicide cases aged 11–24 years; only 5% (n = 21) were positive for antidepressants but it is unknown which antidepressants were tested for in this study (21). The present study supports these results. Of the 36 suicide cases in this study, two (5%) tested positive for antidepressants. Neither of the suicides was due to an antidepressant overdose. The most common drugs detected were venlafaxine and bupropion and metabolites. It is recommended to test for antidepressants in all childhood suicides and accidental deaths. During the 5-year study period, there was one positive tricyclic antidepressant (amitriptyline), one selective serotonin reuptake inhibitor (sertraline), two serotonin–norepinephrine reuptake inhibitors (venlafaxine), and three antidepressants of other classes (bupropion, trazodone).

In the miscellaneous drug category, the majority of positive results occurred in children 1 day–12 years (69%). The most common manner of death in this drug category was undetermined death (n = 6). The cause of death in two of the cases was acute intoxication by a specific miscellaneous drug (propoxyphene, oxycodone). The remaining four deaths were caused by medical complications. This category of drugs included a wide range of medications from prescription painkillers to acetone. Therefore, it is difficult to render any conclusions from this data. A thorough investigation of the circumstances surrounding the death in these cases should be performed to adequately make testing decisions.

In Cuyahoga County, Ohio, it is common for individuals to have been transported to a medical facility prior to death. This observation is supported by the data in this study which demonstrated that the majority of drugs detected in the pediatric population were administered by medical personnel. No drug in this category was determined to be the cause of death. This suggests that hospital medication errors are less likely to occur in this population. A meta-analysis of 39 prospective studies, performed by Lazarou et al. estimated the incidence of patients being admitted to a hospital due to an adverse drug reaction (ADR) and the number of ADRs which occurred as a result of hospital treatment. The overall incidence of serious ADRs was found to be 6.7% and fatal ADRs contributed 0.32%. The authors suggested that age, length of hospitalization, and the specific drug are factors which influence whether or not an ADR would occur in a patient (22). Information on length of hospitalization for each case in the present study was not available and therefore this evaluation was not possible. The data in this study suggest that testing for these drugs in the pediatric population is necessary only when there is suspicion of inappropriate treatment.

Carbon monoxide deaths accounted for 8% of the positive results in this study. Eighty percent of the CO deaths were children under the age of 12. It has been suggested that young children are more susceptible to succumbing to CO poisoning in a fire than older children (23). A major factor in surviving a fire is removing oneself from the location of the blaze. Older children are more able to do this on their own, while younger children are more likely to require the help of a caregiver to escape (24). The Przepyszny and Jenkins study supports the finding in this study of a high percentage of CO deaths in children under 12 years. Although there was one suicide in this study positive for CO, it was not the cause of death.

In 35% of the positive cases, multiple drugs were detected. The most common combination was resuscitative/treatment drugs with other resuscitative/treatment drugs followed by illicit with other illicit drugs and illicit drugs with ethanol. Cases involving multiple drugs were violent in nature on 75% of occasions.

In 19% of the positive cases, the presence of a drug was determined to be the cause of death. The majority of these cases (n = 21/47, 45%) were children under the age of 15 days who died due to complications from maternal cocaine use. All these cases were ruled accidents. Thirty-six percent (n = 17) of the drug-related deaths were caused by CO intoxication. The remaining cases were due to acute intoxication by a number of drugs (cocaine, heroin, morphine, propoxyphene/norpropoxyphene, oxycodone, DPH).

In conclusion, to the authors' knowledge this is the first comprehensive report of drug prevalence in pediatric postmortem cases. The study showed that 38% of cases were positive for drugs. The most common drugs detected were those administered during resuscitative attempts and medical treatment. Other drugs commonly detected were illicit drugs and ethanol. The presence of cannabinoids and cocaine and metabolites were more likely to be detected in homicide victims aged >12–18, and < 1 day, respectively. The presence of ethanol was most likely to be detected in >12–18 years. Due to prevalence in the pediatric population, these drugs should be targeted if limited testing is available. In addition, other drug classes should be considered based upon the circumstances of death. For example, it appears to be prudent to test for over-the-counter drugs in children less than 2 years, and antidepressants in all child suicides. While the presence of drugs was determined to be the cause of death in only 6% of all cases, drug use may explain behavior prior to death, and corroborate or refute investigation findings.

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