JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

PEDIATRIC PHARMACOLOGY

Payal Patil[1]*, Supriya Kirdat[2], Santosh Waghmare[3], Ashwini Andhale[4], Dr. H.V Kamble[5]

Department of pharmacology, Loknete Shri Dadasaheb Pharate Patil College of Pharmacy, Mandavgan Pharata, Shirur, Pune, Maharashtra, India, 412211.

Corresponding Author:

Payal Patil
Loknete Shri Dadasaheb Pharate Patil College of Pharmacy, Mandavgan Pharata, Shirur, Pune, Maharashtra, India, 412211.

E-mail: payalpatil975@gmail.com

Abstract:

Pediatric clinical pharmacology is a relatively young field in pediatrics that studies drugs in children. In the last ten years, pediatric pharmacology research has changed dramatically. Both officially and privately supported activities are expanding. A variety of pharmacokinetics studies and multi-site controlled effectiveness trials have been done, allowing for more informed and evidence-based treatment of children and adolescents. Ethical considerations in clinical trials, as well as pharmacokinetics and drug metabolism investigations in children, are critical. Pediatric patients require formulations that are suitable for young children in particular. To guarantee that medicines are used rationally in children, scientific evidence from clinical trials, pharmacokinetic studies, and drug toxicity studies must all be incorporated.

Keywords: Pediatrics, Pharmacology, Drug Toxicity.

Introduction:

A secure and powerful medicine for youngsters calls for an essential expertise and integration of the position of ontogeny within side the disposition and movements of medicines. as maximum essential prerequisite, one has to take into account the fundamental precept that children's aren't small adults! Over the final years there had been several improvements in drug development for pediatric patients. In 2014 and 2015 the Food and Drug Administration (FDA) authorized greater than 70 product label adjustments associated with pediatric populations, ensuing in more than 530 standards for the reason that enactment of the Best Pharmaceuticals for Children Act (BPCA) in 2002 and the Pediatric Research Equity Act (PREA) in 2003. There had been over 10 approvals of recent tablets specially for the remedy of pediatric warning signs within side the final 2 years, inclusive of numerous for uncommon or ultra-uncommon diseases, which displays the primary advancements which have come about for drug development for these populations. The well-known

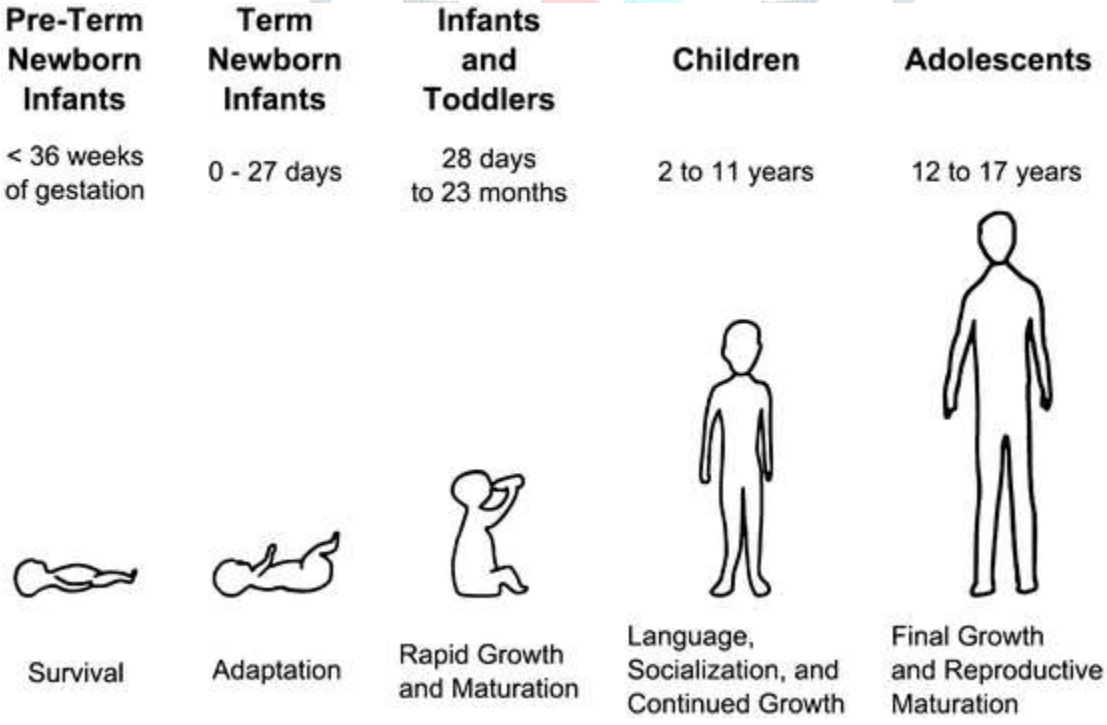
American pharmacist and pediatrician, Harry Shirkey (1916-1995), wrote in his textbook on pediatric Therapy with other words: "The long list of dosage rules based on age, body weight or surface and their respective authors in testimony that no rule is entirely satisfactory in producing an exact fraction of the known adult dose that is applicable to a particular child". This essential information of figuring out the pediatric dosage of a remedy is even today - one hundred years later - frequently ignored. Therefore, as a first step towards a successful pediatric therapeutic approach, it is necessary to evaluate the typical characteristics of the pediatric subgroup and the differences in health problems, nonlinear and dynamic maturation processes. Ontogenesis of basic physiological processes provides guidance for understanding the mechanisms underlying the differences between the various stages of development in pediatric and adult populations.

