BIOP211 – Pharmacology
Tutorial Session 2 – Pharmacokinetics & Lifespan Aspects of Drug Dosage Regimens

Activities on factors of lifestyle that can affect drug dosing regimens including
- Individual and lifespan aspects of drug therapy
- Drug use during pregnancy and lactation
- Pharmacokinetic aspects of drug use in children and the elderly – Case Study elderly client

2.1 Each student is to give one advantage and / or one disadvantage of these routes of administration. Then compile a table of all the class / online forum ideas.

a) Enteral
b) Parenteral
c) Topical
d) Inhalation

2.2 Read the Handout below in 2.3 then answer the Case Study on an Elderly Client called Janice. Post your ideas to the forum or discuss them in class.

Case Study
Janice is 92 years old and is on multiple drugs for hypertension, diabetes and depression. She is experiencing dizziness when standing and has had some ‘falls’ of late that have resulted in minor bruises but no broken bones. She has not had her medications reviewed for a year and is still on the same dosages as she was 20 years ago.

a. What might be contributing to her increased incidence of falls?
b. As a Natural Health Practitioner, what recommendations might you give to her regarding her medication regime?
c. What systems/organs are affected in old age and how do these alter the pharmacokinetics of drugs in Janice’s case?
2.3 INDIVIDUAL AND LIFESPAN ASPECTS OF DRUG THERAPY

Read the following information and answer the Case Study questions. Discuss with your peers in tutorial or online discussion forum.

2.3.1 Lifespan
- Recommended drug therapy, dosage and administration is usually calculated based on a healthy adult.
- There are several special groups that have different drug therapy needs:
  - pregnant/breastfeeding women
  - infants
  - children
  - elderly

2.3.2 Pregnancy
- During pregnancy, any chemical or drug substance consumed and absorbed may potentially reach the foetus.
- Use of medicines during pregnancy should be avoided in general, or only used when the risk outweighs the benefits.
- Women who are trying to/or are at risk of conceiving, should try to avoid drug therapies where possible.
- Many complementary therapies may also be potentially hazardous to the foetus, and should be used with caution if there is a risk of conception, unless safety in pregnancy has been documented.
- Potential for a drug/medicine to cause adverse effects on the foetus will depend on:
  - type of drug
  - concentration of drug
  - foetal age:
    - 1st trimester - risk of congenital malformations (thalidomide)
    - 2nd & 3rd trimester - affects functional and growth development (alcohol)
    - close to labour - may affect birth process and neonate (pethidine)
- When assessing risk of drug therapy during pregnancy factors to consider include:
  - gestational age of foetus
  - duration of therapy planned/required
  - any other drugs taken concomitantly
  - drug dose and dosing interval
  - nature of drug itself (pregnancy risk categories)
- Terminology:
  - teratogen – a substance that causes transient or permanent physical or functional disorders in the foetus without causing toxicity to the mother.
  - mutagen – a physical or chemical agent that causes genetic material (DNA) to undergo a detectable and inheritable structural change.
  - carcinogen – any agent that by either direct or indirect actions causes a normal cell to become a neoplastic cell.
Variation in teratogenic susceptibility of organ systems during stages of human intrauterine Development

**Categories of Drugs in Pregnancy**

**Category A**
Drugs that have been taken by a large number of pregnant women and women of child-bearing age without any proven ↑ in the frequency of malformation or other direct or indirect harmful effects on the foetus having been observed

**Category B1**
Drugs that have been taken by only a limited number of pregnant women and women of child-bearing age without an increase in the frequency of malformations or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have not shown evidence of an increased occurrence of foetal damage

**Category B2**
Drugs that have been taken by only a limited number of pregnant women and women of child-bearing age without an increase in the frequency of malformations or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of foetal damage

**Category B3**
Drugs that have been taken by only a limited number of pregnant women and women of child-bearing age without an increase in the frequency of malformations or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans

**Category C**
Drugs that, owing to their pharmacological effects, have caused or may be suspected of causing harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible

**Category D**
Drugs that have caused, are suspected to have caused, or may be expected to cause an increased incidence of human foetal malformations or irreversible damage. These drugs also have adverse pharmacological effects

**Category X**
Drugs that have such a high risk of causing permanent damage to the foetus that they should not be used in pregnancy or where there is a possibility of pregnancy
The ethical implications of undertaking research on pregnant women means that we have significantly less knowledge about the safety of drugs during pregnancy. Most drugs are placed into categories based on reports from women actually taking the medication as opposed to information collected from controlled drug trials.

