Depression during pregnancy and lactation

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Recommendations

• Depression should be treated, because untreated disease could itself have major negative consequences for the mother and child **(strong recommendation)**
• Non-pharmacological therapy are first-line treatment for mild to moderate symptoms **(recommendation)**
• Women with severe depressive symptoms, who are using antidepressants when they become pregnant, can continue to do so after careful risk-benefit assessment **(recommendation)**
• Pregnant women with severe depressive symptoms in pregnancy, with good response to pharmacological treatment pre-pregnancy, can be offered pharmacological treatment after careful risk-benefit assessment **(recommendation)**
• If the woman is well-stabilized on one antidepressant, switching from this antidepressant to another is often discouraged due to risk of relapse and little evidence of clinically significant differences in safety profiles between the SSRIs **(proposal)**
• Selection of antidepressants should be made according to the drug's safety profile in pregnancy, and when possible according to previous good response:
o SSRIs (citalopram (Cipralex®, Cipramil®), escitalopram (Cipralex®), sertraline (Zoloft®), fluoxetine (Fontex®)) is preferred over the older TCA (amitriptyline (Sarotex®), clomipramine (Anafranil), trimipramine (Surmontil®)) because of toxicity (recommendation)
o Paroxetine (Seroxat®) is not first choice in the first trimester due to a possible small increased risk of heart defect in the child (recommendation)
o Less data are available for the newer antidepressants (agomelatine (Valdoxan®), mirtazapine (Remeron®), reboxetine (Edronax®), duloxetine (Cymbalta®), venlafaxine (Effexor®)) **(recommendation)**
• When using antidepressants or lamotrigine (Lamictal®), serum concentrations should be monitored due to pharmacokinetic changes during pregnancy **(proposal)**
• Newborns who have been exposed to antidepressants in utero near birth should be observed for perinatal complications, especially respiratory problems **(proposal)**
• Women who use antidepressants can breastfeed **(recommendation)**
o Fluoxetine (Fontex®) is not first choice during lactation due to high transition into breast milk and a long half-life **(proposal)**

Literature search
McMaster PLUS (Premium LiteratUre Service), Up to date, PubMed, National Institute for Health and Clinical Excellence (NICE), Cochrane Database, Royal College of Obstetricians & Gynecologists, Danish and Swedish guidelines.

Definition

A depression that occurs in pregnancy or after birth.
Traditionally, three conceptual categories have been used in the period following childbirth: maternity blues, postpartum depression and postpartum psychosis (1).

Prevalence
According to international data, 10-15% of all pregnant and lactating women experience depression (1, 2). Approximately 1/3 of all postpartum depressions begin during pregnancy. Postpartum psychosis occurs in 0.1- 0.2%. In Norway, approximately 2% of all pregnant women use antidepressants during pregnancy (3). This corresponds to approximately 1200 pregnancies annually in Norway. In North America, antidepressant use during pregnancy is estimated between 8 and 13% (4). One study showed that of the 26 deaths of mothers in Norway in 2005-2009, four were suicides - making maternal mental illness the most common indirect cause of death (5).

Etiology / symptoms
A depression that occurs in pregnancy or during maternity has the same symptoms as depression that occurs in other periods of life, but the clinical picture may be colored by the circumstances (1,2).

Risk factors

Negative life events, poor partner relationship, previous depressive episodes, substance abuse problems (2).

Consequences
Depression during pregnancy and postpartum should be treated, because untreated or inadequately treated mental illness itself is associated with increased risk of complications in both the mother and child (4,6). These complications include risk of poor prenatal care follow-up, poor nutrition status, use of alcohol and / or other harmful substances, and self-destructive behavior. There is also an increased risk of pre-eclampsia and miscarriage. For the child, lack of treatment of maternal depression raises the risk of prematurity and low birth weight. Severe depression postpartum is also shown to have a negative impact on the mother-child relationship and the child's cognitive and socio-emotional development. Depressed pregnant women who discontinue antidepressants have an increased risk of relapse compared with pregnant women who continue with pharmacotherapy (4,6).

