

Drug Misuse in Adolescents Presenting to the Emergency Department

Yaron Finkelstein, MD, ABCP(Dip), *† Gautam Goel, MD,‡ Janine R. Hutson, MD, PhD,†
 Jeffrey Armstrong, BESC, * Carl R. Baum, MD,§ Paul Wax, MD,||
 Jeffrey Brent, MD, PhD,¶ on behalf of the Toxicology Investigators Consortium (ToxIC)

Objectives: Drug misuse is a disturbing, common practice among youth. One in 4 American adolescents reports consuming prescription medications without a clinical indication. We sought to explore current trends of drug misuse in adolescents.

Methods: Using the 37 participating sites of the ToxIC (Toxicology Investigators Consortium) Case Registry, a cross-country surveillance tool, we conducted an observational cohort study of all adolescents (aged 13–18 years) who presented to emergency departments with drug misuse and required a bedside medical toxicology consultation between January 2010 and June 2013.

Results: Of 3043 poisonings, 202 (7%) involved drug misuse (139 [69%] were males). Illicit drugs (primarily synthetic cannabinoids and “bath salts”) were encountered in 101 (50%), followed by prescription medications (56 [28%]) and over-the-counter (OTC) drugs (51 [25%]). Dextromethorphan was the most commonly misused legal medication (24 [12%]). Polypharmacy exposure was documented in 74 (37%). One hundred sixty-three adolescents (81%) were symptomatic; of these, 81% had central nervous system impairments: psychosis (38%), agitation (30%), coma (26%), myoclonus (11%), and seizures (10%); and 66 (41%) displayed a specific toxidrome, most commonly sedative-hypnotic. Benzodiazepines were the most frequently administered medications (46%). Antidotes were administered to 28% of adolescents, primarily naloxone, physostigmine, *N*-acetyl-cysteine, and flumazenil. No deaths were recorded.

Conclusions: Adolescents presenting with drug misuse may be exposed to a wide range and combinations of therapeutics or illicit substances and frequently display central nervous system abnormalities, compromising the ability to obtain a reliable history. Frontline clinicians should maintain a high index of suspicion, as routine toxicology screenings fail to detect most contemporary misused legal and designer drugs.

Key Words: adolescents, drug misuse, poisoning

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Drug misuse continues to be a disturbing, common practice among youth in the United States. In 2011, nearly 26% of grade 12 students reported consuming prescription medications without a prescription or clinical indication,¹ frequently from their

home drug cabinet. Recent survey data indicate initiation rates of prescription drug use without a medical indication have remained second only to marijuana initiation rates in 2010 and 2011.² An increase in narcotic use in the mid-2000s has resulted in illicit drug and alcohol use in grade 12 students at 49% and 24%, respectively, in 2012.³ The number of emergency department (ED) visits due to drug misuse rose by 52%, or approximately 844,000 visits in the United States between 2004 and 2011,⁴ the majority of which related to prescription drug misuse.⁵ In teenagers, there are an estimated 500 ED visits annually for emergencies involving alcohol or drug exposures per 100,000 people.⁵

Given the varied and exploratory nature of drug misuse in the teenage population, their symptoms and signs at presentation to the ED are highly variable. Often, exposure history may not be readily available. Thus, knowledge of contemporary drugs misused by youth could help physicians devise appropriate diagnostic and management strategies. In addition, exposure trends are important from an epidemiological and regulatory standpoint, as many agents used are prescription drugs, and prescribing patterns continuously evolve.

We sought to identify the drugs that were most commonly misused by teenagers presenting to EDs across the United States and describe their presentation and management.

METHODS

Setting

The Toxicology Investigators Consortium (ToxIC) Case Registry, a nationwide prospective toxicosurveillance system, was established by the American College of Medical Toxicology in January 2010.^{6,7} ToxIC includes 37 sites from 21 states across the United States, the majority of which are university-affiliated academic institutions, including 20 (87%) of the 23 currently active national medical toxicology fellowship training programs. Participating sites prospectively register all cases managed by medical toxicologists at the bedside into an online, password-protected database, which is maintained centrally by the American College of Medical Toxicology. Prospectively compiling all cases, the ToxIC Registry database allows for the identification, extraction, and pooling of patient-deidentified information on toxicological exposures across all sites. ToxIC functions after clearance by the Western Institutional Review Board, and sites contribute cases pursuant to the approval, policies, and procedures of their respective institutional review boards. A detailed description of the registry has been published,⁶ and its findings previously reported.^{7–9}

