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Review article

A screening study of antidepressant treatment rates and mood symptoms in pregnancy

S. M. Marcus[1], **H. A. Flynn**[1], **F. Blow**[1,2], and **K. Barry**[1,2]

[1] Department of Psychiatry, Women's Mood Disorders Program, University of Michigan Medical School, University of Michigan Depression Center, Ann Arbor, MI, U.S.A.
[2] V.A. Serious Mental Illness Treatment Research and Evaluation Center (SMITREC), Health Services Research and Development (HSR&D), Department of Veterans Affairs Medical Center, Ann Arbor, MI, U.S.A.

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Summary

Study design: As part of a large screening study of perinatal depression, pregnant women were screened for demographic, depression and treatment variables in obstetrics clinics. Women taking antidepressant medication prior to conception were included in the sample as the study aimed to document rates of antidepressant medication use, and relationship to depressive symptomatology.

Results: Among women who reported using antidepressant medications within 2 years prior to screening (n = 390, or 11% of all women), 22% reported current use of these medications. Women who reported using antidepressant medications (52%) and those who discontinued them (49%) evidenced elevated depressive symptoms during pregnancy.

Conclusions: Both women who discontinue and some who continue antidepressants during pregnancy demonstrate depressive symptoms, suggesting sub-optimal management of both groups. Future studies should carefully assess the adequacy of treatments prescribed as well as the monitoring and adherence of recommended treatments. Full symptom remission should be the goal for antenatal and postnatal depression in order to minimize risk to mother and baby.

Keywords: Antidepressants; pregnancy; depression.

Introduction

Depression is one of the most common conditions to complicate pregnancy. One systematic recent study suggests that 10% of gravid women meet criteria for major depressive disorder (Cohen and Rosenbaum, 1998). Untreated depression is an important risk factor for unfavorable pregnancy outcomes. These include poor weight gain, lack of prenatal care, and substance abuse (Miller, 1991). Human studies demonstrate that perceived life-event stress, as well as depression and anxiety in pregnancy predicted lower infant birth weight, decreased Apgar scores, prematurity and smaller head circumference (Steer et al., 1992; Zuckerman et al., 1990; Sandman et al., 1994).

While depression poses threats to a pregnancy, decisions about antidepressant treatment during pregnancy, remains a common obstetric conundrum. Because depression so often presents in childbearing years, women are often taking antidepressant medications at the time of conception. The bulk of the literature suggests that the tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRI's) are unlikely to contribute to major congenital anomalies when used in pregnant women (Altshuler et al., 1996; Pastuszak et al., 1993; Kulin et al., 1998). Careful monitoring of women using antidepressants during pregnancy is essential. Earlier studies with the tricyclic antidepressants suggested that as maternal plasma volumes increased, antidepressant blood levels fall with consequent re-emergence of mood symptoms during later pregnancy (Altshuler and Hendrick, 2000). While plasma levels of the SSRI's are not frequently monitored, it is a common clinical phenomenon to observe increases in mood symptomatology in the late 2nd and 3rd trimester, which responds to increasing doses of the antidepressant medication.

This study examined the rates of recent and current antidepressant medication and their relationship to mood

symptoms as measured by the CES-D administered in the waiting areas of obstetrics clinics.

Material and methods

Procedures

As part of a larger pregnancy screening and intervention project which took place from February 2000 through January 2002, a total of 390 pregnant women were identified who had used antidepressant medication within two years prior to conception. The majority of women approached (90%) agreed to complete the screening questionnaire. Confidentiality was maintained and all study procedures were approved by the University of Michigan Medical School Institutional Review Board.

Participants

The mean age of participants was 28.6 (s.d. = 6) years. Most were married (74%), others had a live-in partner (10%), were separated (1.3%), divorced (1.8%), widowed (0.1%), never married (12.8%). The racial distribution of the sample reflected that of southeast lower Michigan based on the 2000 Census data and were as follows: 73% Caucasian, 13% African American, 9.3% Asian, 2.4% Hispanic, 0.7% Native American, and 1.6% ''other'' race. Women were screened at an average of 24 gestational weeks (s.d. = 10.4).

Measures

The screening questionnaire consisted of items assessing demographic and depression related variables. Women were questioned regarding their antidepressant medication use in the past 2 years and whether they had discontinued medication as a result of the pregnancy. Depressive symptomatology was measured by the Center for Epidemiological Studies Depression Scale (CES-D). The CES-D is used widely as a depression screening instrument in non-clinical populations, with good correlation to the Beck Depression Inventory (Beck et al., 1961). The standard cut-off point of 16 was used to determine significant elevated depressive symptomatology.

