Drugs affecting breast milk and lactation

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@ = introduction

!! = imp.

green = notes

@LACTATION

- ***Breast feeding*** **is very important because breast milk is the healthiest form of milk for babies.**
- **Provide the baby with immunoglobulins (IgA, IgM) that are essential for protection against gastroenteritis.**

@ DRUGS AND LACTATION

- **Most drugs administered to breast feeding woman are detectable in milk.**
- **The concentration of drugs achieved in breast milk is usually low.**
- **Even small amounts however may be of significance for the suckling child because his drug metabolic and eliminating mechanisms are immature.**

We have to know that the PKs approached regarding neonates is different than others (baby, children, adult)

- **Neonates have very limited rate of metabolism due to immaturity of liver enzymes that is not fully developed until 8 weeks of age (**actual development = 2months old**).**
- **Renal clearance is less efficient: well developed after 3-5 months.**

Special concern should be on:

- **Premature babies and newborn (less than 1 month of age) have much more limited capacity for metabolism and excretion.**

Normal gestation age "full term neonates" = 38 – 42 weeks
Before 38 week → preterm neonates

Why even when we give small amount of the medication it affect the neonates?

↓ immunity
↓ fat (body weight)
Immature blood brain barrier
↓ metabolizing capacity of the liver & ↓ renal clearance

***some of the antibiotics could be given to full term but avoided in preterm neonates.**

Most of the drugs metabolize in the liver by 2 phases:

1- liver microsomal enzyme (CYP 450)

2- conjugation (inactivation after this phase) ,it happen by transferase enzyme
Usually conjugation occurs b\w metabolized coming from phase 1 and internal substances in our body (ex.: AA, methyl group …etc)
In neonates not only the liver microsomal enzyme is retarded (not developed) also the substances required in conjugation is reduced

- **The epithelium of the breast alveolar cells is most permeable to drugs during the 1st week postpartum, so drug transfer to milk may be greater during the 1st week of an infants life.**

-We must pay attention when we give medication in the 1st week b\c there are gaps between epithelium of the breast
they start to reduce and have tight junction during the 2nd week

@ Factors controlling passage of drugs into breast milk

1. Physiochemical character of the drug

- **Lipid solubility of the drug:** lipid soluble drugs pass more freely in the breast milk
- **Molecular weight:** low molecular weight drugs are more likely to be transferred to breast milk than high molecular weight

Even when warfarin has LMW it is not contraindicated in breast feeding women b\c it has other characteristic that limit it's transportation and excretion to milk → it is highly bounded to plasma protein→ no harmful effect on the neonates
(but heparin is better as anticoagulant)
Remember warfarin in pregnant women is contraindicated b\c it has a teratogenic effect.

@ Factors controlling passage of drugs into breast milk

- **Degree of ionization:** nonionized form of drugs are more likely to be transferred into breast milk.

Ionized → polar → soluble in water → retarded when it try to cross the membrane
Non-ionized → non-polar→ lipid soluble →cross easily

- **pH of the plasma and milk:**
  - Weakly alkaline drugs tend to be concentrated in milk.
  - Weakly acidic drugs don't enter the milk to a significant extent and tend to be concentrated in plasma.

2. Plasma protein binding of drugs

highly plasma protein-bound drugs pass less into milk.

3. Drug concentration in maternal serum

-High conc. Of drugs in the mother →crossing to milk .

Transfer of drug from mother's blood to milk is low with :

1. drugs with large Vd(volume distribution).
2. drugs with short t ½(avoid long acting preparation.)

@The amount of a drug to which the baby is exposed as a result of breast feeding depends on:

- **The concentration of the drug in the milk at the time of feeding.**
- **The amount of milk consumed.**
- **The amount of drug absorbed (by neonates).**
- **The ability of the baby to eliminate the drug.**

@ General considerations to minimize risk to nursing infant

- **Whenever possible use a topical form of medication instead of an oral form.**
- **Choose medications with the shortest half-life(cleared from mother`s circulation rapidly) and highest protein-binding ability(decease crossing from blood to milk).**
- **Choose medications with the lowest lipid solubility.**

@ General considerations to minimize risk to nursing infant

- **Lactating mother should take medication just after nursing and 3-4 hours before the next feeding.**
- **The safest drug should be chosen e.g. Acetaminophen than aspirin for analgesia**
- **Drugs with no safety data should be avoided or lactation should be discontinued.**

Drugs that should be avoided during lactation (due to harmful effect)

