Dynamic Chiropractic

Cisapride	Propulsid	4.0	Acid/peptic disorders
Indomethacin	Indocin	3.8	NSAIDs
Nitric oxide	INOmax	3.4	Medicinal gases
Azithromycin	Zithromax	2.1	Lincosamides/macrolides
Acetaminophen	Tylenol, Infantol, Anacin, Feverall	1.6	General analgesics
Fluconazole	Diflucan	1.5	Antifungals
Ibuprofen	Advil, Provel, Motrin, Excedrin	1.3	NSAIDs
Respigam	Respigam	1.3	Immune serums
Ceftriaxone	Rocephin	1.1	Cephalosporins
Cefaclor	Cefaclor, Ceclor	1.0	Cephalosporins
Cefoperazone	Cefobid	1.0	Cephalosporins
Zidovudine	Zidovudine, AZT, Retrovir	1.0	Antivirals
Erythromycin	Emgel, Akne-Mycin	0.9	Lincosamides/macrolides
Vincristine	Vincristine, Oncovin	0.8	Antineoplastics

NEWS / PROFESSION

The Baby Killers

1% OF DRUGS LINKED TO 54% OF SERIOUS/FATAL OUTCOMES

Ryan Lockwood, associate editor

A major review of adverse drug reactions has found that almost 250 infants under age 2 may die annually from adverse drug reactions, with more than half of deaths and serious adverse events linked to less than 1% of the drugs identified in the study.

The risk of adverse drug events (ADEs) in infants and young children exceeds that of adults because infants' detoxification mechanisms are immature, and children have a wider range of body sizes than adults. Prescribing drugs to infants or children under age 2 also can be dangerous because of a relative lack of clinical testing in this group of patients. U.S. Food and Drug Administration (FDA) clinical trials for medication approval often do not include children, so labels on new drugs provide physicians with minimal or no guidance as to a drug's safety or dosage requirements in this age population.

In the study, published in the journal Pediatrics, Center for Health Services Research and Policy researcher Thomas J. Moore, et al., examined nearly 600,000 adverse drug reaction reports received by the FDA from November 1997 to December 2000. Protocol dictates that health professionals who observe ADEs in practice that may be related to drugs submit a report to the FDA or the drug manufacturer. The FDA's Adverse Event Reporting System (AERS), published in quarterly extracts, helps monitor the safety of prescription drugs.

Of the adverse drug reactions reported to the FDA, 7,111 involved children age 2 or younger. Almost all (94%) reports were prepared for the FDA by drug manufacturers, not health professionals.

The authors determined whether the suspected drug was transmitted from mother to infant during pregnancy, delivery or lactation, or if the infant was administered the drug directly. Also, they divided reactions into four subgroups of decreasing severity: death; congenital malformation or disability; serious but nonfatal reactions; and either "other" or "no outcome given."

On average, 243 deaths per year were associated with adverse drug reactions in infants and children under age 2, with an increasing trend from less than 200 in 1998 to 326 in 2000. Seventeen drugs (less than 1% of the 1,902 drugs identified in adverse drug reports) were associated with 54% of serious or fatal ADEs. These 17 drugs met the following criteria:

- identified as a primary suspect in at least 20 reports;
- administered directly to infants; and
- related to death or a "serious adverse event."

The drug *palivizumab*, despite being on the market for only 24 of the 38 months in the study period, topped the list of drugs related to ADEs, and was linked to 28% of all cases and 15% of all deaths. Palivizumab is used for prevention of severe respiratory infections in high-risk patients. Note the key word, "prevention": The drug, known by the brand name Synagis, is not used for treating a pre-existing illness. A list of the top 17 drugs, along with their classes, is shown in Table 1.

Table 1: Drugs Most Commonly Suspected in Fatal or Serious Outcomes

Drug or Product	Common Brand Names	% of Outcomes	FDA Drug Class
Palivizumab	Synagis	27.9	Immunologics
Cisapride	Propulsid	4.0	Acid/peptic disorders
Indomethacin	Indocin	3.8	NSAIDs
Nitric oxide	INOmax	3.4	Medicinal gases
Azithromycin	Zithromax	2.1	Lincosamides/macrolides
Acetaminophen	Tylenol, Infantol, Anacin, Feverall	1.6	General analgesics
Fluconazole	Diflucan	1.5	Antifungals
Ibuprofen	Advil, Provel, Motrin, Excedrin	1.3	NSAIDs
Respigam	Respigam	1.3	Immune serums
Ceftriaxone	Rocephin	1.1	Cephalosporins
Cefaclor	Cefaclor, Ceclor	1.0	Cephalosporins
Cefoperazone	Cefobid	1.0	Cephalosporins
Zidovudine	Zidovudine, AZT, Retrovir	1.0	Antivirals
Erythromycin	Emgel, Akne-Mycin	0.9	Lincosamides/macrolides
Vincristine	Vincristine, Oncovin	0.8	Antineoplastics
Sevoflurane	Ultane, Sevorane	0.8	General anesthetics
Vancomycin	Vancocin	0.8	Miscellaneous antibacterials

*Maternal drug exposure excluded from list.

Deaths linked to adverse events were far more likely in the first months after birth (41% in the first month), and ADEs overall were more likely in males than females (57% vs. 43%, respectively). Most ADEs were considered "severe," with 61% categorized as death, disability, congenital anomaly, hospitalization or other serious outcomes; 84% of deaths linked to ADEs occurred in the first year of life.

In 24% of cases, drugs were administered to the mother, then transferred to the infant through pregnancy, lactation, etc. In these cases, congenital deformation or disability was the most likely outcome (41% of events). Approximately 25% of these drugs were intended to prevent the transmission of HIV.

Of the nearly 2,000 "drugs" listed linked to ADEs, types included: therapeutic drugs; vaccines; biological products; nontherapeutic chemicals; over-the-counter medications; dietary supplements; vitamins and minerals; illegal substances; and blood products.

While these results may seem frightening enough, the authors bring up an even more disturbing point. "It is almost certain that the overall total of death and serious injury associated with drug adverse events is substantially higher than reported here. According to a recent FDA report, 'About 90% of serious or fatal adverse drug reactions are never reported. Some studies have found reporting rates around 1%.'"

The researchers conclude, "The results of this study underscore the need for additional testing in the youngest pediatric patients and for greater vigilance in the use of higher risk drugs and in medications for pregnant or lactating women."

Editor's note: The full text of this study can be accessed for free online at www.pediatrics.org/cgi/reprint/110/5/e53.

Reference

Moore TJ, Weiss SR, et al. Reported adverse drug events in infants and children under 2 years of age. *Pediatrics*, November 2002:110(5), p. e53.

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