# Approach to Optimize Pharmacological Treatment in Children

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children, drugs, pharmacokinetic, pharmacodynamics, therapeutic drug monitoring

# **Pharmacological Treatment of Children**

The different stages of life are marked by processes of immaturity, maturity, and aging where the body undergoes different changes such as anatomical, physical, and biochemical. These processes alter the pharmacokinetics of drugs, individual comorbidities, and the patient's nutritional status.<sup>1</sup> Hence, it is extremely important to know the pharmacokinetics of drugs being administered to patients in order to individualize their use in medical therapeutics. During the pharmacological treatment in children, it should be noted that the physiological changes that occur in the pediatric age not only influence the drug distribution but also the absorption, biotransformation, and elimination and therefore the therapeutic response.<sup>2</sup> So, unintentional overdose in this population is more common, because the pediatrician usually does not consider these changes when indicating a medication.

Unfortunately, only the body weight is considered in administering the dose of a drug with the belief that the therapeutic response obtained would be good and would be similar in different groups of patients, without considering the homeostatic vision of the organism and biological variability. Pharmacological success is evaluated based on empirical test and error criterion; therefore, the pharmacological dose can be increased or decreased depending on the response obtained. It is not generally questioned whether the therapeutic dose is adequate to achieve and maintain plasma levels within the therapeutic range, which is very important to ensure the obtention of the required pharmacological goal.

Pediatric stage embraces the period that goes from birth to adolescence and this entails the possession of characteristics very different among individuals derived from the effect of growth and development.<sup>3</sup> Undoubtedly, these changes influence on drug distribution and response. The body composition and the processes of biological and physiological maturation constitute important variables worthy of consideration in the effort to adequately satisfy the therapeutic necessities of all the age groups, since different formulations are required to achieve optimum therapy which commences by ensuring the rational use of drugs.

Technological advances in the last decades, of which we are a living witness, have endowed us with the facilities to painstakingly analyze biological samples and thus give way to a potential progress in the study of pharmacokinetics and pharmacodynamics. From this knowledge, it becomes clear that the body is a dynamic model and thus brings to limelight the necessity to individualize treatment regimens based on parameters of each and every one, which in the past were not believed to be important.<sup>4</sup>

There are instruments that contribute to optimize drug management and safety in pediatric population as recommended even by the World Health Organization. The fundamental point of these instruments is the application of drug monitoring strategies that would contribute on ensuring the safety of the patients and on improving treatment schemes to guarantee the use of drugs in safe and effective manner.<sup>5</sup> However, there are some important situations that must be taken into account in order to carry out therapeutic drug monitoring (TDM): When drugs with narrow therapeutic range are administered; due to lack of desired pharmacological response; for the presence of toxicity manifestations using therapeutic doses; to adjust doses to conditions that alter pharmacokinetics<sup>6</sup>; to adjust doses in specific physiological conditions for example hepatic or renal dysfunction<sup>7</sup>; when drugs are administered with a close doseresponse relationship; and drugs that follow a nonlinear

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kinetics. This is important because the most effective therapeutic range of many drugs, far from unnecessarily high concentrations with potential risk of producing toxicity in those taking them, is still unknown.<sup>8</sup>

It is of paramount importance that pediatric doctors as well as specialists in the health sector who are dedicated to childcare have complete knowledge of pharmacokinetics, based on new therapeutic strategies ensuing from information furnished by research works. The consideration of these concepts would definitely permit the elaboration of optimum, specific, and individualized treatment for pediatric patients.<sup>9</sup>

It is necessary to emphasize that the pediatric population is vulnerable to presenting adverse reactions to medications due to the physiological characteristics of the developmental stage and the changes in the pharmacokinetic constants and therapeutic effect, compared to the adult age. Because children have greater adverse reactions compared to adults, it is necessary to perform pharmacovigilance in this population. Even consider that adverse effects to medications can occur even in the breastfeeding stage, and that drug interactions may influence the presence of adverse reactions. Although there is little information, however, it has been noted TDM has contributed in the surveillance of dedicated disease.<sup>10</sup>

# **Optimization of Drug Prescribing in Children**

One of the research lines that cropped up, for its need and nature, is pediatric clinical research. Undoubtedly and due to its characteristics, this research area has turned out to be extremely interesting but at the same time difficult for many researchers due to restrictions, especially the ethical aspects. These restrictions arose when it becomes obvious that during the phases of pharmacological research, the groups of population involved in the final work are special groups such as the pediatric population, pregnant women, and the elderly population. By nature, these population groups have lesser pharmacological therapeutic alternatives when compared with normal population.

In their part, the pharmaceutical industries consider these special groups in their research works only when they are completely sure of a market for the sale of their products. The lack of studies backing up the safe use of drugs in this special groups has cornered the specialists attending these patients into the dilemma of using medications that are probably devoid of studies guaranteeing their reliable use, which is why the legend saying "The use of this drug is the sole responsibility of whom prescribes it" that is commonly found in most of the products.

Having being aware of this problem, the National Institute of Pediatrics (INP), Mexico City, formed a group of researchers led, since its inception, by Dr Hugo Juarez Olguin to address this issue in the absence of alternative drug formulas for use in children. Dr Juarez Olguin is a renowned researcher in Clinical and Experimental Pharmacology, a PhD holder in Medical Research, member of National System of Researchers with level 2 category, and counts with 30-year teaching experience as a professor of Pharmacology in the Faculty of Medicine, UNAM. For more than 20 years and with extensive experience in pharmacological studies in pediatrics, Dr Juarez Olguin and his team of collaborators have been carrying out studies to know the adequate and safe formulation for children of various drugs whose presentation is only for adults.

Outstanding among his studies are those performed for the development of propafenone pediatric suspension, an efficacious pediatric antiarrhythmic, the patent of which was authorized to him, and the proper use of sildenafil in the treatment of pulmonary arterial hypertension.<sup>11,12</sup>

One of the strategies in the obtention of knowledge that supports clinical-hospital decision-making is pharmacokinetic and pharmacodynamic study. From all these immense works arose the notion to transfer his research experiences in the book "Optimization of Drug Prescribing in Children," recently published by Nova Science Publishing House, where he has documented in black and white his years of invaluable knowledge which he puts to the disposition of the readers seeking information on the proper management of medicines in the pediatric population.

Worthy of citing in this synopsis are some important, easyto-read and knowledge-enriching chapters, for example, "Pharmacokinetics, Growth and Development," that brings into limelight the changes that occur from childhood until maturity which unquestionably affect the basic organic functions of children and which directly and indirectly present in the pathologies that could affect this population group; and "Main Diseases in Pediatrics Population," a chapter that describes the principal diseases that afflict the pediatric population and their treatments. In the chapter "Pharmacology for the Fetus and the Newborn," a deep in-look of the biomedical aspects from early life stage and how these changes impact in the future of the infant were rigorously and vividly undertaken.

Without sounding sensationalist, 2 outstanding topics "Unintentional Poisoning with Drugs in the Pediatric Population" and the chapter "Suicidal Attempts by Consumption of Drugs in Children" have attracted attention since it was first published. These topics are totally updated and contain critical analysis of the causes, medical attention approach, and recommendations when faced with these situations as well as the challenges a pediatrician may confront in his professional performance.

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