CASE REPORTS

OLMESARTAN INTAKE DURING PREGNANCY LEADING TO REVERSIBLE RENAL FAILURE AND SKULL HYPOPLASIA IN A PRETERM NEWBORN

Lata Bhat, Supriya Bisht, Kavita Khanijo

Abstract
Drugs acting on renin angiotensin aldosterone system are contraindicated during pregnancy, since they cause severe fetopathic effects like renal failure, oliguria, prematurity and skeletal hypoplasia. Renal failure is progressive in majority of cases. We present a preterm infant who presented with renal failure and skull hypoplasia. Mother had taken olmesartan (angiotensin-II receptor antagonist) throughout her pregnancy. Baby had deranged renal profile and was managed conservatively. Postnatally, renal failure improved after conservative management. Her hypoplastic skull bones also showed improvement. We conclude that selection of antihypertensives during pregnancy should be rational to avoid fetotoxicity.
Keywords: Olmesartan, renal failure, reversible, skull hypoplasia, newborn

Introduction

Angiotensin-II receptor 1(AT1) antagonists, also known as "sartans" are one of the commonly used drugs for managing hypertension. Their mechanism of action is inhibition of angiotensin II/AT1-receptor interaction, leading to decreased effect of angiotensin II. This suppresses renin-angiotensin system (RAS). Maternal intake of the drug, in the second or third trimester of pregnancy can cause fetotoxic effect in view of decreased RAS activity in the fetal circulation. As fetal renal function and urine production starts at the end of first trimester (by 20 weeks), fetal urine constitutes over 90% of the amniotic fluid. (1,2) The decreased renal vascular tonus suppresses fetal urine output. Fetal renal dysfunction subsequently cause oligohydramnios, and leads to further complications. (1) We report a rare case of antenatal olmesartan intake in mother which led to severe oligohydramios, renal failure and skull hypoplasia in the newborn. The renal failure and skull hypoplasia improved completely after conservative management.

Case Report

A twelve day old female baby was referred to us with deranged renal function test since birth. Baby was born vaginally in a private hospital at 32 weeks preterm to G2P1 mother. Birth weight was 1.6 kg. Mother had history of irregular periods. She was hypertensive, for which she was taking olmesartan 20 mg and hydrochlorothiazide 12.5 mg combination since many years. Mother did not go for antenatal check-ups, and continued with the medications. Her first antenatal ultrasound done at 32 weeks was suggestive of oligohydramnios with fetal renal hypoplasia. Soon, she developed leaking per vaginum, and delivered within 48 hours. Baby required resuscitation after birth, and developed respiratory distress which was managed initially with continuous positive airway pressure (CPAP) and antibiotics. At 30 hours of life, baby developed pulmonary hemorrhage, and was started on mechanical ventilation. Subsequently she developed renal failure with decreased urine output (<1ml/kg/hour) and metabolic acidosis. Investigations revealed blood urea 65.6 mg/dL, serum creatinine 1.4 mg/dL, serum sodium 118 mmol/L and potassium 7.2 mmol/L. Baby was managed conservatively. Her respiratory distress settled and she was extubated on ninth day. Though urine output improved, creatinine increased progressively to 4.3 mg/dL, blood urea increased to 127 mg/dL and thus was referred to us on twelfth day of life for further management. At admission in our unit, baby had mild tachypnea. Rest of the parameters were normal. She had high arched palate and widely separated sagittal suture > 1.5 cm, with anterior and posterior fontanelle felt in continuation. Systemic examination was normal. Investigations revealed pH: 7.35, bicarbonate of 22 mmol/L, sodium 138 mmol/L, potassium 3.1mmol/L, calcium 7.7 mg/dL, creatinine 4.5 mg/dL and blood urea 65 mg/dL. Urinalysis showed trace red blood cells, spot urine albumin/creatinine ratio was 171.11 suggesting microalbuminuria. Sepsis screen was negative and urine output was adequate (>4ml/kg/hr). Liver function tests (LFT) were slightly deranged. Ultrasound abdomen revealed mildly enlarged and hyperechoic kidneys with normal corticomedullary differentiation and no hydronephrosis. X-ray skull revealed bilateral parietal bone hypoplasia. Ultrasound cranium, echocardiography and hearing assessment was normal. Baby was managed conservatively with appropriate electrolyte and fluid correction. Serum creatinine decreased to normal on tenth day of hospitalization. Repeat X-ray skull done after four weeks revealed progressive ossification of parietal bone with reduction in the width of parietal suture. Baby was discharged later on request by parents.

