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Research Article

DEVELOPMENT AND EVALUATION OF PEDIATRIC DRUG FORMULARY IN TERTIARY CARE HOSPITAL, ERODE

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ABSTRACT

Objectives: The objectives of the study were to develop and evaluate a pediatric hospital formulary in a tertiary care hospital erode and to provide updated information about the use of medicines to physicians, pharmacists, and other health-care professionals in the hospital for appropriate use of the drugs.

Methods: The prospective developmental study was carried out in a tertiary care hospital, Erode, Tamil Nadu, for a period of 6 months. A survey was conducted using a validated questionnaire for the identification of the need and content of pediatric formulary among physicians in the hospital. The pediatric formulary was developed, and the quality was evaluated using a validated questionnaire form. The content of the formulary was framed based on the opinion of physicians.

Results: The prepared pediatric formulary was assessed with the validated feedback questionnaire. Out of 58 doctors 50 (86.2%) doctors were satisfied with the developed formulary for about 29 (50%) doctors formulary was very useful in their clinical practice and. The necessity of pediatric formulary was supported by 80% of physcians at first but after the implementation of formulary 86% were highly satisfied with the formulary and appreciated the work that was carried out to a great level.

Conclusion: The formulary was handy, user-friendly and saves the precious time of busy physician. It may also promote the safe and effective use of medicines thereby minimizing drug-related problems in the pediatric population.

Keywords: Formulary, Pediatrics, Clinical practice.

INTRODUCTION

Even though pediatric patients comprise a wide proportion of the patient population, but concern about their medication safety has been neglected for a long time. Drug prescribing for pediatric patients offers special challenge [1]. They are the most vulnerable group of the population suffering from frequent but usually non-serious illness. Children are more often exposed to unlicensed and off-label medication use, which potentially forms a greater risk for adverse drug reactions (ADRs). Pediatric practitioners should be aware of the fact that growth and development are an important signal of a child's general well-being [2].

Pharmacokinetic and pharmacodynamic changes in pediatrics

There is the high importance of clinical pharmacokinetics in the optimization of drug therapy. Safety and efficacy of drugs may vary among different groups of pediatric patients it can either be effective, ineffective or toxic, so it is essential to be aware of the variability in drug disposition if children are to receive rational and appropriate drug therapy. Lack of data on important pharmacokinetic (absorption, distribution, metabolism, and excretion) and pharmacodynamic differences (medicine targets, such as receptors, transporters, and channels are certainly also subjected to developmental processes [as are metabolizing enzymes]) has led to several terrible situations in pediatric care. Inability to obtain true informed consent is the primary issue and the second issue is inherent to children; the rapid growth and changes occur in children. Hence, drug studies must be performed on children at each stage of their development to determine appropriate usage. Highly critical aspects in child treatment are pharmacokinetic parameters, method of drug administration, dose, and dosage forms.

Consequences of the lack of studies of medicine development in children and authorization of pediatric medicines

Medicines of major clinical importance, even essential medicines, are not readily tested and not officially approved for use, especially in the very young. This led Harry Shirkey in 1963 to state that, children constitute therapeutic orphans. Among the 340 medicines in the WHO model List of essential medicines 2007 [3] those that have relevance for pediatric populations should be the top priority for documenting pediatric experiences, wherever these medicines are being used. However, all drugs that are tested in adult population probably cannot be met therapeutic needs in children if medicines are not tested and labeled for pediatric use. Once a medicine becomes available on the market for adults, it is possible to use it in children in an off-label way. Even though unlicensed and off-label medicines for children became a practice for decades; this does not provide the same quality, safety, and efficacy of medicines as adults [4]. Therefore, it is not surprising that pediatric patients are exposed to a rate of potentially dangerous medication errors 3 times higher than that for adult patients [1].

Problem arise during the use of medication in children

Wrong dosage causes short-term toxicity or treatment failure. Health care providers forced to administering the crushed tablets, dissolving tablets in solvents or administering the powder contained inside the capsule due to lack of non-availability of appropriate pediatric formulations.

