



A Rough Obscurity: Using Antidepressants in Pregnancy

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Most of the obstetricians have provided consultancy for their pregnant patients about starting, continuing or discontinuing antidepressant treatment, at least once in their professional life. While making a decision, clinicians should take into account the consequences of an untreated psychiatric condition as well as possible effects of medication both on the mother and the baby. Over the last decade, in concordance with an increase in antidepressant use in pregnancy, numerous studies have discussed the effects of antidepressants and found contradictory results.

Possible Risks for the Offspring

Antidepressants have been associated with spontaneous abortion, anencephaly, craniosynostosis, omphalocele, low birth weight, preterm birth, small for gestational age, low APGAR scores, increased pulmonary vascular resistance, intraventricular and subarachnoid hemorrhage, jitteriness and withdrawal syndrome (1,2). In most of these studies, the data is confounded by the gestational age, underlying maternal psychiatric or medical condition. Contrary to positive associations, there are many reviews pretending no relationship between antidepressant use and congenital malformations (3). In a study by Jimenez-Solem et al, authors submitted that women using antidepressant treatment tend to visit health care providers for screening their children and this tendency might be accepted as a confounding factor (4). In addition to vast literature about results of antidepressant use in pregnancy suggesting no significant increase in malformations in the offspring, no concrete evidence about their teratogenicity has been emerged (5).

Tricyclic Antidepressants

After their first launch to the market in 1959, literature pointed out some associations between tricyclic antidepressant (TCA) use and congenital malformations. Amitriptyline and nortriptyline were thought to be associated with fetal malformations including limb anomalies, whereas an association with clomipramine use in pregnancy and cardiovascular anomalies (atrial and ventricular septal defects) was demonstrated. However, designs

of these studies are not sufficient for figuring out a causal relationship between TCA use and birth defects. Studies were unable to investigate some confounders such as polypharmacy, the direct effect of mental illness and alcohol use (6). Second or third trimester use of TCAs, especially clomipramine, might increase both the risk of cardiac defects and some perinatal complications such as lethargy, jitteriness and seizures (6).

Selective Serotonine/Noradrenaline Reuptake Inhibitors

These group of antidepressants show better safety and tolerability when compared with TCAs. Although Food and Drug Administration (FDA) categorizes TCAs and paroxetine as "indicating a risk to the fetus but the use of these drugs in pregnancy may be acceptable despite the risk" (7), Bonari et al (8) postulated that antidepressants have no bigger risks than gastrointestinal medications or antibiotics on the fetus. Citalopram has the highest placental passage, while sertraline and paroxetine have the lowest placental transfer rates. Beside this fact, in accordance with the recent scientific evidence, escitalopram is accepted safer than fluoxetine, sertraline and citalopram in terms of fetal cardiac malformation risk. Fluvoxamine, with the highest safety profile among SSRIs, has a common side effect such as nausea and vomiting (9).

Risks for Breast-Feeding

Available data in the literature is derived from case reports and studies consisting of small sample sizes. And also, there is still no consensus on a reliable lactation safety index. In addition, while making a decision, infant's metabolism should be better taken into account. In a meta-analysis, it is found that antidepressant levels peaked 8-9 hours after dosing and feeding the baby after this period is recommended in order to minimize fetal exposure

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(10). Although short-term and small side effects were described, among all SSRIs/SNRIs, paroxetine and sertraline are recommended during breastfeeding. Fluvoxamine is considered safe, in terms of adverse effects up to 300 mg/day doses (11).

Disorders of Childhood

Except one study reporting an increased risk of autism spectrum disorders (ASD) with use of antidepressants before pregnancy (12), some of the studies concluded an increased risk for ASD in pregnant women using antidepressant treatment. The results indicate a 1.5 to 2.5 fold increase in ASD risk (13). There are inconsistent results in published studies and one study reported risk for developing attention deficiency and hyperactivity disorder-not ASD with antidepressant exposure in the first trimester (14). On the other hand, these associations might be linked to some confounding factors seen more commonly in women taking antidepressants, such as being overweight, smoking, alcohol use, co-administered medications and medical conditions etc. The effect of clinical diagnosis on the fetus, genetic factors, postnatal care provided by parents are not evaluated and none of the studies have identified a causal relationship. And also, with more frequent visits to the physicians, the possibility of detecting ASD might be increasing. There is more convincing evidence indicating that antidepressants do not cause ASD.

Although there is a marked increase in antidepressant use during pregnancy, women at reproductive ages have an increased risk perception than the scientific data. Due to this perceptual bias, women have a tendency to stop or avoid their pharmacotherapy. Because most of the studies in the literature questioned the association based on databases derived from health records, some methodological limitations such as study design should be considered by the clinicians while evaluating these results. While making decisions, obstetricians should consider the risks and benefits of all treatment options, taking into account the woman's individual medical condition. Discontinuing the medication might exacerbate the symptoms of illness and maternal psychiatric illness may be associated with higher rates of morbidity and hospitalization. Depression and anxiety is relatively common during pregnancy period and after childbirth, and untreated illness have potentially serious consequences on both the mother and the baby (15). Monitoring both the baby and the mother during and after second trimester and adequate patient education is recommended. Different treatment options including psychotherapies, somatic treatments such as transcranial magnetic stimulation and social interventions can be helpful for certain cases.

Ethical Issues

Not applicable.

Conflict of Interests

The authors declare that they have no conflict of interest. We certify that we had no relationship with companies

that may have a financial interest. All authors contributed equally to this study.

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