

Course Name :An Overview on Maternal Health Antenatal, Intranatal and Postnatal Care

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Teratology, Teratogens and fetotoxic agents (part 2)

Good morning students. I welcome you all to today's session for the NPTEL online certified course on the topic and overview on maternal health, the antenatal, intranatal and postnatal care. I am Dr. Barnali Ghosh, an obstetrician and gynecologist working as assistant professor at B.C.Roy Medical College and Medical Research Center, IIT Kharagpur. Today we are going to continue our discussion on teratogenicity right. So, in the last class we have discussed the meaning of teratogen, the different stages of fetal development and the most teratogenic period that is the period of organogenesis which is between 3 to 8 weeks post fertilization that is day 31 to day 71 from LMP right.

So, exposure to any type of teratogen by the mother can pose serious risk for the fetus cause congenital malformations and lead to various syndromes. We have discussed the FDA categorization of drugs where category X drugs are strictly prohibited or contraindicated during pregnancy. Then we discussed the different effects of lithium exposure, warfarin exposure, alcohol exposure, phenytoin exposure, isotretinoin exposure. So, different types of drugs and its effects on the fetus.

So, we will continue with our discussion and today first drug to be studied is your valproic acid right. So, what is valproic acid? Valproic acid is a type of anti-epileptic drug ok. So, it is a type of anti-epileptic drug and this also is a category X drug. Say the mother was taking valproic acid before her conception, she was on anti-epileptics. So, the day when she starts to plan her conception to plan her pregnancy right, then only the doctor needs to change valproic acid to some other anti-epileptic drug which can be continued throughout the pregnancy.

As such if the anticonvulsants are being used, they should be used at you know the minimum possible dose which is required to prevent relapse of convulsions in the mother during the period of pregnancy. What happens with valproic acid? It can cause neural tube defect of which most common is the spina bifida. So, neural tube defect is number 1, then it causes impairment in the folate absorption right. So, folic acid is actually required for the neural tube development, it helps in cell division right. So, this folic acid being absent there causes neural tube defects.

Also there may be facial defect right like cleft lip and cleft palate right. So, that can also occur then it can lead to polydactyly right polydactyly. It can lead to different you know skull abnormality, craniosynostosis you can see here in the picture. There are no abnormalities in the skull bone formation and also see narrow palpebral fissure, mid facial defect, depressed nasal bridge, flat nose and your absence of philtrum absence of philtrum. So, these are you know the effects on the fetus in case of valproic acid exposure.

Now, coming to the different androgenic hormones right. So, these hormones will have a detrimental effect mostly if the offspring is a female. In case of female offspring, you know androgenic hormones like danazol, androgens or testosterone. If these get you know the female fetus gets exposed to these androgenic hormones, there can be masculinization of the female offspring. There can be you know change in the genitalia, masculine genitalia can occur or ambiguous genitalia of the female offspring if it is exposed to these androgenic hormones in the early stages of pregnancy during the formation of the external genitalia period right.

So, that is between your 14 to 18 weeks of gestation. Another hormone to note is the diethylstilbestrol. It is also written as DES. Previously it was used, but then nowadays it has been totally banned because of its stereogenic effects. What are the effects? It causes vaginal adenosis right.

So, say this is the uterus in case of your female offspring. So, the uterus is also hypoplastic, hypoplastic uterus. Next, T- shaped that uterus is in the you know instead of being pear shaped here it is t shaped uterus right. Then cervix there is a cervical hood like structure. Fallopian tubes may be blocked.

Ovaries are atrophic, atrophic ovaries. So, these females who have been exposed to your DES in utero will have a premature menopause right. In the vagina there can be vaginal adenosis. And sometimes it has been noted that these females have a increased chance of clear cell adenocarcinoma of vagina and cervix which appears at a very early age. You know in teen age there can be presence of clear cell adenocarcinoma of vagina and cervix.

So, these are the effects on the you know female reproductive tract due to DES exposure in utero. Also it can lead to cancer that is breast cancer. Yes, if in case the offspring is male then what happens with DES exposure? In males or in male offspring it leads to cryptorchidism or undescended testes right. Next it can cause hypospadias. It can also lead to various renal defects.

