MEDICATIONS TO TREAT AD/HD AND THEIR USE DURING PREGNANCY

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The recent recognition of AD/HD as a life-long disorder affecting 3% to 5% of the adult population has left thousands of women of child-bearing age asking questions about the safety of taking medications used to treat this disorder during pregnancy.

Medications used to treat ADHD

To date, stimulants remain the treatment of choice for AD/HD. These include methylphenidate (**Ritalin, Metadate CD, and Concerta**), the amphetamines (**Dexedrine and Adderall**), and pemoline (**Cylert**). In addition, antihypertensives (**Catapres and Tenex**) and the tricyclic antidepressants (**Desipramine and Imipramine**) have been first line choices for the treatment of AD/HD over the years. Other antidepressants, either alone or in combination with the stimulants, may also be prescribed for AD/HD or related conditions. These include the SSRIs (Selective Serotonin Reuptake Inhibitors such as **Prozac, Zoloft**, and **Paxil**) and, more recently, **Wellbutrin**.

Safety issues

When evaluating the safe use of any product during pregnancy, several issues usually arise. Will the medication have a deleterious effect on the developing fetus, resulting in physical deformities or residual neurologic, behavioral or cognitive deficits? Does the use of medication predispose mothers to premature delivery or to giving birth to undersized infants? Does taking medication throughout the pregnancy result in withdrawal behaviors in the newborn, when he is no longer exposed to the medication? Are there other long-term conditions associated with exposure before birth?

The answers to these questions are not always easy to discern. Human studies may present ethical limitations and animal studies are not always perfect solutions. Doses given to laboratory animals usually far exceed those customarily used in adults, thus not allowing for generalizations to pregnant women.

Available information
To date, there have been no controlled studies specifically designed to investigate the safe use of the stimulants in a pregnant population. However, the question of whether amphetamines cause damage to offspring has been looked at in animal studies and in several published case histories of women who were addicted to amphetamines as well as other drugs.

Amphetamines
In animal studies, cardiac defects were reported in the offspring of mice injected with 41 times the usual human dose of amphetamine. However, no negative effects on offspring were found in rabbits given the drug at 7 times the human dose or in rats given 12.5 times the maximum human dose.

There have been numerous outcome studies looking at the infants of women who have taken amphetamines either during the first trimester or throughout the pregnancy. Women in these studies were usually taking amphetamines as appetite suppressants or were addicted to methamphetamine. These studies are summarized in the book, ***Drugs in Pregnancy and Lactation - A Reference Guide to Fetal and Neonatal Risk, 4h edition*** by Briggs, Freeman, and Yaffe, published by Williams & Wilkins, Baltimore, 1994, (p44a-51a).

One of these studies looked at 52 mothers with documented exposure to **Dexedrine** and 50 non-exposed mothers. No cardiac abnormalities were found in either group initially. However, when the **Dexedrine**-exposed children were seen at follow up three years later, investigators did report a relationship to heart defects in this population.

At this time, as a result of all the available evidence, the prevailing recommendation is that "amphetamines should be used during pregnancy only when the potential benefits to the mother outweigh any risk to the fetus."

Methylphenidate
Adequate animal studies to establish the safe use of methylphenidate (MPH) during pregnancy and lactation have not yet been conducted. It is therefore not known, at this time, whether methylphenidate causes harm to the fetus when taken by pregnant women. Several studies have, however, reported on the outcome of newborns exposed to methylphenidate before birth. In one study, the Collaborative Perinatal Project, involving 3082 mother-infant pairs, 11 women were found who were exposed to MPH without adverse outcome in their infants. A second group of women were identified in 1993. Of the 13 newborns in this group, one had a cardiovascular defect. In addition, there has been a case report of I.V. MPH abuse during pregnancy. In this case, the abuse of the drug was associated with premature birth, growth retardation and neonatal withdrawal, but not with any defects or developmental delay in the infant.

