Medication Errors: Common Pitfalls and Recommendations in Pediatric Dentistry Practice

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Parallel to the development of new medications for various diseases run the threat of medication errors. These errors though common, very few are fatal and so goes unnoticed. Such errors occurring with pediatric population can be a major predicament. This review aims to address the various parametric variations and considerations in pediatric population so as to minimize medication errors. A detailing about various causes, types and levels of errors, ways of analysing the amount of error and the essential knowledge about prescription writing which could reduce the incidents have been paid attention to. The article also discusses possible recommendations to the stakeholders and caregivers that could encompass the reason of lack of information for the ever-increasing medication errors.

Keywords: *medication, prescription, pediatric, medication errors.*

INTRODUCTION

One of the startling discoveries in today's era is medication that promote healing and reduce suffering. But indeed, thousands of new drugs have been developed recently thereby increasing the risk for medication errors[1]. The phrase "medical error" is a highly detailed umbrella term that covers all errors occurring in the health-care system and one thing to be extremely careful about is that the "trial and error" principle is not acceptable in an extremely vulnerable crowd like the pediatric population[2]. Thus, ensuring medication safety by taking utmost care from the point of hospital admission to the discharge time is a pre requisite[1].

Drug use being an extremely complex process, for its success, according to the 'hedgehog principle', there is a need to 'marry the mechanism of action of drug to the pathophysiology of the disease'[3,4]. Alertness about the need for remedial actions related to drug complexities took a long time even though medical errors are not uncommon[3]. Children are the ones prone to non-serious but usual illnesses which mostly are self-limiting but treated inappropriately with irrational use of antimicrobials leading to serious complications[5]. Optimizing such pharmacotherapy by detailed study of the drug use therapy specifically in pediatric population has become the need of the hour[6,4]. All institutions must have a quality improvement process inculcated which would not only identify but also correct these errors through interventions[7]. For the purpose of this review article, a 'PubMed', 'Scopus', 'Science Direct', 'Cochrane Library' search was done using English as the language. One hundred sixty-seven articles were obtained, out of which, after relating the tittle and abstract to the key words 'medication', 'prescription', 'pediatric', 'medication error' the most relevant 68 full text articles from January 1962 to February 2021 were selected.

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Dose considerations among pediatric population and adult population

Infants and children were once considered to be "miniature men and women" but as rightly brought up Abraham Jacobi, 1830-1919, they definitely are more than that. The dynamic process of maturation wherein there is a substantial change in body proportion and composition constitutes to the differences between the pediatric and the adult populations. Such developmental changes influence the efficacy, toxicity and dosing regimens of medicines used in children. Thus, drilling these changes of growth and making the notable changes to circumvent any drug complications can be one of the many[2].

***Gastrointestinal tract and oral absorption**:* Various factors like gastric acidity, gastric emptying time, gut motility, gastrointestinal medicine-metabolizing enzymes and transporters, secretion of enzymes, first-pass metabolism, diet at different ages and diurnal variations have shown wide number of developmental changes. For example, gastric acid secretion is remarkably less in preterm and term infants. Also, another point worth mentioning is regurgitation of medicines in children due to high gastric reflux[8]. Certain suggestions that must be considered are avoiding the widespread unnecessary use of acid suppressive medications[9]. Additionally, studies have suggested that left lateral positioning (LLP) has resulted in reduction in the total number of reflux episodes. Additionally, 40-degree elevation while administering the medication, reduction or elimination of cow's milk protein in patients having medications, having formula milk with extensively hydrolyzed protein has also shown marked reduction in regurgitation episodes[10].

***Medicine distribution**:* New-borns show a relatively high level of extracellular fluid and less fat contents and this will affect the distribution of various drugs based on their solubility. For an instance, while prescribing antibiotics to infants, like aminoglycoside and cephalosporins which are highly water soluble, a larger dose has to be administered to attain a high plasma concentration. On the other hand, lipid soluble drugs like anaesthetic, sedatives or hypnotics need a very low concentration to attain the effect seen in children and adults[2].

