Prescribing in Pregnancy and Breast Feeding

Abstract

In this article in the series of 'bite sized' pharmacology, we will look at the pharmacological considerations when prescribing for the pregnant or breast feeding patient. This article will illustrate the common issues to consider when prescribing in these groups. Focus will be on pharmacokinetics and pharmacodynamics but the types of harm that can occur when medications are given in pregnancy will also be discussed. There will also be some consideration of prescribing in women of child bearing age. Exercises provided will help you apply this knowledge to your prescribing practice.

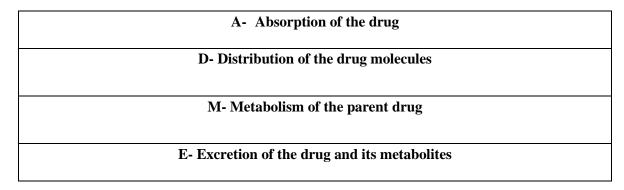
We must remember as prescribers that a drug has to be:

- Absorbed into the body fluids and tissues
- Distributed to its active site
- Metabolised, primarily by the liver
- Excreted, primarily by the kidneys

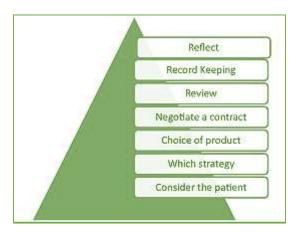
These actions that occur after administration are pharmacokinetics and we shall begin by exploring the differences in this population of patient.

Pharmacokinetics is the action of the body on the drugs that we take. It can be broken down into four processes as can be seen from table 1. (More detail on each of these processes is found in the article on pharmacokinetics in Volume 15, issue3).

Table 1- The four pharmacokinetic processes that occur after oral drug administration



As with all areas of prescribing, it is wise to consider the seven principles of good prescribing practice when dealing with all patients



Prescribing Pyramid (NPC 1999)

When considering prescribing in the pregnant or breast feeding woman, it is important to remember additional information may need to be gathered by consultation and examination and the way that you gather and use this information may be different. We will go on to explore the relevant areas of the framework.

Exercise

Using the BNF, choose a common drug from your area of practice. Review the guidance on prescribing in pregnancy and breastfeeding given for the drug in its monograph and reflect on how this may affect your prescribing practice.

Consider the Patient

Consideration of the patient should be modified to reflect the additional considerations required when prescribing for the patient who may be pregnant, trying to conceive or is breastfeeding after the birth of a child. On some occasions women may still be breast feeding a child while pregnant with another and this can further complicate prescribing regimes. The main factors to consider in addition to normal consultation and examination are:

- Changes to the normal pharmacokinetic processes
- The stage of gestation
- Increased risk to the developing foetus
- Potential for increased risk of poor compliance
- Continuation of essential medicines in pregnancy
- Changing medications during pre-conception period

Changes to Pharmacokinetics in Pregnancy

Absorption

Absorption of drugs from the oral route can be compromised in certain gastrointestinal conditions that can be found in any stage of pregnancy.

Morning sickness in pregnancy can reduce the amount of drug that is available to be absorbed in the gastrointestinal tract if the drug has been given by the oral route. For that reason consideration of the level of nausea and vomiting, the frequency and the duration should be done before prescribing by this route. Administration times should be targeted at the period when the sickness is at its least or an alternative route of administration may need to be sought.

Indigestion in pregnancy, at all stages of gestation can be problematic to the patient but may also be a sign of changes in gastric acid secretion.

For the most part gastric acid secretion during the gestational period can be decreased and the amount of mucus secreted can be increased, both of these things can lead to changes in gastric pH. These changes can reduce the absorption of some drugs that are taken by the oral route while increasing the absorption of other drugs. It is also known that intestinal transit time can be changed changing drug bioavailability, however these changes have little overall effect on actual drug bioavailability in the pregnant woman. (Feghali, Venkataramanan & Caritis 2015)

Distribution

Distribution of drugs from the absorbing site to the plasma and then from plasma to cell and tissues can be compromised. Plasma proteins play a crucial role in drug distribution and bioavailability and they can be reduced in concentration in the pregnant women. The actual number of proteins does not change but as the general circulation increases with incorporation of the foetal circulation the concentration drops. This can lead to higher levels of 'free drug' and a risk of side effects and toxicity as the unbound drug is free to cross the placenta. In pre-eclampsia, the low levels of serum albumen can compound this and allow the even higher levels of free drug to cross to the foetal circulation. Another factor is the change in body composition. There is a change to the body fat and water ratio in that the total body water is increased.