Discussion

Fetotoxic effects of "sartans"-angiotensin-II receptor antagonist losartan was first reported in 2001. These were similar to those seen in exposure to angiotensin converting enzyme (ACE) inhibitors during pregnancy. (3) Abnormalities are oligohydramios, pulmonary hypoplasia, hypoplastic skull bones, limb contractures, with subsequent fetal or neonatal death. (1-3) The expression of AT1 receptors is less during the initial stages of renal development, and increases later in pregnancy in mature renal tissues. (2) Adequate amniotic fluid is necessary for normal fetal lung maturation. Hence, oligohydramnios due to any cause may result in pulmonary hypoplasia.

Fetal membranous bones are highly vascular and require high oxygen tension for growth. (2) Possible reason of skull hypoplasia is decrease in fetal blood flow due to reduced activity of the RAS. It may cause low oxygen supply, which may inhibit mineralization and ossification of the skull. Oligohydramnios may further cause the uterine muscles to exert direct impact on the developing fetal skull, which may interfere with skull ossification. (4)

In a study of 15 newborns with maternal intake of "sartans" in second/third trimester, outcome

was poor as 6 (40%) cases died due to severe hypotension, pulmonary hypoplasia, and anuria. Renal failure improved with treatment in only 3 (20%). Hypoplastic and poorly ossified skull bones, and widely open sutures, was seen in 9 cases. (2) In another case report, fetal ultrasound at 29 weeks gestation suggested oligohydramnios with normal fetal kidneys. Stopping olmesartan, maternal rehydration along with furosemide reversed the renal impairment. Baby was born at term with normal renal function, suggesting that renal impairment due to olmesartan may be reversible. (5) In a similar study of seven newborns, oligohydramnios was present in all and fetal kidneys were hyperechogenic on ultrasound. Four did not survive, 2 had renal impairment requiring chronic dialysis, and only 1 had complete recovery of renal functions. Other features seen in these patients were cranial ossification defect, flaccid paralysis of hands and feet and sensorineural hearing loss. (6) In our patient, the renal parameters of the baby improved completely with conservative management.

Thus, we conclude that angiotensin-II receptor antagonists are contraindicated in the second and third trimester of pregnancy because of the risk of adverse fetal effects. It is advised to change the antihypertensive in hypertensive mothers during pregnancy if they are on angiotensin-II receptor antagonists. (2)

Contributor Statement

LB was involved in patient management and finalization of the draft. SB was responsible for draft preparation and patient care. KK was responsible for development of draft and investigation support.

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References :

1. Oppermann M, Padberg S, Kayser A, Weber- Schoendorfer C, Schaefer C. Angiotensin-II receptor 1 antagonist fetopathy--risk assessment, critical time period and vena cava thrombosis as a possible new feature. Br J Clin Pharmacol 2013 Mar;75(3):822-30.
2. Alwan S, Polifka J E, Friedman J M. Angiotensin II Receptor Antagonist Treatment during Pregnancy. Birth Defects Res A Clin Mol Teratol 2005; 73: 123–30.
3. Saji H, Yamanaka M, Hagiwara A, Ijiri R. Losartan and fetal toxic effects. Lancet 2001; 357: 363.
4. Brent RL, Beckman DA. Angiotensin-converting enzyme inhibitors, an embryopathic class of drugs with unique properties: information for clinical teratology counselors. Teratology 1991; 43:543–546.
5. Celentano C, Prefumo F, di Vera E, Lanicco A, Gallo DP, Liberati M. Reversible acute fetal renal failure due to maternal exposure to angiotensin receptor blocker. Paediatr nephrol 2008 Feb;23(2):333-4. Epub 2007 Sep 26.
6. Hunseler C, Paneitz A, Friedrich D, Lindner U, Oberthuer A , Korber F et al. Angiotensin II receptor blocker induced fetopathy: 7 cases. Klin Paediatr 2011 Jan; 223(1):10-4.

From: Department of Neonatology, Fortis Hospital, Noida, Uttar Pradesh, India.

Address for Correspondence:
Dr Supriya Bisht, Department of Neonatology, Fortis Hospital, B-22, Sector 62,Noida, Uttar Pradesh, India.

Email : supriyabisht07@gmail.com

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