DEPRESSIVE DISORDERS IN PREGNANCY – A CHALLENGE REQUIRING MULTIDISCIPLINARY APPROACH

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ABSTRACT

Pregnancy is considered to be one of the most special moments of a woman's life. Soon-to-be mothers are expected to be awaiting their baby's arrival with excitement and jubilance. But sometimes, due to depressive disorders (DD), the course of the pregnancy may not meet the blissful expectations. DD might impact fetal development and have consequences reaching far after pregnancy and delivery. Untreated DD may be the cause of premature delivery, low birth weight, gestational hypertension or even perinatal death and may also affect child's physical and emotional development. But unfortunately, drugs used in pharmacological treatment of DD are also considered as potentially harmful for the child, causing pregnancy and delivery complications such as poor neonatal adaptation syndrome and respiratory distress in newborns. Finding the "gold standard" in treatment of DD in pregnant patients should become one of the main goals both for gynecologist and psychiatrist and doctors of both these specialties should work together to destigmatize mental health problems of expecting mothers.

BACKGROUND

Undoubtedly, depression is a growing sociomedical problem, becoming one of the leading causes of disability worldwide [1]. Since in the Western World it is more often diagnosed among women than men [2], it is crucial for obstetricians to take into consideration that 1 in 5 of their patients might be treated for this disorder or have a history of depressive episodes. Our aim is to elucidate this issue to the readers, which is extremely important, since there are no official guidelines neither from the Polish Society of Gynecologists and Obstetricians nor the Polish Psychiatric Association.

THE INFLUENCE OF DEPRESSIVE DISORDERS ON THE COURSE OF PREGNANCY AND FETAL DEVELOPMENT

The term 'perinatal depression' is pertinent when depressive episode is experienced by a woman during pregnancy or within the first year after the childbirth. To establish the risk of developing depressive disorder in a pregnant patient a doctor may for example ask two simple Whooley questions [3]. Positive response, as well as reported depressive episode in the past, should lead to the referral to the psychiatrist. Although pregnancy is generally a condition in which we are reluctant to prescribe new medications, we should consider possible negative influence of untreated depression on both the mother and the child. Depending on how severe the depressive episode is, there may be changes in woman's behavior such as: unhealthy diet, less intense physical activity, irregular sleep, alcohol consumption or abuse of other psychoactive substances, not to mention the higher risk of attempting suicide. There are also studies suggesting that hypothalamic-pituitary-ovarian (HPO) axis may be dysfunctional, which can negatively affect fetal development [4].

We are not able to distinguish which factors are determinant, but the studies suggest that mother's depression may be associated with premature delivery, low birth weight, gestational hypertension or even perinatal death [5, 6]. Mother's mental condition probably also affects child's emotional and behavioral development, especially in early stages. Higher maternal cortisol levels may be responsible for augmented emotional reactivity in children [7]. Relation between prenatal and postnatal depression is also thought-provoking – the first one is clearly considered a risk factor for developing the second one. Determining whether the postpartum depression emerges from undiagnosed and thus untreated prenatal depression might be extremely helpful in understanding the postnatal depression phenomenon.

HOW THE TREATMENT OF DEPRESSIVE DISORDERS MAY IMPACT THE CHILD?

We are lacking strong evidence for safety antidepressants use in treating pregnant women – there are no randomized control trials, although the risk is considered to be minimal. Meta-analysis of 27 studies showed no significant relation between exposure to any antidepressant with prevalence of congenital malformations. There was a statistically significant association between developing cardiovascular malformations (i.e. atrial septal defects or ventricular septal defects) in the fetus and exposure to paroxetine yet the clinical significance of this finding is questionable [8]. Still, that is the reason why paroxetine is not recommended for pregnant women according to most of guidelines. Also, fluoxetine, which together with paroxetine are the oldest selective serotonin reuptake inhibitors (SSRIs) in use, is considered "unfavourable" in couple of guidelines, because of its pharmacokinetics and pharmacodynamics (long biological half-time and presence in breast milk) [9]. Other SSRIs, such as sertraline, citalopram and escitalopram are so far known as safe when it comes to risk of congenital malformations. Still, it is important to remember that several studies showed both statistical and clinical significance in increased risk for occurrence of poor neonatal adaptation syndrome and respiratory distress in newborns. For this reason, it is important for neonatologists to be informed about the maternal depression treatment [10]. Fewer studies examined further development of children prenatally exposed to antidepressants. For example, there are surmises that there is slightly increased risk of poorer motor development [11].

There is no doubt that both untreated depression and medication may be harmful for the fetus, though it is the doctor's task to evaluate the risk, present the issue to the patient and discuss it together to choose the best possible solution.

WHAT ARE THE GUIDELINES FOR DEPRESSIVE DISORDERS TREATMENT IN PREGNANT WOMEN?

So far there have been no official Polish recommendations established for treating depression in pregnancy. Clinical Practice Guidelines in different countries are mostly consentaneous (i.e. in the USA - by the American College of Obstetricians and Gynecologists and the American Psychiatric Association; in Germany - by Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde; in the UK - by the National Institute for Health and Care Excellence and by the Scottish Intercollegiate Guidelines Network) [12, 13, 14, 15]. In the international review of 16 guidelines published in March 2018 by Molenaar et al. authors point out that most of recommendations indicate psychotherapy, especially cognitive behavioral therapy (CBT), as the first step in treating mild to moderate depression and antidepressants as the second step - or the first one in severe cases [16]. What is interesting, the American College of Obstetricians and Gynecologists recommends medical therapy as the first step regardless of depression severity. Patients who had been already taking antidepressants before conception, should be informed about the possible risk of the relapse when discontinuing the therapy, but the studies show different results in this matter [17, 18].

As for favoring a particular substance, guidelines point out sertraline or citalopram, if any.

THE TREATMENT OF DEPRESSIVE DISORDERS AFTER CHILDBIRTH

Next step included in the clinical practice guidelines is postpartum period. Half of them advise breast-feeding, no matter which anti-depressant medication the patient is taking [19]. Recent analysis of excretion ratios of three antidepressants (sertraline, citalopram and venlafaxine) in the breast milk of 17 women had shown, that all of them are present in milk, but the concentration of the drug to which infants are exposed is low - median from 0.0016 mg/kg b.w./day for sertraline to 0.077 mg/kg b.w./day for venlafaxine [19]. The study found no correlation between daily dosage and the concentration of drugs in breastmilk, except for venlafaxine. Although this finding could be clinically important, as it implies relative safety for the child exposed to the medication, there is a need for further research on bigger samples and more precise studies on pharmacokinetics and pharmacodynamics of antidepressants during lactation period.

WHAT PROBLEMS COULD WE FACE IN THE FUTURE?

We are lacking complete statistical data about the course of DDs treatment in pregnant patients and patients' compliance. How many women actually take the medication in a prescribed dose? How many of them discontinue the therapy and why – is it because of their fear for their child's health or because of the possible side effects they think they may experience? These questions should be answered if we want to provide the best care for soon-to-be mothers suffering from DDs. Performing studies on these matters is in the best interest of psychiatrists and obstetricians.

CONCLUSIONS

Since obstetricians are usually the first and often the only medical contact for pregnant women, it is crucial to sensitize them to the delicate issue of possible DDs in their patients. Providing them with suitable guidelines, directions and tips is crucial for the wellbeing of their patients. Fighting the stigma associated with any type of mental illness, including DDs, should encourage soon-to-be mothers to reach out for help out of their own initiative.

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ABBREVIATIONS

DD – depressive disorders
HPO – hypothalamic-pituitary-ovarian
SSRIS – selective serotonin reuptake inhibitors

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