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Recommendations of the Polish Psychiatric Association for treatment of affective disorders in women of childbearing age. Part I: Treatment of depression

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Summary

Treatment of depressive disorders in women of childbearing age requires special attention due to the possibility of planned or unplanned pregnancy and the specificity of mood disorders associated with the perinatal period. A doctor who treats depression in a woman of childbearing age should openly discuss with the patient her sexuality and the possibility of becoming pregnant. A psychiatrist may encounter various problems, such as: a therapeutic decision regarding a woman suffering from recurrent depression who receives preventive or maintenance antidepressant medication and becomes pregnant or plans to conceive; proceedings in the case of a depressive episode in a woman who is already pregnant; proceedings in the case of postpartum depression; antidepressant treatment in the context of breastfeeding. The recommendations were prepared by the working group of the Polish Psychiatric Association based on the latest worldwide standards as well as opinions and consensus of experts. The recommendations provide general principles of therapeutic approach and include data on the safety of antidepressants.

Key words: depression, pregnancy, recommendations

1. Introduction

Depressive disorders remain among the most prevalent mental disorders, and a leading cause of disability, especially when following a chronic course, and the subject of antidepressant treatment still dominates the literature on mental health in the perinatal period. Depressive disorders often affect women who are planning to start a family and have offspring. The possibility of an unplanned pregnancy, as well as the woman's desire to have children and be a mother despite her illness should all be considered in treatment of female patients of childbearing age. Given the current state of knowledge and progress of treatment, mental disorders should not be an obstacle to achieving life goals, such as having a family and children.

A doctor who treats depression in a female patient of childbearing age should be ready to openly discuss the issues of her sexuality and pregnancy options. It is of paramount importance to educate the patient about different forms of birth control. There are no reports on interaction between oral contraceptives and antidepressants, with most women reporting good tolerance of hormonal contraception and less frequent mood swings than prior to its use, but in rare cases depressive symptoms or relapse of depression may occur. Negative mood effects are usually linked to the use of triphasic contraceptives and their occurrence is an indication for gynecological consultation and switching to a different drug [1].

Depression is associated with a number of serious social and health consequences for both the mother and her child. Of particular importance is the socioeconomic status of the woman [2]. Although both scientific research and clinical care place the greatest emphasis on the postnatal period, the occurrence of depressive symptoms in pregnant women is also significant. A high-quality review and meta-analysis of studies on depression in pregnancy and the postnatal period estimated the point prevalence of major depression as 3.8% at the end of the first, 4.9% at the end of the second and 3.1% at the end of the third trimester of pregnancy [3].

In the same review, the incidence rate of postpartum depression was estimated to range between 1 and 5.7% in the first postnatal year, with the highest rates at 2 months (5.7%) and 6 months postnatally (6.5%). Gavin et al. [3] calculated the period prevalence of depressive disorders (i.e., rate over a specified time interval) as 12.7% during pregnancy, 5.7% from birth to 2 months postnatally, 6.5% after 6 months, and 21. 9% after 12 months. The authors emphasize that, based on available research findings, it is not possible to state with any certainty whether incidence rates of depression vary between different pregnancy trimesters or months postnatally [3]. However, all above studies are clear that pregnancy is not a protective factor against depressive disorders.

Low mood after childbirth (sometimes referred to as 'baby blues') is a very common phenomenon, affecting 30 to 80% of women in the first 2 weeks after childbirth, but is usually mild and transient and therefore should be differentiated from clinical postpartum depression [4]. There has been some debate over the presumed increase in the incidence of depression in the postpartum period, with previous reports suggesting its threefold increase during the first 5 weeks after childbirth [5], while recent longitudinal population studies have indicated only a generally higher incidence of depression

in the postnatal period [2, 6]. In some cases, the incidence of postpartum depression may reflect lack of proper diagnosis of depression having its onset already during pregnancy. Recent studies have shown that at least one-third of cases of 'postpartum depression' begin during pregnancy or pre-pregnancy [7, 8].

Similarly to other forms of depression, postpartum depression is often self-limiting within a few months. However, in approximately 30% of women symptoms persist even beyond the first year postnatally and there is high risk (about 40%) of subsequent relapses [9–11].