The passage of drugs from the maternal to the foetal circulation can be beneficial, for example we can give steroids to the mother for passage to the foetus to promote lung maturation if there is significant risk of pre-term delivery. But passage of drug can largely be considered to have potential detrimental effects and the highest risk of these is during organogenesis in trimester one. (Griffiths and Campbell 2015)

Causes of Foetal Harm

Harm to the foetus can be divided into two categories;

- Indirect due to impact on blood flow
- Direct due to harmful substance reaching foetus

Types of Harm

The types of harm that can be identified due to drug or medication use in pregnancy are usually linked to the time of gestation the medication is given at;

- Death and miscarriage up to week 3
- Structural Injury weeks 3-11 e.g. Spina bifida
- Functional injury weeks 8-12
- Retardation of growth second and third trimester

Exercise

Using the BNF, or other drug resource, look up an essential drug you are likely to prescribe in practice (for example anticonvulsants or antidiabetic drugs), where the risk to the mother in stopping the drug is great. Identify if there are any restrictions on prescribing in pregnancy. Reflect on any changes you would need to make to dose or prescribing regimes in light of this.

Metabolism

As we know drug metabolism and biotransformation primarily occurs in the liver. Some evidence exist that suggests there is an increased activity of the livers drug metabolising enzymes, the cytochrome P450's, during pregnancy (Isoherranen & Thummel 2013). This means that if the enzymes responsible for drug metabolism are increased in activity then they will be clearing the drug through the liver ready for excretion at a faster rate. This may affect

the duration of action of some medications. This does however seem to be variable between women and can also be affected by ethnicity and age (Feghali, Venkataramanan & Caritis 2015)

Excretion

Drug excretion is largely carried out by the kidney for expulsion in urine and is dependent on glomerular filtration, tubular secretion and tubular reabsorption for maximum efficiency in elimination of drugs and metabolites. It is known that the glomerular filtration rate increases in pregnancy. This occurs in the first 3 months of gestation and continues until delivery in line with the increase in maternal circulation found during term. This means that for drugs that are primarily eliminated due to renal excretion then the clearance rate through the kidney will be higher and affect duration of action and circulating plasma levels.

Pharmacokinetic considerations relate to the 'which strategy' and 'choice of product' areas of the prescribing pyramid.

Exercise

Using the online medicines compendium look up a drug you are likely to prescribe in pregnancy and identify its primary route of elimination (hepatic metabolism or renal excretion) and reflect upon how the removal of the drug from the body may be affected by the state of pregnancy.

Prescribing in the Breast Feeding Woman

It is known that small or trace amounts of drugs given to a woman can be passed to her nursing infant during breast feeding. Lipid soluble, low molecular weight drug molecules are more likely to pass into breast milk, due to its high relative fat content, and be passed onto the child whose own pharmacokinetic processes may be as yet not fully developed. However

withholding breast feeding is not a no risk option and the prescriber should be able to assess any risk to the child.

The BNF is an invaluable resource when prescribing in the breast feeding woman as it will identify drugs that pose a risk. It classifies the risk as follows

- Drugs that should be used with caution or are contra-indicated in breast-feeding
- Drugs that can be given to the mother during breastfeeding because they are present in milk in amounts which are too small to be harmful to the infant
- Drugs that might be present in milk in significant amount but are not known to be harmful

Retrieved from BNF online https://bnf.nice.org.uk/guidance/prescribing-in-breast-feeding.html

Prescribing in the Woman of Childbearing Age

For some medications the wariness of prescribing in pregnancy and breast feeding also extends to women and girls of childbearing age. A good example of this is the drug valproate. This is a drug, previously used in many patients for its anticonvulsant properties but now a NICE recommended second line treatment for the prevention of relapse in bipolar disorder (NICE 2014). Its known teratogenic effects had led to dose restrictions and prescribing cautions, and changing to another drug in planned pregnancy. It even returned to black triangle status so that intensive monitoring could be carried out. This monitoring led to the banning of prescribing valproate in women and girls of child bearing age unless a pregnancy prevention programme is in place in early 2018 after the publication of findings and of audits took place (Paton, Cookson, Ferrier, Bhatti, Fagan and Barnes 2018).

Exercise

Using the most current resources you have available, look up sodium valproate and identify the risks of prescribing to women and girls of child bearing age. Reflect on the prevalence and type of birth defects that can occur and why this drug has now be banned from prescription to this patient group unless a pregnancy prevention programme is in place.

Adherence to Medication Regimes

Compliance with or adherence to medication regimes can be problematic in the pregnant woman as she may feel that taking any medication may be detrimental or harmful to the baby. It is important as prescribers that we ensure that the drug benefit to the mother outweighs the risk to the developing foetus and that the mother is fully informed about any risks in taking medication and the risks of not taking essential medication during pregnancy. We should still always try to reach a concordant agreement and this falls under the 'Negotiate a Contract' section of the prescribing pyramid.

Exercise

Can you identify drugs in your area of practice that would be essential to continue in pregnancy and how you could manage the prescribing of these in a patient who may not be compliant due to her perceived risk to the child?

Can we put in some pictures to break the text up a bit?

References, Suggested and Further Reading

Barber and Robertson (2015) Essentials of Pharmacology for Nurses 3rd Edition McGraw Hill London

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