A review on factors influencing the prescribing patterns in paediatrics

Experience, Human Nature

INTRODUCTION

Paediatrics is the branch of medicines dealing with the development, diseases, and disorders of children1. Infancy and childhood is a period of rapid growth and development. Compared to adult medicine, drug use in paediatrics is not extensively researched and the range of licensed drugs inappropriate dosage form is limited. Drug therapy is considered to be a major component of paediatric management in the health care setting like hospital2, 3.

Prescription auditing is a type of vigilance activity, which is beneficial in a clinical practice in terms of reducing the burden of disease because of medication errors. Rational use of drugs is multifaceted. Its medical, social and economic aspects are well reflected in the WHO definition: “ Rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, at the lowest cost to them and their community”.

Irrational prescribing is a global problem. The rationality of prescribing pattern is of utmost importance because bad prescribing habits including misuse, overuse and underuse of medicines can lead to unsafe treatment, exasperation of the disease, health hazards and economic burden on the patients and wastage of resources. Examples of irrational use of irrational use of medicines include: Polypharmacy, inadequate dosage, and use of antimicrobials even for non-bacterial infections, over use of injections when

oral forms are available and inappropriate, self-medication and non-compliance to dosage regimes4.

Studies on proper drug utilization are necessary tools to evaluate whether drugs are appropriately utilized in terms of efficacy, safety, convenience and economic aspects at all stages in the chain of drug use5. Knowledge of prescribing patterns are important tools for a rational drug therapy. For all drug users rational drug therapy is important, but it is of utmost importance for paediatrics6. Several drugs were frequently used for children; though they were having been investigated in adult's only. Nevertheless pharmacokinetics as well as pharmacodynamics in paediatrics differs from that of adults7-9. Children are among the most sensitive groups to possible harmful effects of drugs as they are physiologically different from adults. It is therefore important to establish which drugs can be used for children and to dicover those which are not harmful. So, rational prescribing pattern and providing correct information during dispensing is good for proper utilization of drugs10.

Over 60% of children in hospitals and 90% of those in intensive care units receives unlicensed or off-label drug. Example of such drug is captopril, levofloxacin, gabapentin, dexmeditomidine e and morphine. Often, information about the dose in milligrams per kilograms of body weight for their drugs is not available and the practitioner is left to estimate a children dose based on the adult dose, using certain formulae give below11.

Clark's Rule:

(Weight in pounds)× (Adult dose)

150

Fried’s Rule:

(Age in months)× (Adult dose)

150

Young’s Rule:

(Age in years)× (Adult dose)

Age+12

Prescribing indication measurements12

The WHO prescribing indication was pretested and slight modification was made to make it application in Indian scenario before using in this study. The formula adopted from WHO manual for the assessment prescribing indicators used in this study are as follows:

1. Average number of drugs par encounter= Total number of drugs prescribing/ Total number of encounters sample. Combinations of drugs prescribing for one health problem were counted as one.
2. Percentage of drugs per encounter = (Number of drugs prescribed by generic name/ Total number of drugs prescribed) × 100.

3. Percentage of encounters with an antibiotic prescribed = (Number of patient encounters with an antibiotic/ Total number of encounter sample) × 100
4. Percentage of encounters with an injection prescribed = (Number of patients encounters with an injection prescribed/ Total number of encounters sample) × 100
5. Percentage of drugs prescribed from essential drugs list = (Number of drugs prescribed from essential drugs list / Total number of prescribed drugs) × 100.

PHARMACODYNAMIC CONSIDERATIONS

Pharmacodynamic Covariates

Considerable strides have been made recognizing Pharmacodynamic covariates. Bradycardia during anaesthetic persuade with sevoflurane was common in children with Down syndrome13. Severe illness is a major explicit for the clearance midazolam14. Opioid administration was decreased in healthy children with altitude induced chronic hypoxia when compared with non hypoxic children undergoing identical operations under similar anaesthetic regimens15. Opioid dose also appears to different geographically; that is, children in central and South America receive less opioid intra operatively than children in Africa and India, under standardized anesthesia for cleft surgeries. Culture may contribute to this observation. There were differences in the episodes of adverse effects after morphine administration between Latino and non Latino Caucasian children.