Antidepressants

Tricyclics

The tricyclic antidepressants are currently not recommended for use during pregnancy because of isolated reports of congenital abnormalities, although a cause and effects relationship has not been established. (Drugs and Pregnancy, Catz & Abuelo, *Drug Therapy* , 4, p 90)

Selective Serotonin ReUptake Inhibitors

Results of the first prospective study on the effects of the SSRIs (**luvox, paxil, and zoloft**) on the fetus in utero were only recently released. In this study 267 women from nine medical centers who were taking one of these drugs when they learned that they were pregnant were compared to 267 women who were not exposed to anything known to cause birth defects. No differences were found in women who took these antidepressants throughout their pregnancies and those that took them only during the first trimester. It was concluded that there was no increased risk of major malformations from these drugs when used at recommended doses. There was also no increased risk of miscarriage, stillbirth, or premature delivery noted. These findings agree with previous studies and animal research with the drug **Prozac**. This study however did not address later behavioral effects in children. Previous studies did find a link between fetal exposure to **Prozac** and later behavioral abnormalities in the children. (JAMA 279 (8): 609-610, 1998)

Antihypertensives

Clonidine

Studies performed in rabbits at doses up to three times the oral maximum recommended doses in humans produced no evidence of damage to the offspring. No adequate well-controlled studies have been conducted in pregnant women, but because animal studies are not always predictive of human response, this drug is not recommended for use during pregnancy.

Drugs during breastfeeding

Current information indicates that the **amphetamines** are concentrated in breast milk and can cause symptoms of addiction and withdrawal in the infant. It is therefore recommended that these drugs not be used while nursing. **Wellbutrin** is also secreted into the milk and should not be taken by nursing mothers because of the "potential serious reactions in nursing infants." **Prozac** is excreted into milk and it is not recommended that mothers take it and nurse their infants. It is not known whether **Zoloft** is excreted in milk, but, because of that possibility, caution is recommended when nursing. A recent study has shown that breast fed infants of mothers taking **Paxil** had no detectable trace of that medication in their blood, although low concentrations were found in the milk. These infants experienced no adverse events reported by their parents or pediatricians. As **clonidine (Catapres)** is excreted in human milk, caution is also recommended when administering this medication to nursing mothers.

Conclusion

As with any medication regime, the pros and cons of treatment should be thoroughly discussed by the prescribing physicians with their patients before embarking on a course of treatment. In cases where the patient is or may become pregnant, the health risk to the developing fetus must also be taken into consideration.

Many women with AD/HD, report that pregnancy with its high estrogen levels and increased sense of well being is a time when they feel and function at their best even without medication. Stimulant medication may not be needed during this time and the continued use of antidepressants may also need to be discussed.

For other women, who may still need medication to function, a frank discussion within their family and with their therapist is recommended. If they chose to forgo medications during pregnancy, taking extra steps to ensure that they continue to function well will need to be part of their plan for a healthy pregnancy. Pregnant women with AD/HD should take extra measures to insure that their lives run smoothly during this time. Increasing structure, taking more time for herself, and reducing stress whenever possible should all be given a high priority. Hiring babysitters for younger children, and having someone come in to clean or to do the laundry may help keep things organized and running smoothly. Working with a coach or a therapist to keep you focused on your goals may also be an important step to consider.

After the baby comes, help will also be needed. Scheduling extra help while nursing or deciding not to nurse the baby so that you can get back on your medication regimes are both options you should discuss with your therapist and the baby's pediatrician. Remember, a calm, together mom may be more important to your baby and the rest of the family than breastfeeding this new infant.

It is hoped that the information contained in this article will assist women in their discussions with their physicians, and that they will be better able to make informed decisions about the benefits to themselves and their families when pursuing a course of treatment for their AD/HD symptoms. It, however, should never be considered a substitute for medical advice. The decision to use medication during pregnancy may have serious consequences and should be made only in consultation with your treating physician, who can offer advice based on knowledge of a woman's unique history and current health and circumstances.

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