Patients

We searched all prospectively collected reports in the ToxIC Case Registry database between January 1, 2010, and June 30, 2013. The following search criteria were used to identify eligible cases: patients 13 to 18 years old, who presented to a participating hospital with a history, signs, and/or laboratory confirmation of

From the *Divisions of Emergency Medicine and †Clinical Pharmacology and Toxicology, Hospital for Sick Children, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; ‡Department of Family and Community Medicine, St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; §Center for Children's Environmental Toxicology, Yale–New Haven Children's Hospital, Yale University School of Medicine, New Haven, CT; ||Department of Surgery (Emergency Medicine), UT Southwestern School of Medicine, Dallas, TX; and ¶Department of Medicine, University of Colorado, School of Medicine, and Colorado School of Public Health, Aurora, CO. Disclosure: The authors declare no conflict of interest.

Reprints: Yaron Finkelstein, MD, ABCP(Dip), Divisions of Emergency Medicine and Clinical Pharmacology and Toxicology, Department of Pediatrics, Hospital for Sick Children, University of Toronto, 555 University Ave, Toronto, Ontario, Canada M5G 1X8 (e-mail: yaron.finkelstein@sickkids.ca).

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alcohol or illicit drug exposure or of prescription drug misuse. The latter is defined by the National Survey on Drug Use and Health as “use of any form of prescription drugs that were not prescribed for the [patient] or that the [patient] took only for the experience they caused.”^{10–12} The etiology of subsequent clinical manifestations was determined by an attending medical toxicologist at the bedside.

Data Collection

All potentially eligible cases were evaluated to determine each patient’s exposure and identify the most likely etiologic agent(s) without exclusion of any medications or substances. All substances revealed in the exposure history and laboratory testing were recorded. The medical toxicology service caring for the patient then assigned and graded the most likely causal agent(s), which were reviewed by the authors for likelihood. Exposures recorded in the registry are characterized by detailed history and physical examination performed by medical toxicologists, and additional diagnostic tests (eg, urine toxicology screens, serum drug levels) were ordered as clinically indicated. Data were tabulated, including age, source of referral, circumstances regarding the exposure, signs and symptoms at presentation, and antidotes administered.

RESULTS

A total of 21,748 poisonings were reported to ToxIC Registry during the study period, including 3043 adolescents (14.0%) between 13 and 18 years. Of this latter subset, 202 (6.6%) presented for drug misuse, of whom 139 (69.0%) were males.

Drug Exposure

A total of 294 drug exposures were documented in the 202 patients in our cohort (Table 1). A single-agent exposure was present in 128 patients (63.4%), 2 agents in 55 patients (27.2%), and 3 or more in 19 (9.4%). When categorized by legal drug schedules, illicit/recreational drugs (primarily synthetic cannabinoids, cannabinoids, and “bath salts”) were the most commonly encountered substances, reported in 101 (50.0%) of 202 patients, followed by prescription medications (56 [27.7%]), OTC drugs (51 [25.2%]), and ethanol (31 [15.3%]). Dextromethorphan was the most commonly misused legal medication (n = 24). The remaining substances encountered are presented in Table 1.

Signs and Symptoms

The majority of patients (163/202 [80.7%]) manifested significant clinical effects of their substance misuse at presentation. Central nervous system manifestations were the most common (131/163 [80.4%]), including delirium or acute psychosis (62 [38.0%]), agitation (49 [30.0%]), coma/central nervous system (CNS) depression (42 [25.8%]), myoclonus/tremor (17 [10.4%]), and seizures (16 [9.8%]). Furthermore, 66 (40.5%) of 163 individuals displayed a specific toxidrome, most commonly sedative-hypnotic (17 [10.4%]), followed by sympathomimetic (16 [9.8%]), anticholinergic (12 [7.4%]), and opioid (7 [4.3%]) toxidromes or serotonin syndrome (6 [3.7%]). Other signs at presentation are shown in Table 2. No deaths were recorded in this series.

