Pediatric Pharmacotherapy

A Monthly Review for Health Care Professionals of the Children's Medical Center

Volume 2, Number 3, March 1996

Preventing Pediatric Poisonings

- Overview
- Current Statistics
- Preventing Accidental Poisonings
- Poison Prevention Resources
- References

Pharmacology Literature Reviews

- Clonazepam pharmacokinetics in children
- Dornase alpha Review
- Enhancing Cyclosporine Absorption
- Famotidine in children
- Pain management and conscious sedation
- Respiratory depression with Opiates
- Review of Surfactant

Formulary Update

On September 16, 1961, Congress passed a joint resolution authorizing the President of the United States to annually proclaim the third week of March as National Poison Prevention Week. The purpose of this law is to provide an ongoing source of public education regarding the dangers of accidental poisonings and methods to prevent them. This year's Poison Prevention Week will be March 17th -23rd. The motto for this campaign is "Keep Safe: Keep it Up and Away," focusing on the need for proper storage of medications and hazardous household products. As in previous years, the Pharmacy Department of the University of Virginia Medical Center and the Blue Ridge Poison Control Center will be participating in activities designed to educate families in Charlottesville and the surrounding areas about the dangers of accidental poisonings. The purpose of this review is to call attention to these activities and provide basic poison prevention information for health care professionals who care for children.

Current Statistics

The combined efforts of health care professionals providing poison prevention education and governmental regulations such as the Poison Prevention Packaging Act of 1970 have made a significant impact on the number of poisoning deaths in the United States. The National Center for Health Statistics reports a decline from 450 childhood deaths due to ingestion of household toxins in 1961 to only 42 in 1992.[1]
Additional information is available from the American Association of Poison Control Centers (AAPCC). The Toxic Exposure Surveillance System was originated in 1983 to collect information on poisonings from the members of the AAPCC.[2] Each year, a report summarizing data collected from the previous year is published in The American Journal of Emergency Medicine. For 1994, only 26 fatalities due to poisonings were reported in children under six years of age. Despite the reduction in deaths due to poisonings, there is still a significant number of potential exposures. More than one million poison exposures occurred in children less than six years of age during 1994, accounting for 54% of all exposures. In contrast, only 121,512 poison exposures were reported in children aged six to 12 years. In addition to the morbidity and mortality associated with poisonings, these events also result in a significant use of health care resources. Approximately 24% of all poisonings (adult and pediatric) reported in 1994 required management in a health care facility. Three percent of poisonings resulted in admission to a critical care unit.[2]

Preventing Accidental Poisonings

There are several basic methods for reducing the risk of poisonings in the home. Tenebein and Rodgers have developed a simple method for poison prevention education: the four A's- increasing awareness, decreasing attractiveness, decreasing accessibility, and decreasing availability. [3] The age group most at risk for accidental ingestions are children between the ages of one to three years;[4] and therefore, a discussion of poison prevention strategies should be conducted well before the child begins to crawl or walk. The following list of questions may be useful for initiating a discussion with the families of young children:

1. Do all potentially harmful products in your home have child-resistant caps? Medications, as well as most household cleaning supplies, can be purchased in containers with child-resistant packaging. Particular attention should be given to iron supplements. Iron is the most common cause of death due to poisonings in children under six years of age.[3,5] In addition to prescription medications, families should be made aware of the potential risk associated with herbal remedies and nonprescription medications.[6,7]
2. Are all potentially harmful products in their original containers? Transferring products to other containers may delay identification of a toxic substance in a poisoning. In addition, storage of hazardous products in the same type of storage containers used for food may confuse young children.

