Pediatric Pharmacotherapy

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

Volume 5 Number 10, October 1999

Preventing Medication Errors in Children

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Literature Reviews:

Formulary Update

A recent review conducted by a national organization of malpractice insurers revealed that although pediatrics was ranked sixth out of the 16 medical specialties evaluated for the number of medication-related malpractice claims, it ranked second in the amount of damages awarded. On average, pediatric settlements were twice that of any other medical specialty.[1] These numbers are hardly surprising. The significance of an error in a child is magnified by the implications of life-long medical expenses and loss of productivity.[2] Reducing or eliminating sources of medication errors is paramount to providing optimal pediatric health care.

Errors in prescribing

The pediatric population encompasses a very heterogenous group, from the smallest premature infant to fully-grown adolescents. As a result, doses of the same drug within one institution's pediatric patient population may vary by more than ten-fold. When dosages must be calculated by patient weight, and very small amounts of drug are needed, there is considerable risk for mathematical errors.[3]

Several studies have documented the risk for mathematical errors by prescribers.[4-8] Lesar performed a retrospective review of 200 medication orders involving dosage calculations for both adults and children in a 631-bed tertiary care teaching hospital.[7] A significantly greater number of errors involved pediatric patients than adults (4.94 errors per 1000 patient days vs. 0.13). Of those errors made in children, 56.1% would have resulted in an overdose if not detected. The most frequent type of serious error was decimal point misplacement, occurring in 27.9% of the pediatric errors reported. Failing to divide the total daily dose into individual doses occurred in 16.3% of the cases.

Rowe, Koren, and Koren examined the same problem, but through different means.[8] In 1998, they published the results of a standardized test evaluating the ability of medical residents to determine the appropriateness of drug dosages for children. The authors compared results from 1993 (34 residents) and 1995 (30 residents). Nineteen of the residents in the first examination and nine in the second made at least one error, showing a significant decrease ($p = 0.03$). The total number of wrong calculations also decreased, with 26 in the 1993 test and only 13 in the test given two years later ($p = 0.01$). The authors speculate that these improvements may have been the result of a concerted effort to train residents in dosage calculations. Serious errors, however, showed no decline. Three residents in 1993 and four in 1995 made a ten-fold dosing calculation error on the examination, despite the use of calculators. The examinees also frequently failed to recognize doses deliberately set to be excessive for the test patient.

Reducing prescribing errors requires careful attention to detail (Table). Decimal point errors are particularly dangerous for drugs with significant dose-related toxicity, such as morphine and other opioids. Errors also have been made when doses are not rounded to the nearest whole number. This can be confusing to pharmacists and nurses if the unrounded dose looks like the standard adult dose. For example, a medical resident calculating a 10 mg/kg acetaminophen dose for a 3.25 kg infant might order 32.5 mg of acetaminophen. To someone accustomed to seeing adult orders, this could easily be misread as one adult 325 mg dose. Transcription errors also are more frequent in pediatrics; where, depending on the prescriber, drugs may be ordered in milligram or gram amounts. In other cases, errors have been made when trailing zeros are used (e.g. an order for 1.0 mg is misinterpreted as 10 mg).

Table. Tips for Prescribers

- know the patient's current therapy, identify potential allergies and drug interactions
- use an accurate patient weight; write or enter the weight as part of your order
- use generic drug names
- do not abbreviate drug names
- watch for "look alike" and "sound alike" drug names (e.g. Celebrex® and Cerebyx®, prednisone and prednisolone)
- check doses in a current dosing reference
- round doses to nearest whole number, when appropriate
- use leading zeros (e.g. 0.1 mg)
- eliminate trailing zeros (e.g. 15.0 mg)
- double-check all calculations and units
- give specific dosing instructions; avoid prn or titrate as instructed
- minimize the use of verbal orders
- discontinue orders no longer needed

Errors in preparation and administration

In some cases, the order may be correct, but the dose prepared is incorrect. For example, some commercially-available products, such as digoxin and phenytoin, are available in "pediatric" strengths that may be confused with the more frequently used "adult" preparations by those

unaccustomed to working with pediatric patients. The use of extemporaneous dosage formulations and restrictions on intravenous fluids causing the need for highly concentrated drug products can also lead to errors. Compounding dosage forms can result in mathematical errors in determining the correct amount of drug or diluent to use.