***Hepatic and renal function and the elimination process**:* Proportions of body water, fat, and protein continuously change during infancy and childhood. Growth and development occur particularly rapidly during the first 2 years of life. Body weight typically doubles by 6 months of age and triples by the first year of life. Body surface area (BSA) doubles during the first year[11]. Liver and kidney reach the maximum size only in the first and second year of life and this affects the hepatic and renal function, increasing the half-life and the excretion time. Lipid soluble drugs like paracetamol needs to be metabolised to a more polar and water-soluble drug while water soluble drugs are directly excreted from kidney thus decreasing the half-life and excretion time when compared to the lipid soluble drugs. However, following 2-3 years of age, hepatic and renal function slowly matures posing lesser drug associated risks as compared to early infancy[12].

Another clinical scenario that requires attention in pediatric dental practise are children with natal teeth that interferes with breastfeeding or suggestive of Riga-Fede disease. The extraction of the natal tooth is considered after 10 days of birth. This waiting period is essential for the commensal flora of the intestine to become established and produce vitamin K, which is essential for the production of prothrombin in the liver. However, if the extraction is an emergency, it is advisable to evaluate the need for administration of vitamin K by a paediatrician. Vitamin K (0.5–1.0 mg) is administered intramuscularly to the baby as a part of immediate medical care to prevent haemorrhagic disease of the newborn[13].

***Pharmacodynamics during development**:* Medicine targets, receptors, transporters and channels undergo various developmental changes over a period of time. For an example, new-borns are more prone to opioid related respiratory depression and bradycardia when compared to adults and is the leading cause of infant fatalities. This is basically because of the earlier development of these receptors in the medulla and pons region where the respiratory and cardiovascular centres are located, when compared to the receptors located elsewhere in the body. All these factors bring to the limelight the need for independent studies on pediatric medicines[14].

Levine *et al*[15] highlights several factors that place pediatric patients at increased risk for adverse drug reactions including the varying pharmacokinetic parameters, constant need for calculation of individualized doses based on patient's age, weight (mg/kg), body surface area (mg/m^2), and various systemic conditions. The other factors include lack of standard dosage forms and concentrations, need for appropriate drug delivery systems and published information or FDA-approved labelling regarding efficacy and safe dosing in pediatric population[15].

Medication Errors

Achieving a defined therapeutic outcome, while simultaneously negating the patient's risk is the primary goal of drug therapy. The recent National Audit Commission report marks the Medication errors (7% of all incidents) to be the second most common incident reported[1]. It was Richard Clark in 1910 who published the first study that confined at error rates in clinical diagnosis. "To Err is Human- Building a Safer Health System" released in 2000 gave an estimate of about 44,000-98,000 preventable deaths each year from medical error[16].

Classification of Medication errors:

The classification system based on psychological principles divides errors into mistakes, slips or lapses. It includes:

a. Errors – Forgetting to act as planned/actions intended but not performed. Eg. AZT- intended drug: Zidovudine, mistaken as: Azathioprine or Aztreonam[1,3,17]

b. Mistakes – errors in planning actions. Eg. TIW (thrice a week) misinterpreted and planned for "three times a day" or "twice a week"

c. Knowledge-based errors- lack of knowledge. Eg. Use of penicillin in allergic patients

d. Rule-based errors
   - Bad rules or failure to apply good rules. Eg. Wrong drug dosage
   - Good rules misapplied. Eg. Correct drug but into wrong injecting site

e. Skill-based errors (slips and lapses) – errors in executing correctly planned actions. Eg. When HS for half strength is misinterpreted as 'Hour of sleep'

f. Action-based errors (slips) – Eg. Writing the more familiar chlorpropamide instead of chlorpromazine

g. Memory-based errors (lapsed) – Eg. Giving a drug to a patient with known allergy[1,3].

Types of Medication errors

Following are the common types of errors encountered in practice[1,18-20]

- Prescribing error–Incorrect drug selection, dose, dosage form, quantity, route.
- Improper dose error–Dose greater than or less than the amount ordered by prescriber
- Wrong dosage-form error–Drug product in a different dosage form. Eg. 5ml mentioned as 1 teaspoon
- Wrong drug-preparation error–Incorrectly formulated or manipulated drug product.
- Wrong administration-technique error–Inappropriate procedure or technique. Eg. Heparin to be administered subcutaneously given intramuscularly instead
- Deteriorated drug error–Administration of an expired drug.
- Omission error–Failure in administration of first dose before the next scheduled dose.
- Wrong time error–Medication administered beyond the predefined time interval.
- Unauthorized drug error–Self-medicating a non-authorized/prescribed drug.
- Compliance error–Inadequate drug intake due to inappropriate patient behaviour. Eg. Uncooperative and agitated children, children with high gag reflex
- Monitoring error–Lack of review of appropriateness of administration of medication. Eg. Negligent parent allowing young children to self-administer liquid medications prescribed with specific dosing units.