The suitable formulations are not available for administration to neonates, infants, and young children. Adult formulations should be diluted or administered in miniscule volumes over a period of time. This leads to administration errors, especially in circumstances that require urgent action (as in emergency units, premature units, and NICU).

Complications in pediatric populations

Most of the medicines have not been adequately tested and/or formulated and authorized for use inappropriate pediatric age groups therefore in pediatric patients many medicines are prescribed on an unlicensed and off-label manner. The lack of reliable data in the

pediatric population is associated with specific problems including: Less availability of safety data due to the shortage of clinical trials in the pediatric population; under- or over-dosing in some age groups due to the lack of pharmacokinetics data; maturation, growth, and development of the pediatric population susceptible to drug-induced growth and development disorders as well as to delayed ADRs not findable in adults. The spectrum of adverse reactions in children may differ due to the variability in pharmacodynamics and pharmacokinetics in children from adults [5]. Furthermore, children are more often exposed to unlicensed and off-label medication use, which potentially forms a greater risk for ADRs [6,7]. More knowledge on occurrence and content of ADRs in the pediatric setting is necessary, thereby can prevent those events.

Pre-marketing trials are do not manage to establish a safety profile but it can able to provide information about the benefits of drugs [8]. To promote reasonable warning signs spontaneous reporting of ADRs plays a key role. The World Health Organization defines ADRs as unintended and harmful responses to a drug and which occurs with doses normally used in humans for prophylaxis, diagnosis or treatment of a disease or modifying a physiological function. It is a condition which rarely is associated with a significant impact on the health system. The occurrence of ADRs is natural to the use of medicines, and in some cases, the hospital admission is needed. In children, ADRs risk factors are relatively unknown. Pharmacokinetics and pharmacodynamics in children differ from adults, and therefore the range of adverse reactions in children may differ as well [5]. Furthermore, children are more often exposed to off-label and unlicensed medication use, which potentially forms a greater risk for ADRs [6,7]. Because part of these events may be preventable, more knowledge on occurrence and content of ADRs in the pediatric setting is necessary.

Limitations of available hospital formulary

There is a lack of availability and reliability of pediatric drug dosing guidelines in present hospital formulary. The lack of adequate and evidence-based dosing recommendations for pediatric patients reflects the lack of drug studies in this population.

Necessity of pediatric formulary

Medication and its management is central to the quality of care received by most hospitalized children and is dependent on an evidence-based formulary that ensures safe, effective, and rational use of medicines. It is the fundamental responsibility of drug and therapeutics committees to evaluate medicines for addition to the hospital formulary. For pediatric hospitals, committee decisions also have a strong impact on access to medicines to treat rare conditions, transition to adult services, outpatient medication supply, and hospital drug budgets. In India, few hospitals are having hospital formulary of their own. Among those hospitals, only a few hospitals are having their own pediatric drug formulary. Therefore, the presence of the pediatric formulary might help in the pediatric prescribing pattern.

Pediatric formulary should be complete, concise, updated, and easy to use since it is a tool for health-care professionals mainly medical and nursing staffs make use of this tool periodically [9]. Pediatric formulary aims to provide prescribers, pharmacists, and other health-care professionals with sound updated information on the use of medicines for treating children. Many fields of pediatric practice have suffered from inadequate information on effective medicines. By providing practical information on the use of medicines in children of all ages from birth to adolescence pediatric formulary addresses this significant knowledge gap. Against emerging evidence, best practice guidelines, and crucially advice from a group of clinical expert's information in pediatric formulary have been updated. This is essential because licensed indications frequently do not cover the clinical needs of children; in some cases, products for use in children need to be specially manufactured or imported. For unlicensed interventions, to establish the clinical needs with respect to the evidence and experience of their safety and efficacy careful consideration has been given; clinical literature has been invaluable in this process.

Therefore, the presence of the pediatric formulary might help in the pediatric prescribing pattern, and the main objective of developing this pediatric formulary is to set standards for best practice, promoting high quality and evidence-based prescribing thereby minimizing the variation in the level of treatment provided to the patients.

