Introduction

During gestation, the fetus receives food stuff's from the mothers blood and excretes all the excretory products back to the mothers blood through the placenta ***(Guyton, 2002)***.

The term placenta is believed to have been introduced by ***Realdus Columbus in 1559*** when he used the latin word for the circular cake. The human placenta of villous type, consists of multiple fetal villi which branch progressively throughout gestation, thereby increasing its surface area ***(Kaufman, 1993)***.

Placental transfer of drugs across the placenta is mainly made by simple diffusion so, the maternal –fetal concentration gradient, uterine and umblical blood flow and other factors determine the fetal exposure to the maternal administrated anaesthia, all this may be expressed by the following formual based on fick's law of diffusion ***(Russel et al., 1998)***.

The, formula:

$$\frac{Q}{T} = K(\frac{A(Cm - Cf)}{D}$$

where: $\frac{Q}{T}$ = quantity of drug transferred per unit time.

K= Diffusion constant of the drug.

A= Area of placenta available for transfer

D= Thickness of the placental membrane.

Cm-Cf= Maternal fetal concentration gradient.

There are many factors that affect transfer of drugs across the placenta:

Molecular weight, lipid solubility, degree of ionization, protein binding, maternal-fetal concentration gradient, placental factors.

1- Molecular weight:

As a general principle, the larger the molecule the less likely placental transfer to occur, compounds with a molecular weight Below 600 readily cross the placenta, whereas the placenta is relatively impermeable to those above 1000, the majority of drugs given to mother during labor have molecular weight in the region 250 to 450, so other factors are of more importance in determining placental transfer ***(Corke, 2001)***.

2- Lipid solubility:

The placental membrane contain much lipoprotein, drugs which are soluble in lipids can therefore easily pass through the placental membrane ***(Moir and Carty, 1980)***.

3- Degree of ionization:

The degree of ionization of a drug is an important determinant of placental transfer because only non ionized drug readily crosses the placenta. The degree of ionization of a substance depends on the nature of the substance (acid or base), its dissociation (pka) and the pH of the medium in which it is present. The (pka) of a drug is the pH at which is 50% ionized and 50% unionized ***(Yentis et al., 2001)***

Maternal and fetal blood pH may influence the degree of ionization and hence the placental transfer of a drug. The pH of umbilical vessel blood is normally 0.10 to 0.15 units lower than that of maternal blood and consequently there is a small pH gradient across the placenta. Basic drugs are thus more ionized in the fetus, while acidic drugs tend to be more ionized in maternal blood. The concentration of unionized basic drug is higher in maternal blood as compared with fetal blood and as it is

unionized drug that diffused across the placenta most readily, there will be a net transfer of basic drug from mother to the fetus ***(Cork, 2001)***.

4- Protein Binding:

This is an important factor that may reduce the quantity of certain drugs reaching the fetus. Only unbound moiety of a drug to plasma protein is a available for transmission across the placenta ***(Karemer, 1997)***.

Many drugs have been joined to decrease binding in neonate as compared to the mother,. For example, local anesthetics, antibiotics, propranolol and phenobarbital. The plasma binding of Bupivacaine is higher in maternal blood than neonatal blood and at delivery following the epidural administration of bupivacaine to mother, the total umbilical venous plasma concentration of bupivacaina is lower than the total maternal venous plasma concentration, however the concentration of free or unbound bupivacaine in umbilical venous and maternal venous plasma at delivery is the same, this is bacause it is the free drug that crosses the placenta and eventually the free drug, concentration on each side of the placenta becomes equal, therefore differences in protein bounding in total drug concentration on each side of the placenta, although the free drug concentrations are in fact equal ***(Corke, 2001)***.

5- Maternal- Fetal concentration gradient:

Drug transfer occurs down a concentration gradient (which is usually from mother to fetus but can occur also from fetus to mother) the drug concentration on the maternal side depends on the route of administration, total maternal dose, volume of distribution, drug clearance and metabolism ***(Yentis et al., 2001)***.

6- Placental factors :

Placental circulation, diffusion rate across the placenta, drug metabolism, in the placenta and the disease of the placenta all affects the drug transfer from maternal to fetal circulation. The distance over which diffusion occurs is related to the maturity of the chorionic villi. As the maternal – placenta fetal approaches term, the villi decrease from 25um to 2u at the. Certain disease of pregnancy may increase the diffusion substance e.g. pregnancy induced hypertension ***(Ostneimer, 1992)***.

The anaesthiologist being the personal dealing with pregnant females during anaeasthia using different drugs, he has to be aware of placental transfer of each drug he uses. This essay has been suggested to review placental transfer of all drugs used in anaesthetic practice.