

## PRESS RELEASE

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### **Pregnancy study finds strong association between two antidepressants and heart anomalies**

Women who took the antidepressant fluoxetine during the first three months of pregnancy gave birth to four times as many babies with heart problems as women who did not and the levels were three times higher in women taking paroxetine.

Although some of the conditions were serious, others were not severe and resolved themselves without the need for medical intervention, according to a three-country study in the November issue of the **British Journal of Clinical Pharmacology**.

Researchers have advised women taking the drugs to continue unless they are advised to stop by their doctor or consultant. But they are being urged to give up smoking, as the study also found that more than ten cigarettes a day was associated with a five-fold increase in babies with major heart problems.

The team has also suggested that women on fluoxetine should be given a foetal echocardiogram in their second trimester to diagnose possible heart anomalies.

International researchers from Israel, Italy and Germany followed the pregnancies of 2,191 women - 410 who had taken paroxetine during pregnancy, 314 who had taken fluoxetine and 1,467 controls who hadn't taken either of the drugs.

"After we excluded genetic and cytogenic anomalies, we found a higher rate of major heart anomalies in the women who had been taking the antidepressants" says lead author Professor Asher Ornoy from the Israeli Teratology Information Service in Jerusalem, Israel.

"Further analysis showed a strong association between major heart anomalies and taking fluoxetine in the first trimester. Women who smoked more than 10 cigarettes a day also had more babies with heart anomalies."

Women taking paroxetine or smoking less than ten cigarettes a day also faced elevated risks, but not to the same extent.

The women had all contacted either the Israeli Teratology Information Service in Jerusalem, Israel, the Servizio di Informazione Teratologica in Padua, Italy, or the Pharmakovigilanz-und Beratungszentrum für Embryonaltoxikologie in Berlin, Germany.

All three belong to the European Network of Teratology Information Services, which comprises organisations that investigate, and provide counselling on, environmental exposure during pregnancy.

The women in the control group had contacted the services because of concerns about exposure to substances that are not known to cause birth defects and the women in the medication groups because of their use of paroxetine and fluoxetine.

When the researchers looked at the outcomes of all of the pregnancies they found that:

- The prevalence of major heart anomalies was 2.8% in the fluoxetine group, 2% in the paroxetine group and 0.6% in the control group. There was no increase in other major congenital anomalies.
- Previous pregnancy terminations were also higher in the fluoxetine and paroxetine groups than the control group (7.8%, 4.8% and 2.8%). All groups included some terminations because of diagnosed anomalies.
- Birth weights were slightly lower in the fluoxetine and paroxetine groups than the control group (3200g, 3250g and 3300g).
- Women taking fluoxetine and paroxetine were more likely to smoke than women in the control group (20.1%, 20.7% and 7.5%) and more likely to smoke more than ten cigarettes a day (12.3%, 14% and 4.4%).

Taking all the factors into account, the authors calculated that the overall risk posed by antidepressant use and cigarette consumption was as follows:

- Women who took fluoxetine during pregnancy were 4.47 times more likely to have a baby with a heart anomaly and women who took paroxetine were 2.66 times more likely.
- Those smoking more than ten cigarettes a day were 5.40 times more likely to have a baby with a heart anomaly and women smoking less than ten cigarettes a day were 2.75 times more likely.

“These findings clearly show a significant association between major heart anomalies and taking fluoxetine and smoking during pregnancy” says Professor Ornoy.

“There is an ongoing debate in the medical literature about the possible association between women taking one of these two drugs during pregnancy and having a baby with a heart anomaly and we are keen to see further research in this area.

“We should point out that there is no evidence of any increased risk posed by citalopram and sertraline, which belong to the same group of antidepressants.”

The authors say that it is important that women are aware of these findings, especially if they smoke. However if they are taking fluoxetine, they should speak to their family doctor or consultant and should not stop taking their medication unless advised to do so.

“It’s estimated that as many as one in seven women suffer from clinical depression during pregnancy and clinicians need to weigh up the individual risks of pregnant women taking, or not taking, drugs like fluoxetine” stresses Professor Ornoy.

“Many heart anomalies can now be treated, so it is important to bear that in mind when making a decision about whether or not to continue with one of these drugs during pregnancy. The health of the mother and the baby are both important.

“We hope that this study will provide both doctors and pregnant women on antidepressants with some of the information they need to help them make those difficult decisions.”

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#### Notes to Editors

- Paroxetine and fluoxetine in pregnancy: a prospective multicentre, controlled, observational study. Diav-Citrin et al. **British Journal of Clinical Pharmacology**. 66.5, p 695-705 (November 2008).
- Published on behalf of the British Pharmacological Society, the **British Journal of Clinical Pharmacology** contains papers and reports on all aspects of drug action in man: invited review articles, original papers, short communications and correspondence. [www.bjcp-journal.com](http://www.bjcp-journal.com)
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