Aronson[3] in Table 1 lists the causes of medication errors at each stage.

Table 1: Stage of Medications errors

Stage	Cause
Choosing	Inappropriateness, Ineffectiveness, Under-prescription, Over-prescription
Prescribing	Prescription errors like illegibility
Manufacturing	Wrong strength, Ineffective packing, Presence of contaminants or adulterants
Dispensing	Wrong drug, Wrong formulation, Wrong label
Administering	Wrong dose, Wrong route, Wrong frequency, Wrong duration
Monitoring	Incorrect erroneous alterations

Measuring medication errors

Measuring the medication error is the only way of overcoming this issue at the root level. Hartwig, Denger and Schneider[21] defined seven medication error severity levels that are listed in Table 2. Reporting the errors, analysing the cause and structuring a systematic solution can help improve patient's safety and encourage a safe culture[17,22]. Three methods of measuring have been used in most medication error research: spontaneous reporting, chart review and observation[22].

a. Spontaneous reporting: This involves immediate reporting of the incident into the incident chart by the person who witnessed, committed or discovered the error. This method has shown a high level of inefficacy due to underestimation and inability in identifying the error.

b. Chart review: This is only moderately effective as this involves the clinical skill of the investigator who has to constantly review the prescription, prescription chart and make note of the errors.

c. Observation: Constant observation of the prescriber by the investigator, while the prescriber prepares and administers the drug is needed. It has been proven to be a valid method.

Table 2: Levels of Medication errors

Levels	Description
0	Non-medication error occurred
1	Error with no patient harm
2	Error with no patient harm or change in vital signs but with a need for increased patient monitoring
3	Error with no patient harm but with a change in vital signs and increased need for patient monitoring
4	Error with a need for treatment with another drug
5	Error resulting in permanent patient harm
6	Patient death due to error

Prescription errors

Prescription errors were ignored until 1962. Later it was Barker and McConnell in the United States of America (USA) who evaluated the frequency of error and estimated it to be 16 per 100 doses[23]. In 1995, National Coordinating Council for Medication Error Reporting and Prevention was formed. It defines medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the health-care professional patient, or consumer[24].

Prescription error can be encompassed by prescribers and other experts by careful evaluation and monitoring for which the prescribers should be updated about the errors made and the decision taken to overcome complications. Chart review, observations method are ten times more effective than spontaneous reporting[25-27]. Three major interventions strategies can be adopted and monitored that includes use of automation wherever possible, thus reducing complexity; constant education programmes for prescribers and the use of on-line aids or feedback control systems[28,29].

Factors associated with the act of writing a prescription is prescription error, whereas faults due to erroneous medical judgement encompassing irrational prescribing, inappropriate prescribing, under-prescribing, overprescribing, and ineffective prescribing are prescription faults[30,31]. A definition states that 'a clinically meaningful prescribing error occurs when there is an unintentional significant reduction in the probability of treatment being timely and effective or increase in the risk of harm when compared with generally accepted practices'[32].

Prescription writing

Prescription is considered to be one of the most important transactions between the prescriber and the patient. It not only implies responsibility of the health care professionals but also have associated legal implications. Certain recommendations for the elements of a prescription can help avoid many errors. The following elements must be considered as a prerequisite while writing any prescription for the completeness of the same[15]. The Patient's full name, age (date of birth), current weight, known allergies; the prescriber's name and pager or telephone number; diagnosis; drug name, dosage form, drug strength, calculation expressed and the numbers/amounts to be dispensed (expressed in metric units)[33]. Products are to be labelled with complete instructions. Counselling the patient before discharge as well as asking the patient or caregiver to demonstrate method of administration is an appropriate practice to advocate[34,35].

