Medicine Use in Children: A Critical Area

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Children are particularly a challenging group of patients when trying to ensure the safe use of medicines. Their variable weight, body surface area and organ system maturity affect their ability to metabolize and excrete medications. In addition, there are few standardized dosing regimens for children, with most medication dosing requiring body weight calculations. These challenges in pediatric medication use contribute to an increased risk of medication errors including serious drug dosing errors. This manuscript addresses the pediatric dentists to focus on the issues related to pediatric medication.

***Keywords**: Drug dosing errors, Medication errors, Pediatric medication errors, prescribing errors, safe prescribing, pediatric prescribing.*

***Abbreviations:** **IOM**–Institute of Medicine, **USP**–United States Pharmacopeia, **SDR**–Safe dose range, **CPOE**–Computerized physician order entry, **CDSS**–Clinical decision support systems.*

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INTRODUCTION

Medication mistakes (type or dosage) are the most common[1] and the most preventable medical mishaps that can harm the pediatric patient during treatment.[2] Pediatrics has been ranked sixth among other specialities in regard of medication errors.[3,4] The United States Pharmacopeia (USP) defines medication errors as any preventable event that may cause or lead to an inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient or consumer.[5]

Medication errors are classified as physician related, pharmacist related, nurse related and patient related. Prescribing errors, transcribing errors, dispensing errors and administration errors, etc are the types of medication errors.[6,7] In pediatrics, prescribing error is the most common type of medication setback.[8,9,10] Most medications for children are prescribed on the basis of patient weight, which requires practitioners to calculate a patient specific dose and frequency regimen for each medication. Therefore, increasing the likelihood of mistakes. [11]

Every health care provider has an occasional bad day or lapse in personal performance that could result in a medication error and pediatric dentists are no exception. The aim of this article is to highlight the critical areas of medicine use in pediatric patients. Such that potential pitfalls are identified and pediatric dentists practice safe prescribing.

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Children are a challenging group

Children are at a greater risk than adults for medication errors because childhood is a period of maturation. Pharmacokinetic and pharmacodynamic components of drug response change from birth onwards because of organ maturation, changes in body composition and enzymology. Dosing must reflect these changes. The range of dosages in pediatrics is broad compared to adults dosages that are more standard. Determining pediatric dosages can be complicated because of the need to calculate them according to the child's weight, body surface area and clinical condition. The ability of the child to manage different dosage forms also changes. Their developmental limitations affect their ability to communicate and self-administer medications.[12,13]

There is lack of evidence-based data in children to establish efficacy, safety and more specifically, optimal dosing procedures. Lack of data can lead to the creation of arbitrary therapeutic ranges.

Research has identified children receiving chemotherapy;[14] IV medication;[14,15]children who are in ICUs, especially neonatal ICUs;[16,17,18] children who are seriously ill, between the hours of 4 AM and 8 AM or on weekends,[19] children younger than two years of age[19] and children whose weight has not been documented[20] to be the most vulnerable group to medication errors.

THE INTRICACIES OF PEDIATRIC DRUG DOSING

PEDIATRIC DRUG DOSAGE RULES

When to use? It is often unclear when to switch from weight-based dosing (pediatric) to daily dosing (adult).

Standard pediatric-dose conversion formulas can be used in children 12 years of age and younger and in those weighing less than 40 kg.[21,22]

Which one to use? Drug dosage rules are based on age, weight and body surface area. Almost all pediatric drug dosage rules use percentage of adult dose to calculate an appropriate child's dose, with mg/kg regimen being the exception. Despite disadvantages mg/kg regimen has widespread popularity.[23,24] It is more advisable to base one's calculation on the ideal weight for the child's height and age.[25] (Refer Table 1)

TABLE 1. [58,59]

BASED ON AGE	**Fried's Rule**	Age in Months x Adult Dose ÷150
	Young's Rule	Age in Years x Adult Dose ÷ Age + 12
	Dilling's formula	Age in years x adult dose
BASED ON BODY WEIGHT	**Clark's Rule**	Weight in lbs or kg x Adult dose ÷ 150 lbs or 70 kgs.
	Penna's Formula	Adult dosage x child's weight ÷ child's weight/2 + 30.
	Salisbury's Formula	Children weighing less than 30 kg = weight x 2 = % of the adult dosage. Children weighing more than 30 kg = weight + 30 = % of the adult dosage.
	Mg/kg regimen	*Ratio-proportion method:* - multiply the means and the extremes (eg-3 : 4 = *x* : 8) *Formula method*: D/H x Q = X D - dosage desired or ordered; H - what is on hand (available); Q - unit of measure that contains the available dose. X - The unknown dosage you need to administer.
BASED ON BODY SURFACE AREA	A nomogram or fomula can be used to determine BSA.	$\frac{\text{BSA of the child x adult dose}}{1.73m^2}$

