

PRESCRIPTION OF DRUGS IN SPECIAL GROUPS

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Overview

- ▶ **Medicines** are meant to help patients get relief from the effects disease conditions (diagnosis, prevention and treatment)
- ▶ For this to be actualised there is an interaction between drugs and the body's biological systems
- ▶ These interactions may sometimes lead to the occurrence of other unwanted effects i.e. side effects, adverse effects and sometimes fatalities in unfortunate situations
- ▶ This is why **quality, efficacy** and **safety issues** surrounding drugs should be put into considerations to ensure the **optimisation of benefit** while reducing the **harmful effects** of drug therapy

Factors affecting drug safety and efficacy

- ▶ There are a number of established biological variables that can alter the response to drugs in particular patients

- ▶ Below are the examples of those factors affecting drug effect or under which special care should be taken when administering drugs;
 - i. Age
 - ii. Disease
 - iii. Pregnancy
 - iv. Lactation

EFFECT OF AGE ON DRUG EFFICACY AND SAFETY OF DRUGS

AGE

Regarding age, it will be great to appreciate the following classification;

- ▶ Preterm Neonate (Preterm Newborn Infant) (born at < 37 weeks gestation)
- ▶ Neonate (New born infant) – from birth to 27 days
- ▶ Infants or toddlers – 20 days to 23 months (about 6 months)
- ▶ Young children – 2 to 5 years
- ▶ Older children – 6 to 11 years
- ▶ Adolescents – 12 to 18 years
- ▶ Adults – 18 years
- ▶ Geriatrics – the aged

Neonates

- ▶ The capacity to metabolize and excrete drugs especially in premature infants is reduced because of low level of biotransformation enzymes
- ▶ Oxidative reactions and glucoronate conjugation occur at a lower rate in neonates than in adults
- ▶ Sulfate conjugation is well developed in neonates
- ▶ Some drugs that primarily depend on glucoronate conjugation in adults like acetaminophen are metabolized chiefly by sulfate conjugation in neonates
- ▶ Overall, the rate of biotransformation of most drugs is lower in neonates and infants than it is in adults

Geriatrics

- ▶ In comparison with children and young adults, elderly adults tend to have reduced capacity to metabolize drugs
- ▶ Biotransformation via oxidative reaction declines more than biotransformation via drug conjugation
- ▶ It would therefore, be safer to choose drugs that are conjugated e.g. benzodiazepines which undergo glucuronidation are more preferred compared to those that undergo oxidation
- Benzodiazepine which undergo conjugation; Lorazepam and temazepam
- Benzodiazepines which undergo oxidative biotransformation; diazepam

Medication reviews at the point admission

- ▶ Review all medications being taken by the patient prior to their admission
- ▶ These may include relevant over the counter drugs (OTCs), herbal, vitamins, etc
- ▶ Assess previous compliance when it comes to taking of medicines
- ▶ Avoid unnecessary poly-pharmacy by using drugs that treat more than one condition where practical e.g. beta-blockers for both hypertension and angina pectoris
- ▶ Discontinue drugs unnecessary in hospital e.g. urinary antispasmodic when catheter has been placed

Safe prescribing habits

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When initiating a new medication:

- ▶ Choose agents whose pharmacokinetics properties in elderly patients are known
- ▶ Begin with a short-acting agent but by discharge convert to an agent that is given once or twice daily in order to enhance patient compliance
- ▶ If patients require multiple medications, avoid drugs that are inhibitors or inducers of CYP P450 hepatic metabolism or are highly bound to albumin
- ▶ Examples: ceftriaxone, diazepam, lorazepam, phenytoin, valproic acid, warfarin (If in doubt, consult a pharmacist)
- ▶ When the maintenance dose of a medication is not established, **“start low and go slow,”** to allow time to titrate the dose against the desired clinical effect
- ▶ Use lower than usual maintenance doses of medications that are renally excreted e.g. digoxin

Renal function

- ▶ Renal function is lower in neonates and the elderly adults compared to the young adults
- ▶ This affects the renal excretion of many drugs e.g. the half lives of aminoglycoside antibiotics are greatly prolonged in neonates
- ▶ Glomerular filtration declines 35% between the ages of 20 and 90 years which corresponds to reduced elimination of many drugs
- ▶ There is increased sensitivity to drugs in the very old and very young and therefore, the dosage per kilogram of body weight should be reduced

EFFECTS OF DISEASE ON DRUG EFFICACY AND SAFETY

DISEASE

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- ▶ Hepatic and renal disease may reduce the capacity of the liver and kidneys to bio transform and excrete drugs
- ▶ This reduces the drug clearance thereby necessitating a dosage reduction to avoid toxicity
- ▶ Heart failure and other conditions that reduce hepatic blood flow may also reduce drug biotransformation
- ▶ Oxidative drug metabolism is usually impaired in patients with hepatic disease while conjugation process may be little affected