Diagnostics
An instrument that focuses on the psychological symptoms of depression should be chosen, as many of the somatic symptoms are normal conditions in pregnancy. Relevant diagnostic instruments are EPDS (Edinburgh Postnatal Depression Scale) (validated for Norwegian conditions) (7) and MADRS (Montgomery and Åsberg Depression Rating Scale).

Treatment
Depression during pregnancy and in the postnatal period is treated like any other depression, but non-pharmacological methods such as sessions with therapists and psychosocial interventions are more important than elsewhere. Non-pharmacological therapy (psychotherapy, family therapy, cognitive-behavioral therapy, etc.) are first-line treatment for

mild to moderate symptoms (6).

The American College of Obstetricians and Gynecologists and the American Psychiatric Association recommends that women with severe depressive symptoms who are planning on becoming pregnant or are already pregnant, can begin or continue to use antidepressants (6). Pharmacological treatment should always be combined with non-pharmacological treatments (4,6).

Antidepressants

SSRIs (selective serotonin reuptake inhibitors)

Studies provides some conflicting results regarding risk for the fetus (3,4,8), however, if there is any risk, this risk is probably small. Conflicting results can possibly be explained by the difficulty in distinguishing between the effects of the underlying mental illness and the pharmacological effects.

The following findings are highlighted:

• Data from the Norwegian Mother and Child Cohort Study showed no increased risk of structural malformations (3). Data from the Nordic Prescription Databases linked to Medical Birth Registries showed no increased risk of malformations (including cardiac defects), stillbirths or neonatal mortality (12, 13).

• Use of paroxetine (Seroxat®) is advised against during the first trimester due to a possible increased risk of cardiovascular malformations (4).

• Use of SSRIs in late pregnancy is associated with a slightly increased risk of persistent pulmonary hypertension in the newborn (absolute risk: 1-2 of 1000 exposed) (4).

• Use of SSRI close to birth increases the risk for perinatal complications (irritability, hypertonicity, lactation problems) (absolute risk: 20-30% of the exposed) (4).

• Few studies have examined the risk of complications during pregnancy (bleeding, preeclampsia) or long-term effects on the central nervous system in children exposed to SSRIs in utero (4).

SNRIs (serotonin noradrenaline reuptake inhibitors)

There is less evidence on the safety of SNRIs (i.e. venlafaxine (Effexor depot®), duloxetine (Cymbalta®)) in pregnancy than other antidepressants. Therefore, other antidepressants are usually recommended to pregnant women (4,6).

TCA (tricyclic antidepressants)

The majority of studies have not shown increased risk of structural abnormalities or psychomotor and cognitive developmental disorders. Treatment with TCA in the third trimester increases the risk of transient neonatal symptoms (respiratory disorders, convulsions, irritability and tremors) (4,6).

Lamotrigine (Lamictal®)

No increased risk of teratogenicity has been shown for lamotrigine in doses up to 400 mg daily (8). Large individual pharmacokinetic differences during pregnancy indicate a need for

regular monitoring of serum concentration of this drug during pregnancy.

Follow-up

Women who use antidepressants need close supervision during pregnancy and after delivery. Some women may need to stay longer at the hospital after birth, both for the assessment of maternal mental state and for observation of the child with respect to possible adverse reactions.

Breastfeeding and antidepressants

Women who use antidepressants can breastfeed (10,11). Sertraline (Zoloft®) has the lowest transfer to breast milk. Fluoxetine (Fontex®) is not first choice when breastfeeding due to relatively high transfer to breast milk, long half-life (including active metabolite norfluoxetin) and some reports of adverse reactions in children. In cases where side effects (irritability, sedation) have been reported, the child has usually also been exposed to the drug before birth and has been younger than two months (immature kidney and liver function). Caution is recommended with use of lamotrigine during lactation (11).

Patient information

Some pregnant women need to begin or continue treatment with antidepressants during pregnancy because the psychiatric disease itself carries greater risk for mother and child than pharmacologic therapy. Women who use antidepressants can breastfeed.

Keywords

• Antidepressants
• Depression during pregnancy
• Postpartum depression

ICD-10

O99.3 Mental disorders and diseases of the nervous system complicating pregnancy, childbirth and maternity
F53 Mental and behavioral disorders associated with maternity, not elsewhere classified

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