Maternal Depression and Perception of Teratogenic Risk

Gideon Koren, MD, FRCPC

Motherisk Program, Division of Clin Pharmacology-Toxicology, Department of Pediatrics, Hospital for Sick Children and University of Toronto, Toronto, Canada

ABSTRACT

Depression in pregnancy is characterized by unrealistically heightened perception of teratogenic risk. Appropriate counseling regarding the exposure at hand can assist in reducing maternal concerns. Addressing depression during pregnancy and, in parallel, providing evidence-based counseling and reassurance regarding different antidepressants in pregnancy may avert major health risks.

The majority of pregnant women are exposed to medications during pregnancy. Since the thalidomide disaster of the 1950-60s, medicine is commonly practiced with blatant over estimation of the potential teratogenic effects of various exposures in pregnancy (1-4). We have shown that women tend to assign an unrealistically high teratogenic risk to medications even when they are not known to be teratogenic, as well as to drugs that have been proven to be safe to the fetus (1-2, 4). This misperception of teratogenic risk may lead to serious consequences such as discontinuation of medication for life threatening disorders as well as consideration of pregnancy termination of an otherwise wanted pregnancy (1-5). In the case of psychotropic drugs, abrupt discontinuation of medications may lead to exacerbation of depression (6). In a large multicenter trial Cohen et al. (7) explored the effects of medication discontinuation on pregnancy course. The authors followed up a group of women suffering from major depression treated with antidepressants in pregnancy. A proportion of these women decided to discontinue their antidepressants while others elected to continue. The risk of major depression relapse was 70% in the group that discontinued therapy, as compared to only 25% among those who continued. This study and similar others highlight the dangers of discontinuation of important medications during pregnancy. In the case of antidepressants, this can be associated with increased suicidality.

PERCEPTION OF TERATOGENIC POTENTIAL OF PREGNANT WOMEN

In 1989 we studied for the first time the perception of teratogenic risk in a group of 80 women attending our Motherisk antenatal counseling service (2). These women were exposed to medications not known to be teratogenic, yet they assigned high teratogenicity potential to their exposures (mean 25%), and expressed a high rated likelihood of pregnancy termination. The good news was that these unrealistic perceptions and intentions changed following an evidence-based counseling session. We recently published additional work exploring maternal perception of teratogenic potential (8). Our results corroborated the earlier findings regarding the heightened perception of teratogenic potential among pregnant and planning women, exposed to a variety of fetal-safe agents. As expected, women exposed to proven teratogens (such as anticonvulsants or anticoagulants) exhibited an even higher risk perception and likelihood of pregnancy termination (8).

MEASURING MATERNAL PERCEPTIONS

In different teratology centers, women are counseled in the early stages of pregnancy or in the planning phase. Typically these women are exposed to a variety of medications, some may constitute teratogens, or are suffering from medical disorders that may have adverse fetal impact on
the pregnancy course and or outcome. The components of a typical counseling session include a detailed demographic and medical questionnaire followed by evidence-based counseling on safety/risk of the specific context of the women. In an attempt to capture maternal perceptions and intentions prior to, and following the counseling session, we have developed a specific Visual Analog Scale (VAS) (2, 8). This VAS was validated for quantification of maternal teratogenic risk perception and the rated likelihood of pregnancy termination in pregnant women. The first item of the visual analog scale quantifies maternal tendency to terminate the present pregnancy (on a scale of 1 to 100). The second item refers to the woman’s perception of her unborn baby’s risk for birth defects, and the third refers to the risk of birth defects in the general population. As one would expect, the first and second items of the VAS are significantly inter-correlated. In other words, women who perceive their personal risk of having a child with a birth defect to be high are more likely to consider pregnancy termination. Some maternal characteristics have been shown by us to have a significant effect on maternal intention to terminate the pregnancy, such as age and marital status (8). Despite depression being so prevalent in pregnancy, very few studies have been conducted on the possible impact of undiagnosed maternal depression on these perceptions and intentions.

