Captopril Therapy in Preeclampsia

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Dear Sir,

We have read the paper by Coen et al. [1] with great interest. Until now, the administration of captopril to pregnant women has been rarely reported, as some authors consider that the therapeutic use of the converting-enzyme inhibitor in pregnancy bears the risk of inducing neonatal renal failure. We report the case of a pregnant patient presenting with a high risk of eclampsia and the effect of captopril intake at the 32nd week of gestation in such a patient.

Case Report

A 31-year-old woman (case 1) had presented with severe hypertension, proteinuria and edema during 3 prior pregnancies which failed spontaneously at the 3rd trimester. At the 32nd week of her 4th pregnancy she presented with preeclampsia; at the 36th week a cesarian section was performed and she gave birth to a 1,600-gram baby. During her 5th pregnancy, the patient exhibited high blood pressure (170/120 mm Hg) at the 23rd week. Intrauterine growth retardation (2 SD below normal values) was diagnosed clinically and by ultrasound scan at the 28th week. The patient's condition gradually worsened and at the 32nd week, massive proteinuria appeared (10 g/24 h) and uricemia increased (0.51 mmol/liter). Hypertension failed to improve under acebutolol (800 mg/day). Labetalol was substituted (1,200 mg/day) in combination with dihy-dralazine (75 mg/day). As her blood pressure remained uncontrolled, captopril (75 mg/day) was prescribed at the 32nd week, whereas dihydralazine was withdrawn. Her average blood pressure was 140/90 mm Hg. Alphamethyldopa (500 mg/day) was started 2 days prior to delivery because of relapsing hypertension. At the 35th week, a girl who was small for gestational age (birth weight: 1.4 kg, head circumference: 29 cm, chest circumference: 23 cm) was delivered by cesarian section. Apgar scores at 1 and 5 min were 7 and 10, respectively. There was no respiratory distress or any other particular clinical symptoms. Plasma free captopril concentrations in ma-

1 We thank Prof. J.F. Giudicelli for the assays of plasma captopril and angiotensin-converting enzyme activity.

ternal and umbilical venous blood were 27 and 92 ng/ml, respectively (last captopril dose was supplied 10 h before delivery). Angiotensin-converting enzyme activity was below 2 nmol/min/ml in maternal (normal: 23.2 ± 1.7) and in fetal blood (normal in preterm infants: 23.3

± 1.3). On the 11th day, the infant's heart rate was 150/min, with polypnea, and cardiac failure symptoms appeared. An intense systolic murmur was diagnosed. Echocardiography showed a massive ductus arteriosus (6 mm diameter), which was dealt with surgically when the baby was 1.5 month old. The further evolution was favorable. Maternal blood pressure reverted to normal values and all hypertensive agents could be stopped.

Various studies demonstrated that the renin-angioten-sin (RA) system is activated during pregnancy, whereas its role in gravidic hypertension remains unclear. The fetal RA system is stimulated in the newborn when the

Table I. Plasma free captopril and angiotensin-converting enzyme activity in maternal blood and in cord blood

Mother at delivery	Cord blood	
Plasma captopril, ng/ml		
Boutroy et al. [5]	< 100	< 100
Fiocchi et al. [6]	29	undetectable
This study (case 1)	27	92
This study (case 2)	310	330
Angiotensin-converting enzyme activity, mmol/min/ml		
Boutroy et al. [5]	9.7	13.9
This study (case 1)	< 2	< 2
This study (case 2)	6	6
Normal values	23 ± 1.7	23.3 ± 1.3

Table II. Maternal and neonatal plasma renin activity (PRA) and aldosterone in case 2 of this study

Mother at delivery	Cord blood	
PRA, µg/ml/h	0.45 (0.2–2.8)	6.8 (13–14)
Aldosterone, ng/ml	180(12–125)	300(450–700)

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delivery is difficult [4]. Captopril was shown to cross the placenta [5, 6] and could suppress the physiological effects of the fetal RA system and impair the hemodynamic adaptation of the fetus in perinatal distress. Neonatal renal failure has been reported [2, 3], but in those studies maternal treatment required captopril and furosemide. Renal failure thus appeared to be induced by salt depletion as well as by angiotensin II suppression. In the first case, as in the case of Boutroy et al. [5], captopril inhibited fetal angiotensin-converting enzyme activity (table I). Fiocchi et al. [6] mentioned that the RA system was not much impaired, and that the captopril concentration was very low in fetal blood. Coen et al. [1] demonstrated that plasma renin activity as well as aldosterone can be considered to be within normal limits, thus suggesting that the drug was biochemically inefficient. We observed a quite similar case (case 2) in a 28-year-old woman, who presented with preeclampsia and was administered captopril (75 mg/day) at the 31st week (table II). The last dose of captopril (25 mg) was supplied 3 h before delivery of a 1.4-kg baby. Plasma free captopril concentration and angiotensin-converting enzyme activity are reported in table I.

The effect of captopril therapy on the fetus is difficult to determine. What was the role of captopril and other drugs in the retarded intrauterine growth in these women presenting with high-risk pregnancies (thus with a potentially compromised fetus)? We also reported the

persistence of a ductus arteriosus which was surgically treated at 14 months [5]. A few months later, the baby did not show any abnormalities. In this case, as well as in case 1, the ductus arteriosus can be ascribed to prematurity. This could be explained by the potentialization of kinin sys-

tem by converting-enzyme inhibitors, for kinins appeared to be able to stimulate prostaglandin release (involved in the patency of the ductus arteriosus). We conclude thus that converting-enzyme inhibitors can be used – without any diuretics – for the treatment of hypertension and concomitant severe preeclampsia when other drugs are ineffective.

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