So, these occur in case of male offspring. Now, coming to a very important topic which we you know regularly use in different types of infections or say upper respiratory tract infection

any subcutaneous edema or you know skin infections gastrointestinal infection. So, when the pregnant female comes with any such infection before prescribing the antibiotics you should be very cautious. So, these antibiotics which are mostly listed here these antibiotics should not be used in pregnancy. Number 1 is the aminoglycoside under which we can say the streptomycin the kanamycin should not be used because of its oto toxicity causes 8th cranial nerve damage and also leads to nephrotoxicity.

Number 2 is chloramphenicol used mostly in GI tract infection it should not be used because it leads to gray baby syndrome right. So, there will be peripheral vascular collapse. Okay, next is sulfonamides. Sulfonamides can cause kernicterus neonatal jaundice due to hemolysis within the fetus right.

Then quinolones. Now, quinolones like ciprofloxacin, ofloxacin these are used mostly in urinary tract infection nowadays, but they should not be used in pregnancy because it can lead to bone and cartilage damage or cause arthropathy right. Tetracyclines no it is a strict no no because it can cause permanent discoloration of the teeth right. So, there will be no yellowish permanent discoloration of the teeth of the fetus and also it leads to inhibition of bone growth right. We use nitrofurantoin, nitrofurantoin, but to remember nitrofurantoin can be used in a case of UTI in pregnancy, but it should not be used at term should not be used at term why? Because it can cause hemolysis in case of G6PD deficiency right. So, that can also lead to jaundice and kernicterus in the neonate right.

So, these are some of the antibiotics which we have you know we prescribe very frequently. Another one to add here is I do not have space I can write it here is metronidazole right. So, metronidazole given in case of stomach infection, loose motion, dysentery sometimes also in case of vaginal trichomonas infection right, but metronidazole as such is safe in pregnancy, but it should not be used should not be used in very high dose. 500 milligram BD for 3 days can be used, but not more than that right. So, that were regarding the antibiotics yes tetracycline we have read can you know causes permanent see these are the you know staining of the teeth permanent teeth staining and also lead to impaired bone growth can cause enabler hypoplasia right altered growth of teeth and bones.

Why because there it causes chelation of the circulating calcium which will prevent the development of bones. Now, coming to the antibiotics which can be prescribed in pregnancy if required right where the benefits will outweigh the risk. Say if the mother is you know having upper respiratory severe upper respiratory tract infection or any type of you know severe skin infection that time what antibiotics to prescribe best is penicillin. Penicillin in the form of ampicillin or amoxicillin cephalosporin can also be prescribed and in case she is penicillin allergic or you know that is penicillin resistant bacteria then you know sometimes we use erythromycin macrolides erythromycin azithromycin which are also safe in pregnancy. So, that

was regarding the antibiotics use.

Gray baby syndrome this is a picture I have told that it is seen in case of chloramphenicol use what happens the skin turns pale or blue and the eyes become lethargic it is associated with peripheral vascular collapse right.

Next, in a nutshell all live vaccines live vaccines are not to be used in pregnancy it is contraindicated right. So, MMR vaccine it is contraindicated, chicken pox vaccine contraindicated, rubella vaccine contraindicated right. Then other live vaccines say your measles mumps rubella these types polio vaccine these are all live vaccines. So, these are all contraindicated in pregnancy.

Smoking, smoking is also contraindicated because nicotine carbon monoxide and other polycyclic hydrocarbon they can cause placental abruption. They are notorious for causing placental abruption can lead to placenta previa and also for the fetus it can cause intrauterine growth retardation and prematurity. So, that will be complicating the pregnancy. So, no smoking we have previously read no alcohol and if she is taking alcohol then also it should be you know in a limited amount no binge drinking because binge drinking is highly dangerous in pregnancy can lead to growth impairment can lead to neurodevelopmental impairment can lead to you know malformation causing facial dysmorphism in the fetus. So, that way alcohol should not be used cocaine use is also a no for pregnancy.