Classification of the pediatric population:

The pediatric population is a continuous process of growth and development from the smallest premature infant to childhood, adolescence and to young adulthood.

Classification of the pediatric population is as follows:

- Preterm infants (<37 weeks gestation)
- Term newborn infants (0-28 days)
- Infants and toddlers (> 28days to 23 months)
- Children (2-11 years)
- Adolescents (12 to 16-18 years, depending on the region)



Clinical Trials:

It is good practice to scientifically evaluate drugs that may benefit children in clinical trials. Previously, many medicines had not been studied in children, and children were deprived of the basis of evidence for rational use of medicines. A new European law, passed in 2007, recognizes the need to study all new drugs if necessary, but discourages studies of different drug methods in children. Clinical trials in pediatric patients should always be less invasive than clinical trials in healthy adult volunteers. Blood sampling and other invasive procedures should be minimized or avoided entirely unless clinically relevant.

The safety of clinical trials in children is very important. Unfortunately, there have been clinical trials in children where children experienced severe toxicity because researchers did not fully address the safety issue in the first place. Previously, many clinical trials in children did not have an independent safety monitoring committee/data monitoring committee. Fortunately, it is now essential for clinical trials of the drug in pediatric patients.

Important developments within various therapeutic areas:

ANESTHESIA

Pain management:

In August 2015, the FDA approved controlled release oxycodone hydrochloride (OxyContin) for patients 11 years of age and older who are in pain, are opioid tolerant, and receive a minimum daily dose of 20 mg oxycodone. This approval is based on an open clinical study of 155 pediatric patients with opioid tolerance and moderate to severe chronic pain. The median duration of treatment (range) was 20.7 days (1-43) and the daily dose was 33.30 mg/day (20-140). Over 50% of patients experienced side effects, the most common being vomiting, nausea, headache, fever and constipation. Pain was assessed using the modified FACES Pain Rating Scale, assessed by patients at screening, after the first dose, twice daily (morning and evening) for each dose. The mean score (standard deviation) at baseline was 4.44 (3.250), 3.13 (2.569) in the morning of the 4th week, and 3.42 (2.974) in the evening. Therefore, this study concluded that controlled release oxycodone is safe and effective for pain relief in this opioid-resistant pediatric population.

INFECTIOUS DISEASE

Hepatitis B:

Entecavir (baracrud) is a reverse transcriptase inhibitor approved in 2004 for the treatment of chronic hepatitis B in adults. In 2014, FDA expanded the age range of indications to include pediatric patients 2 years of age and older. It is based on two clinical trials in pediatric patients aged 2-18 years who are positive for hepatitis B envelope antigen (HBeAg) with chronic hepatitis B infection and compensated liver disease.

