

Antidepressants Pregnancy Risk: Babies Adversely Affected

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Thanks to the BBC 3-part Panorama series (beginning October 2002), it is no longer a secret that coming off SSRI antidepressants can cause serious symptoms of withdrawal in some users. Christopher Pittman is on trial for killing his grandparents while taking Zoloft when he was 12 years old.

Tonight at 10:00 p.m. AHRP board member, Dr. Joseph Glenmullen, will debate Dr. William Callahan on CNN about the potential risk for an SSRI such as Zoloft to trigger violent behavior.

The latest SSRI withdrawal study (published in The Lancet) by a team at the University of La Laguna in Spain suggests that unborn babies could also be at risk from their mothers' use of SSRIs. Symptoms of neonatal withdrawal syndrome resemble withdrawal symptoms of infants born to Crack Cocaine addicted mothers - they include, convulsions, irritability, abnormal crying and tremor.

The hazardous effects of antidepressants have not been generally known or acknowledged - much less, the adverse effects on newborn babies. The FDA had failed to require warnings about the activation, suicidal risks for children, and the risks of withdrawal syndrome for newborn infants. However, several published reports do exist. [See: <http://www.ahrp.org/infomail/04/06/29.php>]

In 1996, Chambers et al (1996) reported that 31.5% of 73 infants exposed to Prozac in the third trimester exhibited symptoms of "poor neonatal adaptation" including respiratory difficulties, irritability, jitteriness, cyanosis (turning blue) on feeding. [Birth outcomes in pregnant women taking fluoxetine. N Engl Med 335:10101015]

In April 2004, the NTP-CERHR panel issued a report about published evidence of infants exposed to an antidepressant in utero and / or breast fed by mothers who took an antidepressant: The REPRODUCTIVE and DEVELOPMENTAL TOXICITY of FLUOXETINE http://cerhr.niehs.nih.gov/news/fluoxetine/fluoxetine_final.pdf. Following the publication of the NTP-CERHR report, the FDA convened an advisory committee, June 9 that recommended class labeling for the neonatal toxicity/withdrawal syndrome related to in utero exposure of SSRI/SNRI's. The committee also strongly supported a package insert for patients (pregnant or considering pregnancy) which provided detailed information at the 6th to 8th grade level as to what is known about the risk/benefit issues for the fetus/newborn and for the mother when choices have to be made about the use of these agents in pregnancy.. See synopsis of the advisory committee recommendations at: <http://www.ahrp.org/infomail/04/06/29.php>

In the new study the researchers used World Health Organization records. They found more than 100 such cases. Based on the treating doctors' original reports, the researchers narrowed those down to 93 that could be linked

strongly to an antidepressant medication. After conducting a statistical analysis, the authors concluded that the withdrawal reports were more common than would be expected by chance, and should be published to alert doctors and patients.

"In 13 of the 93 cases, the study found, newborns suffered convulsions, a reaction that has not been widely noted in adults who discontinue antidepressant use."

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<http://news.bbc.co.uk/1/hi/health/4229851.stm>

BBC

Anti-depressants pregnancy risk

Babies whose mothers use a type of anti-depressant during pregnancy are at risk of being born with withdrawal symptoms, research suggests.

Babies can be affected by their mother's drugs

If you can avoid medication in pregnancy do."

Dr Patrick O'Brien

Spanish research found use of selective serotonin reuptake inhibitors (SSRIs) was associated with neonatal withdrawal syndrome, the Lancet reports. The researchers say doctors should avoid prescribing SSRIs to pregnant women, or use them cautiously. SSRIs have become a standard treatment for depression in the past seven years. However, it is now known that coming off the drugs can cause serious symptoms of withdrawal in the user.

The latest study by a team at the University of La Laguna in Spain suggests that unborn babies could also be at risk from their mothers' use of the drugs. Symptoms of neonatal withdrawal syndrome include convulsions, irritability, abnormal crying and tremor.

Database

The researchers screened the World Health Organization database of adverse drug reactions for cases of neonatal convulsions and neonatal withdrawal syndrome associated with the use of SSRIs. They found that by November 2003, a total of 93 cases of SSRI use associated with either neonatal convulsions or withdrawal syndrome had been reported. Of these cases 64 were associated with Seroxat (paroxetine), 14 with Prozac (fluoxetine), nine with sertraline and seven with citalopram. The dose was only reported in 13 of the cases associated with paroxetine and ranged from 10mg to 50mg per day.