2.3.3 Lactation
- Almost all drugs or their metabolites can potentially be present in breast milk and can therefore be transferred to the infant
- There is very little data on how the infant is able to handle this small amount of drug, and the information available is often conflicting
- Assuming that the infant’s hepatic and renal systems are still immature, one can assume that the infant’s ability to handle drugs will be limited
- In general, the risks and benefits of use of drug therapies needs to be assessed on an individual basis
- Data is available on some drugs – however as with pregnancy, clinical trials are unethical, therefore most of what we know has been accumulated over time due to experience with the drug
- The specific drug characteristics will also be predictive of the likelihood of safety in lactation
- Factors to consider:
  - if a drug is fat soluble, it will be more highly concentrated in breast milk at the end of feeding and at midday
  - infants have a lower total plasma protein concentration compared to adults, so more free drug may be available in circulation
  - metabolic reactions in the infant’s liver are slower, thus drug metabolism may be delayed
  - drug excretion via the kidney’s may be impaired due to immaturity of the renal system

2.3.4 Children
- Neonates
  - Drug administration in neonates should only be conducted by those with a specialised knowledge as newborns lack many of the usual protective mechanisms to cope with drugs
- Infants and children
  - Once a child is > 1 year, most pharmacokinetic patterns (other than liver) are similar to those of an adult
  - Children metabolise certain drugs at a faster rate than adults – dosage adjustments may be required
  - Many drugs that are safe in adults have not been tested in children, safe doses have not been established
  - Dosage is often calculated based on the child’s age and weight
  - The risk: benefit ratio of the drug needs to be assessed before giving drug therapies to children
  - Many will be inappropriate for use in children based on a lack of safety data
2.3.5 Elderly

- The average life expectancy of Australians – According to the Australian Bureau of Statistics (ABS) a baby boy born in 2008-2010 will average 79.5 years lifespan; while a baby girl born in 2008-2010 could expect to live 84.0 years (ABS, 2012)
- The elderly represent a significant percentage of the general population and:
  - Consume a high proportion of all OTC and prescribed drugs
  - Often take multiple medications
  - Take 3x more medication than younger adults
  - Are more likely to be admitted to hospital for adverse drug reactions
- Many elderly people take multiple drug therapies for multiple medical conditions – leading to what is termed “polypharmacy”
- This leads to a significantly higher risk of adverse drug reactions, interactions and iatrogenic disease
- Physiological changes occurring with ageing will also alter drug pharmacokinetics (absorption, distribution, metabolism, excretion)
- Physiological changes in the elderly:
  - Blood-brain-barrier more easily penetrated by lipid soluble drugs e.g. B-blockers
    - Risk of dizziness and confusion
  - Reduced baroreceptor response exaggerates the hypotensive effects of anti-hypertensives and diuretics
  - Declining liver function increases risk of toxicity with many drugs
  - Increased abdominal fat can lead to increased drug toxicity of fat soluble drugs
  - Altered peripheral venous tone exaggerates the hypotensive effects of anti-hypertensives and diuretics
  - Decreased renal blood flow and filtration can reduce the rate of excretion of some drugs, with an increased risk of toxicity
  - Slower gastric emptying time and an increase in gastric pH will increase the risk of stomach irritation (e.g. NSAIDs)
  - Loss of body weight as seen in many elderly means lower doses may be required
- Potential altered Pharmacokinetics in the elderly:
  - Absorption
    - Increase in gastric pH
    - Altered gastric emptying time and intestinal blood flow
    - Decrease in first pass metabolism in the liver
  - Distribution
    - Altered body composition (decreased lean body mass, increase in adipose tissue)
    - Decrease in total body water
    - Decrease in plasma albumin
    - Decrease in blood flow and cardiac output
  - Metabolism
    - Decrease in oxidative metabolism (cytochrome P450 system)
    - Decrease in hepatic blood flow
  - Excretion
    - Decrease in glomerular filtration rate
    - Most persons lose 10% renal function per decade after age 50
How Pharmacokinetics change with age,
Adapted from (Goodman & Gorin, 1977 in Bryant & Knights, 2007)
How pharmacokinetics change with age

- Alterations in Pharmacodynamics:
  - Changes in target organ or receptor sensitivity in the elderly may lead to either a decreased or increased drug effect
  - In general, the elderly are more sensitive to the effects of CNS-acting drugs
  - Close monitoring and appropriate dosage adjustments are required

- Practical suggestions for drug use in the elderly:
  - Use non-pharmacological measures where possible
  - Review medication frequently
  - Simplify their medication and dosing regimens as far as possible
  - Use as few drugs as possible
  - Discontinue drugs that are no longer required
  - Consider that new symptoms may be an adverse reaction – investigate this avenue before adding in another drug
    - Choose drugs that are associated with the least risk of adverse effects within a therapeutic class
    - Use the lowest dose possible to achieve the desired effect
    - Provide simple instructions to aid in compliance
    - Altered body composition (decreased lean body mass, increase in adipose tissue) Elderly patients may not be able to open certain containers due to diseases such as arthritis
    - Drugs that cause dizziness or disorientation increase the risk of falling, which can lead to fracture in osteoporotic patients

2.4 True / False – terminology. Use your textbook, explain your answers. Discuss with your peers during tutorials or Loop post / online discussion forum. Feedback is available on the subject website.

