# Olmesartan medoxomil-induced acute renal failure in a premature newborn following maternal exposure during pregnancy: A case report and review of the literature

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## ABSTRACT

Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers (ARBs) are widely used antihypertensive with well-recognized renoprotective and cardioprotective effects. Although treatment with these agents generally does not result in adverse metabolic consequences, their use during human pregnancy has been associated with negative reactions. Here, we report a premature baby with a history of oligohydramnios and maternal exposure to the ARB olmesartan medoxomil who was transferred to our institution with acute renal failure.

**Key words:** *Acute renal failure, Oligohydramnios, Olmesartan medoxomil*

Angiotensin receptor blockers (ARBs) are antihypertensive medications, prescribed especially for patients with coexistent diabetes mellitus [1]. Their mechanism of action is inhibition of angiotensin II and angiotensin II - receptor interaction, leading to decreased effect of angiotensin II. This suppresses renin–angiotensin system (RAS). ARBs, as well angiotensin-converting enzyme (ACE) inhibitors [2], are contraindicated during pregnancy, due to the high incidence of fetal complications such as anuria, renal tubular dysplasia, renal insufficiency, oligohydramnios, malformations, and intrauterine death after maternal exposure.

## CASE REPORT

We report a 4-day-old 30 weeks, appropriate for gestational age neonate, presented with complaints of not voided urine since birth. Baby was born to 30-year-old G5P2L2A2 mothers with no antenatal risk factors. All antenatal scans until 23 weeks of gestational age were normal. At 30 weeks, ultrasound study showed severe oligohydramnios with amniotic fluid index <1 cm. Doppler study was within normal limits. There was no preterm premature rupture of membrane or any features suggestive of chorioamnionitis. In view of severe oligohydramnios, baby was delivered by emergency lower section cesarean section after administering two doses of antenatal steroids. Baby cried immediately after birth and Appearance, Pulse, Grimace, Activity, and Respiration scores were normal. Birth weight was 1.4 kg which was between 10$^{th}$ and 50$^{th}$ centile as per Fenton's chart. Baby was appropriate for gestational age with no features of growth restriction. Serum creatinine at 18 h of life was 1.3 mg/dl with no urine output. Medical management was initiated with fluid restriction and with correction of dyselectrolytemia. Fluid requirement was calculated according to insensible water losses and urine output which was assessed every 6 h. By 72 h of life serum creatinine increased to 3.9 mg/dl along with serum potassium of 6.9 mEq/L and serum sodium of 129 mEq/L. Baby was started on salbutamol nebulization and intravenous calcium gluconate injection. Baby was started on peritoneal dialysis by 76 h of life. Serial investigation reports are summarized in Table 1. Ultrasound study of the abdomen with careful evaluation of kidney, ureter, and bladder was within normal limits. On careful and meticulous history review, it was found that mother was taking Olmesartan medoxil 20 mg once daily and the cause of acute kidney injury was attributed to antenatal exposure of ARBs medication. Mother is not suffering from hypertension, and she did not have a prescription for the drug. She stated that she purchased this drug over the counter for complaints of gastritis and she never knew that it is an antihypertensive medication. Baby started voiding urine by day 5 of peritoneal dialysis and catheter was removed by day 10 of peritoneal dialysis as the urine output was >1 ml/kg/hour and renal parameters and serum electrolytes were within normal limits. However, by day 15 of life, baby started developing features of nosocomial infections (sepsis and peritonitis), and baby expired on day 19 of life in spite of adequate antibiotic coverage.

## DISCUSSION

Experiments on animals and human reports have described fetal anomalies, fetal anuria with renal abnormalities, stillbirth,

**Table 1 : Serial investigation reports**

| Investigations | Day 1 of life | Day 3 of life | Day 5 of life | Day 7 of life | Day 10 of life |
|---|---|---|---|---|---|
| Blood urea (mg/dl) | 110 | 185 | 160 | 95 | 66 |
| Serum creatinine (mg/dl) | 1.3 | 3.9 | 2.6 | 1.3 | 0.8 |
| Serum sodium (Meq/L) | 138 | 130 | 134 | 138 | 140 |
| Serum potassium (Meq/L) | 4.2 | 6.9 | 5.8 | 4.2 | 4 |
| Urine output (ml/kg/hour) | 0 | 0 | 0 | 0.6 | 1.2 |

and neonatal death following maternal treatment with ARBs and ACE inhibitors during pregnancy. In the literature, unfavorable fetal outcomes following exposure during late pregnancy are disturbingly frequent. As is also well known for ACE inhibitors [2], the gestational age of a fetus exposed to ARBs is of great importance, with kidney lesions appearing in the second part of the pregnancy [3]. The expression of the angiotensin receptor II gene could be considered the reason for this critical gestational window for the drug-induced renal lesion. The acquired abnormality in renal function due to olmesartan medoxomil exposure seems, therefore, not necessarily lethal. The recovery of renal function observed in our patient suggests that fetal renal damage may be reversible for a period whose length is perhaps gestational age - and dose-dependent. As there is no evidence to identify safely the length of this reversibility period, withdrawal of ARBs must still be considered at the earliest time possible in pregnancy. Fetotoxic effects of angiotensin-II receptor antagonist losartan were first reported in 2001. These were similar to those seen in exposure to ACE inhibitors during pregnancy [4]. Abnormalities are oligohydramnios, pulmonary hypoplasia, hypoplastic skull bones, and limb contractures, with subsequent fetal or neonatal death [4-6]. The expression of angiotensin II receptors is less during the initial stages of renal development and increases later in pregnancy in mature renal tissues [5]. 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 [5]. Possible reason of skull hypoplasia is decreased 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 a direct impact on the developing fetal skull, which may interfere with skull ossification [7]. In a study of 15 newborns with maternal intake of ARB's in the second/third trimester, the 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 were seen in 9 cases [6]. 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 [8]. 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 [9].

## CONCLUSION

Fetal exposure to ACE-Is or ARBs has relevant neonatal and long-term complications. The neonatal outcome appear to be poorer following prenatal exposure to ARBs compared with ACE-Is. 30 years after the first description of ACE inhibitor-induced fetopathy, relevant complications are regularly described, indicating that the awareness of the deleterious effects of prenatal exposure to drugs inhibiting the RAS should be addressed.

## REFERENCES


1. Cooke CE, Fatodu H. Physician conformity and patient adherence to ACE inhibitors and ARBs in patients with diabetes, with and without renal disease and hypertension, in a Medicaid managed care organization. J Manag Care Pharm 2006;12:649-55.
2. Pryde PG, Sedman AB, Nugent CE, Barr M Jr. Angiotensin converting enzyme inhibitor fetopathy. J Am Soc Nephrol 1993;3:1575-82.
3. Daikha-Dahmane F, Levy-Beff E, Jugie M, Lenclen R. Foetal kidney mal development in maternal use of angiotensin II Type I receptor antagonists. Pediatr Nephrol 2006;21:729-32.
4. Saji H, Yamanaka M, Hagiwara A, Ijiri R. Losartan and fetal toxic effects. Lancet 2001;357:363.
5. 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;75:822-30.
6. 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.
7. Brent RL, Beckman DA. Angiotensin-converting enzyme inhibitors, an embryopathic class of drugs with unique properties: Information for clinical teratology counselors. Teratology 1991;43:543-6.
8. 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;23:333-4.
9. Hünseler C, Paneitz A, Friedrich D, Lindner U, Oberthuer A, Körber F, *et al.* Angiotensin II receptor blocker induced fetopathy: 7 cases. Klin Padiatr 2011;223:10-4.


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