Data from *the Confidential Enquiries into Maternal Deaths* report [12] consistently point to mental health problems being among the main causes of maternal death in the United Kingdom, with more than half of these deaths occurring as a result of suicide. Four enquiries found that more than half of women who died of suicide had previously experienced some form of severe mental illness (bipolar disorder or severe depression); whereas around one third of suicide cases were consistently linked with comorbid drug misuse (suicides of pregnant women remain relatively rare, and most occur after childbirth) [12]. Most cases of suicide in pregnant and postnatal women (approximately 60%) occur within 6 weeks before and 12 weeks after childbirth [12].

In 1987, *the Edinburgh Postnatal Depression Scale* (EPDS) was designed to screen women for depressive symptoms during pregnancy or the postnatal period. It is a 10-item psychological rating scale for measuring the severity of postnatal depressive symptoms, with a maximum total score of 30 points, and a cut-off of 10 points or self-harm ideation considered indicative of high likelihood of postpartum depression. Such score requires further thorough clinical mental state evaluation [13]. In a Polish study of 434 women, postpartum depression defined as 13+ points on the EPDS, was found in 15.2% of the subjects [14].

2. Methodology

The recommendations were created at the initiative of the PPA expert group and were developed in 3 phases: (1) review of available scientific literature; (2) subsequent round table discussion leading to a consensus among the experts; and (3) development of a common expert position. The recommendations include a discussion of the diagnostic, therapeutic and rehabilitation process of major depressive disorder in women of childbearing planning pregnancy, during pregnancy and postnatally, with practical recommendations referring to the current legal status of pregnancy management in Poland. The final form of the recommendations has been agreed upon by all of the experts.

3. Classification of perinatal disorders

The ICD-10 authors recommend that psychiatric disorders be diagnosed as associated with the puerperium if they commence within 6 weeks of delivery, they do not meet the criteria for disorders classified as F 00–F 48. They recommend that mental disorders associated with postpartum period be classified with two ICD-10 codes.

(1) Chapter V

- F 53 Mental and behavioral disorders associated with the puerperium, not elsewhere classified;
- F 53.0 F Mild mental and behavioral disorders associated with the puerperium, not elsewhere classified (including postnatal depression NOS and postpartum depression NOS);
- F 53.1 Severe mental and behavioral disorders associated with the puerperium, not elsewhere classified (including puerperal psychosis NOS);
- F 53.8 Other mental and behavioral disorders associated with the puerperium, not elsewhere classified
- F 53.9 Puerperal mental disorder, unspecified

(2) Chapter XV

- O 99.3 Pregnancy, childbirth, puerperium – mental disorders and diseases of the nervous system complicating pregnancy, childbirth and the puerperium.

The latest classification of the American Psychiatric Association – *the Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) from 2013 in the chapter on depressive disorders defines diagnostic criteria for major depressive disorder (code 296). It allows the use of 'depressive disorder specifiers', including 'with peripartum-onset' specifier. The DSM-5 diagnostic criteria clarified that: this specifier can be used to describe the current or, if currently necessary criteria for a mood disorder episode are not met, the last episode of major depressive disorder, if the onset of symptoms falls on pregnancy or within 4 weeks after delivery

Due to the high prevalence and serious consequences of perinatal mood disorders for women, their children and their entire families, from 1 January 2019, new standards of perinatal care in Poland include obligatory, three-time mental state assessment screening for symptoms of depression [15].

4. Review of guidelines on pharmacological treatment of perinatal depression

The review [16] included only Clinical Practice Guidelines (CPGs), i.e., recommendations intended to optimize patient care, based on systematic reviews of evidence and assessment of both benefits and harms of alternative forms of care. Selected guidelines had to comply with the quality criteria of the Appraisal of Guidelines for Research and Evaluation (AGREE, www.agreetrust.org). To avoid documents not meeting these quality criteria, consensus statements and guidance papers were excluded from the review. There were no restrictions on the date or language of publication. Guidelines that did not relate to the perinatal management of mood disorders and/or on the perinatal use of antidepressants were excluded. Only the latest or most complete version of a guideline was selected when several versions of the same guideline were available. Presented below are the most essential parts of 16 guidelines from 12 countries [17–33].

4.1. Guidelines on treatment of pre-pregnancy depression

Three guidelines advise against switching antidepressant medication. The Dutch Society of Obstetrics and Gynecology (NVOG, the Netherlands) recommends to continue antidepressant treatment if the patient's mental state is stable.

Detailed recommendations for the initial treatment of the first depressive symptoms formulated by the American Psychiatric Association (APA, USA), the Center of Perinatal Excellence (COPE, Australia) and the National Institute for Health and Care Excellence (NICE, UK) advise the use of psychotherapy as first-choice treatment. In more severe cases of depression, the COPE and NICE guidelines recommend the use of antidepressants as the initial form of therapy.

