PSYCHIATRY

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PSYCHIATRIC DISORDERS IN PREGNANCY AND THE POST-PARTUM PERIOD - ETIOLOGY, DESCRIPTION AND IMPACT, TREATMENT - REVIEW

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ABSTRACT

Pregnancy and the first year after birth are special periods for the monitoring and treatment of mental illness. During these periods, numerous conditions are diagnosed including depressive disorders (11%), anxiety disorders (15%), bipolar disorders (20.1%) and psychotic disorders (0,1-0,2%). Of interest is the potential impact of psychiatric treatment on plans to have children and the need for treatment during pregnancy.

Aims: To identify the factors enabling the psychiatrist, in collaboration with obstetricians, anesthesiologists, and psychologists, to take the risk of prescribing in pregnancy and the postpartum.

Methods: A literature review was conducted using the PubMed database with the search items identical to keywords.

Results: Still many psychiatric disorders in pregnancy and the postpartum left unrecognized and undertreated, which might increase the risk of complications and development problems for foetus and infant due to medical and psychological factors. Mental disorders are the leading causes of maternal death which might be associated with stigma and fear, making it impossible to ask for professional help.

Conclusions: The appropriate medical care for pregnant women and mothers with psychiatric disorders should include the whole service of medical professionals familiar with all the complexity and difficulty of mental disorders. The decision of treatment in such cases always has an impact not only on mothers but also on newborns.

Keywords: depression in pregnant women; postpartum depression; postpartum psychosis; anxiety disorder; tokophobia

INTRODUCTION

A concern of a potential impact of treatment on plans to have children is especially justified in cases of psychiatric disorders and the need for their treatment during pregnancy. These fears are completely

understandable, however, frequently ignored. Pregnancy is generally accepted as a time of "hormone storm", so you can expect an absolutely full range of moods and behaviors from a woman and treat them as the norm. Contrary to appearances, the situation is much more complicated. A much more important risk factor for mental disorders during pregnancy is their previous occurrence, e.g. a past episode of depression, lack of support from the environment, complications during pregnancy or unplanned pregnancy, as well as natural stress related to the new situation and fear of childbirth. Pregnant women most often suffer from depression and anxiety disorders. This is also a vulnerable period that might induce the development of postpartum psychiatric disorders including a rare but severe postpartum psychosis.

The objective of this review is to show how widespread and complex are factors on which the psychiatrist with the help of obstetric, anesthesiologic and psychological care makes the decision of prescribing pharmacological treatment to psychiatric patients during pregnancy or early postpartum.

METHODS

A literature review was conducted using the PubMed database with the search items: "depression in pregnant women", "postpartum depression", "postpartum psychosis", "anxiety disorder" and "tokophobia". The studies were carefully reviewed and analyzed in order to ensure full relevance to the subject.

RESULTS AND DISCUSSION

EPIDEMIOLOGY

In pregnancy, depressive and anxiety disorders are common, with recent population estimates of 11% for depressive disorders and 15% for anxiety disorders. [1] Also panic disorder and obsessive-compulsive disorder are the diagnosis set in pregnancy more frequently than at other times. [2] On the other hand, depression and antenatal anxiety are two of the greatest risk factors for postpartum psychosis. [3] For around 50% of women, postpartum psychosis will be their first onset of psychiatric disorders [4] and occurs in 1-2 in 1000 women after birth [5] Maternal suicide due to postpartum mood disorders (including unipolar and bipolar depressive disorders) is a leading cause of maternal mortality. [6] There is a particular vulnerability in women with bipolar disorder making them experience psychotic episodes in the postpartum period when they are the most prevalent. [7] The postnatal depression occurrence is estimated at 17%. [8] The conditions of the poor socioeconomic environment and limited access to health care increase the risk of developing these diseases even though there are countermeasures with inadequate social support in many countries. [9]

Severe psychotic disorders should not be confused with baby blues since they are regarded as transient, mild mood and anxiety symptoms that often persist for ≤2 weeks and usually resolve spontaneously with no sequelae. [10] Psychiatrists might diagnose postpartum disorder when the symptoms of the baby blues persist too long or get worse than expected.

ETIOLOGY

Childbirth might turn out as the one of the most influential triggers of psychiatric disorders. The etiology of all psychiatric conditions is always a complex interaction of psychological, social and biological factors, including the effect of genetic and environmental influences on the risk.

Biological factors have a huge impact on triggering of postpartum psychosis, whereas psychological factors might have an important role in postpartum depression. [11] As an example of pathophysiological impact there is a small group of women with postpartum psychosis who were diagnosed with autoimmune encephalitis [12]. This might be a proof of biological impairment involved in the onset of the mental disease.