Data analyses

The primary analyses for this study are focused exclusively on women who reported that they had taken medications for treatment of depression in the two years prior to the screening date (n = 390, 11% of all pregnant women screened). Two groups emerged: women who reported that they had discontinued use of these medications, thus were not currently taking them (n = 248) and women who continued to use antidepressant medications while pregnant (n = 68). Women who omitted information on whether they were currently using antidepressant medications were not included in this grouping (n = 74). T-test was used to examine group differences between the women who were not taking antidepressant medications and those who were taking antidepressants in CES-D total scores. Chi-square analysis was used to examine the relationship between antidepressant medication use (yes/no) and elevated CES-D (scores <16 vs scores ≥ 16). A CES-D cutoff score of 22 was also examined in this manner, with similar results.

Results

Overall, 11% of all women screened reported use of antidepressant medications in the past 2 years. Among the 316 women who reported use of antidepressant medication in the 2 years prior to completing the screening measure (and provided current medication data), 78% (n = 248) reported no current use of antidepressant medications in pregnancy, and 68 (22%) reported current use of these medications. A subgroup of women who recently discontinued antidepressant medications (57%, n = 141 out of 248) reported that they discontinued as a direct result of conception. Many women not taking antidepressant medications during pregnancy (who had used these medications in the past 2 years) evidenced depressive symptomatology during pregnancy, with 49% having elevated CES-D scores (i.e. $\geq$ a score of 16) at the point of screening. 52% of those taking medications showed elevated CES-D. No significant differences on elevated CES-D were found between those taking and not taking antidepressant medications during pregnancy (based on Chi-square test). Both groups of women showed mean elevated CES-D scores (group taking medications mean CES-D = 17.4, s.d. = 11.6; group not taking medications mean CES-D = 18.3, s.d. = 12.4), with no difference found between the groups based on t-test results. When the CES-D was examined after omitting 3 items that pertain to difficulties with sleep, appetite and energy (symptoms that may be confounded with pregnancy related experiences), the results were similar.

Discussion

These data show that, regardless of antidepressant medication use in pregnancy, many women with recent use of antidepressant medications (i.e. prior 2 years) showed elevated symptoms of antenatal depression. Medication discontinuation was associated with high prevalence of depressive symptoms, with 49% of non-medicated women having elevated CES-D. It is also noteworthy that even women who continued medication did not have complete quiescence of their mood symptoms. These findings suggest that, among a sample of women screened in obstetrics settings, adequate remission of symptoms is not being achieved.

In this project, we were not able to assess the reasons for incomplete symptom remission among women who

reported current use of antidepressant medications. It is possible that poor treatment adherence and/or inadequate prescribing or monitoring of symptoms and medication management may be implicated. In a related study, Cohen and colleagues (2002) found that relapse rates were much higher in *unmedicated* women. However, in that study medicated women were monitored within more highly structured psychiatric outpatient settings. Further information about the antidepressant treatment regimen, antidepressant blood levels and concurrent therapies would be essential to better understand the adequacy of the medication treatments.

When medicated, women should be closely monitored for persistent symptoms despite use of antidepressants or other treatments. Physicians treating pregnant women at risk for depression could monitor such symptoms using a symptom severity measure such as the Beck Depression Inventory prior to office visits each trimester, making pharmacotherapy adjustments accordingly. It is not clear from this study whether obstetricians were aware of their patients' use or non-use of antidepressant medications, their depression risk or other forms of mental health service use. Most of the women who discontinued medication were not in mental health treatment, and unlikely to have been engaging in prevention strategies or receiving regular medication visits or adjunctive psychotherapy.

This is one of the few studies to document the rates of antidepressant medication use around the time of conception, and rates of discontinuing these medicines due to conception. There are several practical and methodological difficulties inherent in a large screening study such as this. This study relied on self-reports of medication discontinuation and mood symptoms. Although every effort was made to increase accuracy of reporting (assurance of confidentiality and not notifying clinicians about study data), future studies should include other objective measures of mood and mood treatment, such as inspection of medical records and of pharmacy data. Finally, more data about those women choosing to continue their antidepressant medication would have been informative. Specifically, those blood values correlating with rates of breakthrough symptoms of depression, frequency of medication monitoring, information about medication adherence, and what types of psychological treatment the women were receiving may have helped determine which factors contributed to these breakthrough symptoms. Studies employing careful assessment of these important factors are needed.

Both women who continue medication and those who discontinue their antidepressants during pregnancy merit close follow-up to ensure full remission of symptoms. Minimizing risk to the fetus is paramount, and there may be increased risks inherent in exposing the fetus simultaneously to sub-therapeutic levels of medication and to depressive symptomatology throughout the pregnancy. All decisions regarding medication in pregnancy must consider the risks of fetal exposure, the risks of untreated psychiatric illness in the mother and the risks of relapse when maintenance medications are discontinued.

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Correspondence: Sheila M. Marcus, M.D., 2101 Commonwealth, Ann Arbor, MI 48105-0722, U.S.A.; e-mail: smmarcus@ umich.edu