Incomplete differences in morphine or polymorphisms examined, explained these findings16.

The management of postoperative pain can only improve with greater understanding of its severity and duration. Children experience notable pain and severe functional limitation up to 7days after tonsillectomy or orchidopexy; effects that may persist into the second postoperative week17. Substantial pain continue on day 2 even after laparoscopic appendicectomy18. With intellectual disability (e. g., Trisomy 22) suffer post-operative pain to a identifiable effects as unaffected children, leading many to advocate similar preoperative analgesia care for the two groups19, 20.

“ Jet Lag” After Anesthesia

Children often experience sleep disturbance after anesthesia. Part of this effect may be assign to disruption of the internal circadian clock. The honey bee has a circadian clock that is alike to that found in humans. After a 6hr anaesthetic, bees showed a delay in the start of hunt and whole-hive locomotor- activity rhythms that were slowed by an average of 4. 3 h. Messenger RNA of circadian clock genes was altered by anesthetic exposure, recommend that general anesthesia changes the circadian clock in a manner consistent with jet lag21.

PHARMACOKINETICS22

Pharmacokinetics deals with the processes of drug absorption, distribution, metabolism, and elimination.

Absorption

Absorption from the GI tract is simulated by

Gastric acid secretion

Bile salt formation

Gastric emptying time

Intestinal motility

Bowel length and effective absorption surface

Microbial flora

All these factors turn down in neonates (full-term and premature) and all may be reduced or increased in an ill child. Reduced gastric acid secretion increased bioavailability of acid-labile drugs and decreases bioavailability of weakly acidic drugs. Reduced bile salt formation decreases bioavailability of lipophillic drugs.

Reduced gastric emptying and intestinal motility increase the time it takes to reach therapeutic concentrations when enteral drugs are given to infants below 3 months. Drug-metabolizing enzymes present in the intestines of infants are another cause of reduced drug absorption.

Injection

Injected drugs are often absorbed due to

Divergence in their chemical characteristics

Differences in absorption by the site of injection (IM or SC)

Variability in muscle mass among paediatrics

Illness among paediatrics

Difference in depth of injection (too deep or too shallow)

Transdermal

Transdermal absorption may be increased in neonates and young infants because their stratum corneum is thin and because the ratio of surface area to weight is very much greater than for children and adults.

Transrectal

Transrectal drugs therapy is generally appropriate only for emergencies when an IV route is not available (e. g., use of rectal diazepam for status epilepticus). Site of administration of drug within the rectal cavity may influence absorption because of the variation in venous drainage systems.

Inhalation

Absorption of inhaled drugs from the lungs (e. g., beta-agonist for asthma) varies less by physiologic factors and by reliability of the delivery and patient or caregiver technique.

Distribution

The volume of distribution of drugs changes in children with aging process. These age-related changes are due to changes in body composition (especially the extracellular and total body water spaces) and plasma protein binding.

Higher doses (per kg of body weight) of water-soluble drugs are required by younger children because a higher percentage of their body weight. Conversely, lower doses are required to avoid toxicity as children grow older because of the decline in water as a percentage of body weight.

Metabolism and elimination

Drugs metabolism and elimination differs with age and depend on the substrate or drug, but most drugs, and most notably phenytoin, barbiturates, and cardiac glycosides, have plasma half-life 2 to 3 times greater in neonates than in adults.

The cytochrome P-450(CYP 450) enzyme in the small bowel and liver is the most important known system for drug metabolism. CYP450 enzymes inactivate drugs via

Oxidation, reduction, and hydrolysis (phase I metabolism)

Hydroxylation and conjugation(phase II metabolism)

Phase I metabolism activity is decreased in neonates, increases progressively during the first 6 months of life, exceeds adult rates by the first few years for some drugs, slows during adolescence, and usually attains

adults rates by late puberty. However, adult rates of metabolism may be achieved for some drugs (e. g., phenytoin) 2 to 4 weeks postnatal.

Phase II metabolism varies mainly by substrate. Maturation of enzymes responsible for bilirubin and acetaminophen conjugation is slowed.

