

ABSTRACT

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Antidepressant drugs in pregnancy and lactation with special reference to citalopram and fluoxetine.

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Mood and anxiety disorders are common in women during their childbearing years. Therefore there is a clinical demand for effective and safe treatment of pregnant or nursing mothers with psychotropic medication, taking at the same into consideration the effects of maternal drug therapy on the developing fetus and infant.

In present study, the transplacental transfer of amitriptyline, citalopram and fluoxetine was investigated by using an *ex vivo* placental perfusion method. Pharmacokinetics of citalopram and fluoxetine and their demethylated metabolites during pregnancy, delivery and lactation were examined in a clinical trial with 42 mother-child –pairs. In addition, the effects of SSRI exposure on the pregnancy outcome and the growth and neurodevelopment of infants during the first year of life were characterized.

Amitriptyline, citalopram and fluoxetine, and also their primary demethylated metabolites were found to cross the human placenta in *ex vivo* placental perfusions. In the clinical study, common clinical doses of citalopram and fluoxetine were found to result in relatively low maternal drug and metabolite concentrations, which may partly be explained by physiologic changes occurring during pregnancy and partly by increased CYP2D6 activity during pregnancy. Infants exposed to SSRIs during late pregnancy were found to be in increased risk for serotonergic central nervous system adverse effects and the severity of these symptoms was recognized to be in relationship with cord blood 5-HIAA levels. Citalopram and fluoxetine both were excreted into breast milk, but the infant drug concentrations were found to be low or undetectable during breast-feeding. The growth and neurodevelopment of all infants were found to be normal at the age of one year.

In conclusion, maternal citalopram and fluoxetine concentrations were found to be low during pregnancy, which might indicate that these low blood levels could lead to therapeutic failure, and clinicians should be alert to this possibility so that depression or anxiety disorders are not undertreated. Also psychiatrists prescribing SSRIs during pregnancy, as well as the pediatricians treating the newborns should be aware of the possibility for serotonin related neurological symptoms during the first days of life.

Keywords: amitriptyline, citalopram, fluoxetine, transplacental transfer, pregnancy, breast-feeding, serotonin, and 5-HIAA.