CASE REPORT

ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND AORTIC ARCH OBSTRUCTIVE MALFORMATIONS

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ABSTRACT

We describe two newborn infants with aortic arch obstructive malformations who became anuric after initiation of captopril. Since angiotensin converting enzyme inhibitors can alter renal blood flow by reduction in angiotensin II and blocking autoregulation phenomenon, it is important to use them with great caution in neonates with aortic arch obstructive malformations, while monitoring their renal function closely.

Key words: Captopril, coarctation, renal failure

Captopril, an angiotensin converting enzyme inhibitor (ACEI), has been used for a variety of indications such as cardiovascular diseases among adults and pediatric patients. Renal failure has been frequently described in fetuses or newborns with antenatal exposure to ACEIs, but it has been reported in only few cases of newborn infants who have been given ACEIs postnatally.[1,2] Furthermore, since administration of ACEIs in cases of aortic arch obstructive malformation makes this potential side effect much more important, we describe two newborn infants with interrupted aortic arch and coarctation of the aorta who suffered from acute renal failure after initiation of Captopril.

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CASE REPORTS

Case 1

The patient is a full-term 10-day-old male neonate of nonconsanguineous parents, who was born to a 28-year-old multigravida mother with an uneventful course of pregnancy and delivery. He was admitted with the presumptive diagnosis of sepsis at 4 days of age. Echocardiogram demonstrated interrupted aortic arch just distal to the left subclavian artery (type A), no aortic valve stenosis, large muscular ventricular septal defect (VSD), small patent ductus arteriosus (PDA) with bidirectional flow, a gradient of 60 mmHg between pulmonary artery and descending aorta (PA-DAO) with pulmonary hypertension [Figure 1]. Laboratory exam

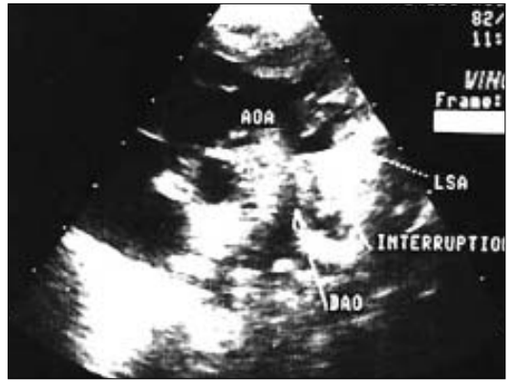

Figure 1: Two-dimensional echocardiogram (suprasternal view) showing interrupted aortic arch type A; AOA = Ascending aorta, DAO = Descending aorta, LSA = Left subclavian artery.

showed normal renal function (BUN = 4 mg/dl, Cr = 0.3 mg/dl). Due to congestive heart failure, Digoxin, Furosemide, *Captopril* (0.5 mg/kg/day) and prostaglandin E1 were initiated. Two days after initiation of Captopril, the patient became anuric and edematous. Creatinine increased to 2.4 mg/dl and BUN to 14 mg/dl. There was no clue in favor of interstitial nephritis in the lab data (e.g., eosinophilia, eosinophiluria). All cultures were negative. Ultrasonography of kidneys and bladder was normal. Doppler ultrasonography of both kidneys showed no evidence of renal artery stenosis. Fluid was restricted and Captopril was discontinued. Forty-eight hours after discontinuation of Captopril, urinary output improved to 2.5 ml/kg/h. His serum creatinine and BUN level gradually decreased to 0.6 mg/dl and 4 mg/dl respectively. Staged repair of arch and pulmonary trunk band was carried out. One week after surgery while renal function tests remained within normal ranges, he suddenly died due to cardiac arrest.

Case 2

A male newborn of 36 weeks' gestational age, product of consanguineous parents, was admitted due to tachypnea and respiratory distress on the first day of his life. Echocardiography showed severe juxtaductal coarctation of the aorta (a gradient of 50 mmHg), muscular VSD (6 mm), PDA and pulmonary hypertension. Renal function tests were within normal limits. He was given Digoxin, Furosemide and *Captopril* (0.5 mg/kg/day) and was discharged after clinical improvement. Again he was admitted due to recurrence of respiratory distress on the 25th day of his life. Blood pressure in both upper and lower limbs was 50 mmHg systolic. He was anuric for the preceding 24 h. Laboratory examination revealed impaired renal function (BUN = 68 mg/dl, Cr = 10.8 mg/dl and K = 6.9 mEq/l). Urine microscopic examination was normal. Ultrasonography of kidneys (Doppler ultrasonography of renal arteries) and bladder was normal. Captopril was discontinued. Supportive management of fluid and electrolytes and temporary peritoneal dialysis were initiated. Urinary output improved 48 h later. Serum creatinine and BUN level gradually decreased to 0.4 mg/dl and 8 mg/dl respectively. Subclavian flap aortoplasty was performed after initial stabilization. The patient had an uneventful postoperative recovery.

DISCUSSION

ACEIs prevent conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. During the fetal period when the placenta acts as the main excretory organ, the fetus has

very high renin and angiotensin II levels to maintain a high renal vascular tone and decreased renal blood flow. Postnatally, angiotensin II will gradually decline and fall with age to reach the adult values.[2,3] Conditions causing renal hypoperfusion typically increase renin secretion or angiotensin II production. Angiotensin II constricts the efferent arterioles more than the afferent arterioles such that glomerular hydrostatic pressure and glomerular filtration rate (GFR) can be maintained despite renal hypoperfusion.[4] If efferent vasoconstriction is blocked by the reduction in angiotensin II caused by ACEIs, then autoregulation does not occur and glomerular capillary pressure and subsequently GFR will fall. It is speculated that high levels of renin and angiotensin II in perinatal period increase the propensity of newborns treated with ACEIs to develop renal failure.[5]

As a fact, disturbed renal perfusion pressure in neonates with severe coarctation of the aorta may be the consequence of: a) low pressure distal to the obstruction, b) congestive heart failure with poor perfusion, c) volume depletion either from increase in diuretic therapy or nondiuretic-induced cause such as gastroenteritis or sepsis. Some experts believe that the beneficial effects of ACEI therapy are seen as long as mean arterial pressure does not fall below 60 to 65 mmHg.[4]

Experimental studies showed that during ACE inhibition, the natriuretic and diuretic responses to Furosemide were attenuated and there was also an increase in the urinary excretion of prostaglandins F_2, $F_{1\alpha}$ and E_2.[6] Withdrawal of ACEIs and interacting drugs, supportive management of fluid and electrolytes and temporary dialysis when indicated are the mainstays of therapy. In addition, underlying causes of volume depletion and reduced renal perfusion must be reversed as much as possible like the way we managed our patients.

To the best of our knowledge, less than 10 cases of newborn infants have been reported in literature to date to have developed renal failure following postnatal exposure to Captopril.[7-10] In contrast to the survival of only 2 neonates from the 5 reported infants with renal failure following postnatal exposure to Enalapril,[2] all Captopril-induced renal failures were reversible after dose reduction or discontinuation, dialysis and aggressive management.

In conclusion, since ACEIs can alter renal blood flow, it is important to monitor renal function in critical conditions such as aortic arch obstructive malformations. It is also recommended to initiate ACEIs in doses less than usual and with great caution in such circumstances.

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