Drug metabolites are eliminated primarily through bile or the kidneys. Renal elimination depends mainly on

Plasma protein binding

Renal blood flow

GFR

Tubular secretion

All of these factors are altered in the first 2 years of life. Renal plasma flow is low at birth (12ml/min) and reaches adult levels of 140 ml/min by age 1 year. Similarly, GFR is 2- 4 ml/min at birth, increases 8 to 20 ml/min by 2 to 3 days, and reaches adult levels of 120ml/min by 3-5 months

Drug dosing

Because of the above factors, drug dosing in children less than 12 yrs is always a function of age, body weight, or both. This approach is practical but not ideal. Even within a population of approximately same age and weight, drug requirements may differ because of maturational differences in absorption, metabolism, and elimination. Thus, when practical, dose

adjustments should be depending on plasma drug concentration (however, plasma drug concentration may not reflect the drug concentration in the target organ).

DRUG UTILIZATION EVALUATION

Rational drug use is an important factor to be checked for the optimal benefit of drug therapy in patient care23. In India, many factors like illiteracy poverty, use of multiple health care system, drug advertising and promotion, sale of prescription, competition in medical and pharmaceutical market place and limited availability of drug information are the main reasons for not achieving the optimal health care 24. Inappropriate use of drug also leads to increased cost of medical care, antimicrobial resistance, adverse effects and utilization evaluation (DUE) studies becomes one of the potential tools in evaluation of health system23, 25. Drug utilization studies focuses on factors related to prescribing, dispensing, administering and taking of medication and associated events23.

Classification of Drug Utilization Evaluation

DUR is typically classified into three different categories,

Prospective DUR:

Prospective review evaluation a patients planned drug theory before a medication described. This DUR helps the pharmacist to access the prescription medications and resolve drug related problems23, 25, 26.

Concurrent DUR:

It is performed during the course of treatment and the ongoing monitoring of drug therapy for the positive patient outcomes23, 26.

Retrospective DUR:

It is a review of drug therapy after the patient has received the medication. A retrospective review aims to detect the pattern in prescribing, dispensing or advertising drugs and it helps to prevent recurrence of inappropriate medication use. The advantage of this DUR is ease of data collection, as records are assessed at the data collector’s convenience. A disadvantage is that some information may be unclear or missing and reviewed patients may not gain immediate benefit, as interventions are delayed until the intervention phase23, 25, 26.

Steps in DUE23, 25

Drug utilization evaluation process is divided into four phases

PHASE 1: PLANNING

Develop a DUR committee.

Write policies and procedures.

Describe about the departments of the hospital, where drugs are utilized (intensive care unit, radiology, surgical department, medical department).

Select specific drugs for possible inclusion in the program.

Assess resources available for critical development, data collection, and evaluation.

Consider the indications, dosing, dosage form, frequency of drug used to monitor and evaluate.

Select criteria and establish performance thresholds.

Develop the methodology for data collection, evaluation and create a schedule.

Educate hospital staff about DUE study and current criteria.

PHASE 2: DATA COLLECTION AND EVALUATION

Start the data collection in proper way.

Evaluate the collected data and determine if drug use problem exist.

PHASE 3: INTERVENTIONS

Send the results to hospital staff.

If a drug use problem was found, design and implement interventions.

Collect new data on problem drug to determine with drug use has improved as a result of the intervention.

Disseminate results of re-evaluation.

PHASE 4: PROGRAM EVALUATION

Evaluate all DUR program activities at the end of the year, and plan the new activities for the upcoming year.

Conclusion:

Prescription auditing gives a clear picture of the prescribing practices in our hospital setting. The WHO core indicators helped to improvise the prescribing pattern, identify significant problems involved in the knowledge gap of patients or caretakers understanding of instructions provided by consultants and even to minimize the cost burden on patient. With the help of pharmacokinetic of a drug, interactions between drugs, and the Pharmacodynamic effects of these findings in different subpopulations of infants and children, we can identify the key covariates that will enable clinicians to prescribe effective doses of drugs while limiting the adverse effects in the individual child.