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CASE REPORT

Eplerenone use in primary aldosteronism during pregnancy

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Key Clinical Message

Primary aldosteronism (PA) in pregnancy is rare. Due to pharmacological limitations and risks associated with surgical intervention during pregnancy, clinical decision making in this area is difficult. We report the short-term use of eplerenone in the management of hypertension and hypokalemia due to PA in pregnancy.

Keywords

Conn's syndrome, eplerenone, pregnancy, primary aldosteronism.

A 31-year-old woman was referred to our unit 10 weeks into in her fifth pregnancy. She had a complex obstetric history: following an uneventful first pregnancy aged 22, she subsequently had a stillbirth at 32 weeks, a spontaneous abortion at 15 weeks, and a neonatal death following an emergency cesarean section for pre-eclampsia at 34 weeks. Hypertension was found in, and persisted after, her second pregnancy but clinical details from her native Ghana were scarce.

Our investigations revealed hypokalemia (2.1 mmol/L, reference range 3.5–5.1), a recumbent plasma renin activity of <0.2 pmol/mL per h (1.1–2.7), and a plasma aldosterone concentration of 750 pmol/L (135–400), respectively; results strongly suggestive of PA. Left ventricular hypertrophy was evident on an echocardiogram, but there was no hypertensive retinopathy or proteinuria. An MRI scan showed a 1.1 × 8 mm focal left lipid-rich adrenal lesion with decrease in signal intensity on out-of-phase scan, in keeping with an adenoma. A dating ultrasound scan at 16 weeks showed a normal size live male fetus with normal movements.

Treatment with amiloride, methyldopa, doxazosin, and high-dose oral potassium supplements was commenced, but uncontrolled hypertension and hypokalemia persisted. After detailed discussion and informed consent, eplerenone was added at 18 weeks gestation, starting at 50 mg and quickly titrating to 200 mg daily in divided doses. Hypokalemia rapidly resolved, but average inpatient blood pressure recordings remained sufficiently high to be considered a major obstetric risk. An uneventful left laparoscopically assisted adrenalectomy was performed at 20 weeks gestation after a total period of exposure to eplerenone of 2 weeks. Hypertension persisted postadrenalectomy, but was easily controlled with methyldopa and doxazosin. Serum potassium levels remained normal. Histological examination confirmed a Conn's adenoma.

Pre-eclampsia developed at 28 weeks gestation, requiring an emergency cesarean section. The male neonate had significant growth retardation, but there was no evidence of feminization. After 3 months continuous treatment in a high dependency neonatal unit he died from sepsis. The patient defaulted from endocrine follow-up. Four years later, during her sixth pregnancy, despite well-controlled hypertension on three antihypertensive agents, she developed pre-eclampsia and required an emergency cesarean section to deliver a healthy female infant. The successful sixth pregnancy, with normokalemia, would suggest that treatment of her Conn's syndrome had allowed better control of her underlying hypertension, although attempts to confirm biochemical cure of PA have not been successful due to non-attendance.

Diagnosing primary aldosteronism in pregnancy can be difficult as the level of aldosterone can be physiologically twice or thrice levels [1] compared to levels in non-pregnant

women. However, renin levels are also raised [2] in pregnancy and low or suppressed levels should raise suspicion of underlying primary aldosteronism. In our patient, although the level of aldosterone was not elevated in the context of pregnancy, the suppressed renin level, persistent hypokalemia, and refractory hypertension made the diagnosis of primary aldosteronism more apparent.

Eplerenone is a selective aldosterone blocker, currently licensed for use in hypertension and heart failure post myocardial infarction [3]. Unlike spironolactone, it has fewer androgenic effects (gynecomastia, mastalgia, feminization, impotence) [3]. Its main side effects include hyperkalemia [3], hypotension, and renal impairment. Since the first case of PA in pregnancy [4] was described in 1964, only around 20 cases have been reported [5], making informed therapeutic decision making in this area difficult. Spironolactone crosses the placenta and its potent antiandrogenic effects dictate that it has the potential to cause ambiguous genitalia in a male fetus. The lack of affinity of eplerenone for the androgen receptor suggests that it has the potential to be a safer option than spironolactone in severe situations such as the one described here. Clinical trials are clearly neither feasible nor appropriate and any information to guide clinicians will have to come from anecdotal reports such as this. To the best of our knowledge, this is the fourth report of the use of eplerenone in pregnancy and only the second of its use for the treatment of PA in this setting (the others being in the context of Gitelman's syndrome [6] and congestive heart failure [7]). In the previous case of PA in pregnancy [8], a healthy male infant was born at 35 weeks after the mother had received 8 weeks of eplerenone 50 mg twice daily to control resistant hypertension and hypokalemia. In the other two cases, the infant gender was female (eplerenone used from conception to delivery) and in the other case the gender was not reported (eplerenone used from 32 weeks' gestation onwards). A postmarketing surveillance report ("yellow card") is being submitted.

As described, the clinical outcome in our patient was poor, although her previous and subsequent episodes of pre-eclampsia requiring emergency obstetric intervention would suggest that this was related to hypertension rather than the use of eplerenone. The purpose of this report is simply to document, as part of cumulative world experience, the efficacy of the temporary use of eplerenone on blood pressure control and potassium homeostasis in pregnancy. No overt feminization was observed, although neonatal death precluded any subsequent documentation of psychophysical development. The optimum management of PA in pregnancy remains very challenging.

Conflict of Interest

None declared.

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