FOETOPATHY ASSOCIATED WITH EXPOSURE OF A BLOCKER OF THE RENIN-ANGIOTENSIN SYSTEM- A CASE REPORT AND REVIEW OF LITERATURE

Mautusi Datta¹, Jaharlal Baidya²

¹Tutor, Department of Pharmacology, Agartala Government Medical College, Agartala, Tripura, India.

²Associate Professor, Department of Obstetrics and Gynaecology, Agartala Government Medical College, Agartala, Tripura, India.

HOW TO CITE THIS ARTICLE: Datta M, Baidya JL. Foetopathy associated with exposure of a blocker of the renin-angiotensin system- a case report and review of literature. J. Evolution Med. Dent. Sci. 2018;7(26):3077-3078, DOI: 10.14260/jemds/2018/690

PRESENTATION OF CASE

A 36 years old multiparous woman was on antihypertensive agents- Olmesartan Medoxomil for last 2 years for essential hypertension. She had conceived for second time without pre-conceptional counseling and had continued with same drugs throughout pregnancy without knowing the consequences. Even though she was registered and had regular antenatal care by local general practitioner, the antihypertensive continued without switching over to safer one. She has been referred at her late third trimester of pregnancy with clinical suspicion of Intrauterine Growth Restriction (IUGR) and oligohydramnios along with non-reassuring foetal well-being. Her general physical examination suggests fairly good control of hypertension. Obstetric examination and obstetric USG confirms IUGR and anhydramnios. Doppler USG revealed abnormal wave pattern (Signs of hypovolaemia or increased resistance to foeto-placental blood flow) at umbilical artery and middle cerebral artery of foetus, which warrant immediate termination of pregnancy by caesarean delivery. An asphyxiated male baby weighing 2.25 kg with features of IUGR, hyperflexible major joints was born, who survived only for few hours.

Angiotensin II receptor blockers or antagonists (AT-1 subtype) also called "Sartans" group of drugs are most potent antihypertensive pharmaceutical agents with well recognised renoprotective and cardioprotective agents. Although, treatment with this hypertensive agent is generally not associated with any adverse effects, their use in human pregnancy has been associated with foetopathy.

ACE inhibitors and angiotensin II (AT-II) receptor blockers (ARBs) the most potent antihypertensives and renoprotective pharmaceutical agents also recognised for their cardioprotective activity have been widely applied to a number of illnesses.¹ Clinical consequences are well understood. The side effects are extensively studied in animals and humans. Some of the important side effects related to hypoperfusion of foetal vasculature include renal insufficiency, tubular dysplasia, foetal anuria with oligohydramnios, hypocalvaria, pulmonary hypoplasia and intrauterine foetal death.²

The present short communication describes a registered antenatal mother, who was on "Sartan" group of antihypertensive (Olmesartan Medoxomil) before starting her pregnancy and continued throughout pregnancy due to lack of knowledge of treating clinician. The lady is being referred to a specialist for clinical suspicion of intrauterine growth restriction and oligohydramnios at late third trimester of pregnancy (36 weeks) along with non-reassuring foetal movements.

DIFFERENTIAL DIAGNOSIS

Intrauterine growth restriction with anhydramnios is due to intrauterine infection; congenital malformation of foetus mostly genitourinary anomalies like bilateral renal agenesis; placental hypoperfusion in cases of hypertensive disorder of pregnancy.

CLINICAL DIAGNOSIS

Intrauterine Growth Restriction with severe oligohydramnios with non-reassuring foetal well-being at term pregnancy, exposed to ACE inhibitor.

PATHOLOGICAL DISCUSSION

The renin-angiotensin system is very active during foetal organogenesis and plays an important role, particularly in renal development. ARBs result in hypoperfusion and a decrease in the glomerular filtration rate, which likely affects the development of the foetus. Moreover, these pharmaceutical agents are excreted by the kidneys and can cross human placenta to be excreted into the amniotic fluid and presumably be swallowed by the foetus.³ Therefore, foetal hypoperfusion and the consequent anomalies involving the kidneys are not only indirectly related to the mother's hypotensive status, but also directly related to the drugs in the foetal circulation. Additionally, it is possible that exposure to a pharmaceutical toxic agent could also influence the expression of renin-angiotensin system genes.³

Foetopathy induced by the use of Angiotensin Receptor Blockers (ARB) are reported in literature, mostly it happens if women fail to stop such medication or the woman is lost for follow-up or wrongly prescribed by treating physicians.² More than 15 cases reports described oligohydramnios, foetal growth restriction, pulmonary hypoplasia, limb contractures, and calvarial hypoplasia in various combinations.⁴ Still birth or early neonatal death is frequent to find and surviving infants may have renal damage.⁴ The foetal abnormalities are almost similar to ACE inhibitors during second and third trimester of pregnancy, probably due to extreme sensitivity of the foetus to the hypotensive action of the drug. Interestingly, animal studies fail to demonstrate any teratogenic effects of large doses of "Sartans" group drugs during organogenesis and unfortunately very little is known in human pregnancy.

'Financial or Other Competing Interest': None.

Submission 13-05-2018, Peer Review 07-06-2018,

Acceptance 14-06-2018, Published 25-06-2018.

Corresponding Author:

Mautusi Datta,

Tutor, Department of Pharmacology,

Agartala Govt. Medical College,

Kunjavan, Agartala, Tripura.

Pin-799006

E-mail: mautusidatta77@gmail.com

DOI: 10.14260/jemds/2018/690

In our case, the lady planned her pregnancy while on Olmesartan without switching over to safer antihypertensive agents. Unfortunately, she continued the same throughout her pregnancy as she was asked to do so by the treating clinician. This probably had happened due to lack of knowledge of treating clinician.

DISCUSSION OF MANAGEMENT

Pregnancy was terminated by emergency caesarean section in view of IUGR with absence of amniotic fluid at term with non-reassuring foetal well-being.

FINAL DIAGNOSIS

Fetopathy due to exposure to antihypertensive agent renin-angiotensin blocker during pregnancy.

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