3. Are all potentially harmful products stored out of the reach of children? A locked cabinet is the best method for storing medications and hazardous substances. Don't forget to check the garage and work areas where children may play.
4. Do you discard all medications you no longer need? Flush all old medications down the toilet. When purchasing hazardous household chemicals, buy only what you need and discard the rest.
5. Do you always measure all medication doses carefully? Teach your children to treat medications with respect; never refer to medications as "candy."
6. Do you know the phone number for the nearest Poison Control Center and emergency department? Place these numbers on or near the phone. Make sure baby-sitters or other care providers know how to contact these agencies.
7. Is syrup of ipecac available in the home and other places visited by the child? When used on the recommendation of a poison control expert, ipecac can significantly reduce the toxicity associated with many medications and hazardous substances.[8,9]

Improper storage of medications and hazardous substances remains one of the major factors leading to childhood poisonings. In a recent study of antecedents to pediatric ingestions, Brayden and colleagues[10] found that improper storage was cited in 51% of 50 consecutive cases reported to the Middle Tennessee Poison Center. Distraction and improper monitoring of the child was also reported by 39% of the care providers. Behavioral attributes in the child which may have been a factor included noncompliance with parental instructions (reported in 44% of cases), imitation of observed behavior (26%), and curiosity (33%). It has also been suggested that hyperactive, impulsive children and those recently exposed to stress may be at greater risk.[11] It should be noted that poison-warning stickers introduced in the 1970's, such as Mr. Yuk, have failed to provide a deterrent effect in clinical trials and should not be relied upon as a solitary prevention strategy.[12]

Educational efforts must be continued throughout childhood. It has been estimated that nearly 30% of all children less than six years of age who experience an accidental ingestion will be involved in at least one more episode before the age of six.[13] In a recent study by Woolf and colleagues[14], the authors found a 3.7% recurrence rate within a 3-month surveillance period. These authors also demonstrated the limitations of follow-up intervention following a poisoning incident. The rate of parental compliance with preventative strategies was no different in those parents who received a mailed packet of information on poison prevention than the group of parents who did not receive follow-up information. Temple[4] has suggested an outline for incorporating poison prevention information into routine pediatrician visits.

While households with small children are often the focus of poison prevention education, it is estimated that 1/5 of all childhood poisonings occur outside the home. Grandparents and other family members should be aware of the need to store medications and hazardous substances appropriately, both at home and

when visiting children.[1] Providers of day-care facilities and pre-schools also should be in compliance with poison prevention techniques.

Poison Prevention Resources

Many excellent resources are available for counseling families with young children on methods to reduce the potential for poisonings in their homes. Poison prevention posters and a pamphlet on storing hazardous substances may be obtained from the Poison Prevention Week Council (phone 301-504-0580). A booklet entitled "Preventing Accidental Poisonings" and a brochure, "Stop Poisonings," are available from the National Safety Council (phone 800-621-7619). Information on basic first aid tips and choking prevention are available from the American Academy of Pediatrics. You may place an order for these educational materials by phone 800-433-9016, by fax 1-708-22801281, or by mail to AAP Publications, PO Box 927, Elk Grove, IL 60009-0927. Copies of several different brochures and pamphlets will be available for UVA patients at the Primary Care Center Pharmacy and the Barringer Pharmacy throughout Poison Prevention Week.

The successful reduction in childhood poisonings has been the result of a multifaceted approach. Legislative measures, such as those requiring child-resistant packaging, as well as improvements in toxicology reference sources, and an increase in parental education have played a role in this success.[15] Continued efforts are necessary to further reduce the incidence of accidental poisonings in children.

References

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Pharmacology Literature Review

Clonazepam Pharmacokinetics in Children

Clonazepam is a benzodiazepine used for the treatment of refractory seizures. Although this drug has been in use for many years, little is known about its disposition in pediatric patients. In this study, the pharmacokinetic properties of clonazepam were studied in 10 children with epilepsy (aged 2-18 years). The authors attempted to control dosing and serum sampling times, but were limited by their small sample size. As anticipated there was considerable variation among the patients studied, with clearance values ranging from 7 to 64 ml/hr/kg. The two major steps in clonazepam metabolism, nitroreduction and acetylation, appear to be genetically determined and may explain this variation in clearance. Walson PD, Edge JH. Clonazepam disposition in pediatric patients. Ther Drug Monitor 1996;18:1-5.

Dornase alfa Review

This review focuses on the basic pharmacology of dornase alfa, also known as recombinant human DNase I. While more in-depth reviews of this therapy are available, this brief article may be more useful for health care professionals in training. Of particular value for clinicians in practice, the article contains a section on patient instructions as well as pharmacoeconomic issues which may be discussed with patients and their families before starting therapy. Witt DM, Anderson L. Dornase alfa: A new option in the management of cystic fibrosis. Pharmacotherapy 1996;16:40-8.

