Panic Disorder and Pregnancy: Challenges of Caring for Mother and Child

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Panic disorder is a common psychiatric illness that can have a chronic, relapsing course. The question of whether pregnancy represents a time of increased risk for recurrence of panic symptoms has been a matter of debate.

Panic disorder (PD) is a common psychiatric illness that can have a chronic, relapsing course. Epidemiological data has documented a lifetime prevalence of 0.4% to 3.5%, and the illness usually begins during early to middle adulthood with a female to male preponderance (Weissman et al., 1997). Other data have shown that after remission of panic symptoms, women may be more likely than men to experience recurrence of panic attacks (Yonkers et al., 1998).

The question of whether pregnancy represents a time of increased risk for recurrence of panic symptoms has been a matter of debate. Several authors have suggested that pregnancy may provide a protective effect in the course of panic disorder. For example, George et al. (1987) reported a small case series of three women with PD who showed marked improvement in their panic symptoms during pregnancy. Villeponteaux et al. (1992) conducted a small retrospective study on pregnant women with pre-existing PD and reported that a majority of women had an improvement in panic symptoms during pregnancy. Altshuler et al. (1998) found that whereas pregnancy appears to exacerbate symptoms of obsessive compulsive disorder, patients with PD may remain well during pregnancy even after discontinuing medication. In contrast to the above findings, Cohen et al. (1996) conducted a small prospective study on the course of pre-existing PD during pregnancy and found that most patients continued to experience panic attacks during all three trimesters and required anti-panic medication.

Our group has conducted a seven-year, naturalistic follow-up study in order to examine the effect of pregnancy on the course of pre-existing panic disorder. Our results demonstrated that pregnancy may confer an increased risk of relapse in PD. Moreover, when compared to patients who develop PD while not pregnant, patients who have the initial onset of PD during pregnancy appear to have a higher risk of relapse at the time of a subsequent pregnancy (Dannon, unpublished data). While the effect of pregnancy seems to have a variable influence on the course of PD, multiple studies have demonstrated that the postpartum period appears to be associated with an increased risk of relapse (Cohen et al., 1996; Northcott and Stein, 1994; Sholomskas et al., 1993; Wenzel et al., 2005). It should be noted that Wisner et al. (1996) conducted a historical, prospective study of women with panic disorder (n=22) and found no change in the course of panic symptoms postnatally, as compared to the pre-pregnancy baseline. On the other hand, one interesting observation from this study was that first lifetime onset of PD was common postpartum. While it is well accepted that PD has disabling effects in terms of social and occupational functioning, there is also evidence that untreated anxiety in pregnant women may adversely affect the developing fetus. In a cohort of 100 pregnant women with a mean gestation of 32 weeks, Teixeira et al. (1999) found a significant association between uterine artery resistance and maternal scores for state and trait anxiety. Another finding was the strong correlation between plasma levels in the mother and in the fetus, leading the investigators to postulate that elevated maternal cortisol may have a direct effect on the development of the fetal brain (Glover, 1999). In support of this theory, it has been suggested that the hypothalamic-pituitary-adrenocortical (HPA) system (elevated cortisol levels) or sympathetic activation may have contributed to the findings of increased uterine artery resistance in anxious mothers (Field et al., 2003).

The approach to treating the pregnant woman with symptomatic PD must take into consideration the potential risks to the fetus of pharmacotherapeutic intervention versus the possible risks of untreated maternal anxiety. Benzodiazepines are widely prescribed for the treatment of panic disorder, but their use should generally be avoided in women who are pregnant or who wish to conceive. Benzodiazepines used in the first trimester have been associated with a small but
increased risk of oral cleft and congenital malformations of the central nervous system and the urinary tract (Altshuler et al., 1996). Maternal use of benzodiazepines in the perinatal period has also been shown to produce neonatal withdrawal symptoms and may cause respiratory depression and muscular hypotonia in the neonate.

Selective serotonin reuptake inhibitors are highly effective anti-panic agents and are commonly used in treating young women with PD (Ballenger et al., 1998). Several prospective studies of SSRIs have shown no increase in the incidence of miscarriage or major malformations associated with their use (Kulin et al., 1998; Wisner et al., 1999). The SSRIs, however, have U.S. Food and Drug Administration use-in-pregnancy ratings of either B or C, indicating that the risks and benefits of treatment must be considered on a case-by-case basis, and treatment options must be discussed carefully with the patient. Among the SSRIs, fluoxetine (Prozac) has been the best studied in terms of reproductive safety while information regarding the use of sertraline (Zoloft), paroxetine (Paxil), fluvoxamine (Luvox) and citalopram (Celexa) during pregnancy is limited, due to small sample size (Nonacs and Cohen, 2003). A prospective study of the serotonergic noradrenergic reuptake inhibitor (SNRI) venlafaxine (Effexor) during the first trimester of pregnancy showed no increase in the risk of major malformations as compared with non-exposed controls (Einarson et al., 2001). It should be kept in mind that the use of paroxetine prior to delivery has been associated with a high rate of neonatal complications such as respiratory distress and hypoglycemia (Costei et al., 2002).

Cognitive-behavioral therapy (CBT) for PD has been shown to be effective in terms of controlling acute panic symptoms and preventing relapse (Barlow et al., 2000; Dannon et al., 2004). It may be combined with medication therapy or may be used alone, and the ability to treat panic symptoms without the inherent risks of pharmacotherapy represents a distinct advantage for CBT in pregnancy. Treatment with CBT requires both the availability of clinicians who have training in CBT, as well as motivation and cooperation on the part of the patients. Robinson et al. (1992) reported that CBT could be successfully adapted in order to treat panic disorder during pregnancy.

In a recent survey of perinatal care (n=387), only 11% of women with panic disorder were referred for psychiatric consultation during pregnancy at their prenatal visits (Smith et al., 2004). Improved detection of PD during pregnancy, as well as improved early intervention, are important in order to prevent unnecessary suffering in the mother and to maximize the well-being of the fetus. Care of the mother-child dyad continues to be critical in the postpartum period, which appears to be associated with increased risk of relapse. Both mother and child benefit when panic symptoms are well controlled throughout the pre- and postnatal periods and when thoughtful consideration is given to weighing the risks and benefits of pharmacotherapy for PD in pregnancy.

In summary, the treatment of panic disorder in women of childbearing age requires attention to possible teratogenic risks of anti-panic medication. Prior to conception and during the first trimester, patients should be advised not to use or to use the lowest possible doses of medication recommended. Ideally, for women with a stable course, anti-panic medication may be tapered and discontinued prior to pregnancy. Given the possibility of an unplanned pregnancy, patients should be routinely educated about the reproductive safety profile of medication that is prescribed for the treatment of PD. In a subgroup of patients with pre-existing panic disorder, pregnancy may be associated with an increased risk of relapse, and therefore optimal prenatal care includes careful monitoring of panic symptoms throughout all three trimesters.

Among the SSRIs, fluoxetine and citalopram appear to be the best studied in pregnancy and have not been associated with an increased rate of major malformations. Women should be counselled to taper and discontinue benzodiazepines prior to planning a pregnancy. It is also recommended to taper SSRIs and benzodiazepines during the late third trimester in order to prevent the risk of neonatal withdrawal symptoms.

References:

4. Barlow DH, Gorman JM, Shear MK et al. (2000), Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: a randomized controlled trial. [Published errata JAMA 284(19):2450;


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