18/MHS07/022

PHARMACOLOGY

PHS 212

ASSIGNMENT: Elucidate the Physiological adaptations of the female to pregnancy?

ANSWER:

Pregnancy is a unique period in a woman's lifetime. A number of anatomic, physiologic, biochemical and psychological changes take place. These changes may easily be misinterpreted by physicians who lack experience in regards to pregnancy effects on a woman's body. It is important that physicians caring for women understand the implications of these physiological changes in order to avoid any diagnostic errors and errors of management. One has to remember that nature does not waste energy or effort. In that respect all the physiological changes that happen during pregnancy, happen for a purpose. As it will be appreciated later on in this chapter, almost every organ system of a female body is affected to some degree. An attempt was made to present the information by organ systems although there may be some overlap since most of the organ systems interact with each other and affect each other. Some organ systems will be discussed in detail more than others. This distinction will be solely based on the significance of the particular organ system changes.

**SKIN CHANGES**

 A number of changes take place in the skin of pregnant women. Mechanical stretching of the skin over the abdomen and breasts can lead to striae. The increased levels of estrogen and progesterone have also been implicated. Usually striae remain permanently with some change in color. Prevention may be achieved with moisturizing creams, especially those containing lanolin and other oily substances. It should be realized, however, that striae may develop despite any preventative measures. Vascular spider nevi and palmar erythema happen also during pregnancy. There is no clear explanation for these changes, but they most likely represent the result of vasodilatation that happens in the skin during pregnancy. Chloasma and other pigmented lesions can happen as a result of increased melanocytestimulating hormone activity which in turn is a result of increased estrogen and progesterone levels. These lesions usually begin at about five to six months gestation. One way that these lesions may be prevented is by the use of screening agents and avoidance of direct sunlight. Skin pruritus affects a number of women and it may be related to increased retention of bile salts in the skin secondary to estrogen effects. Scratching of the skin can then lead to infected excoriations. Local measures with anti-pruritic creams and lotions usually are sufficient.

CHANGES IN THE GASTROINTESTINAL SYSTEM

 Nausea and vomiting are the most frequent complaints involving the gastrointestinal system and usually happen in early pregnancy while heartburn happen primarily in late pregnancy. The gums become hyperemic and edematous during pregnancy and tend to bleed. The muscular wall of the esophagus is relaxed and this may cause reflux, which in turn can lead to esophagitis and heartburn. The stomach and the intestines have decreased motility presumably due to the effect of progesterone on smooth muscle contractility. This causes an increase in the time that it takes for the stomach to empty. Reduced gastric secretion has also been documented and it could account for the improvement of peptic ulcers sometimes observed in pregnancy. Decreased motility of the large intestine may lead to constipation. The liver is affected significantly by pregnancy. Cholestatic jaundice is considered to be the result of estrogen effect on elimination of bilirubin by the liver. The effect of estrogens also, is to increase protein synthesis in the liver, which leads to increased production of fibrinogen and binding proteins. The liver enzymes are usually unaffected with the exception of alkaline phosphatase, which is increased at approximately two fold to four fold that is a result of a placental production. Pregnancy increases the size and decreases the motility of the gall bladder. The decreasing motility and increase in volume, combined with changes in the bile's composition, explain the correlation between the incidence of cholelithiasis and pregnancy.

**CARDIOVASCULAR CHANGES**

Of all changes that happen in pregnancy, the single most important is the one involving the cardiovascular system. Adequate cardiovascular adaptation secures good placental development and thus appropriate fetal growth. In brief, the cardiovascular changes involve a substantial change in the blood volume, cardiac output, heart rate, systemic arterial blood pressure, systemic vascular resistance, oxygen consumption and alterations in regional blood flow of various organ systems.

* Blood Volume

 Significant increases in the blood volume start taking place in the first trimester and continue until the mid third trimester, at approximately the 32nd to the 34th week. Beyond this point in gestation, the blood volume plateaus. This pattern was established with studies that kept the patients in the leftlateral position to avoid vena cava compression. However, studies that kept the patient in the supine position had controversial results indicating a decline in the blood volume after 34 to 36 weeks. The average absolute increase in blood volume during pregnancy is about 1600 ml and in terms of percent change one should expect a 40 to 50 percent increase above prepregnancy levels. The increase in the blood volume is achieved by a combination of increases in the plasma volume and the RBC mass. The calculated plasma volume expansion is approximately 1300 ml and the volume of the RBC increases about 400 ml. This discordance in the change between the cellular elements of the blood and the liquid portion leads to the so called "physiologic anemia of pregnancy". The mechanisms leading to hypervolemia in pregnancy are still not entirely understood and seem to be multifactorial. Increased estrogen levels in pregnancy cause increased production of renin from the kidneys, the uterus and the liver and thus cause elevated renin plasma levels. The increase in renin, which stimulates aldosterone secretion, is associated with sodium retention and an increase in total body water. The roll of atrial natriuretic factor (ANF) in mediating changes in fluid balance during gestation is still not clearly understood. On the other hand increased levels of human chorionic somatomammotropin and prolactin increase the amount of erythropoiesis and thus causes the necessary increase in the red blood cell mass. The increase in blood volume with pregnancy appears to serve the essential physiologic needs of both the mother and fetus. It ensures adequate supplies required for normal fetal growth and oxygenation even under circumstances that affect the maternal cardiac output (inferior vena cava compression). This increased blood volume also helps normal pregnant women to withstand hemorrhage equal to the volume of blood added to the circulation during the course of the normal pregnancy without any signs of decompensation.

