

Pediatric Poisoning Fatalities: Beyond Cough and Cold Medications

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For more than 10 years, there have been Food and Drug Administration recommendations and manufacturer labeling changes in place advising against the use of cough and cold medications (CCMs) in young children.^{1,2} In this issue of *Pediatrics*, Halmo et al³ present concerning findings characterizing fatalities associated with CCMs in recent years. Identifying cases through the Pediatric Cough and Cold Safety Surveillance System and then using an expert panel for review, the authors report 40 CCM-related fatalities in children under 12 years old that occurred from 2008 to 2016. Although overall fatalities associated with CCMs were rare, they found that most fatalities were in children <2 years old and were of nontherapeutic intent, with more than one-half of nontherapeutic intent cases determined to be malicious in nature. Diphenhydramine, a commonly used antihistamine, was found to be the index-ingredient most often involved in CCM-related fatalities. This important fatality review demonstrates that despite safety efforts, young children remain at risk for death from CCMs.

The strengths of the study include the use of a cough-and-cold-specific safety surveillance system that includes data from several national sources and data collection that covered several years after advisory and labeling changes. The surveillance system was limited, however, by self-report and potential misclassification of cases as well as

inconsistencies in detailed case information. Autopsy reports were also reviewed, but reports were only available in 55% of cases.³ Therefore, the expert panel could not determine the contributory factors that led to the child's death in almost one-half of fatalities. Thus, these limitations likely have led to an underestimation of CCM-related fatalities and CCM-related fatalities determined to be due to malicious intent, which may occur even more frequently than classified in this study.

The 2019 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS) describes a 16.3% increase in fatalities in children <20 years of age, compared with 2018.⁴ Although Halmo et al³ focused on CCMs, pediatric fatalities can be associated with a wide range of substances including alcohols, hydrocarbons, disc batteries, laundry detergent pods, opioids, amphetamines, acetaminophen, and benzodiazepines.⁵ In a case series of infants and toddler poisonings between 2010 and 2011 reported to the Toxicology Investigators Consortium Registry, 6810 poisonings were identified. The top substances ingested included cardiac drugs, psychotropic agents, recreational drugs, alcohols and controlled narcotics, analgesics, and cleaning compounds; 14% of cases involved multiple agents.⁶

Fatalities from pediatric poisonings in general are particularly disturbing and may result from unintentional

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exposures as well as from neglect and/or malicious intent, as highlighted in the study by Halmo et al.³ Neglect may be difficult to determine, but unsafe environments where ethanol, opioids, and other recreational drugs are easily accessible are especially concerning.

In a sentinel article, researchers examined pharmaceutical exposures coded as “malicious” in children <7 years old, as reported to the NPDS from 2000 to 2008; 1439 cases met the inclusion criteria.⁷ There were at least 1 sedating agent in 51% of cases and 18 deaths, including 17 children exposed to a sedating agent; in fact, the use of a sedating agent was 3.6 times more likely to be associated with a major outcome or death. Age ≤ 2 years was also significantly associated with death or a major outcome, similar to the CCM study. A total of 8 of the children were exposed to antihistamines, and 8 of the ingestions involved opioids. When nonpharmaceutical malicious ingestions were investigated with these same research parameters, 4053 cases were identified.⁸ A total of 4 children died, and 18 sustained injuries that were classified as life-threatening; cleaning substances, chemicals, alcohols and fumes, gases, and vapors were the most common substances implicated. Other studies have shown that risk factors for child abuse include community poverty levels,⁹ and the dynamic between a child’s potential behavioral difficulties, parental antisocial and/or psychiatric problems, and the environment (physical violence and low socioeconomic status) may contribute to child neglect.¹⁰ In recent study of child maltreatment in siblings of abused children, researchers found that maternal age <20 years was the strongest predictor of abuse.¹¹ Pediatricians should be aware of these findings

and advocate for screening and interventions, such as home visitation programs that work with first-time mothers in lower socioeconomic groups.¹²

As mentioned, ethanol is a common household product implicated in harming children. Gaw et al¹³ looked at 10 years of data reported to NPDS in infants <12 months of age from 2009 to 2018 and found that 1818 infant exposures to beverage ethanol were reported.¹³ Infants who were 0 to 5 months of age had higher odds of admission to both critical and noncritical hospital units than infants in the 6- to 11-month-old group; these younger infants also had an almost 5 times increased rate of serious outcomes, with 5 fatalities reported. Marijuana has also been implicated in 1 pediatric fatality; an 11-month-old boy presented with central nervous depression after a seizure at home and subsequent cardiac arrest.¹⁴ Myocarditis was diagnosed postmortem; cardiac blood at autopsy confirmed the presence to Δ -9-carboxy-tetrahydrocannabinol, with parents later admitting to cannabis possession. Prevention efforts, aimed at safe storage of ethanol and marijuana products up and away, combined with flow restrictors, liquid medications dosed only in milliliters, and unit dose (blister) packs for solid medications, are key in keeping children safe.¹⁵

Opioid poisonings are also an incredibly important cause of morbidity and mortality in children. Numerous deaths from ingestion of fentanyl patches have been reported,¹⁶⁻¹⁸ in which neglect may have been a contributing factor. In a study in which researchers looked at adverse outcomes in pediatric buprenorphine exposures, 4 deaths were reported overall, but none were in the film preparation group, suggesting that the formulation itself

may be a key difference.¹⁹ In fact, analysis of NPDS calls for prescription opioids in children <20 years of age for the years 2000–2015 showed that children 0 to 5 years accounted for ~90% of buprenorphine exposures.²⁰ Reports of pediatric methadone deaths have existed for decades, including 4 children in a case series from Michigan²¹ and 29 deaths identified in children aged 3 weeks to 13 years in a systematic review from the United Kingdom; 11 infants (<12 months old) were thought to have been deliberately poisoned.²² In a salient article, Gaither et al²³ describe 8986 children <20 years of age who died of prescription and illicit opioids between 1999–2016, and the pediatric mortality rate increased from 0.22 to 0.81 per 100 000, an increase of 268.2%. A total of 38% of children died at home or other residential setting, and homicide was the cause of death in 24.5% of children <5 years of age.

In conclusion, the findings from this study by Halmo et al³ highlight the need for continued targeted interventions to promote medication safety and specifically to prevent child abuse by poisoning, which may involve over-the-counter medications such as CCMs as well as prescription medications or illicit substances. Labeling changes and current caregiver education remain inadequate in preventing CCM-related deaths. It is important to note that >40% of CCM-related fatalities in the study were reported to also involve at least 1 non-CCM ingredient,³ indicating that combination drug products or polypharmacy was involved in many cases and demonstrating the need for safety efforts more broadly. The authors highlight comprehensive testing as an opportunity to identify child abuse

by poisoning, although access to testing may be limited. The authors are to be applauded for their efforts in characterizing pediatric fatalities associated with CCMs. However, further study of trends and detailed factors associated with medication-related fatalities in young children is necessary to determine the best interventions for these vulnerable patients and their preventable deaths.

ABBREVIATIONS

CCM: cough and cold medication
NPDS: National Poison Data System

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