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SAFETY OF NADOLOL IN PREGNANCY

Question:
What is the safety of nadolol in pregnancy? It is for the treatment of social/fear responses such as tremor.

Answer:
First trimester
We are not aware of any reported evidence associating nadolol or other β-blockers with causing foetal malformations[1-4]. Nadolol does not appear to be teratogenic in rats or hamsters although there have been reports of embryotoxicity and foetotoxicity when high doses are given to rabbits[1]. Due to interspecies variation, care must be taken when extrapolating this data to humans.

There is limited information specifically describing the use of nadolol in pregnancy[1-4]. In a surveillance study of 229,101 completed pregnancies, 71 babies had been exposed to nadolol in the first trimester. One major birth defect was observed (three expected on the basis of natural chance)[1]. In one case report, an infant was exposed to nadolol throughout gestation without evidence of malformations[5]. In another case report, a woman delivered a healthy female following ingestion of nadolol (80mg daily) and nifedipine for the first 23 weeks of pregnancy[6].

Second and third trimesters
The majority of data on the foetal risks associated with β-blockers relates to their use in the treatment of hypertension in pregnancy. Under these circumstances, treatment of hypertension aims to reduce maternal blood pressure without reducing uteroplacental perfusion. Maternal hypertension and reduced uteroplacental perfusion have been associated with intrauterine growth retardation.

In theory, there are several ways a β-blocker may affect the developing foetus:
(a) sympathetic blockade may impair reflex tachycardia and other foetal responses due to uterine contractions and hypoxia,
(b) spontaneous abortion or premature labour may occur secondary to increased uterine tone and diminished relaxation of the cervix prior to, or during delivery,
(c) decreased placental perfusion due to negative inotropic effect on the maternal heart,
(d) intrauterine growth retardation, possibly as a result of neuroactive influences on brain development,
(e) respiratory depression post-natally due to central nervous system effects,
(f) hypoglycaemia which may develop as a result of β-blockade.

A compilation of 23 studies/reports involving 167 live births with exposure to β-blockers during pregnancy found the following incidence of effects: intrauterine growth retardation (14%), hypoglycaemia (10%), bradycardia (7%), respiratory depression (4%), hyperbilirubinaemia (4%), small placental size (2%). It is difficult to differentiate between the effects of maternal disease, the β-blocker or other drug therapy used concurrently[1].

In the previously described case report[5], the infant developed cardiorespiratory depression, mild hypoglycaemia and growth retardation following in utero exposure to nadolol. These effects may be due to persistent β-blockade. Nadolol has a long serum half-life (17-24 hours) and is primarily excreted unchanged by the kidneys. Given the anatomical and functional immaturity of a newborn's kidneys, these pharmacological properties have the potential to prolong its toxicity in the newborn[1].

Conclusions:

As a class, β-adrenergic blocking drugs do not appear to be overtly teratogenic, however there is very limited data specifically on nadolol. β-blockers have been implicated as a cause of intra-uterine growth retardation and reduced placental weight. Perinatal complications such as cardio-respiratory depression and hypoglycaemia have been reported in infants exposed to β-blockers throughout pregnancy. It would be prudent to be aware of these risks perinatally.

As with the use of any drug in pregnancy, there must be careful assessment of the risks and benefits particularly during the first trimester. If treatment of the maternal condition is indicated in pregnancy, it may be preferable to use an agent that has been used more extensively in pregnancy, given the paucity of data on nadolol. It should be noted that cardioselective agents have been suggested to be the preferred type of β-blocker in pregnancy due to the possibility of less perinatal complications.

References:

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