Effect of Cough and Cold Medication Restriction and Label Changes on Pediatric Ingestions Reported to United States Poison Centers

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Objective To determine the impact of industry and Food and Drug Administration initiatives implemented to limit the use of over-the-counter (OTC) cough and cold medications in children younger than 6 years of age.

Study design This is a retrospective database study of OTC cough and cold medication ingestions reported to US poison centers between 2000 and 2010. Data analyzed from the National Poison Data System included the month and year of ingestion, reason for ingestion, health care utilization, and medical outcome. Ingestion frequencies were stratified by age and reason. Data were divided into pre- and postintervention periods for comparative analysis.

Results Unintentional ingestions of OTC cough and cold medications decreased 33.4% and therapeutic errors by 46.0%. Health care facility referral declined for unintentional ingestions (28.9% <2 years of age, 19.9% 2-5 years of age, $P < .0001$) and therapeutic errors in children younger than 2 years of age (59.2%, $P < .0001$). Moderate and severe adverse outcomes decreased for unintentional ingestions in children younger than 2 years of age by 32.4% and by 21.3% in 2- to 5-year olds, $P < .0001$.

Conclusions The restriction of OTC cough and cold medications has led to a decline in unintentional ingestions, therapeutic errors, health care facility referral, and serious medical outcomes in children younger than 2 years of age. There has also been a decline in ingestions in 2- to 5-year-old children. *(J Pediatr 2013;163:1372-6)*.

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Over-the-counter (OTC) cough and cold medications containing antihistamines, antitussives, decongestants, and expectorants are widely marketed and frequently used to treat cough and cold symptoms in children.[1-5] Although these medications have traditionally been considered safe, misuse and overdose can result in significant toxicity, including death.[2-8]

In October 2007, a joint panel meeting of the Food and Drug Administration's (FDA)'s Nonprescription Drugs and Pediatric Advisory Committees convened to advise against the use of OTC cough and cold medications in children younger than 6 years of age.[2] Prior to the meeting, the Consumer Healthcare Products Association (CHPA) issued a position statement and voluntarily withdrew products marketed for use in children younger than 2 years of age.[2-4] In January 2008, the FDA recommended OTC cough and cold medications not be used in children younger than 2 years of age.[9,10] In October 2008, the CHPA issued warnings regarding the use of these medications in children younger than 4 years of age.[11,12] These actions were supported by the FDA.[13] The FDA continues to review the available data and is considering changing the labeling of OTC cough and cold medications for children between 2 and 6 years of age.[10]

Since the voluntary restrictions of OTC cough and cold medications, there has been a decrease in therapeutic errors, unintentional exposures, and adverse drug events reported in children younger than 2 years of age.[14,15] There is evidence to suggest a decline in emergency department visits in children for adverse events related to these medications.[16] This study evaluated the impact of the CHPA and FDA recommendations and labeling changes on pediatric ingestions reported to US poison centers. The primary hypothesis was that the frequency of therapeutic errors and unintentional ingestions would significantly decrease. The secondary hypothesis was that there would also be a decline in health care facility utilization and serious medical outcomes.

Methods

A retrospective database analysis was conducted. Data pertaining to OTC cough and cold medication ingestions reported to US poison centers from January 1,

CHPA	Consumer Healthcare Products Association
FDA	Food and Drug Administration
NPDS	National Poison Data System
OTC	Over-the-counter

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2000-December 31, 2010 were obtained from the National Poison Data System (NPDS). Data were collected from all participating US poison centers. The number of poison centers in the US declined from 64 in 2000 to 57 at the close of the study period; however, the population served increased.[17] Exposure data were documented by nurse and pharmacist specialists in poison information using standardized data fields and definitions. All ingestions occurring in children younger than 13 years of age, involving OTC cough and cold medications with an exposure reason of "therapeutic error" or "unintentional general" were included. Therapeutic errors are defined as "an unintentional deviation from a proper therapeutic regimen that results in the wrong dose, incorrect route of administration, administration to the wrong person, or administration of the wrong substance." Unintentional general exposures are those unintentional exposures that are not classified as misuse, abuse, environmental, occupational, bite or sting, food poisoning, or unknown.[17] Information calls and confirmed nonexposures were excluded. Products included as cough and cold medications were identified by specific NPDS codes and included agents that were classified as antihistamines, decongestants, expectorants, and cough suppressants. Cough and cold medications could be single agent products or contain multiple ingredients including pain relievers and antipyretics.[17] OTC status was determined from specific product codes when present, or generic codes when specific products were unknown; prescription only formulations were excluded. Cases with multiple substances implicated were included if at least 1 substance was an OTC cough and cold medication.