The specific emerging risk factors for perinatal anxiety disorders are associated with lower educational attainment, the extended family, multiparity, family history of a psychiatric disorder, hyperemesis gravidarum, comorbid sleep disorders and antenatal oxytocin exposure. [13]

The dysregulated hypothalamic - pituitary - adrenal stress axis during the perinatal period might generate depressive and anxiety symptoms in pregnant women. [14] The triggers are fluctuations of the releasing corticotropin hormone produced by the placenta. [15] The levels of the hormones increase significantly during pregnancy and also significantly decline in the postpartum period. The same time levels of gonadal steroids participate in puerperal hypertrophy of the pituitary and adrenal glands, leading to increases in adrenocorticotropic hormone and cortisol levels. [16] It can also lead to the changes in reactivity of the HPA axis in the newborn because maternal depression and anxious mood induce epigenetic changes in the infant glucocorticoid receptor gene (Nr3c1). [17]

An increase in thyroxine-binding globulin concentrations (TBG, which transports thyroid hormones in the blood) during pregnancy might be an index of sensitivity to elevated oestrogen levels. Decreased TBG levels have been suggested as a predictor of perinatal depression in some studies. [18]

The conversion from pregnancy into the postpartum period is characterized by a fast immune response (mediated through both pro-inflammatory and anti-inflammatory mediators for healing and involution) during labor that continues into the early postpartum period. [19] Consequently, immune changes at the end of pregnancy might predict postpartum depression. IL6 levels are increased in women with postpartum depression compared with postpartum women without depression in some but not all studies. However, leptin (a protein hormone made by adipose cells that regulates energy and has inflammatory functions) might also be associated with postpartum depression. Decreased maternal serum leptin levels during delivery are related with a higher risk of postpartum depression and might potentially serve as a biomarker for this disorder. [20]

Schizophrenia and mood disorders are the psychiatric illnesses in which etiology outside of the perinatal period genetic factors were implicated. This statement is based on the data from the twin and adoption studies. [21,22] Genetic epidemiological and linkage studies for postpartum depression have demonstrated the role of genetic factors - the heritability of postpartum depression is increased compared with depression outside of the perinatal period. [23,24] The studies have also suggested that episodes of postpartum psychosis are a marker for a more-familial form of bipolar disorder and triggering of bipolar illness might be a family feature. [25,26]

In patients with the prior history of psychiatric disease, discontinuation or change in the treatment may be also the reason why the period of pregnancy or labor release psychiatric disorder or exacerbate the current one. [27] Also non-psychiatric treatment like oral contraceptives might induce sensitivity to hormonal change and then after labor the patients, diagnosed with for example premenstrual dysphoric disorder previously, will be more burdened with the risk of developing postpartum depression. [28] Apart from medical complications the important risk factors of postpartum depression are perinatal anxiety, family history of these illnesses, life stressors and perceived social isolation [29], low self-esteem [30] and history of physical abuse [31].

SYMPTOMS AND IMPACT ON FETUS

The symptoms of the psychiatric disorders in pregnant women and in the postpartum period might manifest in many various ways and always have an impact on the fetus or infant no matter if the symptoms persist during pregnancy or develop after childbirth.

In case of perinatal depression and anxiety the manifestation does not differ significantly from the non-childbearing presentation. The psychiatrists should stay alert to somatic symptoms of sleep disturbances and fatigue which occur frequently as normal pregnancy related changes. The women with depression during pregnancy might develop symptoms such as hypertension, preeclampsia and gestational diabetes. [32] It is also associated with premature birth [33], low birth weight, fetal growth restriction [34] and postnatal complications. [35] Depressed pregnant women may have a higher tendency not to obey obstetric care and overuse medication, drugs, alcohol, herbal remedies and tobacco. [36]

Some patients present specific anxiety disorders like needle phobia which might challenge anaesthetic care because of the need of general anaesthesia. Tokophobia is a description of a morbid fear from pregnancy and childbirth. For this reason many women decide for delivery by caesarean section. [37]

Unfortunately, maternal depression is often associated with impaired maternal-fetal bonding. [38] All the maternal behaviors which should promote infant development such as engagement with playing or talking to babies and breastfeeding [39] are handicapped. The infants of depressed mothers may have problems with emotional regulation, also in their adulthood, and cognitive development. [40]

Postpartum psychosis has usually a rapid onset, beginning within 2-4 weeks after childbirth and in majority cases should be treated as a psychiatric emergency. Patients are unable to take care of themselves and of the infant which can lead even to suicide or in the worst cases to infanticide how reported some studies. [5] The symptoms might be presented as delusions, hallucinations, confusion and perplexity occur particularly, also severe mood swings, insomnia, agitation and rapid deterioration.

There might also appear a trap with misdiagnosed unipolar depression based on the result from Edinburgh Postnatal Depression Scale if the screening for bipolar disorder were not conducted. [41] Many women with a diagnosis of bipolar disorder during the perinatal period may present depression episode. [42] Therefore if the medical care would like to consider implementation of an antidepressant treatment it will be useful to screen the patient for bipolar disorder. Postpartum depression should be distinguished from hypomania, psychosis, anxiety disorders, substance abuse or when in the family history bipolar disorder has ever occurred. Anyway, perinatal depression and especially postpartum depression have been still undiagnosed and undertreated. That might be the aftermath from the deep sense of responsibility for the foetus and then for the newborn and anxiety of being judged as the insufficient mother and feeling guilty which will appear if the patient would admit her fears and symptoms.