Administration errors are often linked to inadequate information at the patient's bedside. Incomplete medical orders or patient charts can cause clinicians to miss allergies or administer drugs incorrectly. Use of the wrong route (e.g. an intramuscular dose given intravenously), administration of an incorrect dose (e.g. giving a full tablet when the order called for only ½), and administration of a dose at an incorrect time are some of the more common errors at the bedside.

System changes for preventing errors

Recently several professional organizations, including the American Academy of Pediatrics[1] and the Pediatric Pharmacy Advocacy Group,[9] have published guidelines on reducing pediatric medication errors. Both organizations drew heavily from an earlier document published by the American Society of Hospital (now Health-System) Pharmacists.[10] All of these sources recommend following the same basic tenets:

√ educate health care providers

√ use technologic advances to reduce errors, such as computerized prescriber order-entry and automated dispensing devices

√ implement policies to enforce appropriate prescribing and accurate drug preparation and administration

√ develop multidisciplinary continuing quality improvement programs to oversee pediatric drug administration.

Educating health care providers about the need for accuracy in dosage calculations and providing them with current dosing references are some of the most important steps to reduce drug errors. Several studies have documented the impact of educational programs on reducing the frequency of calculation errors made by medical residents.[6,7] The need for educating those in training, however, extends to more than physicians. Early in their training, pharmacy students and residents, as well as nursing students, should be taught the importance of dosing pediatric patients according to patient weight. Educational programs should also be developed for clinicians already in practice. The Pediatric Pharmacy Advocacy Group recommends training programs for health care providers of all disciplines which encourage communication among care providers and build a team philosophy.[9]

While education plays a major role in reducing errors, the development of systems designed to prevent errors, such as physician order-entry, computer-based dose checking, drug interaction alerts, and on-line drug information also should be used to prevent problem orders from reaching the dose preparation stage. The adoption of technologic advances that allow greater dosing accuracy (e.g. infusion pumps and intravenous compounding devices) should be considered vital in reducing drug preparation and administration errors.

Drug prescribing and administration policies should reflect the need for increased safety in pediatrics. All dosages should be clearly and accurately labeled. Whenever possible, drugs

should be provided in ready-to-administer forms, such as oral syringes and cups and intravenous syringes, rather than a multidose supply. Oral dosages should be distinctly different than intravenous products. Many institutions use only amber or specially-colored containers for oral products. Oral syringes should not be compatible with any intravenous set or needle-less system that might encourage inadvertent intravenous drug administration.

In addition to these precautions, the use of floor stock and verbal orders also should be kept to a minimum to allow pharmacists to provide an additional check. The value of pharmacist participation on rounds and in reviewing medication orders has been well described.[2,11,12]

Quality assurance

Periodic review of drug administration practices, as well as an analysis of any error committed, is necessary to develop optimal patient care. Every institution should have a quality assurance plan in place which details the process for responding when an error has been made and methods for counseling the health care providers involved. Committees formed to address these issues should include representatives of all disciplines involved in medication ordering, preparation, and administration.

Summary

Preventing medication errors should be a focus of all pediatric health care providers. Education, implementation of policies to safeguard prescribing, preparation, and administration of medications, and periodic review are needed to ensure that the likelihood of committing an error is kept at a minimum.

References

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Literature Review

Cyclosporine pharmacodynamics

The relationship between age and the degree of immunosuppression caused by cyclosporine was assessed in this *in vitro* study. Fifty-six volunteers were stratified by age into 4 groups: infants, children (<5 years), preadolescents (< 13 years), and adults. Peripheral blood monocytes from these subjects were collected and cultured with standardized concentrations of cyclosporine. Data from the 41 subjects completing the study revealed a distinct relationship between age and peripheral blood monocyte proliferation and interleukin-2 expression. Monocytes from infants demonstrated a much more profound response to cyclosporine than did cells from the three older groups, suggesting a potential need to reduce cyclosporine dosing in infants. Marshall JD, Kearns GL. Developmental pharmacodynamics of cyclosporine. **Clin Pharmacol Ther 1999;66:66-75.**

