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SAFETY OF FLECAINIDE IN PREGNANCY

Question:
What is the safety of flecainide in the third trimester of pregnancy?

Answer:
NOTE: this report does not discuss the use of flecainide in the first trimester.

Flecainide has been advocated as one of the drugs of first choice for treatment of foetal arrhythmias such as supraventricular tachycardia (SVT)[1]. In one study, 14 women with a mean gestation of 31 weeks (range: 23-36 weeks) received flecainide to treat foetal SVT (n=14) or atrial flutter (n=2) and the resultant heart failure. The maternal flecainide dose was titrated to maintain serum concentrations of 400-700 mcg/L (300-400mg/day). Duration of treatment ranged from two days to five weeks. Twelve infants were successfully converted to sinus rhythm. One intrauterine death occurred three days after initiation of flecainide exposure and was postulated to occur secondary to foetal blood sampling or flecainide-induced arrhythmia. The remaining 13 infants were born alive although one died at 4.5 months of age as a result of sudden infant death syndrome. Six of these infants redeveloped tachyarrhythmia after delivery requiring treatment[2].

Case reports:
There are numerous case reports where foetal arrhythmias have been successfully treated with flecainide in pregnancy[3,4]. Some of these are outlined below:

- A 30-week pregnant woman received intravenous flecainide for treatment of digoxin-resistant foetal tachycardia[5]. Sinus rhythm was rapidly attained and the mother continued to take flecainide 300mg daily throughout the remainder of pregnancy. A healthy 3450g infant was born at 38 weeks' gestation and had no evidence of cardiac problems during the first 10 days of life.
- Kofinas *et al* described a woman of 31 weeks' gestation who received flecainide 300mg daily for foetal SVT that was resistant to digoxin. The dose was gradually reduced to 100mg daily. A healthy infant was born by vaginal delivery at 41 weeks gestation weighing 3,480g[6].
- Maternal administration of flecainide 100-200mg daily successfully treated foetal tachycardia and cardiac failure in the 33rd week of pregnancy. She delivered a term-infant with normal initial development and growth out to seven months of age[7].
- Amano *et al.,* [8] described maternal use of flecainide 400mg daily from 27 weeks' gestation to treat digoxin-resistant foetal SVT and associated cardiac failure. Cardioversion occurred six days after initiation and a 'vigorous' baby was born at term. At one year of age the infant was described as being in 'good condition' and was on flecainide 5mg/kg/day.

Flecainide has also been used to treat maternal arrhythmias during pregnancy:

- A woman with ventricular tachycardia and polymorphous ventricular premature complexes received flecainide 100mg twice daily with sotalol throughout pregnancy. A healthy infant was born at 37 weeks by cesarean section. The infant had normal growth at one year of age[9].
- A woman was commenced on flecainide 200-300mg daily at 35 weeks' gestation for Wolf-Parkinson-White syndrome. Foetal heart rate monitoring did not reveal any evidence of distress and a viable infant was delivered 11 hours after drug initiation. An electrocardiogram conducted when the infant was 90 minutes old did not reveal any abnormalities[10].

Use of flecainide near term has been suggested to cause conjugated hyperbilirubinaemia in the newborn:

- Flecainide 300mg daily was initiated in a woman who was 28 weeks' pregnant for treatment of foetal SVT and cardiac failure. Sinus rhythm was attained within 24 hours and flecainide was discontinued after one week. Another treatment course was required at 30 weeks' gestation and was continued until delivery. The infant was born at 36 weeks gestation and developed conjugated hyperbilirubinaemia within a few days of vaginal delivery. Clinical examination revealed hepatomegaly and a systolic murmur. The authors proposed that flecainide may be implicated as it has caused a similar effect in adults. Two month follow-up indicated resolution of abnormal liver function tests[11].

Conclusions:

There is limited data describing the safety of flecainide in the latter stages of pregnancy. However, it has been successfully used to manage potentially fatal maternal and foetal arrhythmias in pregnancy. As always, there must be careful assessment of the risks and benefits prior to using any drug in pregnancy. However, in the case of potentially fatal maternal or foetal arrhythmias, it would seem likely that the benefits will outweigh any risks. The paediatrician involved in neonatal care of the infant should be aware of the potential for hyperbilirubinaemia.
As always, the lowest effective dose should be used for the shortest possible time.

References:

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