METHODS

The prospective developmental study was conducted in tertiary care hospital in South India for 6 months. No pediatric formulary was available in the hospital. Hence, the drug information center which belongs to the pharmacy practice initiated the concept of preparing pediatric formulary.

The study received clearance from the Ethical Committee after submitting the proposal with study title, duration, objectives, and a brief methodology about the work to be carried. The protocols and guidelines approved by Pharmacy and Therapeutic committee of the hospital were collected.

The drug list was collected from hospital pharmacy and categorized the drugs to be included in the pediatric drug formulary which was verified by the pediatrician. Appropriate Drug Information resources such as LEXICOMP and MICROMEDEX were selected and the drugs in the pediatric department as per hospital formulary drug list. Layout of drug monograph was designed. Monograph for all drugs in the list from standard primary, secondary, and tertiary drug information resources was prepared. The developed pediatric formulary was given to the physicians in Government Headquarters Hospital Erode. The feedback form for evaluating the formulary was prepared. The developed pediatric formulary was implemented and later evaluated among 58 doctors using suitably designed feedback questionnaire.

Two types of questionnaires were framed one for the selection of information to be included in each monograph, and other for the evaluation of developed pediatric formulary was evaluated using suitable feedback questionnaire. Based on the information from the questionnaire pediatric formulary was developed.

RESULTS

About 50–75% of drugs that are used in the pediatric population have not been studied adequately to provide appropriate labeling information. Due to the prescriber's reluctance to use a medication for an off-label use pediatric patients may also be deprived of potentially effective medication [10]. Off-label use in pediatrics affects both seriously ill inpatients and the millions of children treated outside the hospital for various types of illness. The problem of off-label use of drugs in pediatrics is international and affects pediatric patients in the United States, Europe, Asia, Africa, and South America [11-14]. Appropriate drug prescribing is quite challenging since DRPs have become a priority, due to the complexity of today's drug therapy [15-17]. Various studies have shown that DRPs in the pediatric population are of major concern [15,18,19].

Of 58 doctors, 50 (86.2%) doctors were satisfied with the developed formulary for about 29 (50%) doctors formulary was very useful in their clinical practice. For third question (Table 1), 50 (86.2%) of them had preferred very useful and 8 (13.8%) of them had preferred useful. For fourth question 50 (86.2%) of them had preferred very helpful, 5 (8.62%) had preferred helpful, and 3 (5.172%) of them had preferred not helpful. For the fifth question 50 (86.2%) of them had preferred to great extend option, 5 (8.62%) had answered moderately option, and 3 (5.172 %) had preferred the option little.

For the sixth question, 29 (50%) had preferred very useful. For the seventh question, 40 (68.96%) of them had preferred the option frequently, 10 (17.24%) of them had preferred occasionally, 5 (8.62%) of them had preferred the option rarely, and 3 (5.172%) of them had preferred never. For the eighth question, 58 (100%) of them had preferred yes. For the ninth question, 50 (86.2%) of them had preferred

Table 1: Response of the doctors based on the need of pediatric formulary

S. no	Feedback questionnaire/comment	Number of doctors n=58 (%)
1	Whether the order of contents in each monograph is convenient to refer?	
	To a great extent	29 (50)
	Convenient	21 (36.206)
	Little	5 (8.62)
	Not at all	3 (5.172)
2	The content in each drug monograph is	
	Sufficient	50 (86.2)
	Average	7 (12.06)
	Below average	1 (1.724)
3	Is it useful to get aware of the contraindications, side effects, and ADRs of pediatric drugs available in the hospital pharmacy?	
	Very useful	50 (86.2)
	Useful	8 (13.8)
4	Dose prediction	
	Very helpful	50 (86.2)
	Helpful	5 (8.62)
	Not helpful	3 (5.172)
5	Whether this formulary promotes the safe and effective use of medicines?	
	To a great extent	50 (86.2)
	Moderately	5 (8.62)
	Little	3 (5.172)
6	Will it be useful in your clinical practice?	
	Very useful	29 (50)
	Useful	29 (50)
7	Extent of usage of the formulary	
	Frequently	40 (68.96)
	Occasionally	10 (17.24)
	Rarely	5 (8.62)
	Never	3 (5.172)
8	Whether the formulary is handy?	
	Yes	
	No	58 (100)
9	Are you satisfied with the developed formulary?	
	Satisfied	50 (86.2)
	Not satisfied	8 (13.8)
10	Do you feel that a clinical pharmacist is required in your daily practice?	
	Agree	50 (86.2
	Disagree	8 (13.8)