4.2. Guidelines on treatment of depression during pregnancy

During pregnancy, four guidelines recommend continuation of pharmacological antidepressant treatment. Five other guidelines mention the possibility of treatment continuation, but neither recommend nor advise against it. Three guidelines advise against modification of pharmacotherapy during pregnancy. In turn, the Danish guidelines recommend a change of medication when antidepressants with an unfavorable profile of action (paroxetine and fluoxetine) are used.

The majority of guidelines consistently indicate psychotherapy as the preferred initial treatment for mild to moderate depression, and antidepressants as the initial form of therapy for severe depression. Only the guidelines of the American College of Obstetricians and Gynecologists (ACOG, USA), recommend the use of antidepressants as the preferred initial form of therapy (instead of psychotherapy), regardless of the symptom severity.

There is a general agreement that potential harms and benefits of antidepressant use during pregnancy should be discussed by the doctor with the patient, so that patients can make informed decisions about the preferred form of treatment.

4.3. Guidelines on treatment of depression in the perinatal period

Most guidelines recommend delivery in a hospital setting, which constitutes a healthcare standard in most countries. Still, since in some countries, like the Netherlands and Canada, home births are still quite common, the guidelines clearly emphasize the superiority of hospital delivery with additional observation as a recommended option.

Postpartum monitoring of the neonate is recommended, with varied recommended length of observation time (from 12 hours to 3 days). The BC (Canada) guidelines recommend more intense observation of the newborn, including pulse oximetry for the early detection of persistent pulmonary hypertension and monitoring of the serum level of antidepressants.

4.4. Guidelines on treatment of postpartum depression

The BC (Canada) and NVOG (Netherlands) guidelines specifically recommend continuation of antidepressant medication to prevent relapse of depressive symptoms. In the case of new episodes, the majority of guidelines consistently recommend psychotherapy as initial treatment of mild to moderate forms of depression and consideration of pharmacological treatment as initial therapy for severe depression. Most guidelines encourage breastfeeding regardless of the type of antidepressants used. The Nordic Federation of Obstetrics and Gynecology (NFOG, Norway) recommends switching antidepressants when unfavorable medication is used during breastfeeding. Sertraline is considered safe for use in breastfeeding women, mainly due to its low concentration in breast milk and infant serum.

4.5. Guidelines on medication preference in treatment of depression in the perinatal period

Recommendations concerning medication preferences are often not specific to pregnancy stage. In general, available guidelines agree that paroxetine should be avoided in pregnant women, as its use is associated with an increased risk of congenital cardiovascular malformations in newborns [34]. In addition, the ACOG (US) guidelines recommend fetal echocardiography if the mother was taking paroxetine during early pregnancy.

Due to its long half-life and its presence in breast milk, fluoxetine was deemed 'unfavorable' in five guidelines. Remarkably, the NHS (Spanish Ministry of Health, Welfare and Equality) mentions fluoxetine as the preferred medication.

There is a general consensus on sertraline as the preferred drug during postpartum and lactation [35]. The Canadian (CANMAT) and Danish guidelines also mention the benefits of using citalopram as the preferred drug due to the minimal risk of its use during lactation and available data on the effectiveness of treatment in the postpartum period [29].

The risk of congenital abnormalities depends on the period of exposure to teratogenic agents:

- in the period of blastogenesis (weeks 1–2) – exposure may lead to the embryo's death;
- during embryogenesis (weeks 3–11) – developmental defects and other teratogenic effects may develop;
- during fetal development (weeks 12–40) – exposure may lead to impaired growth and behavioral disorders;
- in the perinatal and lactation period – exposure may lead to toxic reactions, withdrawal syndromes.

Therefore, the FDA – the American Food and Drug Administration – has divided drugs according to the risk categories of congenital anomalies:

FDA classification of drugs used during pregnancy	
Category	**Definition**
A	Control studies did not show any risk to the fetus in the first trimester and the possibility of fetal damage seems unlikely.
B	Animal studies do not indicate a risk to the fetus, but no human studies have been performed, or animal studies have shown an adverse effect on the fetus, however, studies in the group of pregnant women did not confirm the existence of a risk to the fetus.
C	Animal studies have shown an adverse or fatal effects on the fetus, but no control studies on women have been performed, or no appropriate studies have been performed on animals or humans.
D	There is evidence of adverse effects on the fetus, but in certain clinical situations the potential benefits of its use outweigh the risks (e.g., in life-threatening conditions or diseases in which other safe drugs cannot be used or are ineffective).
X	Studies carried out on animals or humans have indicated fetal abnormalities as a result of the use of the drug or there is evidence of adverse effects on the human fetus and the risk far outweighs the potential benefits of its use.