DEPRESSION IN PREGNANCY
Major depression is the most common mood disorder with high prevalence among women of reproductive age (9). The lifetime incidence of major depression among women is as high as 15% (10, 11). Unfortunately, only half of these women ever seek care. The risk for major depression peaks during the childbearing years and is twice as high in women than in men, both in the childbearing years and during the post-menopausal period (12, 13).

Pregnancy is a major life stressor, and thus may precipitate or exacerbate depressive symptoms. During pregnancy, the risk for active major depression is at least 10% (14), and is associated with a variety of adverse outcomes including poor maternal health; longer hospitalization; suicide ideation and attempt; postpartum depression; higher miscarriage rate in the first trimester and higher rates of pre-term birth (15-18). Maternal depression during pregnancy is therefore a condition that must be screened for and appropriately managed. In reality, depression in pregnancy is often undiagnosed and undertreated, thereby exposing women and their untreated fetuses to a variety of risks (19).

SCREENING FOR DEPRESSION IN GENERAL AND OBSTETRIC PRACTICES
The Edinburgh Postnatal Depression Scale (EPDS) was originally published by Cox et al. in 1987 in an attempt to screen for postpartum depression (20). It consists of 10 items in a self-rated questionnaire. The maximum score is 30. A score of 10 or more is suggestive of a minor depressive disorder, while a score of 13 or more is suggestive of major depression. It is important to remember that this is a screening tool that should never replace full diagnostic workup. Although originally developed for postpartum depression, the EPDS was later validated also for depression during pregnancy (21-24).

In Toronto’s Motherisk program we have integrated the EPDS as part of the counseling session in an attempt to screen for maternal depression in our clinic population. In a sample of over 400 women counseled at the Motherisk Clinic, a quarter of the women scored 13 or more on the EPDS, highly suggestive of major depression (25). A third of the women who had a previous diagnosis of depression scored 13 or more on the EPDS as well. This finding in itself is suggestive of under-treatment in this depressed sub-population. Importantly, a significant number of women coming to the clinic admitted occasional suicide ideation (EPDS question number 10) (25).

MATERNAL DEPRESSION AND PERCEPTION OF TERATOGENIC RISK
Perception of teratogenic risk and maternal decisions are influenced by multiple factors including maternal emotional state. We have recently shown that an EPDS score ≥ 13 (i.e., most probably major depression) is an independent predictor of an heightened perception of teratogenic risk and that EPDS score is significantly and positively correlated with the rated likelihood of pregnancy termination (8). In other words, using the EPDS as a surrogate of the level of depression, a depressed woman (compared to a non-depressed woman with the same exposure) is more likely to have an unrealistically high perception of the risk of having a baby with a birth defect and, possibly as a result, is more likely to consider pregnancy termination.

THE EFFECT OF EVIDENCE-BASED COUNSELLING
Repeating the three VAS items following the counselling session allows a comparison of maternal perceptions and
intentions prior to, and following, counseling and determining whether the session had a significant impact on the patient. Measuring by differences in the maternal assigned risk for having a baby with a birth defect before and after the counseling session, the counselling session has been shown by us to have a significant impact (8). In fact, the assigned risks for all three components of the validated VAS (described above) drop significantly following counseling. Even more important, the rated likelihood of pregnancy termination was shown to significantly decline following a single exposure directed counselling session (2, 3, 8). This effect was shown both for women with high EPDS, as well as for those with lower ones. Thus, appropriate counselling assists in lowering maternal fears, misperceptions, and even the tendency to terminate pregnancy.

**SUMMARY**

Depression is common in women in general and even more so during pregnancy. Maternal depression and its association with the perception of teratogenic risk is a critical, yet neglected, issue. Depressive symptomatology is correlated with both elevated teratogenic risk perception as well as the rated likelihood of pregnancy termination. Appropriate counselling regarding the exposure at hand may assist in reducing maternal concerns. Addressing depression during pregnancy and, in parallel, providing evidence based counselling and reassurance regarding different exposures in pregnancy may avert major health risks.

**References**