1. **Radioactive iodine** →cross→ affect thyroid function in baby)
2. **Anticancer drugs**
   - ***Doxorubicin, cyclophosphamide, methotrexate***
3. **CNS acting drugs (**abused by the mother**)**
   - ***Amphetamine(****CNS stimulus****), heroin, cocaine***
4. **Lithium (** antimanic, secreted in milk in high concentration**)**

Drugs that can suppress lactation

(avoiding them b\c they aren`t harmful BUT suppress lactation)

- **Thiazide diuretics**
- **Levodopa**
- **Bromocriptine (one of the ergot derivatives it ↑ dopamine)**
- **Ergot derivatives**
- **Androgens**
- **Estrogen, oral contraceptives that contain high-dose estrogen and a progestin.**

Lactation influenced by oxytocin & prolactin
Level of prolactin opposite to dopamine
↑ dopamine → ↓ prolactin

→ So we give progesterone only (mini pills).

Drugs that can augment ↑ lactation

Persistent and active suckling release both prolactin and oxytocin to stimulate milk secretion.

Dopamine antagonists stimulate prolactin secretion as

- **Metoclopramide (antiemetic it ↑ prolactine & one of it's Ads is galactorreha)**
- **Haloperidol (antipsychotic)**
- **Phenothiazines (antipsycotic)**
- **Methyl dopa (antihypertensive)**
- **Theophylline (bronchodilator)**

!! Antibiotics

Penicillins ***Ampicillin*** ***amoxacillin***	**No significant adverse effect** **allergic reactions, diarrhea (due to it's action on normal flora)**
Cephalosporins	**No significant adverse effect**
Chloramphenicol	**"Gray baby" syndrome** **Possibility of bone marrow suppression**
Sulphonamides	**hyperbilirubinemia -neonatal jaundice** **Should be avoided in premature infants or infants with G6PD deficiency**

!! Antibiotics

Erythromycin	**No significant adverse effect**
Quinolones	**Risk of arthropathies** **Should be avoided**
Tetracyclines **(ability to bind with Ca++ →not given with dietary product)**	**Absorption by the baby is probably prevented by chelation with milk calcium. Risk of tooth discoloration.** **-Tetracyclines → cross to milk→ bind Ca present in the milk→** **-can be used but better to be avoided cuz→ they lead to staining of the teeth & affect the bones**

!! Sedative/hypnotics

single doses are unlikely to be harmful
Regular use of high doses should be avoided

Barbiturates (phenobarbitone)	**Lethargy, sedation, poor suck reflexes** **Clinical monitoring is recommended**
Benzodiazepines (diazepam)	**Lethargy, sedation in infants** **Clinical monitoring is recommended**

!! Antidiabetics

Insulin	**safe**
Oral antidiabetics	**compatible**
Metformin	**avoid due to lactic acidosis**

- **Oral Antidiabetics can be given but Metformin is avoided b\c it lead to lactic acidosis**
- **Compatible = need regular monitoring**

- **Be aware b\c Oral Antidiabetics can lead to hypoglycemia in neonates. So regular monitoring**

!! Oral contraceptives

Non hormonal method should be used

Avoid estrogens containing pills

Estrogens ↓ milk quantity

Progestin only pills or minipill are preferred for birth control.

Antithyroid drugs **Propylthiouracil** **Carbimazole** **Methimazole**	**May suppress thyroid function in infants.** **Propylthiouracil should be used rather than carbimazole or methimazole.**
Anticonvulsants **Carbamazepine** **Phenytoin**	**Are preferable over others** **Amounts entering breast milk are not sufficient to produce adverse effects** ***Infants must be monitored*** Assess liver function & blood
Anticoagulants **Heparin** **Warfarin**	**Heparin is not present in breast milk.** **Safe (very small quantities found in breast milk).**

Iodine (radioactive)	**Hypothyroidism permanent in infant** **Breast-feeding is contraindicated**
Cytotoxic drugs	**Breast feeding should be avoided**
Lithium	**Large amounts can be detected in milk**
CVS drugs **Atenolol**	**Risk of bradycardia and hypoglycemia** **avoid**

!! Drugs of choice in lactation

Antibiotics	**Cephalosporins, penicillins** **Avoid chloramphenicol, sulphonamides and tetracyclines**
Antidiabetics	**Insulin – oral antidiabetics** **Avoid metformin**
Anticoagulants	**Heparin - warfarin**
Analgesics	**Acetaminophen**
Antithyroid drugs	**Propylthiouracil is preferable over others**
Anticonvulsants	**Carbamazepine - phenytoin**
Oral contraceptives	**Progestin only pills or minipills are preferred for birth control.**
Antiasthmatics	**Inhaled corticosteroids – prednisone**