MATHEMATICS IN PEDIATRIC PRESCRIBING

Almost all pediatric medications require a mathematical calculation, one that may be complex. The most common calculations involve fractions, percentages, decimals and ratios. To prescribe medications to a pediatric patient using mg/kg regimen the prescriber has to perform multiple tasks. Accurate weight should be obtained and correctly transcribed. The weight in pounds may need to be converted to kilograms. Rapid weight-based calculations must be done and the correct preparation and concentration (liquid, chewables, and tablets) of the medicine must be included in the dosage calculation. Then the total daily dose may need to be divided into multiple doses to obtain the appropriate frequency for the medication.[14,26,27] Thus, the prescriber has to compute, convert, conceptualize, and critically evaluate to ensure safe prescribing. [27]

Example 1: Calculate the dose of amoxicillin suspension in mls for dentoalveolar abscess for a child weighing 22 lbs. The dose required is 40 mg/kg/day divided BID and the suspension comes in a concentration of 400 mg/5 ml.

Step 1: Convert pounds to kg:	22 lbs x 1 kg/2.2 lbs = 10 kg
Step 2: Calculate the dose in mg:	10 kg x 40 mg/kg/day = 400 mg/day
Step 3: Divide the dose by the frequency:	400 mg/day ÷ 2 (BID) = 200 mg/dose BID
Step 4: Convert the mg dose to ml:	200 mg/dose ÷ 250mg/5ml = 4 ml BID

SAFE DOSE RANGE (SDR): Many of the medications used in pediatrics have a therapeutic range or safe dose range (SDR). The drug manual provides the "range" information, i.e., the "minimal" and "maximum" limit.[29] (e.g. Amoxicillin 25-50 mg/kg). Many guidelines recommend the lower limit, however the clinical condition dictates the appropriate dosage.[28] The prescriber should be cautious and prescribe drugs within this safe dose range.

STANDARDIZATION OF PEDIATRIC DOSING GUIDELINES

A variety of dosing guidelines is published for pediatric use, with lack of standardized weight-based dosing range. Inconsistencies in the dosing guidelines make defining, under doses and overdoses problematic.[26] Standardization of the various sources of pediatric dosing guidelines, with current and comprehensive dose information would resolve this problem.[24, 29]

CHALLENGES IN PEDIATRIC FORMULATIONS OR DOSAGE FORMS

Potential pediatric patients may include neonates, newborn, toddlers, young children and adolescents and as such, will have widely varying needs. Liquid medicines are usually recommended for infants and younger children. The use of excipients can be harmful when given to children.[30,31,32] Tablets and capsules are more convenient for adolescents. Crushing or splitting some tablets, or opening capsules destroys their release properties and can cause dose inaccuracies. The resulting powder is often mixed with food or beverages, potentially affecting drug absorption.[33] Many of the dosage forms designed for adults, such as granules, fast dissolving 'melt' formulations, oro-dispersible tablets, buccal gels and transdermal patches, would also benefit children if they contain an appropriate pediatric dose. Chewable tablets should be avoided during the transition from primary to permanent teeth. Thus, there is a pressing need for a variety of dosage forms for children, to satisfy their clinical need.[12,26,34]

OFF-LABEL PRESCRIBING

It is the prescription of a registered medicine for an use, which is not included in the product information. This practice is common; with rates up to 40% in adults and up to 90% in pediatric patients.[35] Most clinicians perceive off-label prescribing as appropriate and believe that the benefits outweigh the risks.[36] Legislative and regulatory bodies should take initiative in inducing the pharmaceutical industry to undertake more research in medicine use in children.

Eventually these initiatives may reduce the need to consider off-label prescribing.[37] Until such time, practitioners are expected to "use their professional judgment" to determine the appropriateness of off-label use in individual patients.[38]

CAUSES OF PEDIATRIC MEDICATION ERRORS

Each step of calculation, prescription writing, transcription, dose preparation, and administration is an opportunity for generating pediatric medication errors. The top 10 causes of pediatric errors identified by the USP are, performance deficit, procedure or protocol not followed, miscommunication, inaccurate or omitted transcription, improper documentation, drug distribution system error, knowledge deficit, calculation error, computer entry error, and lack of system safeguards.[3]

Calculation errors comprise majority of prescription errors. **Tenfold dosing errors in children can easily occur due to a misplaced decimal point or a trailing zero.**[39,40,41] The consequences of such errors include transient renal failure, tachycardia, respiratory failure, and cardiac arrest.[42] Research has found that those who make tenfold calculation errors are also more likely to cause other medication errors.[43] The major problems behind many of the miscalculations are associated with an inability to conceptualize the right mathematical calculation to be performed[44] and understand the mathematical process leading to the solution.[45] A lack of math skills needed to solve the problem[46] specifically, the use of fractions, percentages, decimals, and ratios.[47,48] Inexperience in applying these calculations in the clinical setting[18,19] are the other main reasons for errors during pediatric prescribing.

