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Pharmacovigilance in paediatric population

***Darawadi Bhuvana, *H. Parameshwar *SK Sahil Reza, *A.V. Jithan**

**Omega college of Pharmacy, Edulabad, Ghatkesar, Affiliated to Osmania University Hyderabad, Telangana-501301*

Corresponding Author: Darawadi Bhuvana

ABSTRACT

Pharmacovigilance reflection was first published in the British Medical Journal in 1877 by chloroform issues. New era of the Pharmacovigilance was initiated by the children's big issues related to teratogenic effects. To ensure the benefits of use of drugs out weights the risks & thus safe guard the health of the paediatric population. Pharmacology in paediatric population has specific needs in Pharmacovigilance. Altered pharmacokinetics and Pharmacodynamic of drugs make paediatric patients susceptible to drugs adverse drug reactions. A systemic review from past few years starting from 1877 considering the deaths noted due to its adverse effects. The WHO global individual case safety report data base reported the ADRs in children upto7.7% by using the spontaneous reporting system. It is necessary to develop a proactive Pharmacovigilance and patient safety programs with a focus in risk analysis and management, in which ADR reporting should be mandatory.

Keywords: Adverse drug reactions, Paediatric, Intensive Pharmacovigilance, Teratogenic effects.

INTRODUCTION

Pharmacology in paediatric population has specific needs in Pharmacovigilance. Altered pharmacokinetics and Pharmacodynamic of drugs make paediatric patients susceptible to drugs adverse drug reactions [02]. Since the efficacy/safety balance of most available drugs has not been formally evaluated in paediatric clinical trials, optimal dosing is rarely known in paediatrics. The frequent off-label prescribed drug use, usage of the unsuitable dosage forms and the need for continuous dose adjustments increase the risk of the medication errors and thus lead to the adverse drug reactions. NSAIDS the class of anti-inflammatory drugs reported the highest adverse reactions in children especially the ibuprofen. Majority of the adverse drug reactions have shown drugs are related to the cold medicine [03] Paediatric Pharmacovigilance includes the consequences in utero exposure, whether manifestations are present in birth or occurs in early childhood (neurodevelopment disorders). Invasive pharmacovigilance is much needed in paediatric population due to complex diseases; critically ill children in intensive care units have high risk of developing ADR's. The drugs most frequently reported with ADR's are those most commonly in paediatric age group are antibiotics, NSAIDs & vaccines [04]. It is branch of pharmaceutical sciences which evaluated and monitor the adverse drug reactions or any other medication related issue of licenced drug to increase their safety in the market. Paediatrics are at risk of harm from medications because of their organ immaturity and rapid developmental changes in their body. Many drugs which are prescribed to the paediatrics are not formally evaluated and with low accuracy of clinical trials that results in the medication errors to adverse drug reactions [04]. Optimization of drugs became more difficult to prepare due to metabolic changes in the paediatrics [01]. The lack of studies in paediatrics leads to mostly to on falling prescribing and to an increased frequency of adverse drug reaction. Off-labelling refers to unapproved indication or in an unapproved age of groups in dosing of a drug and route of administration.

BACKGROUND

The first instance of safety related problem that led to a pharmacovigilance reflection was published in British medical journal in 1877 by chloroform issues [03]. In 1898, with the commercialization of diacetyl morphine, named as

heroine which people got addicted to it. Later in the beginning of the 1950's di iodo diethyl of tin was added to stalinon for topical application on skin which resulted in the 102 deaths associated with the encephalopathy and hundred patients developed severe, irreversible, neurological after effects. In 1957, thalidomide which was OTC hypnotic / sedative used to treat the morning sickness in the pregnancy women showed the teratogenic effects in the newborns. Considering this thalidomide disaster, the WHO formerly established a programme for International Drug Monitoring in 1968 and founded Uppsala monitoring centre (UMC).

METHODS AND MATERIALS

Implementing the pharmacovigilance in every healthcare department is the easiest way to assess the adverse drug reactions in the health care department and to ensure the quality of patient's health. Intensive pharmacovigilance helps the patients bed side monitoring and reduce the impact of drug-drug interactions and other medication related problems. A systemic review from past few years starting from 1877 considering the deaths noted due to its adverse effects. The WHO global individual case safety report data base reported the ADRs in children upto7.7% by using the spontaneous reporting system. The majority of the UMC reporting are mainly related to the cold medicine. This data collected from the two general wards of hospital at Columbian Caribbean coast.

Age/drug	DM	Guaifen-esin	PE	BH	DH	Codeine
0–27 days	9	4	13	3	25	13
28 days-to-23 months	149	103	76	13	274	136
2–11 years	825	194	79	21	741	429
12–17 years	600	95	37	8	604	277
Total	1583	396	205	45	1644	855

Number of UMC reports in children

DM-dextromethorphan; GUA-guaifenesin; pseudo-, pseudoephedrine; PE-phenylephrine; BH,-brompheniramine; CP-chlorpheniramine; DH, diphenhydramine [03].

