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Pregnancy and Antidepressant: To be or not to be?

KEYWORDS

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ABSTRACT *Depression is common during pregnancy and post partum period. Treatment of it is important as it affects both mother and the baby. But issue regarding safety of antidepressants is always there. Avoiding use of antidepressants is risky as it may be harmful to both mother and child. Using them can atlest treat depression of mother and she can take good care of child. This article is a small attempt to answer some of the queries regarding the same.*

Introduction:
Psychiatric illnesses are common during pregnancy and post-partum period and treatment of these conditions is important as they can affect the health of the mother and the fetus/infant. Prevalance of depression (with anxiety) during perinatal period is 8-30%.[1,2] There is always a fear and controversy regarding use of antidepressants during peripartum and even postpartum period. Treatment options are psychotherapy and antidepressant medications like selective serotonin inhibitors (SSRIs) and tricyclic antidepressants. Though psychotherapy can be used for mild to moderate depression, antidepressants are often required for the effective treatment of severe maternal depression.[3]

Many conflicting studies and sporadic case reports make bias even more confusing. This article highlights this issue and is a small attempt to simplify the available studies and original research articles so that decision making will be easier.

Effects of non treatment:
Many times depression remains untreated during pregnancy and untreated depression is associated with increased odds for premature delivery and decreased breastfeeding initiation. Also seen are poor weight gain, alcohol or illicit drug use, risk of suicide, toxemias of pregnancy and poor mother-child bonding, each of which comprises the health of both baby and mother. There is an increased risk of pre-term delivery, low birth weight, operative delivery, and neonatal ICU admission and high neonatal cortisol levels at birth.[4-10]

Effects of withdrawing treatment:
Voluntary withdrawal of antidepressant medications prior to conception in euthymic women with a history of major depression as compared with the continuation of medication all through pregnancy is associated with a five-fold increase in the risk of relapse during pregnancy. A longer duration of illness and a larger number of past depressive episodes each predict an increased risk of relapse. About half of the relapses occur during the first trimester.[11]

Short-term neonatal effects like increased distress after delivery, less than optimal orientation and motor activity, and disrupted sleep are associated with untreated depression during pregnancy. Longer-term effects on neurobehavioral outcome reported are disruptive social behavior, depression, and changes in the period of sensitivity for language discrimination.[12]

Cohen et. al. carried out a naturalistic study to describe risk of relapse in pregnant women who discontinued antidepressant medication proximate to conception compared with those who maintained treatment with these medications. Of the 201 participants, 86 (43%) experienced a relapse of major depression during pregnancy. Also relapse was higher in those who discontinued (68% vs. 26%).[11] In another longitudinal cohort study by Cohen et. al. wherein 32 women with histories of depression who were euthymic at conception and who either discontinued or attempted to discontinue antidepressant therapy proximate to conception were enrolled. They found that 75% (N = 24) of patients relapsed during pregnancy and majority of relapses (79%, N = 19) occurred in the first trimester, and relapse was more prevalent in women with histories of more chronic depression.[13] Thus it is proved that pregnancy has no protective effect with respect to major depression.

Effects of use of anti-depressants on baby:
Antidepressant exposure during pregnancy is associated with adverse effects on autonomic and motor activity, habituation, and sleep. Potential effects on gross motor function and language development are found in long term studies of neurobehavioral outcomes of in utero antidepressant exposure suggest but not on cognition.[14]

A study conducted by Einarson A et.al. on 1243 females found that the use of antidepressants in pregnancy was associated with a small, but statistically significant increased rate in the incidence of preterm births but they did not find a statistically significant difference in the incidence of small for gestational age or lower birth weight.[15] Metanalysis by Grigoridis et.al. found that antidepressants did not appear to be associated with an increased risk of congenital malformations, but statistical significance was found for cardiovascular malformations.[4]

SSRIs (selective serotonin reuptake Inhibitors) and pregnancy.
In a large, population-based, retrospective cohort study of the teratogenicity of SSRIs done by Pedersen et. al. it

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was found that there was an increased prevalence of septal heart defects among children whose mothers were prescribed an SSRI in early pregnancy, particularly sertraline and citalopram. The largest association was found for children of women who redeemed prescriptions for more than one type of SSRI. Risks of other malformations, including CNS defects, neural tube defects, ocular defects, cardiac defects other than septal defects, cleft lip and cleft palate, gastrointestinal defects, urogenital defects, and other conditions were not statistically significant between SSRI-exposed and unexposed infants. [16]

Louik et. al. found that first-trimester exposure to paroxetine or sertraline was associated with an increased risk of specific but uncommon congenital malformations like omphalocele and cardiac defects.[17]

A large sample size study using US nationwide Medicaid data of 1,06,000 pregnant women aged 12-55 with a diagnosis of mood or anxiety disorder studied found 1.47-fold increased risk of postpartum hemorrhage in women with current exposure to SSRI than non exposed ones and women with current non-serotonin reuptake inhibitor exposure had a 1.39-fold increased risk.[18]

A large study from British Columbia Canada studied outcomes from infants of depressed mothers treated with SSRIs (SE-D) and those not treated with medication (DE) It was found that birth weight and gestational age for SE-D infants were significantly less than for DE infants and an increased proportion of SE-D infants had neonatal respiratory distress, jaundice and feeding problems.[19]

A study by Chambers et.al. found increased risk of persistent pulmonary hypertension of the newborn (PPHN) in SSRI exposed newborn. The normal risk of PPHN in newborns is 1/700 but with SSRI exposure after week 20, this was raised to 7/1000 after controlling for maternal body mass index, diabetes, nonsteroidal anti-inflammatory drug use and smoking. They postulated that SSRIs might promote pulmonary artery constriction after birth by inhibiting the vasodilator nitric oxide or by direct effects on pulmonary smooth muscle cells.[20] Another reason found was that SSRI caused increase in serotonin levels in the fetal circulation and could result in pulmonary vasoconstriction and proliferation of pulmonary smooth muscle, resulting in increased pulmonary resistance.[21]