RECOMMENDATIONS FOR PRESCRIBERS

1) Drug orders should be legible and should contain all components of prescription.[49] 2) Clearly spell The official (generic) or trademarked drug name.[49] 3) Do not use abbreviations. 4) Dosage strengths or concentrations and volumes should be expressed in exact metric units (e.g., mg, units).[49] 5) **A leading zero should always precede decimal expressions less than one (i.e., 0.1 mg), but a trailing zero should never follow a whole number (i.e., 1.0 mg)**[39-41] 6) Calculations used in determining the dose should be included in the medication order.[17] 7) If doses are changed for any patient, new prescriptions should be written and old ones should be canceled.[49] 8) When possible, odd dosages should be rounded-off for more convenient and accurate measurement.[49] 9) Instruct to shake a drug product that is labeled "shake well."[49] 10) Appropriate measuring devices should be recommended for liquid medicaments. The use of household teaspoons and tablespoons should be discouraged because of the variability and resulting inaccuracies. The oral dosing syringe is felt to be the best device for delivery of liquid medication less than 5 ml.[50] 11) The prescriber should also counsel the patient and the caregiver, familiarizing them with the name, indication, route of administration, dose, dose frequency, potential adverse effects, and how adverse effects might be managed for each medication the patient is receiving.[51]

Parents must be reminded to continue drug therapy for the entire period prescribed. Treatment should not be interrupted, even if the child seems to be completely well.

CPOE AND CDSS IN PEDIATRIC MEDICATION

The Institute of Medicine (IOM) report on error in medicine identified computerization of medication prescribing as an important patient safety strategy.[52] The medication use challenges in pediatrics contribute to an increased risk of medication error, hence—Computerized physician order entry (CPOE) and Clinical decision support systems (CDSS) can effectively prevent these errors. Nevertheless, there are many feasibility barriers like the complexity of pediatric prescribing, requirement of large financial resources. Lack of support staff to train and maintain the systems, makes it harder to design and implement CPOE and CDSS systems for pediatric use.[53,54,55]

Preventing pediatric prescribing errors

The first individual who can take steps to prevent the occurrence of a medication error is the prescriber. Therefore, the prescriber has to strictly abide by the elements of a prescription, pursue the prescribers' recommendations and use technologic advances to reduce errors. Regulatory bodies must standardize and make current dosing references available. They must periodically review calculation competency and implement policies to enforce appropriate prescribing. In addition multidisciplinary continuing education programs about pediatric medication errors should be developed.[56,57]

SUMMARY

The pediatric population represents a spectrum of different physiologies. It extends from the very small preterm newborn infant to the adolescent. Pediatric dental patients are often treated with medicines for oral conditions. Hence, pediatric dentists have the moral responsibility to provide the best possible drug treatments for children. It is vital that we gain a better understanding about the intricacies of medication use in children. Future research can shed light on the critical area of medication use in pediatric dentistry. All pediatric health care professionals should prevent medication errors and promote safety of medicine use in children.

Abbreviations: IOM-Institute of Medicine, USP- United States Pharmacopeia, SDR-Safe dose range, CPOE- Computerized physician order entry, CDSS-Clinical decision support systems.

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Table 2. Essentials Of A Pediatric Prescription [49]

Patient's full name
Patient's age (date of birth) and current weight
Information regarding diagnosis and other patient-specific data appropriate to the
circumstance should be included.
Any known allergies should be included.
Drug name, dosage form, and drug strength.
Concentration and quantity should be expressed in metric units.
Include calculations, or at least mg/kg/day dosing, so calculation can be independently double-checked (i.e., amoxicillin 40mg po q 8 hrs (40mg/kg/day). **Doses are often expressed as mg/kg/day or mg/kg/dose, therefore orders written "mg/kg/d" require further clarification from the prescriber.**
Capsules and unscored tablets to be rounded to the nearest whole tablet, scored tablets are rounded to the nearest 1/2 tablet and Liquid medications to be rounded to one decimal place (tenths).
The prescriber's name and contact number should be included.
It should include complete instructions for the patient and or parent/care taker.