Data analyzed included the month and year of the ingestion, age, product ingested, reason for the ingestion, level of health care provided, and severity of outcome. The level of health care provided was stratified into 2 groups: those who were referred to or were already in a health care facility and those who were managed at home. Severity of health outcomes was also stratified into 2 groups: those with no or minor clinical effects into 1 group and those with moderate, major, or fatal outcomes in the second group. A minor outcome is defined as minimal signs or symptoms that rapidly resolve, moderate as more significant symptoms, possibly systemic, that do not result in permanent disability or disfigurement, and major as life-threatening symptoms that may result in permanent sequelae. Cases that were lost to follow-up or that had inadequate follow-up to determine a definitive outcome were excluded from the analysis. For cases with a therapeutic error, 16 therapeutic error scenarios were analyzed.[17]

Population by age was obtained from the US Census Bureau's 2000 and 2010 census data and July population estimates for the years 2001-2009.[18-20] The study population was divided into 3 age groups: younger than 2 years of age, 2-5 years of age, and 6-12 years of age. The 6- to 12-year age group served as a reference group, as they were not directly affected by the interventions. The data were then further divided into unintentional general and therapeutic error as reasons for ingestion, yielding a total of 6 groups based on age and reason. Frequencies of ingestions per million population were graphed by month for the 11-year study period for each of the 6 groups to assess trends in ingestions over time, including seasonal variation. For ingestion frequency, health care facility utilization, medical outcome, and therapeutic error scenarios, data were divided into a pre-intervention period from January 1, 2005-December 31, 2006 and a postintervention period, from January 1, 2009-December 31, 2010 to compare the changes in exposure frequency immediately before and after the intervention. For this portion of the analysis, frequency changes for OTC cough and cold medication ingestions were compared with all other pharmaceutical ingestions reported to NPDS with the same time period, age group, and reason for ingestion. Selection of this comparison group effectively controlled for other factors that might have affected pharmaceutical ingestion frequency during the pre- and postintervention periods. Likewise, for therapeutic error scenarios, a statistical comparison was made between OTC cough and cold medications and all other therapeutic errors reported to NPDS with the same age and scenario in the same time period to limit confounding by any other changes in therapeutic error scenarios over time.

Data were analyzed using χ^2 tests and a P value of less than .05 was considered significant. Statistical analysis was performed using SAS 9.2 (SAS Institute Inc, Cary, North Carolina) and GraphPad InStat 3.10 (GraphPad Software Inc, La Jolla, California), and graphs were prepared using Microsoft Excel 2010. The Institutional Review Board at The George Washington University considered this study exempt from review.

Results

There were statistically significant declines in unintentional ingestions (33.4%) and therapeutic errors (46.0%) in all age groups between the pre- and postintervention periods. For both therapeutic errors and unintentional general ingestions, the greatest decline in ingestion frequency was observed in children younger than 2 years of age (**Table I**). When unintentional ingestions and therapeutic error frequencies were plotted by month, postintervention declines are readily apparent in children younger than 2 years of age and 2- to 5-year olds with a consistent seasonal variation, with peaks coinciding with the cough and cold season (**Figure**).

Health care facility utilization declined for unintentional general ingestions between the pre- and postintervention time periods. There was a 28.9% decrease in children younger than 2 years of age ($P < .0001$) and a 19.9% decrease in children 2-5 years old ($P < .0001$). There was no significant change in the 6- to 12-year age group, compared with ingestions of other pharmaceuticals reported to NPDS involving 6- to 12-year olds in the same pre- and postintervention time periods. When health care facility utilization was examined for therapeutic error cases, there was a 59.2% decrease in health care facility cases in the younger than 2 years age group ($P < .0001$). There was no significant change in the 2- to 5- or 6- to 12-year age groups.