108. Death from diffuse alveolar hemorrhage temporally related to the use of MAB-CHMINACA and N-methyl-2-aminoindane

Edward Bottei[a], Kimberly Zellmer[a] and Julie Breiner[b]
[a]Iowa Poison Control Center; [b]Pathology Medical Services of Siouxland

Background: Deaths from recreational use of a synthetic cannabinoid (SC) or an aminoindane (AI) derivative are rare. No cases have been reported in the literature of the use of either an SC or an AI derivative causing death from diffuse alveolar hemorrhage (DAH).
Case Report: A previously healthy 18 year old teenager collapsed when smoking "K2." The teen had taken two drags from a "K2" joint with no untoward effects. Several minutes later, the decedent took another two drags from the joint and "started freaking out." Within seconds to a few minutes after the second two drags, the decedent vomited, coughed up blood and then collapsed. CPR was initiated and EMS was summoned. Resuscitative efforts were unsuccessful. The autopsy was notable for extremely hemorrhagic, edematous lungs with the right lung weighing 1300 g and the left weighing 1090 g. Average post-mortem lung weight for the decedent's gender for the right lung is 445 g (95% C.I. 155-720 g) and for the left lung is 395 g (112-675 g). Microscopically, the alveolar septal capillaries were markedly congested and erythrocytes were scattered throughout the alveolar spaces. There was no acute inflammation. Aspirated vegetable material was identified within some of the larger bronchioles with no inflammatory reaction. Also notable was blood within the stomach and proximal small intestines without any discrete or localized sites of bleeding noted.
Post-mortem toxicology testing revealed: Blood (tested by LC/quadrupole Time of Flight MS) – MAB-CHMINACA 2.7 ng/mL, A possible MAB-CHMINACA metabolite (M6) was also identified but not quantitated – N-methyl-2-aminoindane 95.4 ng/mL. Urine (tested by LC/MS/MS) – UR-144 metabolites, N-(4-hydroxypentyl) 1.7 ng/mL – N-pentanoic acid 2.6 ng/mL.
Standard forensic drug screen on whole blood was negative for 129 pharmaceuticals and chemicals.
Case Discussion: Acute DAH associated with recreational use of either an SC or an AI derivative has not been previously reported in the literature. The rapidity with which the DAH developed in an otherwise healthy teenage is quite concerning. Whether the DAH was caused by the SC or the AI is unknown. Of note, this is the first report of this particular amionindane being used in humans. Also unknown is whether or not there were other chemicals in the "K2" that caused/contributed to the DAH as the substance specifically smoked was not analyzed. The urine UR-144 metabolites are consistent with previous SC use.
Conclusions: We report the first case of a death from DAH temporally related to the use of MAB-CHMINACA and N-methyl-2-aminoindane.

KEYWORDS MAB-CHMINACA; N-methyl-2-aminoindane; Diffuse alveolar hemorrhage

edward.bottei@unitypoint.org

109. Evaluation of opioids/opiates involved in fatalities in one region 2012–2015

Daniel Baker[a] and Henry Spiller[b]
[a]Franklin County Coroner's Office; [b]Central Ohio Poison Center

Background: Opioid intoxication has been increasing for more than two decades. For much of this time period prescription opioid drug diversion was the primary source of the increase. Coordinated efforts at controlling the number of dispensed opioids have shown results in decrease prescriptions dispensed. In Ohio dispensed opioid prescriptions have decreased 10% from 2010 to 2015 (780M/yr to 700M/yr). However in the same period deaths caused by lethal intoxication have increased.
Methods: review of Franklin county coroner's office records for 2012 to 2015 for lethal intoxication. The office also provides service for 6 surrounding counties, providing a service for central Ohio. The drugs attributed to the fatality were based on the coroner's legal determination after autopsy and post mortem toxicology analysis.
Results: Between 2012 and 2015, 1323 deaths were attributed to lethal intoxications (OD). There was a 29% increase from 301 deaths in 2012 to 388 deaths in 2015. 973 (73.5%) of OD deaths were attributed to an opiate/opioid or polysubstance intoxication including an opioid. Heroin accounted for 504 lethal intoxications (38%), with a linear increase ($R2 = 0.953$) from 93 in 2012 to 155 in 2015. Heroin constituted 52% of opiate/opioid related intoxications. Prescription opioid related deaths decreased 24% since 2012: from 108 deaths in 2012 to 82 deaths in 2015. Fentanyl related deaths increased 240% in 2015 with 58 deaths, from a mean of 17 cases/yr (2012-2014). Prior to 2015 the source of fentanyl was prescription drug diversion (patch). In 2015 illicit fentanyl via the heroin distribution market appeared and is responsible for the sudden increase. Cocaine showed a 50% increase in 2015 with 47 cases, from a mean of 31 case/yr (2012-2014).
Conclusions: The increase in the study period is attributed to dramatic increase in illicit heroin and illicit non-pharmaceutical fentanyl fatalities, During this same period there was a noted decrease in prescription opioid fatalities. Opioid/opiate fatalities continue to increase, despite a decrease in available prescription opioids. The increase appears related to illicit heroin and illicit non-pharmaceutical fentanyl.