Management

All patients received routine supportive care. Specific treatment was administered to 116 patients (57.4%). Of those, neurologically oriented pharmacological interventions were the most commonly used modality (69/116 [59.5%]; Table 3). Benzodiazepines were the most frequently administered class of medications (53/116

TABLE 1. Categorization of Agents by Pharmacologic Class*

| Agent Class | No. Patients | % Patients (n = 202 [†]) | % Exposures (n = 294 [†]) |
|---|--------------|------------------------------------|-------------------------------------|
| Illicit drugs | 101 | 50.0 | 34.4 |
| Synthetic cannabinoids | 33 | 16.3 | 11.2 |
| Cannabinoids | 28 | 13.9 | 9.5 |
| Bath salts | 12 | 5.9 | 4.1 |
| LSD (lysergic acid diethylamide) | 10 | 5.0 | 3.4 |
| Cocaine | 9 | 4.5 | 3.1 |
| MDMA (3,4-methylenedioxy-methamphetamine) | 8 | 4.0 | 2.7 |
| Heroin | 6 | 3.0 | 2.0 |
| Anticholinergics/antihistamines | 38 | 18.8 | 12.9 |
| Dextromethorphan | 24 | 11.9 | 8.2 |
| Diphenhydramine | 8 | 4.0 | 2.7 |
| Doxylamine | 7 | 3.5 | 2.4 |
| Chlorpheniramine | 7 | 3.5 | 2.4 |
| Sedatives | 31 | 15.3 | 10.5 |
| Opioids | 22 | 10.9 | 7.5 |
| Methadone | 5 | 2.5 | 1.7 |
| Benzodiazepines | 19 | 9.4 | 6.5 |
| Alprazolam | 8 | 4.0 | 2.7 |
| Clonazepam | 6 | 3.0 | 2.0 |
| Ethanol | 31 | 15.3 | 10.5 |
| Analgesics | 15 | 7.4 | 5.1 |
| Acetaminophen | 12 | 5.9 | 4.1 |
| Stimulant prescription drugs | 12 | 5.9 | 4.1 |
| Amphetamine | 7 | 3.5 | 2.4 |
| Methylphenidate | 5 | 2.5 | 1.7 |
| Antidepressants | 8 | 4.0 | 2.7 |
| Antipsychotics | 6 | 3.0 | 2.0 |

*Presenting only substances encountered in 5 or more patients; therefore, totals in subgroups may be higher than detailed.

[†]Discordance between the number of exposures and patients because of cases of polysubstance use.

[45.7%]). Pharmacological therapy was administered particularly to patients exposed to illicit substances (52/101 [51.5%]; Table 4). Antidotes were administered to 32 (27.6%) of 116 patients, primarily naloxone (11/116 [9.5%]), followed by physostigmine (10/116 [8.6%]), *N*-acetyl-cysteine (NAC; 6/116 [5.2%]), and flumazenil (6/116 [5.2%]). Decontamination strategies were infrequently used (6/116 [5.2%]) and included whole-bowel irrigation and activated charcoal.

DISCUSSION

Approximately 7% of teenagers requiring bedside consultation by medical toxicology services in EDs across the United States presented with substance misuse. Roughly half of them were exposed to illicit drugs and half to legal medications; more than 80% were symptomatic. Psychoactive agents were the most frequently encountered class of agents, with synthetic cannabinoids being not only the most common psychoactive agent, but the most prevalent agent overall, presenting primarily with CNS signs, including agitation, delirium, and coma, in line with existing literature.^{13–16} More than a third were exposed to multiple substances. Treatment of acute toxicity was largely supportive,

TABLE 2. Signs and Symptoms in Adolescents With Drug Misuse

| Symptom Class | Symptom | n (n = 163) | % |
|----------------------------------|---------------------------------------|-------------|------|
| Toxidrome | | 66 | 40.5 |
| | Sedative-hypnotic | 17 | 10.4 |
| | Sympathomimetic | 16 | 9.8 |
| | Anticholinergic | 12 | 7.4 |
| | Opioid | 7 | 4.3 |
| Notable vital signs and symptoms | Serotonin | 6 | 3.7 |
| | | 56 | 34.4 |
| | Tachycardia | 40 | 24.5 |
| | Hypertension | 21 | 12.9 |
| Cardiovascular | Hypotension | 8 | 4.9 |
| | | 10 | 6.1 |
| Pulmonary | | 21 | 12.9 |
| | Respiratory depression | 17 | 10.4 |
| Nervous | | 131 | 80.4 |
| | Delirium/toxic psychosis | 62 | 38.0 |
| | Agitation | 49 | 30.0 |
| | Coma/CNS depression | 42 | 25.8 |
| | Hyperreflexia/myoclonus/clonus/tremor | 17 | 10.4 |
| | Seizures | 16 | 9.8 |
| Metabolic | Mydriasis | 11 | 6.7 |
| | | 23 | 14.1 |
| | Metabolic acidosis (pH <7.2) | 15 | 9.2 |
| Gastrointestinal/hepatic | Elevated anion gap | 6 | 3.7 |
| | | 14 | 8.6 |
| Hematology | Hepatotoxicity (AST >1000 U/L) | 6 | 3.7 |
| | | 13 | 8.0 |
| Renal/muscle | Leukocytosis (WBCs >20,000/ μ L) | 7 | 4.3 |
| | | 16 | 9.8 |
| | Acute kidney injury (Cr >2.0 mg/dL) | 11 | 6.7 |

*Presenting only specific symptoms present in more than 5 patients.