Pneumonia:

Community-acquired pneumonia is the leading cause of hospitalization in children in the United States. Although most commonly caused by streptococcal pneumonia, due to the nature of the pathogenic uncertainty and susceptibility in the clinical setting, patients are often prescribed broad-spectrum antibiotics as empirical treatment. The Academy of Pediatric Infectious Diseases and the American Society of Infectious Diseases published guidelines for the management of simple community-acquired pneumonia in pediatric patients in 2011 and recommended the empirical use of narrow-acting drugs such as ampicillin and penicillin. A multicenter retrospective cohort study was conducted to compare the efficacy of narrow-band and broad-spectrum therapy. The study included children aged 2 months to 18 years (n = 492) who were discharged with a diagnosis of community-acquired pneumonia and received narrowband or broadband treatment during the first 2 days of hospitalization. The narrow range was defined as amoxicillin, ampicillin, penicillin, and amoxicillin/clavulanic acid, and the broad range was defined as the second or third generation cephalosporin or fluoroquinolone. The study showed that patients who received narrowband therapy had a 10-hour shorter hospital stay (P = 0.4), with no other significant differences in outcomes. Therefore, the researchers concluded that both narrow and broad ranges were associated with similar outcomes. Similarly, in a prospective randomized study of 58 children aged 3 months to 15 years, penicillin G was found to be as safe and effective as cefuroxime in the treatment of community-acquired pneumonia.

HIV:

Significant progress has been made in reducing the incidence of HIV in the pediatric population over the past decade. In 2014, the United Nations Joint Program on HIV/AIDS reported that between 2001 and 2013 new infections in children under 15 years of age decreased by 60%, from 500,000 to approximately 200,000. Childhood HIV/AIDS is currently estimated to affect 3.2 million children worldwide, accounting for approximately 9% of the world's population living with HIV/AIDS. Over the past two years, the FDA has made several changes to the labeling of pediatric HIV drugs. Atazanavir (Reyataz), previously provided as a capsule to patients 6 years of age and older, is now available in a new oral powder formulation for patients 3 months old and older and weighing 5 kg or more. Both abacavir (Ziagen) and lamivudine (Epivir) underwent label modifications to provide new information for once-daily dosing in pediatric patients 3 months and older. When changing the label of the lopinaviritonavir (Kaletra) combination drug, it is recommended to prescribe twice a day to pediatric patients instead of once a day. Ramibudineraltegravir (dutrevis) combination tablet is approved for the treatment of HIV infection in adults and children over 6 years old and weighing 30 kg or more. The indications for rilpivirine (Edurant) and the combination drug abacavir sulfatetramivudine (Epsicom) have been expanded from adults to children. Both CD4% (CD4%) and age are important factors when initiating antiretroviral therapy (ART). Pediatric AIDS Clinical Trials 390 / Investigators from the Pediatric AIDS Treatment European Network 9 (PENPACT1) quantified the effect of initiating ART at various ages and CD4% on CD4% recovery at 4 years of age in pediatric patients aged 0-17 years. Overall, of the 162 vertically infected immunocompromised children, 72% returned to normal CD4% levels within 4 years of initiating ART. Patients with mild or severe immunosuppression as defined by World Health Organization (WHO) criteria were more likely to recover to normal CD4% levels compared to patients considered severe immunosuppressant at baseline. Additionally, for every five-year increase in baseline age, the proportion of children reaching recovery decreased by 19%. The study concluded that the combination of baseline CD4% and age-related effects resulted in >90% recovery after 4 years when

ART was initiated with mild immunosuppression at any age or advanced immunosuppression <3 years of age.

NEUROLOGY

Migraines:

Triptans are agonists of the vascular 5HT1 serotonin receptor, which cause vasoconstriction, and are a therapeutic and prophylactic option for migraine in adults and children. As of 2014, there were only two triptans approved by the FDA for use in children: almotriptan for adolescents (ages 12-17) and lisatriptan for children 6 years of age and older. In the past two years, two additional triptans have been approved for the acute treatment of migraine in adolescents aged 12 to 17 years. The first is zolmitriptan (Zomig), approved in 2014, based on a randomized, double-blind, placebo-controlled study of 310 people diagnosed with migraine for at least 1 year with a common untreated migraine attack lasting ≥ 3 hours. do. Two hours after initiation of treatment, 30% of patients treated with 5 mg of zolmitriptan did not report headache relief, compared to 17% in the placebo group. Sumatriptan and naproxen (Treximet) were also approved in 2014. In terms of efficacy, three different doses of sumatriptan/naproxen were found to be superior to placebo in reducing headache severity from moderate to severe or analgesic 2 hours after administration. (10/60 mg, 30/180 mg and 85/500 mg versus placebo, 29%, 27%, 24% versus 10%, $P < 0.01$).

