ECRONICON OPEN ACCESS

EC PHARMACOLOGY AND TOXICOLOGY
Short Communication

Perspectives in Neonatal Pharmacology

Novy Gupte*

Drug Regulatory Consultant, Science and Policy Unit, Clinical Development Services Agency (CDSA), Department of Pharmacology, All India Institute of Medical Sciences, New Delhi, India

***Corresponding Author**: Novy Gupte, Drug Regulatory Consultant, Science and Policy Unit, Clinical Development Services Agency (CDSA), Department of Pharmacology, All India Institute of Medical Sciences, New Delhi, India.

Received: October 17, 2018; **Published:** December 28, 2018

Abstract

Neonatal pharmacology has not received the deserving attention. The extensive variability in pharmacokinetics and pharmacodynamics in the newborn because of its fast maturation is a glaring feature of the newborn. This, together with the newly-evolving treatment modalities, environmental issues and pharmacogenetics render clinical pharmacological research in neonates important. The challenges have to be met. Moreover, application of pharmacovigilance with regard to adverse drug reactions (ADRs) is urgently needed.

Keywords: *Neonatal Pharmacology; Microdosing; Neonatal Pharmacotherapy; Off-Label Drugs; Pharmacodynamics; Pharmacokinetics; Pharmacological Challenges; Pharmacovigilance; Unlicensed Drugs*

Introduction

Neonatal pharmacology setting is unique [1]. Effective, result-oriented and safe drug administration in neonates should be based on two parameters:

1. Integrated knowledge on the evolving physiological characteristics of the newborn.
2. Pharmacokinetics and pharmacodynamics of the given drug.

Understandably, clinical pharmacology in neonates is as dynamic, varied and diverse as the newborns. Advances in the basic science research have improved our understanding of use of drugs [2].

Unfortunately, neonatal pharmacotherapy remains an area that has not received the deserving attention. Currently, several drugs are being employed notwithstanding lack of specific clinical research in this vulnerable age group. Present day pharmacotherapy in neonates is mainly based on the individual clinical expertise of specialised neonatologists and paediatricians. Most drugs in use in neonates are "off-label". These unlicensed drugs continue to be employed in neonatal drug therapy without undergoing the recommended regulatory phases of drug development.

Peculiarities of the newborn in relation with pharmacotherapy

The peculiarities of the neonate in relation to the drug therapy include [3]:

1. The individual response to a drug in relation to efficacy and safety in the newborn is highly variable. Predicting drug dosing too is complex. This is because of the rapid physiological changes occurring during the perinatal and early postnatal periods affect the pharmacokinetic profile of several drugs.
2. Neonatal disorders (say, renal and hepatic diseases) may also have significant implications for drug pharmacokinetics.
3. Pharmacotherapy in the newborn poses difficulties in accurate drug delivery and, consequent upon that a high risk of adverse drug reactions.
4. The neonates, especially in NICU, are highly exposed to the risk of medication errors, with potentially serious adverse events.

In other words, the extensive variability in pharmacokinetics and pharmacodynamics because of its fast maturation is a glaring feature of the newborn. In view of this, together with the newly-evolving treatment modalities, environmental issues and pharmacogenetics, clinical pharmacological research in newborns assumes a considerable importance. The conduction of such a research is, however, tough and cumbersome [3].

Pharmacological challenges in the newborn

Quite a few problems pose bottlenecks in conduction of research in the newborn [4]. In the first place, the pharmacological trial in neonates are more difficult to perform. Secondly, appropriate dosing is hampered by the rapid physiological changes occurring at this stage of development, and the selection of proper end-points. Thirdly, biomarkers are complicated by the limited knowledge of the pathophysiology of the specific neonatal diseases. Fourthly, there are many ethical challenges in planning and conducting drug studies in the newborns.

These "pharmacological" challenges add to the ethical challenges that are always present in planning and conducting clinical studies in neonates. These challenges justify that clinical research in neonatology should be evaluated by ethical committees with specific expertise.

Overcoming the challenges: Modus operandi

How to overcome the challenges? Tailored tools and legal initiatives, combined with clever trial design are likely to result in more robust information on neonatal pharmacotherapy [5]. This necessitates collaborative efforts between clinical researchers, sponsors, and regulatory authorities. Additionally, patient representatives and society need to make their contribution.

The regulatory framework for model-based neonatal medicinal development needs to be streamlined and initiated wherever it doesn't exist. In trials, success is assured by the implementation of specific pharmacokinetic assessments as a result of accurate drug dosing achieved with a combination of dose validation, population pharmacokinetics and mathematical models of drug clearance and distribution.

Further, age-specific pharmacodynamics need to be considered via appropriate evaluations of drug efficacy with end-points adapted to the peculiar pathophysiology of diseases in this age group

Tailoring the research tools and clinical research facilities through pharmacokinetic and pharmacodynamic modelling is needed. New innovations in pharmacokinetic research, e.g. population pharmacokinetic modelling, offer opportunities to conduct clinical trials aimed at improving the safety and effectiveness of the drugs in newborns.

What is urgently need is the development of dried blood spot techniques and the introduction of micro-dosing and tracer methodology in neonatal drug studies on priority. Secondly, concerted efforts should be made to build research networks and clinical research skills for neonates. Through population modelling, both techniques can be combined with sparse sampling techniques. Boosting the initiatives to develop and integrate knowledge on neonatal pharmacotherapy through dedicated working groups, research networks and clinical research skills can go a long way in meeting the desired goals.

Pharmacovigilance

Over and above all that, pharmacovigilance is needed to recognize specific adverse drug reactions (ADRs). Each and every staff member in the neonatal section involved in carrying out clinical trials needs to be acutely sensitive to the need to report ADRs in keeping with regulatory requirements [3,5]. Even paediatric anaesthesiologists should consider to contribute to improved neonatal pharmacotherapy through clinical trial design and collaboration as well as reporting on adverse effects of specific drugs [6,7].

Bibliography

1. Allegaert K., *et al*. "Neonatal clinical pharmacology". *Pediatric Anesthesia* 24.1 (2014): 30-38.

2. O'Hara K., *et al*. "Pharmacokinetcs in neonatal prescribing: Evidence-base, paradigms and future". *British Journal of Clinical Pharmacology* 80.6 (2015): 1281-1288.

3. Goodyear EW. "Drug therapy in the newborn: What's wrong?" Proceedings, Asian Workshop on Advances in Neonatal Care. Abstract No. AWANC/2016/Part I-03 (2016).

4. Samardzic J., *et al*. "Neonatal medicines research: challenges and opportunities". *Expert Opinion on Drug Metabolism and Toxicology* 11.7 (2015): 1041-1052.

5. Gupte S and Gupte N. "Paediatric Drug Directory". 9th edition. New Delhi, India: Jaypee (2018).

6. Ku LC and Smith PB. "Dosing in neonates: special considerations in physiology and trial design". *Pediatric Research* 77.1-1 (2015): 2-9.

7. Gupte N and Gupte S. "Neonatal pharmacotherapy: Issues, concerns and challenges". *EC Paediatrics* 5.5 (2017): 154-155.

Volume 7 Issue 1 January 2019