HORMONES GIVEN IN EARLY PREGNANCY - DOES IT CAUSE TERATOGENICITY?

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SUMMARY

Drugs given in the early weeks of pregnancy are known to produce congenital malformation in the babies. One important group of drugs, hormones are commonly used by many doctors for postponement or preponement of a menstrual cycle or for withdrawal bleeding in amenorrhoea of early duration. We are presenting 3 babies born in our hospital with multiple congenital anomalies where all 3 mothers gave history of hormonal intake in periconception period or during early pregnancy.

INTRODUCTION

In human pregnancies 2-3% of the babies born have a structural or functional abnormality i.e., a congenital anomaly present at birth (Cousins 1991). It is also estimated that 1-5% of these congenital defects may be drug or chemical related.

Several studies have confirmed that most women ingest drug during pregnancy. In one study it was shown that 82% of pregnant women were prescribed an average of 4 drugs including Calcium and Iron. 65% of pregnant women were also said to consume drugs not prescribed by a physician - like analgesics, antacids, vitamins, antitussives, sedatives and antiemetics.

Most severe malformations occur during 4-6 wks of pregnancy. This observation has serious implications as at this time of pregnancy the women are usually not aware of the early pregnancy. It was also noticed that many a time the general practitioner or even a specialist other than obstetrician often do not enquire about the menstrual cycle or about amenorrhoea

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of early duration, before prescribing any medication which consequently may result in an iatrogenic exposure to teratogenic drugs.

It was also noticed that patients usually will not volunteer this information unless specifically asked for, especially in our country.

We also observed that many of the general practitioners as well as the lay public were under the misconception that taking high dosage of hormonal tablets soon after a missed period will lead to a spontaneous abortion.

Estrogens, Progestrogens and indigenous medicines are frequently used by doctors and Pharmacists over the counter for preponement or postponement of menstruation or for withdrawal bleeding in cases of missed period. Seldom do we realize the potential for fetal teratogenicity when administering these medications. This message was driven home when we noted two babies with phocothelia and one with multiple deformities following administration of Primolut N or Estrogen-Progestrogen combination pills. (Cumorit forte, cycle - norm).

Various teratogenic effects have been attributed to hormonal use in early pregnancy. These are virillisation with or without malformation of urogenital sinus and internal genitalia, neural tube defects, congenital heart disease or a syndrome complex called as VACTREL anomalies.

Many studies have shown that use of hormones in early pregnancy and followed long duration of OC have no effect on the fetus. According to Ambani et al (1977) virilisation is the only problem which seems to be related to hormones.

As to why certain fetuses are only affected when exposed to the hormones in the same age,race, region is not known. Genetic predisposition in certain people in conjuction with the hormones may trigger a malformation. Secondly, the genetically deformed low metabolic clearance of a drug may lead to its abnormal accumulation and may be toxic to the embryo directly or by reducing availability of crucial nutrient.

CASE I

Mrs. R, 20 yrs. old primi gravida had taken Tab. Primolut N 5 mg tid for 7 days soon after her marriage as she had to visit a temple and she did not want to have menstrual period at that time. She also had taken "over the counter" analgesics like tab. Saridon/Anacin quite frequently during Ist trimester. Patient came to us at about 32 wks. of pregnancy and a routine ultrasound scan was done as patient was not sure of her dates. During ultrasound it was noticed that the baby remained static with no body movements or limb movements. As there was oligohydramnios the extremeties could not be visualised clearly. BPD and femur length were measured. Patient was asked to come for a rescan and admission the next day for which she did not agree. 25 days later patient came in spontaneous labour and vaginally delivered alive female baby with apgar 5 and 8 weighing 2 kgs. The baby was found to have phocothelia of both upper limbs. The baby also had excessive hair all over the body, small forehead, calcaneo varus of both feet

and multiple contractural deformity of all long bones. Baby also had bilateral exophthalmus. There was also restricted mobility of all joints.

In this case Primolut N was administered during the periconceptional and postconceptional period.

CASE II

Mrs. J.P., 26 yrs, came with h/o profuse bleeding per vaginum since 3 months immediately following diagnostic laparoscopy and D & C for secondary infertility. The endometrium showed secretary pattern. The patient had received tab. Primolut N in 5 mg tid for 21 days and had ceased bleeding for a few days. After 15 days patient had bleeding again and she came to us. An ultrasound scan showed evidence of 12 wks. Live intra uterine gestation. She was treated as threatened abortion and given tab. Gestatin tid till 8th month. Unfortunately fetal echocardiogram could not be done. She had a preterm rupture of membrane at 32 wks. with breech presentation for which she underwent emergency LSCS. The baby was a premature female weighing 1.85 kg.

The baby was found to have a mild degree of hydrocephalus with cyanotic heart disease. (pulmonary stenosis). She underwent a surgery for the CHD and expired postoperatively at 1 1/2 months of age. After this the patient conceived twice again and both times she delivered healthy normal babies vaginally. The above anomalies could be attributed to an exposure to Norethisterone during organogenesis.

CASE III

Mrs.L, G3) P2) with previous full term normal vaginal deliveries with healthy live babies was admitted to this hospital in labour and delivered a live male baby with unilateral phocothelia of right upper limb. Taking a restrospective history we could elicit the usage of 6 tablet of Cumorit Forte at 35 days amenorrhoea with the purpose of termination of pregnancy.

DISCUSSION

It is well established that succptability to teratogenic agents varies with the developmental stage of the embryo at the time of exposure. The factors that may determine the drugs effects include dosage, duration and time of exposure, mode of delivery, concurrent use of other drugs, generation and accumulation of drug's toxic metabolites and genetic susceptibility. The time of drug exposure during pregnancy may result in different fetal effects i.e., the drug will affect tissues with maxium growth and differenciationat time of exposure.

In all 3 cases, there was exposure to hormones in the Ist 4-8 wks of pregnancy the periconceptional and organogenetic period, thereby stressing that administration of drug during pregnancy should have a valid indication for its use and the risks and benefits should be clearly explained to the patient and her husband so that they are also aware of the pitfalls of medication taken in early pregnancy and opt for termination of pregnancy if consumed accidently. It may be even better to publicise the information that postponement of menstruation or preponement should not be taken lightly and the couple should be advised to be

adequately protected against conception in the cycle.

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