SSRI withdrawal syndrome, which comprises of nonspecific symptoms such as irritability, crying, rapid breathing, poor feeding and sleep disturbances, may develop in about 30% of neonates after prolonged exposure to an SSRI during the last weeks of pregnancy. The withdrawal syndrome peaks in severity during the first two days after birth; but in some cases may not occur until the fourth day of life. [22] Discontinuation syndrome is more frequently seen with fluoxetine, sertraline and paroxetine.[23,24]

Conclusions: Important things to be kept in mind while treating depression in pregnancy are [25]:

- Folate supplementation in all women in the reproductive age group
- Planning pregnancies to minimize fetal exposure
- Discussion with patient and family regarding treatment options and documentation of all discussions and decisions
- Active liaison with obstetricians, ultrasonologists and pediatricians is important
- Non-pharmacological treatments should be preferred wherever possible
- If a psychotropic is necessary, the choice of medication should be guided primarily by its safety data during pregnancy and breast-feeding and by the psychiatric history of the patient.

REFERENCE

1. Bowen A, Muhajarine N. Prevalence of antenatal depression in women enrolled in an outreach program in Canada. J Obstet Gynecol Neonatal Nurs 2006;35:491-8. | 2. van Bussel JC, Spitz B, Demyttenaere K. Women's mental health before, during, and after pregnancy: A population-based controlled cohort study. Birth 2006;33:297-302). | 3. Yonkers K, Vigod S, Ross L. Diagnosis, pathophysiology, and management of mood disorders in pregnant and postpartum women. Obstet Gynecol 2011;117(4): 961–77. | 4. Grigoriadis S, VonderPorten EH, Mamisashvili L, et.al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. J Clin Psychiatry. 2013 Apr; 74(4):e321-41. | 5. Kurki T, Hiilesmaa V, Raitasalo R, et.al. Depression and anxiety in early pregnancy and risk for preeclampsia. Obstet Gynecol 2000;95:487-90. | 6. Nonacs R, Cohen LS. Assessment and treatment of depression during pregnancy: An update. Psychiatr Clin North Am 2003;26:547-62. | 7. Chung TK, Lau TK, Yip AS, et.al. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. Psychosom Med 2001;63:830- | 8. Oberlander TF, Warburton W, Misri S, et.al. Neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. Arch Gen Psychiatry 2006;63:898-906. | 9. Nonacs R, Cohen LS. Assessment and treatment of depression during pregnancy: an update. Psychiatr Clin North Am. 2003 Sep;26(3):547-62. | 10. Alder J, Fink N, Bitzer J, et.al. Depression and anxiety during pregnancy: a risk factor for obstetric, fetal and neonatal outcome? A critical review of the literature. J Matern Fetal Neonatal Med. 2007 Mar;20(3):189-209. | 11. Cohen LS, Altshuler LL, Harlow BL, et.al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. JAMA 2006;295:499-507 | 12. Monk C, Sloan RP, Myers MM, et.al. Fetal heart rate reactivity differs by women's psychiatric status: an early marker for developmental risk? J Am Acad Child Adolesc Psychiatry. 2004 Mar; 43(3):283-90. | 13. Cohen LS, Nonacs RM, Bailey JW, et.al. Relapse of depression during pregnancy following antidepressant discontinuation: a preliminary prospective study. Arch Womens Ment Health. 2004 Oct;7(4):217-21. | 14. Suri R, Lin AS, Cohen LS, Altshuler LL. Acute and long-term behavioral outcome of infants and children exposed in utero to either maternal depression or antidepressants: a review of the literature. J Clin Psychiatry. 2014 Oct;75(10):e1142-52. | 15. Einarson A, Choi J, Einarson TR, Koren G. Adverse effects of antidepressant use in pregnancy: an evaluation of fetal growth and preterm birth. Depress Anxiety. 2010;27(1):35-8. | 16. Pedersen LH, Henriksen TB, Vestergaard M, et.al. Selective serotonin reuptake inhibitors in pregnancy and congenital malformations: Population based cohort study. BMJ 2009;339:3569. | 17. Louik C, Lin AE, Werler MM, et.al. First trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. N Engl J Med 2007;356:2675-83. | 18. Palmsten Kristin, Hernández-Díaz Sonia, Huybrechts Krista F, et al. Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States BMJ 2013; 347:f4877 | 19. Oberlander TF, Warburton W, Misri S, et al. Neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. Arch Gen Psychiatry 2006; 63:898-906 | 20. Chambers CD, Hernandez-Diaz S, Van Marter LJ, et al. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. N Engl J Med 2006;354:579-87 | 21. Andrade C. Continuing medical education: SSRIs and pregnancy. Indian J Psychiatry 2010;52:83-6. | 22. Sanz EJ, De-las-Cuevas C, Kiuru A, et.al. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: A database analysis. Lancet 2005;365:482-7 | 23. Spencer MJ, Escondido CA. Fluoxetine hydrochloride (Prozac) toxicity in a neonate. Pediatrics 1993;92:721–722. | 24. Stiskal JA, Kulin N, Koren G, et al. Neonatal paroxetine withdrawal syndrome. Arch Dis Child Fetal Neonatal Ed. 2001;84:F134–F135. | 25. Desai G, Babu GN, Rajkumar RP, Chandra PS. More questions than answers! Clinical dilemmas in psychopharmacology in pregnancy and lactation. Indian J Psychiatry 2009;51:26-33. |