KEYWORDS Heroin; opioids; fatality

haspiller5@gmail.com

110. Intentional Abuse Cases Mentioning Prescription Opioid Products Following the Hydrocodone Rescheduling

L. J. Fischer[a], S. G. Severtson[a], J. L. Green[a], R. C. Dart[b] and RADARS® System Poison Centers[a]
[a]Rocky Mountain Poison and Drug Center, Denver Health; [b]Rocky Mountain Poison and Drug Center, Denver Hospital Health Authority

Background: In an effort to curb abuse, the Drug Enforcement Administration rescheduled hydrocodone combination products (e.g. Vicodin®) from Schedule III to Schedule II in October 2014. This study examined whether the trend in intentional abuse cases

Table 1. Average Quarterly Change in Intentional Abuse Cases Pre/Post Hydrocodone Rescheduling

Drug	Pre (95% CI)	Post (95% CI)	p-value for difference in trends	Interaction p-value
Hydrocodone	−3.4% (−4.2, −2.6)	−6.2% (−9.9, −2.3)	0.211	REF
Oxycodone	−2.7% (−3.5, −1.9)	3.1% (−0.9, 7.3)	0.010	0.007
Other Schedule II Opioids	−3.1% (−4.0, −2.2)	4.1% (−0.3, 8.7)	0.004	0.003
Tramadol	−1.1% (−2.1, −0.1)	−3.1% (−7.8. 1.8)	0.476	0.817

mentioning hydrocodone products changed following rescheduling and whether this change differed from comparator opioids.
Methods: Data from the Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS®) System Poison Center Program were used. Intentional abuse cases from 1Q2011-4Q2015 mentioning products within drug categories of interest were included. Four drug groups were assessed: hydrocodone, oxycodone, other Schedule II opioids (fentanyl, hydromorphone, morphine, oxymorphone, tapentadol), and tramadol. The Pre-Rescheduling period was 1Q2011-3Q2014, and Post-Rescheduling was 4Q2014-4Q2015. The analysis was restricted to poison centers that provided data every quarter during the study period (n = 44). Negative binomial regression was used to compare the Pre-Rescheduling quarterly trend to the Post-Rescheduling trend with hydrocodone as the reference for interactions.
Results: Table 1 shows the average quarterly change for each drug group Pre/Post-Rescheduling. On average, hydrocodone abuse cases declined 3.4% per quarter Pre-Rescheduling to -6.2% Post-Rescheduling, a statistically non-significant change. Oxycodone declined 2.7% Pre-Rescheduling but displayed a statistically significant change to +3.1% per quarter Post-Rescheduling. Other Schedule II opioids declined 3.1% Pre-Rescheduling but increased to +4.1% per quarter Post-Rescheduling, a statistically significant change. Changes in tramadol trends were not statistically significant. The difference in oxycodone and other Schedule II opioids trends were significantly different from the change in hydrocodone.
Conclusions: After rescheduling, hydrocodone showed non-significant decline while oxycodone and other Schedule II opioids showed significant increases. This suggests regulatory changes in one drug may impact the patterns of abuse in others. Continued monitoring is needed to further determine the potential impact of this intervention on prescription opioid abuse.