* Heart Rate During Normal Pregnancy

The baseline heart rate increases by about 10 to 20 beats per minute. This increase starts early in pregnancy and gradually continues to go upward with the highest values achieved at term. Some investigators, however, suggested that the total increase happens early in pregnancy and remains so throughout the remainder of gestation. In twin gestations, the rise of the heart rate is more pronounced and it can reach as much as 40 percent above the non-pregnant state. A change also from the supine position to the lateral position may cause the heart rate to drop slightly.

* The Heart

A number of changes happen to the heart and are unique to pregnancy. Increasing intra-abdominal contents displace the heart upward with some forward rotation. As a result the anterior posterior diameter and the cardiothoracic ratio are increased. The overall dimensions of the heart are increased during pregnancy as a result of increased diastolic heart volume without any change in the ventricular wall thickness. Systolic ejection murmurs are common in pregnancy while diastolic murmurs are less frequent. The systolic murmurs are usually the result of the hyperdynamic circulation. Electrocardiogram changes have been reported during pregnancy. Transient ST and T changes are common in pregnancy, SRQ waves and inverted T waves in lead III. Left access deviation of the QRS complex has been reported also in pregnancy.

* Blood Pressure

 A slight decrease in the systolic arterial blood pressure and a significant decrease in the diastolic pressure have been observed to occur in normal pregnancy. This decrease becomes evident in the late first trimester and continues throughout most of the second trimester. The lowest values are noted in mid pregnancy and there after the blood pressure returns toward non-pregnant levels before term. The degree of change in the blood pressure parameters has been found to be affected by parity, smoking, preexisting hypertension, maternal age and ethnic background. In the typical normal pregnancy the mean arterial pressure (diastolic plus 1/3 of the difference between systolic and diastolic) is less than 85 mm of mercury. Studies have found that when the mean arterial blood pressure in the mid second trimester is higher than 90 mm of mercury, there is increased perinatal mortality and morbidity.

* Systemic Vascular Resistance

Normal pregnancy is associated with a significant fall in systemic vascular resistance. As a result, the diastolic blood pressure drops as well as the systolic. However, the diastolic blood pressure drops more than the systolic leading to a widening of the pulse pressure. The mechanism for this change is not entirely clear. It has been speculated, however, that a significant portion of this decline is caused by the development of a low resistance circulation in the pregnant uterus. Estrogens, Prolactin, circulating prostaglandins PGE2 and PGI2 may be responsible for the vasodilatation that can cause a drop in the peripheral resistance. In addition, the profound dilatation of the skin vessels as a result of the increased maternal body heat dissipation may contribute to the drop in the systemic vascular resistance.

* Blood Flow Changes in Various Organ Systems During Pregnancy

 The most profound changes in regional blood flow occur in the uterus with a 5 to 10 fold increase. This change starts early in pregnancy and continues until almost term. Approximately 20% of the maternal cardiac output perfuses the uterine vessels (placental and nonplacental). The kidneys also demonstrate substantial increase of the regional blood flow as much as 30 to 80 percent and at the same time a 50 percent increase in glomerular filtration rate is noted. The regional blood flow in the extremities also increases and more so in the hands than the legs. As it was mentioned previously, there is a significant dilatation in the skin vessels which leads to an increase in the regional blood flow. These changes in the skin vessels may cause warm skin, clammy hands, vascular spiders, and palm erythema. The liver circulation is not affected very much and the same is true for the brain blood flow which is autoregulated. The blood flow to the breast is increased during pregnancy to prepare the breast for lactation. The effect of pregnancy on coronary blood flow is still unknown. It is safe, however, to speculate that an increase may happen since augmentation of cardiac function is present during pregnancy.

* Hemodynamic changes in the postpartum period

 In the postpartum period the blood volume decreases by about 10 percent on the patients who undergo vaginal delivery and 15 to 30 percent for those who undergo cesarean section. The cardiac output increases by 60 to 80 percent immediately after delivery and it rapidly decreases to a level slightly above the nonpregnant value. Complete return to normal nonpregnant values will take sometimes a few weeks. The stroke volume increases also significantly and the heart rate drops by 4 to 17 beats per minute shortly after delivery. Blood pressure is usually unchanged unless excessive blood loss has taken place in which case the blood pressure will drop or in other medical complications. The peripheral vascular resistance according to some investigators is increased and according to others is unchanged.