

Position Paper

Paediatric Age Categories to be Used in Differentiating Between Listing on a Model Essential Medicines List for Children

Introduction

Although not specifically excluded from the essential medicines concept, the needs of paediatric age groups has not been sufficiently catered for in previous editions of the WHO Model Essential Medicines List. The report on the 4th Model List of Essential Drugs included guidelines for the selection of pharmaceutical dosage forms, but stated that “[s]pecific paediatric dosages and formulations are included in the list only when indicated by special circumstances”.¹

There are various conventions applied in sub-dividing the paediatric population by age, which to some extent reflect issues of developmental progression. The British National Formulary for Children, for example, provides doses for neonates (under 1 month in age), then for children from 1 month to 4 years, and for children 4 year to 10 years.² Many entries do not, however, follow this age division. For example, the US FDA³ classification is neonate (birth to 1 month), infant (1 month to 2 years), children (2 to 12 years) and adolescent (12 to < 16 years).

Underlying Principle

The division of Paediatric Age Categories for the administration of drugs is largely arbitrary. The majority of drugs are administered on a weight basis (e.g. mg/kg), often until either an adult dose or an arbitrary weight ceiling (e.g. 50 kg) is reached. This practice of weight-based dosing underscores the close, linear relationship between body weight and growth. Nevertheless, the administration of various dosage forms is often limited due to, for example, an inability to swallow a tablet. Individual preferences for older children must also be considered.

¹ World Health Organization. The use of essential drugs. Second report of the WHO Expert Committee. Technical Report Series 722, 1985.

² British National Formulary for Children, 2006.

³ Guidance for Industry – General Considerations for Pediatric Pharmacokinetic Studies for Drugs and Biological products, Draft Guidance, US FDA, 10 November 1998.

Overall Goals :

1. To identify which factors should be taken into account when devising suitable age categories to be used in a Model Essential Medicines List for Children. The following factors are suggested to be considered ⁴ :
 - a. Age – dependent pharmacokinetic characteristics
 - i. Body composition
 1. Body compartment sizes
 2. Protein concentration and function
 - ii. Renal Elimination
 - iii. Hepatic Elimination
 - iv. Absorption
 - v. Pharmacogenomics
 1. Gender
 2. Ethnicity
 3. Genome – specific traits
 - vi. Body Surface Area
 1. Muscle, fat, subcutaneous tissue
 2. Weight and height measurements
 3. *Changing* weight and height
 - b. Pharmacodynamics
 - c. Adverse Reactions
 - d. Practicality (including availability, transport, storage conditions)
 - e. Preferences
 - f. Social stigma

⁴ *Modified after* : Yaffe SJ and Aranda JV. Pediatric Pharmacology – Therapeutic Principles in Practice. Saunders, 1992

2. To recommend suitable age groupings, based on fundamental considerations of paediatric development, metabolic capacity, international regulatory practice, ease of administration and patient/care giver adherence.
 - a. The following age groupings, with slight differences, appear to have received widespread acceptance.^{2,3,5,6} Weight-based drug dosing is recommended up to the adult dose, unless data are available to support a larger absolute dose in children. Gestational age and corrected gestational age are critical for dosing in premature newborns and neonates. These ages must be taken into consideration in addition to weight in this sub-population.

⁵ European Medicines Agency. Reflection Paper : Formulations of Choice for the Paediatric Population, London, 28 July 2006.

⁶ Taketomo CK, Hodding JH, Kraus DM. Pediatric Dosage Handbook, 13th Edition, Lexi-Comp, 2006.

Suggested Age Groupings :

Premature Newborns

< 38 weeks gestational age

Term Newborns

> 38 weeks gestational age

Neonate

0 – 30 days of age

Infant

1 month – 2 years

Young Child

2 – 6 years

Child

6 – 12 years

Adolescent

12 – 18 years

3. To recommend which drug formulations should preferably be made available for each of the age bands suggested. ^(5,7,8) (A detailed discussion is in the Position paper on Dosage Forms.)

	Neonate	Infant	Young Child	Child	Adolescent
<i>Oral</i>					
Suspension	X	X	X	X	X
Syrup	X	X	X	X	
Drops	X	X	X		
Granules		X	X	X	
Disintegration tablet			X	X	X
Tablet			X**	X	X
Capsule				X	X
<i>Buccal</i>				X	X
<i>Rectal</i>					
Suppository	X	X	X	X	X**
Enema	X	X	X	X	X**
<i>Topical</i>	X	X	X	X	X
<i>Parenteral</i>					
IV	X	X	X	X	X
SC	X	X	X	X	X
IM	X*	X	X	X	X
Nasal		X	X	X	X
Metered Dose Inhaler			X	X	X
Nebulizer	X	X	X	X	X

* Although IM is not desired, it may be necessary for initial and subsequent doses in patients with very poor venous access.

** Not preferred by this age category, but in some instances may be required.

⁷ Calle G, Lagomarsimo E. Evaluation of Preferred Dosage Forms in 338 Argentinian Paediatric Outpatients (personal communication).

⁸ Personal experience

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