Lactation risk categories:

L1 – safest;

L2 – safer;

L3 – moderately safe;

L4 – possibly hazardous;

L5 – contraindicated.

Table 1. **Safety of antidepressants during pregnancy and lactation [36–43]**

Category	Antidepressant	Lactation risk category
A	-	-
B and C	Amitriptyline	L2
	Agomelatine	No data
	Citalopram	L3
	Bupropion	L3
	Desipramine	L2
	Doxepin	L5
	Duloxetine	no data
	Escitalopram	L3 in older infants
	Fluoxetine	L2 in older infants; L3 in newborns
	Fluvoxamine	No data
	Clomipramine	L2
	Mianserin	L2
	Maprotiline	L3

table continued on the next page

B and C	Mirtazapine	L3
	Moclobemide	No data
	Nefazodone	L4
	Nortriptyline	L2
	Opipramol	No data
	Reboxetine	L2
	Sertraline	L2
	Tianeptine	No data
	Trazodone	L2
	Venlafaxine	L3
	Vortioxetine	No data
D	Paroxetine	L2
X	-	-

5. Antidepressants and pregnancy

When dealing with a patient planning pregnancy, she should be recommended a comprehensive physical examination, as well as a series of additional tests – complete blood counts, kidney function tests (urea, creatinine, electrolyte levels), as well as – thyroid, liver, glucose, vitamin B12, folic acid, iron, vitamin D level tests. All these tests should be performed prior to planned pregnancy, or at its early stage, as it may be important in further stages of treatment.

5.1. Embryonic period: organogenesis

Animal studies have not demonstrated the teratogenic effect of tricyclic antidepressants. In turn, data from research on humans remain widely inconclusive and uncertain [44].

In the case of selective serotonin reuptake inhibitor antidepressants (SSRIs) and serotonin and noradrenaline reuptake inhibitor antidepressants, a meta-analysis by Einarson and Einarson [45], including research since 1996, found no correlation between the use of citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, reboxetine, venlafaxine, nefazodone, trazodone, mirtazapine, and bupropion and an increased risk of congenital malformations in exposed children. However, the results of other studies [34, 46 47] indicate an increased risk of congenital cardiac malformations (especially ventricular septal defects) in children of women treated mainly with paroxetine, fluoxetine, sertraline, and citalopram, especially when more than one SSRI was used in therapy. Still, the estimated risk may be attenuated with increasing adjustment for confounding [48].

Some studies [49, 50] report an increased risk of pulmonary hypertension in infants whose mothers used SSRIs after the 20th week of pregnancy (compared to the

control group). Due to potential fatality of this complication, a careful harm/benefit assessment is necessary when SSRI antidepressants are considered in treatment of pregnant women [44].

5.2. Fetus and neonate

Children exposed to tricyclic antidepressants or SSRIs during pregnancy are at increased risk of poor neonatal adaptation syndrome (PNA) (including neurological, autonomic, respiratory or gastrointestinal disorders) [51, 52]. To date, the long-term effects of antidepressant use remain unknown [53].

According to a review by Moses-Kolko et al. [54], comparing babies of mothers treated with SSRI antidepressants in early pregnancy, mothers not treated and mothers treated in late pregnancy, the relative risk of PNA tripled in the case of late exposure, especially in response to the use of fluoxetine and paroxetine.

So far, the causes underlying poor neonatal adaptation syndrome are not fully understood – it may be related to withdrawal syndrome or associated with dysregulation of serotonin or atropine levels. Some researchers describe the potential risk of developmental disorders [55] and autism spectrum disorders [56] in children exposed to antidepressants during pregnancy, while others fail to report associations of antidepressant pharmacotherapy with the occurrence of developmental disorders [57].

5.3. Breastfeeding

The NICE recommendations (2018) indicate that when assessing the risks and benefits of treatment for women who are breastfeeding, the limited data about the safety of these drugs and the risks associated with switching from a previously effective medication should be taken into account. As with all drugs, a close pediatric monitoring is recommended.