KEYWORDS opioids; hydrocodone rescheduling; abuse cases

laura.fischer@rmpdc.org

111. Pediatric Cardiac Toxicity Associated with Fentanyl Ingestion

Ryan Chuang[a], Farah Saleh[b] and Bader Alyahya[c]
[a]Poison and Drug Information Services Alberta; [b]Poison and Drug Information Service, Alberta Health Services, Calgary; [c]McGill University

Background: In the United States, opioids such as fentanyl account for up to 40% of drug related deaths. Between 2012-2014, The National Forensic Laboratory Information system reported an eight-fold increase in fentanyl seizures and drug deaths secondary to illicit drugs have increased substantially.
Case Report: A 14-year-old male was found unresponsive, hypotensive, cyanotic (50% oxygen saturation) and diaphoretic 2 hours after a reported ingestion of a half of a round, blue-green unidentified pill. There was hematemesis on his pillow and the patient had continued emesis en route to the hospital. An initial chest X-ray suggested right-sided aspiration pneumonia. Baseline investigations showed a lactate of 6.4 mmol/L, a high sensitivity troponin of 206 ng/L (normal 1-14 ng/L) and undetectable acetaminophen and salicylate levels. GC/MS was positive for fentanyl and its metabolites, cannabinoids, ondansetron, metoclopramide and ranitidine but was negative for xylazine. Chest pain was reported 8 hours post arrival. An electrocardiogram showed ST elevation over the anterior leads and the echocardiogram demonstrated borderline systolic function, though both tests were normalized on subsequent examinations. High sensitivity troponin peaked at 311 ng/L (normal 1-14 ng/L) within 24 hours whereas lactate normalized within a few hours. Cardiac inflammation in the RCA and LAD distributions possibly secondary to vasospasm was evident on a cardiac MRI performed 2 days post hospital admission. Management involved the administration of non-invasive positive-pressure ventilation, and intravenous naloxone, dopamine, norepinephrine and ceftriaxone. Patient was successfully weaned off inotropes 24 hours post admission, switched to room air a few days later and discharged home with a normal physical exam on day 5. A repeat cardiac MRI 6 months later was normal.
Case Discussion: Complications of fentanyl ingestion are usually secondary to respiratory depression. Adverse cardiovascular events have been seen when fentanyl is adulterated with xylazine. We present an unusual pediatric case of cardiac injury in the context of a fentanyl ingestion. In this case, xylazine was not detected and despite the fact that the urine drug screen was positive for cannabinoids and fentanyl, the patient's history and presentation was more consistent with recent fentanyl use. Alternative considerations that could have contributed to cardiac toxicity include a cannabinoid effect, another unidentified cardiotoxic illicit substance or a takotsubo cardiomyopathy incident.
Conclusions: Non-prescription fentanyl may cause cardiac toxicity.

KEYWORDS Fentanyl; Cardiotoxicity; Drug Abuse

ryan.chuang@ahs.ca

112. Adverse effects after the use of ADB-CHMINACA – a case report from the EU Spice II plus project

Maren Hermanns-Clausen[a], Josephine Kithinji[b], Verena Angerer[c], Florian Franz[c] and Volker Auwärter[c]
[a]Poisons Information Centre, Medical Centre - University of Freiburg; [b]Poisons Information Center, Center for Pediatrics and Adolescent Medicine, Medical Center – University of Freiburg; [c]Institute of Forensic Medicine, Forensic Toxicology, Medical Center – University of Freiburg

Background: In 2014, the 'European Monitoring Center for Drugs and Drug Addiction' (EMCDDA) reported about thirty novel synthetic cannabinoids (SC). These included indazole-based valine derivatives carrying a cyclohexyl methyl side chain such as ADB-CHMINACA, which represents a new class of SC. It is a full agonist with a significantly higher affinity and activity at the CB1 receptor compared to JWH-018.
Case Report: A 20 yo male smoked SC with vaporizer. After 3 hours he vomited, grew restless and developed severe headache followed by an increasing clouding of consciousness. On admission in hospital, disorientation, somnolence, and impaired coordination were evident. Subsequent cerebral computed tomography findings and clinical findings were compatible with posterior reversible leucencephalopathy syndrome (PRES), according