The duration of treatment was reported only in eight cases. These ranged from four months to five years. Lead researcher Professor Emilio Sanz said: "The results suggest that symptoms of withdrawal might be a greater problem for paroxetine than for other drugs. "Paroxetine should not be used in pregnancy, or if used, it should be given at the lowest effective dose. "With the other SSRIs, especially citalopram and venlafaxine, their use should be carefully monitored and new cases promptly communicated to drug vigilance systems."

More work needed

Also writing in the Lancet, researchers at Yale University School of Medicine said it would be wrong to assume that neonatal withdrawal syndrome was only associated with paroxetine use.

Dr Vladislav Ruchkin said: "It remains to be seen whether Sanz and colleagues' report ultimately reflects a minor problem for a particular antidepressant, or further evidence of a larger set of serious problems for SSRI use in young people. "From a pessimistic extreme, these reports might jointly herald the beginning of the end for the uncontested SSRI hegemony of the past decade." He said that until further research replicated or refuted the findings, it would be best to focus on non-drug therapies.

Dr Patrick O'Brien, a consultant obstetrician at University College London Hospital, told BBC News the paper was interesting. "There is an increasing tendency to prescribe these drugs in pregnancy because of the perception they are completely safe," he said. "The strength of this study is that it has uncovered so many cases that one would have to accept that it suggests a link. "But the weakness is that nobody has any idea how common these problems are in women taking these drugs in pregnancy. Are we talking about a risk of one in a million, or one in 10?"

Dr O'Brien said doctors had to weigh up the potential risk of prescribing the drugs, with the need to treat women suffering from depression. "My advice is that if you can avoid medication in pregnancy do, but without a doubt there will be women who should be taking medication for depression during their pregnancy," he said.

In December 2003 regulators told doctors to stop prescribing the majority of SSRIs to children amid fears that they could make young patients suicidal.

<http://www.bloomberg.com/apps/news?pid=10000103&sid=aaWQez5K8H1g&refer=us>

Antidepressants Linked to Withdrawals in Newborns, Study Says

Feb. 4 (Bloomberg) -- GlaxoSmithKline Plc's Paxil, Eli Lilly & Co.'s Prozac and other antidepressants may cause convulsions and other withdrawal symptoms in newborns whose mothers took the drugs during pregnancy, according to a study in the Lancet medical journal.

Paxil, also known as paroxetine, was associated with two-thirds of the infant withdrawals from antidepressants known as selective serotonin reuptake inhibitors, or SSRIs, in the study by researchers from the University of La Laguna, Spain. Drawing from reports on adverse drug reactions from a database operated by the World Health Organization, the study identified 93 cases of withdrawals in babies born to mothers who took the drugs.

"Paroxetine emerged as the most likely offending party," said Vladislav Ruchkin and Andres Martin of the Child Study Center at Yale University, in a commentary accompanying the study. "And while there may be plausible explanations for such a distinction, it would be unwise to assume the other SSRIs are immune to the problem."

SSRIs are among the most commonly prescribed drugs in the U.S. with about \$11 billion in U.S. sales, according to IMS Health Inc. They have come under increased scrutiny by health regulators because of reports of child suicide risk and other potential side effects. The European Medicines Agency recommended last year SSRIs not be given to children, and the U.S. Food and Drug Administration ordered that antidepressants carry the strictest warning on child-suicide risk.

In December, EU health authorities also recommended Glaxo strengthen warnings about severe withdrawal symptoms in adults when they stop taking Paxil.

Paxil Label

The U.S. Paxil label cautions that children exposed to the drug in the womb have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Still, the label tells doctors to weigh the potential benefits of the drug against its risk in deciding to prescribe the medicine for pregnant women. "No causal link between the medication and the symptoms has been established," Glaxo spokesman Chris Hunter-Ward said.

In the study, Paxil was linked to 64 cases of infant withdrawal, followed by Prozac with 14 cases, Pfizer Inc.'s Zoloft with 9 and H. Lundbeck A/S and Forest Laboratories Inc.'s Celexa with 7. One of the patients was taking Paxil and Prozac at the same time.

"This is ringing the bell of caution, saying please be careful," said Emilio Sanz, professor of pharmacology at the University of La Laguna and the study's lead author, in an interview. "Careful doesn't mean don't treat the patient, but don't use paroxetine."

'Signal' Raised

Reports of infant withdrawal syndrome first surfaced in 1999, when 12 cases associated with Paxil were reported to the WHO database, raising a "signal" to the organization's drug-monitoring reviewers, the study said. More than one report on an adverse drug reaction is required before a signal is

generated, as well as the seriousness of the event and quality of the information.

At the time, WHO authorities published the signal in the agency's internal bulletin, which is sent to medical agencies around the world. The information, however, was not made available to the public.