ADRs: Adverse drug reactions

satisfied and (13.8%) of them had preferred not satisfied. For the tenth question, 50 (86.2%) of them had preferred agree and 8 (13.8%) of them had preferred disagree.

DISCUSSION

In our study, Table 1 showed the comments for the feedback questionnaires by the physicians of Headquarters Hospital Erode. For the first question, 29 (50%) doctors had preferred to great extent option in the form, 21 (36.206%) had preferred convenient option, 5 (8.62%) had preferred little option, and 3 (5.172%) had preferred not at all option. For second question, 50 (86.2%) of them had preferred sufficient, 7 (12.06%) had preferred average, and 1 (1.724%) had preferred below average.

ADRs in a pediatric population are an important public health problem [20]. Due to the high incidence of drug-induced reactions especially in the pediatric population, despite efforts being made to reduce the incidence of medication-related adverse events, the morbidity, and mortality [21,22].

Unrecognized and/or unresolved DRPs can potentially lead to significant drug-related morbidity and/or mortality [23,24]. Hospitalizations, long-term care admissions, emergency department visits, additional physician office visits, and additional prescriptions are certain consequences associated with DRPs [25].

Regarding ADRs among pediatric patients, several studies have been done in different parts of the world. It has been found that in every year in young children of age group of newborn to 2 years of age, ADRs were associated with 243 reported deaths [26]. A study reported that ADRs occurred more among infants and antibiotics were more commonly implicated. Most of the reactions were of moderate severity [26].

CONCLUSION

The necessity of pediatric formulary was supported by 80% of physicians at first but after the implementation of formulary 86% was highly satisfied with the formulary and appreciated the work that was carried out to a great level. The formulary is handy, user-friendly and saves the precious time of busy physician. It may also promote the safe and effective use of medicines thereby minimizing drug-related problems in the pediatric population. The physicians highly appreciated the pivotal role played by the clinical pharmacists in providing unbiased information and promoting better pharmaceutical care and opined that the services of the clinical pharmacist are very much essential to optimize their daily practice.

New drugs and treatments are emerging all the time, and without evaluation, the formulary may become a collection of older, less effective drug. Therefore, the entire formulary should be reviewed every 2–3 years.

CONFLICTS OF INTEREST

No conflicts of interest.