Methylphenidate pharmacokinetics

Population pharmacokinetic modeling techniques were used in this study in an attempt to isolate sources of variation in patient response. The authors studied methylphenidate serum samples in 273 children between 5 and 18 years of age. A nonlinear regression model was used, assuming a one-compartment model with first-order absorption and elimination. According to this model, the average elimination half-life of methylphenidate in the study subjects was 4.5 hours and the clearance was 90.7 ml/min/kg. As expected, weight and age were the primary factors determining variation in pharmacokinetic response. While the main purpose of this study was to provide basic information on methylphenidate, it also serves as an example of the benefits of population pharmacokinetic methodologies in children. Shader RI, Harmatz JS, Oesterheld JR, et al. Population pharmacokinetics of methylphenidate in children with attention-deficit hyperactivity disorder. J Clin Pharmacol 1999;39:775-85.

Phenothiazines in Children

The authors of this review focus on the potential risks of phenothiazines as sedatives in young children. Two agents within this therapeutic class, chlorpromazine and promethazine, have been used for many years in children. Over the past decade, there has been increasing concern over the potential for respiratory depression with these agents, particularly when used in the office or home setting. The authors propose that the availability of newer drugs that can be more easily titrated and, when necessary, reversed has eliminated the need for phenothiazines in young children. They cite a number of case reports of phenothiazine-induced toxicity as supporting evidence, including a case reported by clinicians from UVA. The authors also include a discussion of the management of phenothiazine overdose. Dyer KS, Woolf AD. Use of phenothiazines as sedatives in children. What are the risks? **Drug Safety 1999;21:81-90.**

Propafenone during CVVH

The removal of propafenone was evaluated in this case report of a 3 year old child receiving continuous venovenous hemofiltration (CVVH). The patient was placed on propafenone for junctional ectopic tachycardia which developed after surgical repair of a congenital cardiac defect. She received a loading dose of 1 mg/kg followed by a maintenance infusion ranging between 2-4 mcg/kg/min for a period of two weeks. At that time, continued low cardiac output led to renal and hepatic failure, necessitating CVVH. Serial measurements of serum propafenone and 5-hydroxypropafenone revealed no significant removal by CVVH. Her mean clearance was 1 L/kg/hr, similar to the values reported previously in the literature for patients without renal or hepatic disease. The authors concluded that dosing should be based on suppression of the arrhythmia and the presence of adverse effects, and should not be arbitrarily adjusted because of CVVH. Seto W, Trope AE, Gow RM. Propafenone disposition during continuous venovenous hemofiltration. **Ann Pharmacother 1999;33:957-9.**

Formulary Update

The following actions were taken by the Pharmacy and Therapeutics Committee at their meeting on 9/24/99:

1. Calfactant (Infasurf®; Forest Labs) was added to the formulary for the prevention and treatment of respiratory distress syndrome in premature neonates.
2. Beractant (Survanta®; Ross Labs) was removed from the formulary.
3. A controlled release formulation of oxycodone (Oxycontin®; Purdue Frederick) was also added to the formulary. Its use is restricted to the Acute Pain Service, the hematology/oncology division, and prescribers at VASC for patients unable to tolerate morphine.
4. Tannic acid suppositories were not included on the formulary, but can be prescribed by selected physicians.
5. Upon recommendation of the hematology/oncology subcommittee, liposomal doxorubicin (Doxil®; SEQUUS) was added to the formulary, but restricted to the

treatment of Kaposi's sarcoma and refractory metastatic ovarian cancer. Liposomal daunorubicin (DaunoXome®; NeXstar) was removed from the formulary. An intravenous formulation of allopurinol (Aloprim®;NABI) was added to the formulary, restricted to the pediatric and adult oncology services. Letrozole (Femara®; Novartis) was added for the treatment of metastatic breast cancer.

If you have any comments or would like to be on our mailing list, please contact Marcia Buck by mail at Box 274-11, University of Virginia Medical Center, Charlottesville, VA 22908 or by phone (804) 982-0921, fax (804) 982-1682, or e-mail to mlb3u@virginia.edu.