Doctors wrote more than 10 million prescriptions for antidepressants last year, according to IMS Health. Sanz said he and other researchers have no idea how many pregnant women are prescribed antidepressants.

Newborn withdrawal symptoms associated with the antidepressants also included irritability, abnormal crying and tremor, the study said. The symptoms usually disappear after a day, Sanz said. The study, however, raises concerns about the long-term effects of infants exposed to antidepressants in the womb, the researchers said.

"Such studies indicate that we need a better understanding of SSRI effects on the growing brain and call for a developmental perspective on the use of psychotropic drugs in younger patients," Ruchkin and Martin said in the Lancet commentary.

<http://www.nytimes.com/2005/02/04/health/04depress.html?pagewanted=print&position=>

THE NEW YORK TIMES

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Treatment Of Depression in Pregnancy Affects Babies

By BENEDICT CAREY

In the wake of a yearlong debate over the risks of antidepressants to minors, an analysis of World Health Organization medical records has found that infants whose mothers took the drugs while pregnant may suffer withdrawal symptoms. The study challenges the assurances that many doctors have long given pregnant women with depression that taking the drugs would not affect their babies.

But experts said that the study, appearing today in the journal Lancet, was not definitive and must be weighed against the benefits of drug treatment. Untreated maternal depression can also harm a developing fetus, the experts said, and may lead to lasting childhood problems; all of the infants in the study recovered completely from withdrawal symptoms within 24 hours.

"This study is important in that it gives us a red flag that babies exposed to antidepressants during pregnancy should be closely observed, and may go through unusual behaviors at first," said Dr. Timothy Oberlander, a developmental pediatrician at the University of British Columbia. Dr. Oberlander was not involved in the research and does not conduct research or act as a consultant for pharmaceutical companies.

Some 10 percent to 15 percent of women suffer bouts of depression during the hormonal chaos of pregnancy, and about a quarter of those women get antidepressant treatment, doctors estimate, usually with drugs like Prozac, Paxil and Zoloft. If not treated, these women may also be at increased risk of postpartum depression, a devastating disorder that not only clouds the relationship between mother and child but can also interfere with the child's social development, according to Dr. Janet DiPietro, a professor at the Johns Hopkins School of Public Health.

In the new study, researchers in Spain and Sweden searched through a database of adverse drug reactions maintained by the W.H.O. since 1968. They looked for reports of newborns who had been exposed in utero to antidepressants and who had symptoms that included heightened agitation, fever and quickened breathing. Psychiatrists have long observed these kinds of reactions in adults who abruptly stop taking certain antidepressants, and a few smaller studies have also recently noted similar symptoms in infants born to mothers who were taking antidepressants.

The researchers using World Health Organization records found more than 100 such cases, and narrowed those down to 93 that could be linked strongly to an antidepressant medication, based on the treating doctors' original reports. After conducting a statistical analysis, the authors concluded that the withdrawal reports were more common than would be expected by chance, and should be published to alert doctors and patients.

In 13 of the 93 cases, the study found, newborns suffered convulsions, a reaction that has not been widely noted in adults who discontinue antidepressant use.

"All we are saying is that the data we have points to the possibility of withdrawal problem, but we would have to investigate each case closely to determine the overall risk," the paper's lead author, Dr. Emilio Sanz of La Laguna Medical School in Spain said in a telephone interview.

That newborns would show some reaction to months of exposure to mood-changing medication in the womb is not surprising to many doctors. The most widely prescribed antidepressants, called selective serotonin reuptake inhibitors, or S.S.R.I.'s, induce alterations in the sensitivity of nerve cells, among other things, and abruptly stopping these drugs forces the brain to readjust, experts say.

The antidepressant most often reported in the study to produce withdrawal effects was Paxil, which is cleared more quickly from the body than similar drugs. Dr. Sanz said the effects were stronger for Paxil but acknowledged that factors unrelated to the drug's chemistry could also account for the difference. "Our monitoring so far has not provided clear evidence that Paxil causes neonatal complications," said Mary Anne Rhyne, a spokeswoman for its maker, GlaxoSmithKline.

The Food and Drug Administration asked antidepressant manufacturers to list possible neonatal complications on labels more than a year ago, after small studies found that infants exposed to the drugs suffered respiratory distress, irritability and seizures, among other troubles. It is not yet clear whether the new study will lead to a new advisory, an F.D.A. spokeswoman said.

Some experts said that severe depression during or after pregnancy was still a larger threat to a child's well-being than the often mild and transient effects from ending a drug. "But for the worried well, for women who want antidepressants to feel better as opposed to treating serious depression," Dr. DiPietro said, "they may want to ask whether the benefit they are getting outweighs the potential risks to the developing child."

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