Enhancing Cyclosporine Absorption

The authors present some interesting findings regarding the concomitant use of aqueous vitamin E with oral cyclosporine. Twenty-six liver transplant patients (7 children and 19 adults) who were unable to achieve therapeutic cyclosporine serum concentrations on standard dosages were given 6.25 IU/kg of a water-soluble vitamin E preparation (Liqui-E®), administered with their cyclosporine dose every 12 hours. In the children studied, the average cyclosporine dose required was reduced from 78.6±34.1 to 53.7±35.0 mg/kg/day ($p<0.02$). Trough serum cyclosporine concentrations rose from 732±187 to 1,052±166 ng/ml ($p< 0.01$). Even greater benefit was observed in the adult patients. The need for less cyclosporine resulted in an estimated daily savings of 26%. Pan S, Lopez RR, Sher LS et al. Enhanced oral cyclosporine absorption with water-soluble vitamin E early after liver transplantation. Pharmacotherapy 1996;16:59-65.

Famotidine Disposition in Children

The pharmacokinetic and pharmacodynamic properties of famotidine, an H_2-antagonist, were studied in 12 children between the ages of 1 and 13 years. The mean volume of distribution for the sample population was 2.4±1.7 L/kg, with an elimination half-life of 3.2±2.0 hours, and a clearance of 0.70±0.34 L/hr/kg. These values are similar to those reported for adults. Approximately 73% of the dose was excreted unchanged in the urine within 24 hours. Pharmacodynamic evaluation revealed a mid-point (50% of maximal effect) at a serum concentration of 26.0±13.2 ng/ml. James LP, Marshall JD, Heulitt MJ et al. Pharmacokinetics and pharmacodynamics of famotidine in children. J Clin Pharmacol 1996;36:48-54.

Pain Management and Conscious Sedation

This timely review covers the broad scope of medications used for providing analgesia and sedation in children. A brief description of the pharmacology of each agent is provided, as well as a discussion of the use of assessment tools and the sedation monitoring guidelines developed by the American Academy of Pediatrics. Concise tables provide dosing recommendations for infants and young children, as well as adolescents. Poon CY. Pain management and conscious sedation for the pediatric patient. **J Pharm Pract 1996;9:57-74.** (Editor's note: This journal is available from the UVA Drug Information Center.)

Respiratory Depression with Opiates

The results of one institution's ongoing adverse medication reaction surveillance system are presented. Fifteen cases of opiate-induced respiratory depression were reported over a three-year period in a London children's hospital. The authors reviewed these cases and identified several predisposing factors: age less than one year, excessive dosage, concurrent respiratory, hepatic, or renal illness, use of other respiratory depressants, and medication errors. Gill AM, Cousins A, Nunn AJ et al. Opiate-induced respiratory depression in pediatric patients. Ann Pharmacother 1996;30:125-9.

Surfactant Review

The author reviews 11 randomized clinical trials which have been published comparing surfactant preparations: synthetic surfactant (Exosurf®), natural surfactant beractant (Survanta®), calf lung surfactant extract (Infasurf®), and porcine-derived surfactant (Curosurf®). Combining the results of seven trials comparing synthetic surfactant with natural surfactant beractant revealed a significant benefit with the natural product in reducing oxygen requirements as well as a reduced risk of mortality, retinopathy of prematurity, and bronchopulmonary dysplasia. In the two trials comparing synthetic surfactant with calf lung surfactant extract, similar trends were found, but did not achieve statistical significance. The remaining trials compared natural products and found little difference in treatment outcomes. Halliday JL. Natural vs synthetic surfactants in neonatal respiratory distress syndrome. Drugs 1996;51:226-37.

Formulary Update

The following actions were taken by the Pharmacy and Therapeutics Committee at their meeting on 2/23/96:

1. Bicalutamide (Casodex®) was added to the formulary. This agent is an antiandrogen indicated for the treatment of prostate cancer.

If you have comments, questions, suggestions, or would like to be included on our mailing list, please send a note to Marcia Buck, Pharm.D., Box 274-11 Children's Medical Center at the University of Virginia, Charlottesville, VA 22908

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Revised: April 9, 1996