Topiramate (Topamax) is an antiepileptic drug that is also used to treat and prevent migraines. In pediatrics, it is approved as monotherapy and adjuvant therapy for the treatment of partial or primary generalized tonic-clonic seizures. In 2014, topiramate was also approved for the prevention of migraine headaches in adolescents aged 12 to 17 years.

ONCOLOGY

The label of anticancer drugs has changed twice in the past two years. For erlotinib (Tarceva) used to treat refractory or relapsed ependymoma, the label change included a statement that safety and efficacy in pediatric patients have not been established. It is based on a phase 2 study in 25 pediatric patients, which was prematurely terminated due to lack of efficacy. For bortezomib (Velcade), a drug used to treat relapsing acute lymphoblastic leukemia (ALL) and

lymphoblastic lymphoma, the label states that it has not been established to be effective in pediatric patients with recurrent pre - B ALL.

Dinutuximab (Unituxin) became the third new drug approved for the treatment of pediatric cancer in the last 25 years. Dinutuximab is a monoclonal antibody that targets GD2, a glycolipid that promotes neuroblastoma cell growth. It is approved for the treatment of high-risk neuroblastoma in combination with isotretinoin (RA), IL2, and granulocyte macrophage colony stimulating factor (GMCSF) in patients who have had a modest response to first-line therapy but require additional treatment. This claim is based on a phase 3 study in 226 patients who had already undergone combination chemotherapy, surgery, radiation therapy, and stem cell transplantation.

Drug toxicity:

Children are prone to many side effects of medications that are found in adults. They may also experience additional side effects due to its direct toxic effect on the developmental organs. Growth Inhibition due to corticosteroid use is drug toxicity specific to pediatric patients. Adverse Drug Reactions are more common in pediatric patients with Hepatotoxicity due to sodium valproate and propofol Infusion syndrome following its use as a sedative. Other Adverse drug reactions only occur in certain age groups. For example, calcium precipitation following concomitant administration of ceftriaxone and intravenous calcium-containing solutions in neonates and young children. It is important to understand the mechanism for side effects of drug in children. For someone to understand the pathophysiology, prevention is often helpful to avoid future drug side effects.

Pharmacovigilance is the scientific study of the safety of drugs. However, pharmacovigilance in children is important for several reasons. First, children experience a wide range of drug side effects, just like adults, but may also experience other reactions. In addition, most adverse drug reactions are not detected due to poor drug quality. Confessed or unregistered. Educating health care providers on the importance of pharmacovigilance has been shown to be effective in increasing the number of reported adverse drug reactions. Over 9% of hospitalized children have adverse reactions to therapy and up to 4% of all hospital admissions are the consequence of ADRs[1-9.] There are some groups of pediatric patients, such as babies in the Neonatal Intensive Care Unit, in whom drug toxicity appears to be quite common (11–30%)[7-9.]

Formulations:

The development of pediatric formulations is an example of how children have historically been neglected. Pediatric formulations are more expensive to develop, and significant advances have been made in recent years, especially with different types of formulations that may be suitable for young children. Lack of proper formulation can be a contributing factor to dosing errors. The Tenfold error is much more common in pediatric patients than in adults. This is especially problematic for newborns, where a single vial, such as morphine, contains more than ten times the amount of a drug that an individual newborn needs.

Conclusion:

It is now widely accepted that drugs used in children must be scientifically evaluated for both efficacy and toxicity. Physicians who want to focus on pediatric drug research now have the opportunity to study Pediatric Clinical Pharmacology. Clinical trials of drugs in pediatric patients have advanced significantly. A challenge for the future Ensure that scientific evidence from clinical trials is used to support rational drug prescribing. Significant progress has been made in drug development for pediatric patients over the past two years. Main research areas include infectious diseases, particularly antiviral, anti-allergic and anti-asthmatic drugs. Other areas in progress include anti-inflammatory drugs used to treat gastrointestinal disorders and anti-epileptic drugs for seizures in children. In addition, drug development to treat rare diseases affecting the pediatric population, particularly hereditary metabolic disorders, has surged in recent years.

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