AST indicates aspartate aminotransferase; WBCs, white blood cells; Cr, serum creatinine.

with intravenous fluids, benzodiazepines in almost half of patients, and specific antidotes in about a quarter.

The current popularity of synthetic cannabinoids in teens is in keeping with an emerging trend in recreational drug use in the general population.¹⁷ Commonly sold on the street or over the Internet under various names,^{15,17} synthetic cannabinoids are increasingly abused.¹⁶ The American Association of Poison Control Centers reported a more than 400% increase in calls related to synthetic cannabinoids and bath salts from 2010 to 2011.¹⁸ With more than 13,000 calls in 2011, approximately 60% of patients were younger than 25 years.¹⁸ Despite many of the most widely used chemicals being scheduled by the Drug Enforcement Administration in March 2011, use among American 12th graders remained unchanged in 2012, with 11.3% of students admitting their use in the past year.³ However, use may be declining following passage of the Synthetic Drug Abuse Prevention Act of 2012, which added both synthetic cannabinoids and cathinone derivatives to the Schedule I controlled substances list.¹⁹

Dextromethorphan, consumed by 12% of our patients, is structurally similar to opioids but has been abused for the dissociative effects attributed to its anticholinergic and anti-N-methyl-D-aspartate receptor properties. It was approved originally as an OTC cough suppressant by the Food and Drug Administration in

1958.²⁰ It is commonly abused by teenagers partly because of its low price and easy accessibility in various OTC products and over the Internet^{21,22} under various street names, such as poor man's PCP, DXM, or Skittles.²³ Emerging in popularity in the early 2000s,²⁴ a 15-fold increase in dextromethorphan abuse-related calls in children aged 9 to 17 years was noted from 1999 to 2004.²⁵ A 2010 survey reported that 5.9% of high school seniors previously abused dextromethorphan,²⁶ and a 2012 survey indicated that 4.4% of American high school students abused cough or cold medications in the previous year.³ In 2004, the American Medical Association released a warning regarding dextromethorphan misuse and recommended restrictions on its OTC use.²¹ Additional warnings from the Food and Drug Administration were raised following the death of 5 youth from dextromethorphan abuse in 2005.²¹ With increasing reports of serious and fatal outcomes after its recreational use,²² there have been several recent attempts in restricting the sale of dextromethorphan-containing products to minors in several states²¹; however, it is not a scheduled drug.

The effects of dextromethorphan are dose dependent and span from mild stimulation at low dose to hallucinations, ataxia, coma, and dissociative sedation at higher doses.^{23–25,27} Presenting symptoms often vary, attributed to the other ingredients in premixed

TABLE 3. Treatments Administered to Adolescents With Drug Misuse*

| Treatment Class | Treatment | No. Cases (n = 116) | % |
|----------------------------------|---------------------------------|---------------------|------|
| Neurologic management | | 69 | 59.5 |
| | Benzodiazepines | 53 | 45.7 |
| | Physostigmine | 10 | 8.6 |
| | Antipsychotics | 8 | 6.9 |
| | Anticonvulsants | 5 | 4.3 |
| Nonpharmacological support | | 52 | 44.8 |
| | Intravenous fluid resuscitation | 40 | 34.5 |
| | Intubation/ventilatory support | 15 | 12.9 |
| Antidotes | | 32 | 27.6 |
| | Naloxone/nalmefene | 11 | 9.5 |
| | N-acetylcysteine | 6 | 5.2 |
| | Flumazenil | 6 | 5.2 |
| Gastrointestinal decontamination | | 6 | 5.2 |

*Reporting only treatments administered to more than 5 patients.

combinations, such as codeine, antihistamines, or analgesics. Although not frequently included in basic drug screen panels, urine testing for dextromethorphan using enzymatic bioassays may produce a false-positive result for PCP.²⁸ Treatment is largely supportive and may include activated charcoal and naloxone.^{23,27}