It can lead to cardiac and CNS defect microcephaly mental retardation, abortion and placental abruption. Narcotic use you know opioids sometimes you know morphine use these should not be taken during pregnancy because it will you know when mother is taking it will pass on to the fetus through the placenta and it will cause depression of the CNS in the fetus causing apnea bradycardia and hypothermia of the fetus. Next coming to prostaglandin synthesis inhibitors NSAIDs why I have introduced it here because indomethacin right aspirin yes in the early stages aspirin can be used, but in the last few weeks high dose of aspirin is not to be used in last few weeks. Last few weeks it is contraindicated should not be used indomethacin why because NSAIDs sometimes we give it for you say ah your ah amniotic fluid oligohydramnios or polyhydramnios amniotic fluid derangements we can you know we sometimes give NSAIDs. So, it should not be used in the later half of pregnancy after 32 weeks why because it can lead to premature closure of ductus arteriosus which will lead to pulmonary hypertension in the newborns right.

So, it should not be used also a NSAIDs will cause you know decrease in the these are the afferent arterioles. Say this is the glomerulus and this is the efferent arteriole right. So, this will decrease the blood supply in the afferent arterioles. It will decrease the blood supply in the

afferent arterioles. So, decreased blood supply to the afferent arterioles will lead to decreased urine formation that will cause oligohydramnios in the later half of the pregnancy. So, as such in indomethacin, aspirin high doses not to be used in the later half of the pregnancy mostly because premature closure of ductus arteriosus. Next if there is hypertension in the female during the period of pregnancy we are not going to use ACE inhibitors angiotensin receptor blocker.

I have already told it causes you know severe urine reduction or urine production. Urine production in the fetus is reduced grossly and it will lead to oligohydramnios which can cause potter's syndrome which is associated with limb defects as well as pulmonary hypoplasia. So, it is contraindicated. Thiazide diuretics no it should not be used can cause electrolyte imbalance. Propranolol calcium channel blockers these are all contraindicated in pregnancy.

Then what to use for pregnancy induced hypertension we can use alpha methyl dopa and labetalol, but alpha methyl dopa should not be used post delivery. In the puerperium because it causes puerperal psychosis. So, you know best to go for labetalol right. So, labetalol and calcium channel blocker that is nifedipine can be used you know in mild hypertension or you know in case of PIH, but it causes drastic reduction of blood pressure sudden reduction and which is associated with tachycardia.

So, you need to monitor the patient. In case of emergency purpose we give IV hydralazine or IV labetalol as in case of a eclampsia as in case of severe hypertension right severe PIH. So, in these two cases we can use hydralazine or labetalol in IV route. So, that was regarding hypertension of the mother in pregnancy. Now, say the mother is hyperthyroid. So, you know hyperthyroid meaning thyrotoxicosis or Graves disease of the mother which is also a high risk pregnancy and in that case anti thyroid medication in the form of propylthiouracil, methylthiouracil, carbimazole or radioactive iodine right these all cross the placenta.

So, these cannot be used because if it goes inside the fetters it will cause fetal hypothyroidism or congenital goiter. So, these all should not be used. What can be used as a anti thyroid medication? Only propylthiouracil which is preferably safe compared to others and that too it should be used in the lowest dose just to treat or keep the thyrotoxicosis features under control and after pregnancy you again have to titrate the dose. So, that was regarding hyperthyrotoxicosis in pregnancy. Lastly, I want to say that habitual use of drugs not for therapeutic purpose when there is no indication for taking the drug right.

So, not for therapeutic purpose only for the presence of you know only for the cause of alteration of one's mood or state of consciousness such any such chemical any such drug any such you know over the counter prescribed drug should not be taken by any pregnant woman because it cause can cause a threat to the fetus right. So, no alcohol, no smoking, no other, no

amphetamine related drugs, morphine related drugs, no cocaine use anything over the counter medication should not be taken by the mother and always always when you go for a checkup or you know outside the pregnancy if there is any ailment or complaint for the mother you need to inform your doctor that yes you are pregnant and this you know this many weeks pregnant right and then the prescribed medications should be taken. So, that was all regarding teratogenicity references have been taken from the this is D.C.Dutta of obstetrics, Williams obstetrics and James book on high risk pregnancy. So, thank you for today and keep reading keep taking notes and keep studying. Thank you.