Intrahepatic Cholestasis of Pregnancy

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Question 1:

You report that oral progesterone (to prevent preterm labor) and combined oral contraceptives have been linked with intrahepatic cholestasis of pregnancy. Has the link between reproductive hormonal medication and intrahepatic cholestasis of pregnancy been shown with other routes of administration?

Response from Drs. Williamson and Geenes:

We are only aware of research using oral hormonal preparations. However, we have also heard of some anecdotal reports of a recurrence of pruritus with intrauterine hormonal preparations (eg, Mirena), but are not aware of an associated biochemical cholestasis with this. We are not aware of any studies or reports of symptoms of intrahepatic cholestasis of pregnancy or biochemical cholestasis resulting from the use of progesterone-containing pessaries used to prevent preterm labor.

Question 2:

Have any measures such as vitamin supplementation, diet, exercise, birth spacing, or aspirin therapy been shown to reduce the risk of recurrent intrahepatic cholestasis of pregnancy? Is there a role for ursodeoxycholic acid in the prevention of recurrent intrahepatic cholestasis of pregnancy?

Response from Drs. Williamson and Geenes:

There is no evidence for vitamin supplementation, diet, exercise, birth spacing, or aspirin therapy in reducing the risk of recurrent intrahepatic cholestasis of pregnancy. Furthermore, there are no reported studies of the use of ursodeoxycholic acid in the prevention of recurrent intrahepatic cholestasis of pregnancy. This would be an interesting future research question.
Question 3:

Is there a difference in perinatal outcomes in women with intrahepatic cholestasis of pregnancy who have known mutations of genes encoding biliary transport proteins compared with outcomes in women with intrahepatic cholestasis of pregnancy without known mutations?

Response from Drs. Williamson and Geenes:

At present, known mutations are reported in less than 15% of cases of intrahepatic cholestasis of pregnancy; therefore, to date it has not been possible to undertake this study.

Question 4:

With regard to the induced preterm deliveries for intrahepatic cholestasis of pregnancy in the United Kingdom, what are the most common indications: patient’s symptoms, elevated serum bile acid concentrations, and/or non-reassuring fetal status?

Response from Drs. Williamson and Geenes:

Current practice in the United Kingdom is based on the Royal College of Obstetricians and Gynaecologists guideline, which states that the decision to deliver should be made on an individualized basis. This would take into account all of the above factors (see RCOG 2011 Obstetrics Cholestasis. Green Top Guidelines No. 43).

Question 5:

Does the severity of the patient’s symptoms correlate with the serum bile acid levels? Is the severity of the symptoms associated with adverse perinatal outcomes?

Response from Drs. Williamson and Geenes:

There are several studies that report that the severity and, indeed, onset of symptoms are not correlated with any of the biochemical markers of disease, including serum bile acid levels. Furthermore, the severity of symptoms do not appear to be related to adverse perinatal outcomes, although it is likely that some pregnancies may be delivered early at maternal request due to severe symptoms. In these cases there may be increased risks of complications related to preterm delivery.

Question 6:

Should measurements of fetal serum bile acid concentrations be used to guide timing of delivery?

Response from Drs. Williamson and Geenes:

There are no studies reporting antenatal fetal serum bile acid concentrations, using either cord blood samples or amniocentesis, to determine the timing of delivery. Many clinicians would feel that it is too invasive to perform cordocentesis or amniocentesis without robust evidence to support the practice.
**Question 7:**
Considering the effect of bile acids on myometrial contractility, are rates of postpartum hemorrhage or cesarean delivery lower in women with intrahepatic cholestasis of pregnancy compared with normal women?

**Response from Drs. Williamson and Geenes:**

*There are four studies, two retrospective and two prospective, which report no increase in postpartum hemorrhage or cesarean delivery in women with intrahepatic cholestasis of pregnancy that have induced labor (see Geenes et al, Hepatology 2014;59:1482–91, Chappell et al, BMJ 2012;344:e3799, Wikstrom Shemer et al, Sex Reprod Healthc 2013;4:17–22, and Webster et al, OBM 2011;4:66–9).*

**Question 8:**
Has intrahepatic cholestasis of pregnancy been associated with maternal obesity or weight gain during pregnancy?

**Response from Drs. Williamson and Geenes:**

*There is no association between intrahepatic cholestasis of pregnancy and maternal obesity or weight gain during pregnancy. The recent prospective U.K. cohort study showed no difference in body mass index between women with intrahepatic cholestasis of pregnancy and those with normal pregnancy (see Geenes et al, Hepatology 2014;59:1482–91).*