REFERENCES

1. Jara MD, Montero AP, Bara MT, Cabrerizo S, Zapatero L, Molero MI. Allergic reactions due to ibuprofen in children. Pediatr Dermatol 2001;18:66-7.
2. World Health Organization. Promoting Safety of Medicines for Children. Geneva: WHO; 2007.
3. Boelsterli UA. Mechanisms of NSAID-induced hepatotoxicity: Focus on nimesulide. Drug Saf 2002;25:633-48.
4. Ramadaniat HU, Tambunan T, Khairani S, Adisty HS. Off-label and unlicensed prescribing in pediatric inpatients with nephritic syndrome in a major teaching hospital: An Indonesian context. Asian J Pharm Clin Res 2017;10:355-9.
5. Kearns GL, Abdel-Rahman SM, Alander SW, Blowey DL, Leeder JS, Kauffman RE. Developmental pharmacology: Drug disposition, action and therapy in infants and children. N Engl J Med 2003;349:1157-67.
6. Horen B, Montastruc JL, Mestre ML. Adverse drug reactions and off-label drug use in paediatric outpatients. Br J Clin Pharmacol 2002;54:665-70.
7. Turner S, Longworth A, Nunn AJ, Choonara I. Unlicensed and off label drug use in paediatric wards: Prospective study. Br Med J 1998;316:343-5.
8. Napoleone E. Children and ADRs (adverse drug reactions). Ital J Pediatr 2010;36:4.
9. Almeida RJ, Acharya LD, Rao PG, Jose J, Bhat RY. Development of hospital formulary for a tertiary care teaching hospital in South India. Indian J Pharm Sci 2007;69:773-9.
10. Roberts R, Rodriguez W, Murphy D, Crescenzi T. Pediatric drug labeling: Improving the safety and efficacy of pediatric therapies. JAMA 2003;290:905-11.
11. Jong WT, Vulto A, De Hoog M, Schimmel KJ, Tibboel D, Van den Anker JN. Unapproved and off label use of drugs in a children's hospital. N Engl J Med 2000;343:1125.
12. Committee on Drugs. Unapproved uses of approved drugs: The physician, the package insert, and the Food and drug administration: Subject review. American Academy of Pediatrics Committee on Drugs. Pediatrics 1996;98:143-5.
13. Gravilov V, Lifskitz M, Levy J, Gorodischer R. Unlicensed and "off label" medication use in a general pediatrics ambulatory hospital unit in Israel. Isr Med Assoc J 2000;2:595-7.
14. Avenel S, Bomkratz A, Dassieu G, Janaud JC, Danan C. The incidence of prescriptions without marketing product license in a neonatal intensive care unit. Arch Pediatr 2000;7:143-7.
15. Rashed AN, Neubert A, Tomlin S, Jackman J, Alhamdan H, Alshaikh A, *et al*. Epidemiology and potential associated risk factors of drug-related problems in hospitalized children in the United Kingdom and Saudi Arabia. Eur J Clin Pharmacol 2012;68:1657-66.
16. Blix HS, Viktil KK, Mger TA, Reikvam A. Characteristics of drug-related problems discussed by hospital pharmacists in multidisciplinary teams. Pharm World Sci 2006;28:152-8.
17. Ibrahim N, Wong IC, Patey S, Tomlin S, Sinha MD, Jani Y. Drug-related problem in children with chronic kidney disease. Pediatr Nephrol 2013;28:25-31.
18. Easton KL, Chapman CB, Brien JA. Frequency and characteristics of hospital admissions associated with drug-related problems in paediatrics. Br J Clin Pharmacol 2004;57:611-5.
19. Rashed AN, Neubert A, Alhamdan H, Tomlin S, Alazmi A, Alshaikh A, *et al*. Drug-related problems found in children attending an emergency department in Saudi Arabia and in the United Kingdom. Int J Clin Pharm 2013;35:327-31.
20. Brunlof G, Tukukino C, Wallerstedt SM. Individual case safety reports in children in commonly used drug groups-signal detection. BMC Clin Pharm 2008;8:1-5.
21. Berry MA, Shah PS, Brouillette RT, Hellmann J. Predictors of mortality and length of stay for neonates admitted to children's hospital neonatal intensive care units. J Perinatol 2008;28:297-302.
22. Neubert A, Dormann H, Weiss J, Egger T, Criegee-Rieck M, Rascher W, *et al*. The impact of unlicensed and off-label drug use on adverse drug reactions in paediatric patients. Drug Saf 2004;27:1059-67.
23. Lassetter JH, Warnick ML. Medical errors, drug-related problems, and medication errors: A literature review onquality of care and cost issues. J Nurs Care Qual 2003;18:175-81.
24. Einarson TR. Drug-related hospital admissions. Ann Pharmacother 1993;27:832-40.
25. Moore TJ, Weiss SR, Kaplan S, Blaisdell CJ. Reported adverse drug events in infants and children under 2 years of age. Pediatrics 2002;110:e53.
26. Priyadharsini R, Surendiran A, Adithan C, Sreenivasan S, Sahoo FK. A study of adverse drug reactions in pediatric patients. J Pharmacol Pharmacother 2011;2:277-80.