Causes and risk factors

Several factors held responsible for medication errors include off-label and unlicensed drug, over-the-counter drug used inappropriately, widespread counterfeit, substandard medicines, teenage abuse and use of non-evidenced new/innovative medicines in the paediatric population[2].

It is noticed that in low-income countries, drugs constantly bypass the health care centre. Availability of drugs without necessity of a prescription from an authorised personal increase the chances of drug related complications. Lack of feasibility for immediate treatment following an adverse drug reaction leads to ignorance by majority of the poor people.

Risk factors that predispose children to develop an adverse reaction to a medicine can be physiological, indirect or iatrogenic[2,16,36,37].

- Physiological causes for increased risk
  Young age. Eg. neonates, infants with greatest physiological differences from adults. Thus, the stage of maturation calls for continuous changes in the medicine dispositional parameters.
- Indirect causes for increased risk
  Greater prevalence of polypharmacotherapy, greater length of hospital stay, critically ill children and look alike, sound-alike brands of drugs available in the market accounts for some of the indirect causes.
- Iatrogenic causes for increased risk
  Factors like insufficient well-trained health-care professionals, use of unlicensed and off-label medicines, lack of information about possible medicine interactions and insufficient long-term surveillance.

However, Roy *et al*.[4] highlights the cause of errors as perceived from pharmacists to be due to too many telephone calls (62%), overload/ unusually busy day (59%), too many customers (53%), lack of concentration (41%), lack of personal for double check (41%), staff shortage (32%), similar drug names (29%), no time to counsel (29%), illegible prescription (26%) and misinterpreted prescription (24%).

Medication errors due to failure to follow label instruction

One of the key factors in avoiding complications that arise due to incorrect amount/technique of drug consumed by the patients is reading the drug labelling/prescription labelling accurately. Thus, the label instructions not only eradicate some of the common medication errors, but it also helps prevent serious side effects caused by the negative reactions with other medications. Some of the common failures in following the label instructions are:

- Failure to "shake well"–Results in over or under administration of drug
- Crushing medications that need not be crushed. For instance, crushing enteric coated medicines can lead to early dissolution or complete disintegration of the medication in the gastric environment[38]
- Food or antacids taken before medications which interferes with the drug absorption. Recommending parents to avoid giving dairy products such as milk, yogurt and cheese which has shown to decrease the absorption of antibiotics is essential[39].
- Swallowing of sublingual tablets reducing absorption. Eg. Sublingual Vitamin B12 supplements.
- Use of inappropriate solvents thereby reducing the efficacy[4]. Honey might decrease how quickly the liver breaks down certain medications and may either increase the effects/side effects of these medications.

It was later concluded that Human factors may therefore be the first identifiable causes of error. According to the 'Swiss cheese' model of accident causation, sequential failures in the system and insufficient defences and counteractions are required for the event to occur[26].

Prevention of Medication Errors

Reducing medication errors is a process of continuous quality improvement[16]. It is called a continuous process as not only reporting of the errors, but continuous and timely evaluation by the experts for acquisition of information and adoption of shared criteria is essential. Both internal and external error reporting system is widely used by healthcare institutions[29,40-42]. Prevention of such errors should be prioritised because the harmful effects caused by these are accounted to be mostly iatrogenic which are well attempted to prevent the illness and not due to presence of any already existing condition in those patients[43].

The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) and Institute for Safe Medication Practices (ISMP) emphasizes on the illegibility of prescriptions to be the most common reasons for injuries, or death of patients. ISMP has incorporated several rules and prevention tools for the safe administration of drugs[4,44]. Utilizing double-check independent systems; forcing functions and constraints like compulsory entry of additional pertinent patient information before the order is completed; following the metric system of drug dosage for completion of any order; including age, weight on the prescription order; considering a medication order as complete only if it includes drug name, exact metric weight, concentration, and dosage form; the avoidance of abbreviations Eg. abbreviations like SC for subcutaneous, mistaken as SL (sublingual) are a few of them.

What should be done is generally known as the five *rights*- the *right* drug, the *right* dose, *right* route, *right* time, and the *right* patient[45]. Some modern ways like the computerised order entry system, use of a prescription chart, training on potential adverse drug reactions, Automated systems dispensing (ADD) and the regular monitoring of various publications (Eg. ISMP Medication Safety Alert, the FDA Medical) on recent updates in medication safety have been put forth to prevent lapse in personal performance that result in medication error.

