Drug Use In Infants & Children

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Pharmacokinetics in Children

1. Absorption

a. ↑ from skin due to thin stratum corneum & better hydration

b. GIT: altered, low acidity, ↑ed gastric emptying time, ↑ed enterohepatic circulation, irregular peristalsis(PCM & phenobarbitone ↓ed & of penicillin G & ampicillin ↑ed)

c. Intramuscular & subcutaneous unpredictable because thin skeletal muscle mass & fat

d. Low bile acid & lipase so less lipophilic drug absorption

e. diarrhoea

2. Drug distribution

a. More in c/o hydrophilic than adult because of higher percentage of body water (65-85%), also 40% is extra cellular in the neonate (aminogycoside)
b. Less fat in pre term (1%) than full term(15%) thus less lipophilic drug concentration in premature
c. Less plasma protein available so more free drug , so more toxicity (diazepam)
d. Competition with bilirubin for albumin may displace it , may cause kernicterus (sulfonamides) & vice versa (phenytoin)

3. Drug metabolism

a. Less liver cytochrome P450 dependent activity , so chances of toxicity high e.g.chloramphenicol causing grey baby syndrome

b.Table shows difference in half life in Neonate & adult p.s.phenobarbital & Phenytoin have low half life during infancy

Drug	Neonatal Age	Neonates $t_{1/2}$ (hours)	Adults $t_{1/2}$ (hours)
Acetaminophen		2.2–5	0.9–2.2
Diazepam		25–100	40–50
Digoxin		60–70	30–60
Phenobarbital	0–5 days	200	64–140
	5–15 days	100	
	1–30 months	50	
Phenytoin	0–2 days	80	12–18
	3–14 days	18	
	14–50 days	6	
Salicylate		4.5–11	10–15
Theophylline	Neonate	13–26	5–10
	Child	3–4	

c. Enzyme induction

Due to mother receiving drugs or child

-enzyme induction may increase interaction

-phenobarbitone is used to treat neonatal jaundice on the same principal

* During toddlerhood metabolite rate of many drugs exceeds adult values .

4. Drug excretion

a. GFR is less , so is tubular secretion, resulting in less renal clearance
b. Normal clearance achieved at the age of 6-12 months
c. Subsequently during toddlerhood it increases than adult value for some (e.g. for digoxin)
d. So appropriate dose adjustment is necessary
e. E.g. penicillin, ampicillin, aminoglycosides

Pharmacodynamic alterations

- Response of drug may be different in children than adults but mechanism remain same
- Due to immature receptors or neurotransmitter system
- e.g. glucocorticoids-premature epiphysial fusion; tetracyclines- malformed bone & teeth also staining of teeth, antihistaminics & barbiturates –excitement, amphetamine- ↓es abnormal hyperactivity

Clinically important

- PDA can be closed with administration of indomethacin
- In case of fallot's tetralogy administration of alprostadil (PGE_1) is life saving

Pediatric Dosage Forms & Compliance

- Use of tablets is inconvenient & injections are rejected by children
- So preferred formulations are liquid e.g. suspension, elixir, drops
- Proper use should be instructed
- Rejection, spitting & vomiting should be considered
- Proper measurement
- Suspensions to be shaken well before use
- Reduce dosing errors
- Encourage children to take medicine themselves

Dose

- Young's rule: dose= Adult dose × Age(years) / Age + 12
- Clark's rule: dose = Adult dose × Weight(kg) / 70
- Determination of drug dosage from surface area

Weight		Approximate Age	Surface Area (m^2)	Percent of Adult Dose
(kg)	(lb)			
3	6.6	Newborn	0.2	12
6	13.2	3 months	0.3	18
10	22	1 year	0.45	28
20	44	5.5 years	0.8	48
30	66	9 years	1	60
40	88	12 years	1.3	78
50	110	14 years	1.5	90
60	132	Adult	1.7	102
70	154	Adult	1.76	103