Dose adjustment in hepatic or renal diseases

- ▶ In patients with hepatic and renal disease, there is need of dosage adjustment according to clinical references
- ▶ Dosage adjustment is done by;
 - i. Reducing the dose
 - ii. Increasing the interval between doses

Determinants of dose adjustment

- ▶ Laboratory measurements of renal and hepatic function
- ▶ Plasma drug concentration

DRUGS IN PREGNANCY AND LACTATION

DRUGS IN PREGNANCY AND LACTATION

- ▶ Pregnant women may require drug therapy for pre-existing medical conditions or for problems associated with their pregnancy
- ▶ This patient population may be exposed to drugs or environmental agents that have adverse effects on the unborn
- ▶ It is important to understand the principles of drug use in these patients because any drug administered to a pregnant woman may directly harm the developing fetus
- ▶ On the other hand, drugs may also adversely influence her pregnancy

Drugs in pregnancy and lactation Cont'd

- ▶ Drugs taken by women during pregnancy or lactation can cause adverse effects in the fetus or infants respectively
- ▶ Risk of drug induced abnormality (teratogenic effects) is the greatest during organogenesis i.e. the period from 4th to 10th week
- ▶ After 10 weeks , the major risk is to the brain and the spinal cord
- ▶ It is estimated that about 1% - 5% of fetal malformations are attributed to drugs

Examples of teratogenic and potentially toxic drugs

- ▶ Vitamin A derivatives: Vitamin A, isotretinoin
- ▶ ACE inhibitors e.g. enalapril
- ▶ Warfarin and warfarin derivatives
- ▶ Estrogen and androgen
- ▶ Ethanol
- ▶ Antibiotics: e.g. Tetracycline, metronidazole, quinolone etc
- ▶ Lithium
- ▶ Anticonvulsants: e.g. Phenytoin, valproic acid, trimethadione and sodium valproate
- ▶ Anti-neoplastics: e.g. Busulfan, chlorambusil, cyclophosphamide and methotrexate
- ▶ Finasteride

Fetotoxic drugs

- ▶ **Fetotoxic** drug effects are the result of pharmacological activity of a drug that may physiologically affect the developing fetus

- ▶ Clinically significant fetotoxic effects include the following
 - I. CNS depression: e.g. Barbiturates, tranquilizers, antidepressants, narcotics, analgesics and anesthetic drugs
 - II. Neonatal bleeding: e.g. NSAIDs, anticoagulant
 - III. Drug withdrawal: barbiturates, narcotics, benzodiazepines, alcohol
 - IV. Reduced birth weight: Pregnant women who smoke cigarettes, consume alcohol or abuse drugs

Drug excretion in milk

- ▶ After a drug is administered to a nursing mother, the drug may be partially activated or inactivated in the maternal liver
- ▶ The drug may be metabolized to active or inactive metabolites
- ▶ The primary hormone responsible for controlling breast milk production is Prolactin

Drugs that decrease serum prolactin levels include;

- a) Ergot alkaloids e.g. ERGOTAMINE
- b) L- dopa
- c) Bromocriptine

Drug excretion in milk Cont'd

The following drugs increase serum prolactin levels;

- a) Metoclopramide
- b) Methyldopa
- c) Amphetamines
- d) Haloperidol
- e) Phenothiazine
- f) Theophylline

Examples of drugs that readily enter breast milk

- ▶ Narcotics, barbiturates and benzodiazepines- Hypnotic effect on the nursing infant
- ▶ Antidepressants and antipsychotics
- ▶ Metoclopramide - CNS effects
- ▶ Anticholinergic compounds - CNS effect

Pharmacokinetic Changes during Pregnancy

Absorption

- ▶ Slowed gastrointestinal motility may delay absorption of oral agents

Renal clearance

- ▶ Glomerular filtration rates increase in pregnancy to 150% of normal range
- ▶ This may call for dose alterations for many medications that are renally cleared
- ▶ For example, digoxin doses may need to be increased to as much as 1.0 mg by the end of the second trimester.