(a) Pharmacodynamics is the study of the concentration of a drug during the processes of absorption, distribution, biotransformation and excretion.

(b) Drugs that bind to and activate receptors are known as agonists.

(c) The action of competitive antagonists can be overcome by increasing the concentration of the agonist.

(d) A drug exerts its effect by conferring new functions on a tissue or organ in the body.

(e) Drugs that have chemical similarity to a neurotransmitter, and therefore, similar actions, are called selective.

(f) Carriers, enzymes, ion channels and receptors are all examples of regulatory proteins.

(g) Drugs resembling enzyme substrates are often termed ‘antimetabolites’.
(h) A drug with high hepatic clearance is extensively metabolised by the liver.

(i) The placental barrier is impermeable to water-soluble drugs.

(j) All drugs have less biological activity than the parent drug after drug metabolism (also called biotransformation).

Reading Activities: BIOP211 - Pharmacology, Session 2

The reading materials listed below are in addition to the text recommended readings above. These will add further understanding of the topics covered.

Add some of the below terms to your growing glossary, and define the terms.

- Interactive Clinical Pharmacology, 2009, Hiltlab NZ, Christchurch Hospital and University of Otago Christchurch, New Zealand. See Pharmacology - Endeavour College of Natural Health LibGuides - LibGuides at Endeavour College of Natural Health
- Here is a link to review the types of proteins targets that drug molecules use: Bioinformatics Research Group, 2011 Drug targets, Advanced Computing Research Laboratory, Institute of Computing Technology, Chinese Academy of Sciences www.bioinfo.org.cn/flash_show/flash_bioinfo/cgnmc07.swf (Just slide 7; not the other material on the human genome project) (Link checked on 1/07/2016) University of Nottingham, 2008, Targets for drug action, RLO-CETL http://www.nottingham.ac.uk/nmp/sonet/rios/bioproc/drug-targets/ncl79_drug_action.swf (Link checked on 1/07/2016)
- Shows how a G-protein coupled receptor works. The example chosen is the adrenoreceptor for adrenaline (adrenaline = epinephrine, symbol A in the BIOP211_SN01toSN04_PharmacologyPharmacokinetics_Notes.pdf)
  DNAtube, n.d., Action of epinephrine, DNAtube Scientific Videos Site and Convert Videos,
  http://www.dnatube.com/video/2952/action-of-epinephrine
  (Please note in your Glossary that epinephrine is called adrenaline in Australia)
- Pharmacognosy video by Navindra Seeram, a natural products researcher from Rhode Island University Seeram, N. 2010, Navindra Seeram: Natural products researcher, University of Rhode Island.
  http://www.youtube.com/watch?v=y1Vvm_Hw4ao&p=D2A2AC62E32D3D80&index=2&playnext=1
- Shows good graphics for ion channels excitatory post-synaptic potentials, (EPSP)or inhibitory (IPSP) and how they are linked to conduction or inhibition of an action potential: GreatPacificMedia, 2009, Neuron synapse.
  http://www.youtube.com/watch?v=LT3VKAr4roo&feature=related
  http://www.youtube.com/watch?v=NB7YfAvez3o&feature=related
- Drug Binding (simplified protein binding for drug action (also shows Na+/K+ excitability)): bmedinago, 2008, Pharmacology: Drug binding.
  http://www.youtube.com/watch?v=07Tr__R_koE&feature=related,


**Revision Questions / Activities from the Reading Guide**

1. What are the four (4) main categories of the routes of administration and outline the advantages and disadvantages of each
2. Why is drug bioavailability less than 100% after oral administration and by which route(s) is it 100%?
3. Describe four (4) methods of absorption of drugs
4. Drug specificity is a theoretical ideal but drug selectivity is what is observed endogenously. Discuss the terms specificity and selectivity, using an example of an endogenous receptor system.
5. Explain these terms: (i) agonist, antagonist; (ii) affinity, potency, (iii) bioequivalent, bioavailability.

**References**


