

MATERNAL DEPRESSION AND PERCEPTION OF TERATOGENICITY

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ABSTRACT

Exposure to various medications and medical conditions during pregnancy is often inevitable. Most of these exposures do not carry an elevated risk of congenital malformations. Nevertheless, misperceptions of the risks associated with different exposures in pregnancy are common and may potentially lead to wrong decisions. Unrealistically high maternal teratogenic risk perception may lead to abrupt discontinuation of therapy during pregnancy and even to termination of an otherwise wanted pregnancy.

Maternal perceptions and decisions regarding pregnancy are influenced by many factors including the emotional well-being. Maternal depressive symptomatology appears to have a significant effect on the perception of teratogenic risk and may further limit the validity of a decision-making process. Both screening and addressing maternal depression, as well as appropriate exposure related counseling by a teratology service, may help in reducing unnecessary fear of teratogenicity and possibly even the likelihood of pregnancy termination.

Key Words: *Depression, teratogenicity, risk, antidepressant therapy, exposure, pregnancy, screening*

Exposures to different types of medication and/or background disorders are not uncommon during pregnancy. Over the years, over estimation of the potential teratogenic effects of various exposures in pregnancy has become apparent.¹⁻⁴ Women tend to assign an unrealistically high teratogenic risk to medications not known to be teratogenic, as well as to some that have been proven to be “safe”.^{1-2,4} This misperception of teratogenic risk may lead to discontinuation of medication for sometimes life-threatening disorders as well as consideration of pregnancy termination of an otherwise wanted pregnancy.¹⁻⁵ Abrupt discontinuation of medication may lead to substantial withdrawal symptoms as well as the exacerbation of the baseline disorder (that in itself, may lead to spontaneous loss of the pregnancy).⁶ Cohen et al⁷ explored the effects of medication discontinuation on pregnancy course. The authors studied a group of women suffering from major depression and treated with antidepressants that entered pregnancy. Some of these women decided

to discontinue their antidepressant therapy while others decided to continue. The risk of major depression relapse was 70% in the group that discontinued therapy (compared to 25% in the second group) a significantly higher rate. The frequency of relapses was also significantly higher in the group that discontinued therapy with a significant hazard ratio of 5.⁷ This study and others remind us of the dangers of discontinuation of important medications during pregnancy.

Maternal Perception of Teratogenic Potential

In previous work by Koren et al,² published 20 years ago, the perception of teratogenic risk was assessed in a group of 80 women attending an antenatal counseling service. These women were exposed to medication not known to be teratogenic. Nevertheless, they assigned high teratogenicity potential to their exposures, and a high rated likelihood of pregnancy termination. These perceptions and intentions changed following an exposure related counseling session. We recently published additional work exploring maternal perception of teratogenic potential.⁸ Our

results corroborated previous publications regarding the exaggerated perception of teratogenic potential, among pregnant and planning women, to a variety of benign exposures. As expected, women exposed to proven teratogens (such as anticonvulsants or anticoagulants) demonstrate an even higher risk perception and likelihood of pregnancy termination.⁸

Measuring Maternal Perception of Teratogenic Potential

In different teratology centers, women are counseled in the early stages of pregnancy or in the planning phase. These women are usually exposed to a variety of medications, possible teratogens, or are suffering from background disorders that may have an affect on the pregnancy course and or outcome. Usual components of a typical counseling session include a detailed demographic and medical questionnaire followed by an evidence-based exposure related counseling session. In an attempt to assess maternal perceptions and intentions prior to, and following, the counseling session, we have added to the counseling session (at Motherisk teratology centre, The Hospital for Sick Children) a 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 the pregnant subpopulation). 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 fetus's risk of a birth defect, 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 correlated.⁸ 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 demographic characteristics may also have a significant effect on maternal intention to terminate the pregnancy, such as age and marital status.⁸ Less studied is the possible impact of undiagnosed maternal depression on these perceptions and intentions.

Depression and Pregnancy

Major depression is the most common mood disorder with millions of women suffering from it annually in the United States only.⁹ The lifetime incidence of major depression in women is as high as 15%.¹⁰⁻¹¹ Sadly, 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 later in life (during the post-menopausal period).¹²

It is well established that estrogen modulates the activity of serotonin and that, in general, hormonal milieu and mood are interconnected. This is evidenced by, for example, post-menopausal depression or premenstrual syndrome. It is also evident by the fact that women who experience post-partum depression have higher levels of estrogen and progesterone, prior to the delivery, and experience greater estrogen withdrawal with the delivery.¹³

Pregnancy is a major life stressor, and as such, may precipitate or exacerbate depressive tendencies. During pregnancy, the risk for major depression is at least 10%.¹⁴ Depression in pregnancy is associated with a variety of adverse outcomes including: poor maternal health; longer hospitalization; suicide ideation and suicide attempt; post partum depression; and 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 treated. Unfortunately, depression in pregnancy is often undiagnosed and/or undertreated thereby exposing women and fetuses to a variety of adverse outcomes.¹⁹

Screening for Depression

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 a 10 item 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. Nevertheless, this is a screening tool and is not diagnostic. Although Cox et al developed this questionnaire for the detection of postpartum depression; it was later repeatedly validated for use during pregnancy.²¹⁻²⁴

We have incorporated the Edinburgh Postnatal Depression Scale (EPDS) as an integral 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 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 later fact in itself is suggestive of under treatment in this depressed sub-population. Of noteworthy is that a significant number of women coming to clinic admitted to occasional suicide ideation (EPDS question number 10).²⁵

Maternal Depression and Perception of Teratogenicity

Perception of teratogenic risk and maternal decision-making are likely to be influenced by multiple factors including maternal emotional state. Data is lacking with regards to the perception of exposure related teratogenic risk in women with depressive symptoms and undiagnosed depression. We have recently shown that an EPDS score ≥ 13 (i.e. most probably major depression) is an independent predictor of an exaggerated perception of teratogenic risk and that EPDS score is significantly and positively correlated with the rated likelihood of pregnancy termination.⁸ In other words, 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.

Does Exposure Related Counseling Make a Difference?

Repeating the three VAS items following a counseling 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 counseling session has 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 importantly, the rated likelihood of pregnancy termination was repeatedly shown to significantly decline following a single exposure directed counseling session.^{2,3,8} Thus, appropriate counseling 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 counseling regarding the exposure at hand may assist in reducing maternal concerns. Addressing depression during pregnancy and, in parallel, providing evidence based counseling and reassurance regarding different exposures in pregnancy may be life saving.

Conflict of Interest

The author reports no conflict of interests.

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