Hepatic clearance

- ▶ An increase in hepatic clearance of pharmacologic agents is often seen during pregnancy

Volume of distribution

- ▶ Plasma volume increases to 150% of normal by 24 to 28 week's gestation, increasing the volume of distribution
- ▶ Drugs may require dosage adjustments

Protein binding

- ▶ Dilution of serum proteins prevalent and is known to be caused by the increase in free water that is responsible for most of the increase in blood volume during pregnancy
- ▶ This may lead to increased free drug levels for a particular total serum level
- ▶ Remember that it is the free unbound drug that is more pharmacologically active compared to the protein bound drug molecule

Categories of drugs in terms safety in pregnancy

- ▶ The safety of many drugs is not yet been determined, FDA has divided drugs into five categories based on their safety in pregnancy

CATEGORY A

- ▶ Have been shown in clinical studies to pose no risk to the fetus

CATEGORY B

- ▶ These may have shown risks in animal studies but not in human studies
- ▶ Generally, drugs in category A and B are considered to be relatively safer

Categories of drugs in terms safety in pregnancy

CATEGORY C

- ▶ Adverse effect on the fetus has been shown in the animals but there is insufficient data in in pregnant women
- ▶ Therefore, risk to the human fetus cannot be ruled out and caution may need to be exercised

CATEGORY D

- ▶ Drugs in this category show positive evidence of risk to the fetus

CATEGORY X

- ▶ These drugs are contraindicated in pregnancy

Choice of drugs in pregnant women

- ▶ Drugs of choice in pregnancy are listed in clinical references based on their safety to the fetus and their therapeutic efficacy
- ▶ Penicillins, cephalosporins and macrolide antibiotic (all category B drugs) are preferred for treating many infections in the pregnancy
- ▶ Tetracyclines, category D and should be avoided in pregnancy
- ▶ Acetaminophen (Category B) is the analgesic of choice in pregnancy but ibuprofen and its related drugs (also category B) may be used when required
- ▶ Pyridoxine (Category A) combined with doxylamine (Category B) are labelled safe for nausea and vomiting in pregnancy

Other drugs of choice in pregnancy

- ▶ For treatment of diabetes, insulin and metformin (Both category B) are safe drug
- ▶ Famotidine and omeprazole (All category B) are safe in reducing gastric acidity
- ▶ Diphenhydramine (category B) is recommended for treating of allergic reactions in pregnancy
- ▶ Despiramin (category B), a tricyclic antidepressant is a safe drug for treating mood depression
- ▶ Most anti epileptic drugs pose some risk to the fetus and hence choice of drugs when treating epilepsy in pregnancy should be carefully done on the basis of risk benefit consideration

Drugs in lactating women

- ▶ Some drugs can be taken in lactating women without posing any risk to their breastfed infant
- ▶ Other drugs place the infant at risk for toxicity

The general rule on breastfeeding

- ▶ Breast feeding should be avoided if a drug taken by the mother would cause the infants plasma concentration to be greater than 50% of the mother's concentration

Summary of effects of drugs in special groups

QUESTIONS	ANSWERS
Why is it always important to consider pregnancy in women of childbearing age?	Drugs can still affect a foetus before women know they are pregnant
When is the most teratogenic part of pregnancy?	3-8 weeks as this is when the organ systems are forming After this point drugs can still cause fetotoxicity
What is usually done about medication for chronic conditions during pregnancy?	They are continued because usually the chronic condition would cause more of a problem than the drug
Why may drugs with a narrow therapeutic index need altering in pregnancy?	Because pregnancy can alter the pharmacokinetics of drugs - blood volume increases, renal excretion and liver metabolism change

Summary of effects of drugs in special groups

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QUESTIONS	ANSWERS
Which drugs cross the placenta?	Presume all drugs cross the placenta unless they have a very high molecular weight, this is why prescribing should be avoided in the first trimester of pregnancy
What are recommendations with breastfeeding?	To avoid prescribing unless necessary drugs will only be found in very small quantities in the breast milk
What drugs can affect lactation?	Dopamine altering drugs due to its effects on prolactin
What are the main pharmacokinetic factors that differ in children to in adults?	Absorption from the GI tract changes with age Distribution differs as children have a higher body water content relative to weight Metabolism varies Excretion is reduced as the kidneys are developing
How is dosing usually calculated for children?	Related to child's body surface area

QUESTIONS	ANSWERS
Which route of administration is preferred in children?	Oral drug administration via flavoured liquids
What are the main changes that occur to the pharmacokinetics in the elderly?	Absorption altered due to changes in gastric motility Distribution Reduced hepatic blood flow causes decreased first pass metabolism Decreased renal elimination with age
What are the changes that occur in the elderly in terms of specific drugs?	Decreased dopamine receptors increase the chances of extrapyramidal effects Decreased baroreceptor response increases likelihood of postural hypotension Increased response to anticoagulants such as warfrin
What are the four 'geriatric giants' in old age?	immobility, instability, incontinence and impaired intellect
What are the main drugs that should be avoided in renal failure?	Nephrotoxic and renally cleared drugs This includes:Gentamycin - toxic and cleared Vancomycin - cleared Nitrofurantoin

QUESTIONS	ANSWERS
What are the main effects liver failure can have on the body?	Hypoproteinaemia Slower clotting due to decreased clotting factors Fluid overload

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