

## 17. Angiotensin-Converting Enzyme (ACE) Inhibitors During First Trimester of Pregnancy: a French Prospective Collaborative Study

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**Background:** A recent study suggested a 2.7-fold increase in the risk of major malformations in children with first-trimester exposure to ACE inhibitors compared to unexposed children,<sup>[1]</sup> but no increased risk in children exposed to other antihypertensive medications. The excess was attributable to cardiovascular and central nervous system malformations.

**Objective:** To assess the risk of major congenital malformations in children or fetuses exposed to ACE inhibitors during the first trimester of pregnancy.

**Methods:** Data collected by the French pharmacovigilance centres and the CRAT were analysed. Pregnancies with confirmed first-trimester exposure to ACE inhibitors were included. Controls were selected from women counselled after exposure to a non teratogenic agent and were match according to maternal and gestational age at the time of request. Details on the maternal history and treatments were collected during the first contact and pregnancy outcomes were prospectively ascertained in both groups. Patients with pre-existing diabetes or exposed to known teratogens were excluded. Children with documented chromosomal defects were excluded in both groups.

**Results:** Data on 159 pregnancies with exposure to ACE inhibitors and 159 controls were obtained. The mean maternal age and the mean gestational age at inclusion were similar in exposed and control patients ( $33.7 \pm 5.9$  vs  $33.4 \pm 5.3$  years, and  $12.3 \pm 6.7$  vs  $12.6 \pm 6.9$  weeks of pregnancy, respectively). Pregnancy outcomes in the exposed and control groups were: spontaneous abortions (10 vs 7), voluntary abortions (12 vs 2), medical terminations of pregnancy (6 vs 2), late fetal deaths (2 vs 0), and live births (129 vs 148). There were 4 (2.9%) major malformations (2 live births, 1 late fetal death, 1 medically aborted foetus) in the exposed group and 3 (live births) in the control group (2%). The rate of major malformations in live births or fetuses with pathological examination was not different between the 2 groups (relative risk: 1.5, 95% CI: 0.3-6.5). The 4 major malformations in the ACE inhibitors exposed group were one tetralogy of Fallot (maternal history of aortic coarctation), one unspecified cardiac malformation (maternal history of cardiomyopathy), one giant naevus and one bilateral multicystic dysplastic kidneys with Potter's sequence in a foetus exposed to fosinopril until gestational week 11.

**Conclusion:** Our data suggest that first-trimester exposure to ACE inhibitors is not associated with an increased risk of major malformations. There were only two major cardiac malformations both with maternal history of cardiac anomalies.

### Reference

1. Cooper WO, et al. Major congenital malformations after first-trimester exposure to ACE inhibitors. *N Engl J Med* 2006; 354: 2443-51