Alcohol use was documented in 15% of patients, often as a coingestant. Alcohol has been commonly consumed by youth in the United States for many decades³ and may be associated with long-term outcomes.²⁹ Epidemiological data indicate that overall alcohol use has declined since 1980, with only 24% of 12th-grade

students reporting binge drinking in the previous 2 weeks, compared with 41% in 1981.³ However, drinking is still a significant concern, as nearly 40% of the 440,000 drug abuse–related ED visits in 2011 by patients younger than 20 years involved alcohol.⁵

Based on the diversity of misused compounds in our study, the majority of which not routinely identified on basic toxicological screens available in most EDs, physicians should be cautious about an overreliance on routine toxicology laboratory testing, as results may be unreliable and are rarely available in time to dictate initial management decisions.³⁰ Screening panels for drugs of

TABLE 4. Analysis of Treatment Modalities Used in Adolescents per Misused Drug Class*

| Treatment | Substance Category | | | |
|----------------------------|----------------------------|----------------------------|----------------------------|------------------------|
| | Illicit (n = 105) | Prescription (n = 58) | OTC (n = 51) | EtOH (n = 31) |
| Antidote | Naloxone, n = 6 | Naloxone, n = 9 | NAC, n = 4 | Physostigmine, n = 1 |
| | NAC, n = 2 | NAC, n = 2 | Physostigmine, n = 5 | |
| | Physostigmine, n = 4 | Fomepizole, n = 1 | | |
| | | Flumazenil, n = 6 | | |
| | | Physostigmine, n = 3 | | |
| Nonpharmacological support | IV fluid, n = 19 | IV fluid, n = 19 | IV fluid, n = 8 | IV fluid, n = 5 |
| | ETT/ventilator, n = 10 | ETT/ventilator, n = 6 | ETT/ventilator, n = 3 | ETT/ventilator, n = 3 |
| Pharmacological support | BDZ, n = 36 | BDZ, n = 10 | BDZ, n = 14 | BDZ, n = 7 |
| | Antipsychotics, n = 9 | Antipsychotic, n = 1 | NaHCO ₃ , n = 2 | Antipsychotics, n = 1 |
| | Anticonvulsants, n = 4 | Vasopressor, n = 3 | | Anticonvulsants, n = 1 |
| | Vasopressors, n = 1 | NaHCO ₃ , n = 2 | | |
| | Bronchodilator, n = 1 | | | |
| | NaHCO ₃ , n = 1 | | | |
| Decontamination | Bowel irrigation, n = 2 | | Activated charcoal, n = 2 | |
| | Activated charcoal, n = 2 | | | |

Note that some patients received an antidote following exposure to more than 1 substance; hence, the total antidote sum may be greater than the total number of patients (n = 116 [57.4%]) receiving that antidote, as reflected in Table 3.

*Table examines the number of patients with exposure and which treatments they received.

BDZ indicates benzodiazepine; ETT, endotracheal intubation; IV, intravenous; NAC, n-acetyl cysteine; NaHCO₃, sodium bicarbonate.

abuse often include only amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine metabolites, methadone, opiates, oxycodone, and phencyclidine.³¹ Clinicians should be familiar with their specific laboratory limitations and common false-negative results (eg, when metabolites are at concentrations less than the established thresholds)³² and false-positive results³³ associated with substance abuse screening tests. A high index of suspicion for substance abuse is warranted in relevant clinical contexts for agents that are not present on routine toxicology screening, such as synthetic cannabinoids and most prescription and OTC drugs, including dextromethorphan. Detection of synthetic cannabinoids, in particular, requires specialized mass spectrophotometry capabilities.³⁴

Several study limitations merit emphasis. As the majority of centers are located in academic tertiary care centers, our data may not necessarily reflect encounters in primary care settings.⁷ Second, as the ToxIC Registry was established as a prospective, nationwide, real-time surveillance tool,⁷ and it exclusively captures cases that required bedside consultation by medical toxicology services, it is likely that novel and more serious exposure cases are overrepresented.^{7,35} Importantly, because all data are obtained by medical toxicologists treating these patients at the bedside, the clinical information obtained is highly reliable. Because of this, the data in the ToxIC database fundamentally differ from those in other commonly used data collection systems such as the National Poisoning Data System maintained by US poison centers.

In summary, teenagers presenting with drug misuse may be exposed to a wide range and combinations of illicit substances and prescription or OTC medications and therefore may display a wide variety of signs and symptoms. The frontline clinician must maintain a high index of suspicion in relevant clinical scenarios, as routine toxicology screens cannot detect a large proportion of the contemporary and commonly drugs misused by teenagers, and as our data show, up to 80% of these children may present with significant neurological abnormalities, compromising the ability to obtain a reliable clinical history.

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