The Edinburgh Postnatal Depression Scale mentioned above, as well as Beck Depression Inventory, and

Patient Health Questionnaire 9 are the validated screening tools while using them doesn't demand a long-term diagnosis. [43] Also mandatory medical supervisions for the pregnant women and after childbirth might be a useful opportunity to provide women, who are in need and would not enter the psychiatric clinic on their own, the access to follow up and psychiatric healthcare with less stigma.

According to the recent reports, it is recommended to regard any act of self-harm in pregnancy or early postpartum period as an indicator of a suicide risk. Any women who have past history psychosis are regarded as being at higher risk of early postpartum major mental disorder as it was indicated in morbidity audit from 2017. [44]

TREATMENT

As it was presented above depression in pregnancy and postpartum period has confounding effects but there also exist the effects of medication exposure however it is difficult to clearly separate them. [45] Some adverse effects may be imputed to antidepressant exposure because all the psychotropic medications are able to cross the placenta. Psychiatrists consider carefully every decision of prescribing medication balancing the risk of prenatal exposure to medical treatment versus the risk of exposure to maternal depression. Psychotherapy is also recommended despite medication treatment both in cases of mild and more severe depression.

Reports from 2016 showed that there is no clinically significant increase in congenital malformations among infants of women taking first- or second-generation antipsychotics in pregnancy, with the exception of risperidone. [46] The dose-related risk might occur in the first trimester of lithium use and may increase the risk of cardiac malformation (like Ebstein's anomaly) in the foetus. [47] Lithium perinatal complications which have been reported were sedation and "floppy infant syndrome" characterized by poor tone and cyanosis.

This medication is also one of the few medications which may be present in increased amounts in breast milk so breastfeeding is not recommended because of the risk of toxicity. [48] Whereas antidepressant exposure in breastfed infants is five to ten times lower than exposure through the placenta during pregnancy. The majority of adverse effects were seen in infants less than two months old and very few adverse effects in infants older than six months. [49]

The antiepileptic drugs like valproate and carbamazepine using in pregnancy might induce significant increase in major malformation - neural tube defects, spina bifida, atrial septal defects, oral cleft, hypospadias, polydactyly and craniosynostosis, also intellectual impairment. [48] Carbamazepine is less associated with those side effects and the risk is lower than that for valproate. [50] Lamotrigine, which might be also used as a mood stabilizer, has no significant connection with major malformation and intellectual impairment. According to the current recommendations valproate should not be used to treat bipolar disorder in pregnant women and used in women of childbearing potential only if they are on the contraception. [51]

Since May 2015 a new labelling system has been functioning, designed to improve the clinician's ability to assess risks and benefits of using individual medications in pregnant and breastfeeding women. It replaced the ABCDX system to provide new categories like fetal risk summary, clinical considerations, and data reports on studies. [52]

Psychotic or severe non-psychotic depression, catatonia and prolonged, severe mania, circumstances where the condition is life-threatening, non-responsiveness to other treatments or where rapid response is required are the indications for use of electroconvulsive therapy. It is a reasonably safe and effective treatment. The most likely adverse effects are premature contractions and preterm delivery but they seem rather uncommon. [53]

CONCLUSIONS

1. The pregnancy and postpartum period as a state of intense emotions, when due to physiological, biological, genetic, psychological and differentiated environmental factors, the likelihood of developing mental disorders may increase. [1-9, 11-31]
2. The skill to distinguish baby blues from more severe symptoms leading to dangerous psychiatric condition is the one which multidisciplinary doctors taking care of women in postpartum period should be in command of [10]
3. If treatment of psychiatric diseases in pregnancy or postpartum is discontinued or changed, this may exacerbate a current psychiatric disorder or even trigger a new one [27]. This presents a challenge for psychiatrists and interdisciplinary teams in prioritizing what should be withdrawn and prescribed.
4. Even though the depression during pregnancy was not diagnosed, the symptoms such as hypertension, preeclampsia and gestational diabetes [32], premature birth [33], low birth weight,

fetal growth restriction [34] and postnatal complications. [35], disobedience of obstetric care and overuse of medication, drugs, alcohol, herbal remedies and tobacco [36] should be considered as the risk of depression by psychiatrists and obstetrician.

5. Worldwide nearly 14% of women suffer from tokophobia, the prevalence of tokophobia was 10% in high income countries and 20-61% in undeveloped countries such as African ones. [54]
6. The mental health of children from mothers with psychiatric disorders in pregnancy and post-partum period may be also affected. They may suffer from emotional and bonding disfunctions, and their cognitive development might be impaired. [38,40]
7. The proper psychiatric and non-psychiatric health care for mother and fetus and later infant should be provided by a multidisciplinary medical counselling team. The attending obstetrician should also have psychiatric knowledge of psychiatric disorders of pregnant and laboring women. In cases of patients without contraindications of analgesia during delivery doctors should encourage patients to choose regional anaesthetic techniques due to benefits in the obstetric setting. [55]
8. If the psychological care is present the conversion from stable, well-controlled mental state into deteriorating one is less likely.

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