Recommendations for stakeholders and caregivers

1. Recommendation for prescribers[1,15,46]

- Clearly spelled generic or trademark name; avoid abbreviation, vague instructions, illegible handwriting, preferably in computer order.
- Exact metric unit for dosages and calculations expressed.
- A leading zero should always precede decimal expression less than one, but a trailing zero should never follow a whole number. Eg. Trailing zero after decimal point (1.0mg) could be mistaken as 10mg and not using a leading zero before a decimal dose (.5mg) could be mistaken as 5mg.
- Any new drug formulary to be noted down in the order/ patient's chart.
- Write a new prescription every time the doses are changed.
- Round off odd doses, make the person at the other end repeat the verbally placed order and familiarize the patient or the caregivers with the drug.

2. Recommendation for Nurses[15]

- Verify patient identification and review patient's Medication Administration Records (MAR).
- Carefully document all verbal orders by repeating it back to the prescriber, double-check the dosage.
- Counsel patients/caregivers about medication use
- Borrowing of a drug from another patient must be a strict 'NO'
- Administer all doses at scheduled time and document immediately

3. Recommendation for pharmacist[7,15]

- Regularly research unfamiliar medications and various developments
- Dispense in a ready-to-administer form with calculations counter checked
- Careful review of the original medication order prior to dispensing
- Careful documentation of verbal orders and repeating back to the prescriber
- Timely arrival of medication according to the order placed
- Mention the name of the drug, dose, frequency on the envelope for the convenience of the patients and counsel about drug usage.

4. Recommendation for patient and caregivers[15]

- Know the name, storage medium, indications, contraindications and other details related of the drug
- Demonstration of drug administration before discharge
- Total involvement and openly questioning about anything unusual

5. Recommendation for institutions[7,47]

- Compulsory Drug and Therapeutics Committee, as suggested by WHO
- Regular quality improvement programme are necessary.
- Safe distribution of all medications by developing comprehensive policies.

Medication safety monitoring

Medicines playing a pivotal role in the pediatric population needs to be constantly assessed. Having the necessary knowledge about the safety of the drugs thus becomes essential when there is a need for assessing. Such monitoring done pre- and post-marketing will help in ruling out various carcinogenicity, mutagenicity and toxicology of the drugs[2]. Pharmacovigilance has nowadays come up for better safety[48]. Also, in 2004, the International Conference of Harmonisation (ICH) published a guideline on Pharmacovigilance planning that helps address the population at risk[49]. One of the pre-marketing measures put forth by WHO has been related to handling the Look Alike-Sound Alike (LASA) drugs which contributes to a large portion of avoidable medication errors[50].

Post-marketing monitoring of medicines is especially crucial in the pediatric population owing to the relatively small sample size used in the pre-authorization clinical trials. Additionally, other reasons for post marketing monitoring in pediatric population would be the constant use of off-labelled medicines, requirement of long-term follow-up in chronic diseases, and those unable to correlate Adverse Drug Reactions (ADRs) in children with adults[51]. Certain approaches that may help in the post-marketing monitoring have a thorough knowledge about the pathophysiology of the disease as well as benefit-risk ratio of the drugs. Such systems not only helps to regularly update the medical records with the prescribed medication list, but also facilities the reporting of ADRs not just from physicians, but also from stake holders in a simple and clear manner[2,52]. A concrete infrastructure containing a full-time commissioner for medicine safety in children's hospitals, regional and National Pharmacovigilance centres and Programmes (NPP) can help evaluate and assess the various modalities required for safety of drugs in a vulnerable pediatric population[2].

CONCLUSION

There has always been a thirst to improve the quality of life of individuals by health care professionals using various medications. Amongst those individuals, children own 1/3rd of the whole population and so are they an indispensable factor. Medication errors which can be highly lethal have become more common in this group of pediatric population due to the lack of literature and tendency of physicians/prescribers to apply the

available information about adult medications into children. What is forgotten in this procedure is that children are not things to be moulded, but people to be unfolded and it is always easier to build stronger children now than to repair older men later. Thus, medication errors in pediatric population, which perhaps are the most preventable cause of patient injury, must be paid attention to and researched in detail.

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