Pharmacokinetic characteristics in paediatrics: Paediatric growth is not a linear process. The pharmacokinetic parameters are varied in paediatrics when compared to the adults they require the dosage adjustments and dose calculations [02]. Dose adjustments are required due to the metabolic immaturity of reduced clearance and prolonged half-life explaining the need to space unit doses during the neonatal period. Paediatrics undergoes some organ developmental changes according to the EMA paediatric age classification [08]. Some of the considerations for the administration of drugs they are: 1. Weight-dosage calculations, 2. Clinical trial evidence in dosage strategy. Weight dosage considerations are related to the body surface area and BMI corresponding to the developmental changes. Evidence based clinical trials are limited in thepaediatrics due to the less statical data on dosage adjustments in paediatrics.

Absorption: Due to the alterations in the gastric acid secretion and gastric emptying time the absorption may vary when compared to the adults. Transdermal administration of any drug to the infants increases the absorption rate due the large surface of area of skin and stratum corneum is thin so absorption rate is faster. Methemoglobinemia seen as adverse effect in children when topical anaesthetics are administered.

Distribution: For most of the water-soluble drugs, the volume of distribution is increased in neonates. Distribution of drugs is affected in vascular perfusion, body composition, tissue binding & plasma protein binding.

Metabolism: Rate of metabolism in paediatrics is 2-3 times longer than the adults. Biotransformation of many drugs is decreased in the neonates, increases from 1-5 years of age and decreases after the puberty to adult values.

Elimination: Glomerular filtration rate of neonate 2-3 ml / min and doubles by 1 week of age and reaches the adult GFR rate by the completion of the 1 year of the age. Kidney of neonates inefficient at drug elimination. Clearance of some drugs may be greater in infants than in toddlers in relation to reabsorption.

Pharmacodynamic changes: Pharmacodynamic studies and extrapolation ofpaediatrics will increase the efficacy. A retrospective study shows currently 50-80% of children are still treated with medication in an off-label manner [10]. Paediatric trails fail because of in evidence on developmental changes when compared to the adults. Drug receptor adherence, comorbidity condition, developmental changes, disease surveillance may impact in improper regimen selection and dose adjustment [09].

Intensive pharmacovigilance: Intensive pharmacovigilance is defined as "the systematic monitoring of the occurrence of adverse events resulting from drug use during the entire length of prescription [03]. It is needed in reducing the predisposing factors of adverse drug reactions and medication related problems for increased susceptibility.

Pharmacovigilance cycle:Detecting, accessing, planning, intervening, monitoring and reviewing in managing and preventing the adverse effects or any drug related problem [03].

Key concepts of pharmacovigilance: Systemic respiratory and antibiotics were the therapeutic groups mostly associated with the adverse drug reaction incidence and the most affected organ in neonates is hematologic [08]. Off-labelling is important in the public health services mainly in young children with rare diseases. However, the paediatrics labelling on drugs is seen in only 50% of the drug labelling's [07]. Pharmacovigilance in paediatrics is necessity to provide the complete information on medication errors to prevent further medicine related problems [05]. Due to the adverse drug reactions and ineffective dose adjustments clearly bound to the repetitive hospital admission who are under critically ill [06]. Changes in the pharmacokinetic and pharmacodynamic properties tin paediatric subjects to adults having an impact on the safety profile of the medicine. ADR's preventable and by preventing them reduces potential readmission to the hospital and can improve the patient health care [07].

RESULTS AND DISCUSSIONS

Physiological changes	Characteristics
Absorption: Gastric pH	weak acids: lower bioavailability weak bases: higher bioavailability
Gastro intestinal motility	delayed absorption
Distribution: Body water	Hydrophilic drugs: higher Vt Hydrophobic drugs: lesser Vt
Metabolism: Phase I enzyme	less hepatic clearance
Elimination: Renal excretion	Low renal clearance

CONCLUSION

ADRs are common among inpatient neonates and children. In neonates, having less than ≤8 days of hospitalization is linked with the nonappearance of ADRs in children; males are more likely to develop ADRs than females. Even when in neonates, males have higher rates of occurrence than females. Systemic antibiotics are correlated with a higher risk of ADRs in children. All these findings mean that ADRs represents an additional burden of morbidity and risk for paediatric patients, particularly in those who used several medicines. Pharmacovigilance in paediatric population needs to be reinforced. It is necessary to develop a proactive pharmacovigilance and patient safety programs with a focus in risk analysis and management, in which ADR reporting should be mandatory. This measure might help us make our health-care systems safer, especially for children, in which this topic must be further investigated. Proposals to improve pharmacovigilance in paediatric population. The increasing number of the published studies and safety warnings from regulatory agencies within the paediatrics demonstrate how awareness about the paediatric pharmacovigilance has been raised.

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