Infant outcomes following maternal perindopril use in a concealed pregnancy – A case report

Oran Milman[1], Rita Wardan[1], Christine Gilmartin[1]

1. Pharmacy Department, The Royal Women's Hospital, Melbourne, VIC, Australia

BACKGROUND

Angiotensin-converting enzyme inhibitors (ACEI) are contraindicated during all pregnancy trimesters.[1] Reports of prolonged exposure to ACEI during pregnancy complicated by maternal renal impairment are limited.

OBJECTIVE

To describe neonatal outcomes following perindopril use in a concealed pregnancy with multiple complex co-morbidities.

MATERNAL CLINICAL FEATURES

A 37 year-old G9P6 woman, without antenatal care, presented with antepartum haemorrhage and in labour at approximately 34 weeks gestation.

Relevant history:

- 4 live term births
- 2 premature live births
- 2 terminations
- 1 missed miscarriage
- Illiteracy
- Peripartum cardiomyopathy
- Hypertension
- Chronic renal disease (Cr=168micromol/L)
- Substance abuse (cannabis, amphetamines, alcohol)
- Schizophrenia
- Stroke
- Asthma
- Smoker

Table 1: Admission medicines and recommendations for use in pregnancy[1]

Medicine	Dose
Perindopril (contraindicated)	10mg daily mane
Bisoprolol (consider alternative)	5mg daily mane
Amlodipine (monitoring required)	5mg daily mane
Olanzapine (monitoring required)	5mg daily mane

The patient's regular medicines (Table 1) were initiated pre-conception and continued throughout pregnancy.
The patient had an etonorgestrel implant *in situ*, but the period of effective contraception had elapsed.

Table 2: Discharge medicines and recommendations for use in breastfeeding

Medicine	Dose
Enalapril (Considered safe to use)	10mg daily mane
Bisoprolol (Consider alternative)	5mg daily mane
Amlodipine (Considered safe to use)	5mg daily mane
Olanzapine (Considered safe to use)	5mg daily mane

Bisoprolol was continued in the post natal period as considered the beta blocker of choice for the patients cardiac condition.

INFANT INTERVENTIONS, CASE PROGRESS AND OUTCOMES

Birth: A baby girl with no obvious congenital anomalies was born by normal vaginal delivery weighing 1946g after one hour of labour. Apgar scores were 7 at 1-minute, and 8 at 5-minutes. Thick meconium was observed at delivery.

Infant complications and progress

Day	Progress
0	• Intubated • Gentamicin (5mg/kg 36-hourly) and benzylpenicillin (60mg/kg 12-hourly) commenced due to presumed sepsis
1	Extubated
2	• High serum creatinine (282 micromol/L) • Low urine output (0.5mL/kg/hour)
3	• Serum gentamicin level recommended • High serum gentamicin level (>2mg/L) • Gentamicin ceased and replaced with cefotaxime (50mg/kg 12-hourly)
4	Urine output improved (2.5mL/kg/hour)
5	Antibiotics ceased
9	Significant reduction in serum creatinine levels (84 micromol/L)

Infant feeding plan

- Day 0 to 5: fully formula fed
  Due to significant maternal substance abuse (cannabis 1g/day)
- Day 6: breastfeeding commenced
  Maternal perindopril changed to enalapril 10mg

Follow up

The infant had normal developmental outcomes at 10 months of age.

DISCUSSION

It is not known if perindopril crosses the human placenta to the fetus. However as the molecular weight of perindopril (368g/mol) is <500g/mol, transfer is likely.[2]

Human reports have described fetal anomalies, neonatal renal failure, and fetal and neonatal death following maternal exposure to ACEI during pregnancy.[3,4]

In this case, the infant's acute kidney impairment was possibly secondary to prematurity and suspected hypoxic injury during delivery. Therefore, these effects could not be exclusively attributed to perindopril use during pregnancy.

CONCLUSION

Adverse neonatal outcomes following maternal perindopril exposure can be difficult to discern from preterm birth complications and contributing maternal conditions. However, the renal compromise resulting from this case is consistent with previous reports of *in utero* ACEI exposure.

REFERENCES

1. The Women's Pregnancy and Breastfeeding Medicines Guide [database on internet]. The Royal Women's Hospital [cited 30/10/2017]
2. Briggs GG, Freeman RK. Drugs in Pregnancy and Lactation. 10th ed. Philadelphia: Wolters Kluwer Health; 2015.
3. Shotan A, WiderhornmJ, Hurst A, Elkayam U. (1994). Risks of Angiotensin-Converting Enzyme Inhibition During Pregnancy: Experimental and Clinical Evidence, Potential Mechanisms, and Recommendations for Use. *The American Journal of Medicine, 96,* 451-456
4. Celentano C, Prefumo F, Di Vera E, Iannicco A, Pio Galllo D, Liberati M. (2008). Reversible acute renal failure due to maternal exposure to angiotensin receptor blocker. *Pediatr Nephrol, 23,* 333-334

For further information regarding this project, please contact the corresponding author on Tel: (03) 8345 3187 or email: christine.gilmartin@thewomens.org.au