General rules for antidepressant treatment and breastfeeding

1. The amount of the drug depends on the dose given to the mother, its half-life, the time between medication intake and feeding, and the length of lactation.
2. Neonate-related factors: poorer renal filtration, immature metabolic mechanisms, liver immaturity, leaky blood-brain barrier, low albumin concentration.
3. Drug use is safer in mothers whose babies are over 10 weeks old.
4. Medication should be administered at lowest (but effective) doses.

Other practical rules

1. all psychotropic drugs are excreted in breast milk, but in small concentrations.
2. Breastfeeding should be avoided when the child suffers from renal or liver failure, circulatory or neurological disorders.
3. Do not breastfeed when drug concentration is the highest.

4. Medication should be administered in one daily dose, before the child's longest sleep, and breastfeeding is recommended just before the drug administration.
5. Child's condition should be monitored: in terms of behavior (crying, drowsiness, irritability), and biochemical parameters (creatinine, hepatic tests)
6. If the mother was treated during pregnancy – the same treatment pattern should be used after delivery (to avoid withdrawal symptoms and exposure of the child to various medications).

6. General principles of psychotropic drug treatment during pregnancy

The rate of antidepressant use during pregnancy ranges from 2 to 7% depending on the country [58–60]. Such relatively high rate is probably related to the widespread use of antidepressants in the general population. The necessity of antidepressant treatment should always be reassessed during the perinatal period, in order to estimate the risk to the infant of exposure to antidepressant agents on the one hand, and the symptoms of mood disorders in the mother on the other. Close monitoring of the fetus during pregnancy and the baby during early neonatal period is recommended.

To conclude:

- It should be ensured that the mother's condition poses such a threat to her and the baby that treatment benefits outweigh the risk of potential fetal damage.
- When indicated and necessary, it is recommended to use:
  - a well-known drug;
  - in monotherapy;
  - at the lowest effective dose, divided over the day to avoid high blood levels.
- The use of medication during the first trimester of pregnancy should be avoided.
- The use of medication in the last 2–3 weeks before delivery should be avoided to prevent the occurrence of toxic and/or withdrawal symptoms in the newborn.

The effects of pregnancy on the pharmacokinetics of drugs should be taken into account due to the following changes:

- increased plasma volume – impaired distribution, and shortening of the half-life of drugs;
- increased cardiac stroke volume, blood flow through the kidneys and renal elimination;
- increased liver metabolism;
- decreased concentration of blood proteins in the third trimester of pregnancy – alpha-1 glycoproteins, weaker protein binding, increased free drug fraction [39].

7. Criteria for selection of drugs and treatment in women with no previous history of antidepressant treatment

- In women of childbearing age, administration of psychotropic drugs should be preceded by a pregnancy test.
- Before starting antidepressant treatment in pregnant women, the effects of the disease and medication on the mother and fetus should be considered.
- The highest fetal sensitivity to toxic factors is between 17th and 60th day of pregnancy.
- When treatment is necessary – it is recommended to use the lowest effective dose, divided over the day and monitor side effects.
- Polytherapy should be avoided.
- Changes in the pharmacokinetics of medication during pregnancy should be considered.
- It is advisable to discontinue medication before delivery (to avoid toxic and/or withdrawal syndromes in the newborn).
- It is recommended to assess whether an attempt to stop medication will not cause relapse and the need for higher doses.
- In such situations, a drug with the lowest teratogenic potential should be selected and the pharmacotherapy should be continued in the lowest effective doses divided over a 24-hour period.
- In order to optimize patient care, cooperation between a gynecologist and psychiatrist is recommended.

8. General NICE 2018 recommendations for the use of tricyclic antidepressants (TCA), SSRIs and SNRIs

When choosing between a tricyclic antidepressant (TCA), selective serotonin reuptake inhibitor (SSRI) or serotonin and noradrenaline reuptake inhibitor (SNRIs), the following should be taken into account:

- the woman's previous response to treatment;
- the stage of pregnancy;
- data on the reproductive safety of the drugs (e.g., the risk of fetal cardiac abnormalities or persistent pulmonary hypertension in newborns);
- increased risk for the fetus and the possibility of other health problems for the woman or baby that are directly attributable to the drugs or may be caused by other factors;
- the risk of withdrawal symptoms in the woman and neonatal adaptation syndrome in the baby associated with the use of the majority of TCA, SSRI and SNRI drugs, in particular paroxetine and venlafaxine.

8.1. Benzodiazepines

- According to the NICE criteria, no benzodiazepine drugs should be used in pregnant and puerperium women, except for the short-term treatment of severe anxiety and agitation.
- If the use of benzodiazepines is indicated and justified, having considered the involved risk, the drugs of choice are those with a short half-life and low transfer into breast milk, mainly lorazepam and oxazepam.
- It is advisable to consider gradual discontinuation of benzodiazepines in women planning pregnancy, pregnant women, or those considering breastfeeding.

8.2. Initiation, use and discontinuation of treatment according to the NICE 2018 guidelines

According to the NICE criteria [61], before starting any treatment during pregnancy and puerperium, it is necessary to discuss with the woman the higher threshold for pharmacological treatment, associated with a change in the risk/benefit ratio for pharmacotherapy at that time, and highlight the benefits of a psychological intervention.

If the optimal form of treatment for a woman suffering from a mental disorder is psychotropic medication combined with psychological interventions, but she refuses or stops taking the prescribed drugs during pregnancy or after childbirth, it is necessary to make sure that she:

- receives adequate support;
- has the opportunity to discuss the risk associated with discontinuation of pharmacological treatment;
- is offered or can continue with psychological interventions.

When treatment with psychotropic medication is started, it is recommended to:

a) choose the drug with the lowest risk profile for the patient and the fetus/baby, taking into account her earlier response to treatment;
b) use the lowest effective dose (this is especially important when the risk of side effects to the woman and the fetus/baby may be dose-dependent); it is of note, however, that the use of subtherapeutic doses is not an effective form of treatment of serious mental health conditions and may pose a risk to the fetus;
c) if possible, use a single drug (instead of 2 or more drugs);
d) take into account that the doses may require adjustments at various stages of pregnancy.

When a woman with a serious mental disorder decides to discontinue psychotropic treatment during pregnancy and the postnatal period, the following issues should be discussed:

- the reasons for her decision;
- the possibility of:

- restarting treatment;
- switching to other medication
- a psychological intervention

– increasing monitoring of her mental state and support.

She should be aware of the risks to her own health and the health of the fetus/baby due to discontinuation of pharmacotherapy.

Discontinuation of medication may result in:

– conversion of the risk to the infant due to antidepressant drug exposure to the risk of exposure to maternal symptoms;
– disrupted cooperation with obstetric care;
– risk of exacerbation;
– improper nutrition;
– smoking, drinking alcohol, other drug and stimulant use;
– disrupted mother-child attachment;
– disrupted family life.

The decision to discontinue medication depends on:

– illness severity (risk of relapse);
– data on drug safety;
– patient's ability to bear the symptoms.

9.1. Treatment of mental disorders during pregnancy and puerperium according to the NICE

Authors of this paper agreed that interventions for treatment of depression according to the NICE 2018 [61] are sufficient in Poland:

– In women with mild to moderate episodes of depression during pregnancy or the postnatal period, cognitive behavioral psychotherapy or facilitated self-help programs should be considered.
– In women with a history of severe depression who are experiencing symptoms of mild depression during pregnancy or postnatally, pharmacotherapy with TCAs, SSRIs or SNRIs should be considered.
– If a woman who is taking a TCA, SSRI or SNRI for mild to moderate depression becomes pregnant, it is advisable to discuss with her gradual discontinuation of the medication and consider facilitated self-help (or cognitive behavioral psychotherapy).
– If a pregnant woman is taking a TCA, SSRI or SNRI due to severe depression, factors such as: previous response to treatment, stage of pregnancy, risk of relapse, drug-related risk, and her preferences should all be considered and she should be offered the following treatment options:

- continuation of the current medication;
- switching to other medication that is effective and offers fewer adverse effects;
- use of high-intensity psychological interventions (e.g., CBT), in combination with pharmacological treatment;
- use of high-intensity psychological interventions (e.g., CBT), if the patient decides to discontinue pharmacological treatment.

It is worth to consider electroconvulsive therapy (ECT) in patients who experience suicidal ideation or in the case of drug-resistant patients [40, 62].

Not using pharmacotherapy in patients with severe depression may have serious consequences: there are reports indicating a significant risk of abnormal or delayed physical and mental development [63, 64]. First of all, there may be obstetric complications such as low birth weight and premature labor, which is partly related to the chronic stress experienced by the mother. Secondly, the symptoms of depression and anxiety in the mother may lead to problems in the newborn – such as anxiety, irritability, attention deficit disorder, or impaired emotional expression. Thirdly, maternal psychological problems can lead to disturbances in the attachment between the mother and the child, which can lead to future behavioral problems or learning disabilities in the child [65].

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