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Review

Depression and anxiety during pregnancy and the postpartum period in women with epilepsy: A review of frequency, risks and recommendations for treatment

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ABSTRACT

Purpose: To review available data and provide treatment recommendations concerning peripartum depression, anxiety and fear of birth in women with epilepsy (WWE).
Method: The PubMed, the LactMed, the DART and the Cochrane database were searched for original articles concerning psychiatric disease in the peripartum period in WWE.
Results: Point prevalence of depression from 2nd trimester to 6 months postpartum ranged from 16 to 35% in women with epilepsy compared to 9–12% in controls. The highest estimates were found early in pregnancy and in the perinatal period. Anxiety symptoms 6 months postpartum were reported by 10 and 5%, respectively. Fear of birth symptoms were increased in primiparous WWE compared to controls. Previous psychiatric disease, sexual/physical abuse, antiepileptic drug (AED) polytherapy, and high seizure frequency emerged as strong risk factors. Depressed WWE rarely used antidepressive medication during pregnancy. No evidence was available concerning treatment effects or impact on the developing child.
Conclusion: Peripartum depression is frequent in WWE and seldom medically treated. Health personnel should screen WWE for psychiatric disease and risk factors during pre-pregnancy planning, pregnancy and postpartum follow up. Treatment decisions should rely on efficacy and safety data in peripartum patients without epilepsy and non-pregnant people with epilepsy. Consequences of in utero exposure to AED therapy in combination with antidepressants are not known, and non-pharmacological treatment should be tried first.

1. Introduction

Peripartum depression and anxiety are the most common complications of childbearing, and associated with substantial adverse effects on pregnancy outcome and the developing child [1,2]. The disorders encompass major and minor depressive episodes and anxiety disorders that occur during pregnancy or within the first 12 months after delivery [3]. The diagnostic criteria are otherwise similar to anxiety disorders and depressive episodes outside the peripartum period [2,4].

Frequency estimates of maternal psychiatric disease vary with the diagnostic criteria and tools used, the time period under consideration and the study population [5]. A systematic review of 28 studies from developed countries assessing peripartum depression by clinical assessment or structured interview found a point prevalence of 6.5–12.5% at different time points during pregnancy and the first postpartum year [3]. A similar diagnostic approach revealed anxiety disorders in 4% of women at a 6 weeks routine postnatal visit [6].

Consequences of depression and anxiety are often more severe in the peripartum period than during other life periods. Suicide in the frame of psychiatric disease is the leading cause of maternal death in the United Kingdom [7]. The majority of suicides were

Abbreviations: AED, antiepileptic drugs; CBT, cognitive behavioral therapy; CYP, cytochrome P450; MBRN, Medical Birth Registry of Norway; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin noradrenaline reuptake inhibitor; WWE, women with epilepsy.

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done by white, married, employed women living in comfortable circumstances [8]. Mother–infant interactions in the presence of depression may be characterized by less face-to-face play behavior, positive touching and appropriate vocal behavior, and more maternal hostility, unresponsiveness and self-focus [5,9,10]. Thoughts of harming the infant is frequent in depressed mothers [11], and the risk of physical child abuse is increased [12]. There is an association between maternal pregnancy-related depression and child behavioral problems [9,13,14], impaired language [15,16], cognitive development [14] and physical health problems [13,17].

People with epilepsy are especially vulnerable to depression and anxiety [18]. The frequency of mood disorders ranges from 10 to 50%, and anxiety disorders from 11 to 46% in adult epilepsy cohorts, depending on the prevalence estimate and whether study populations have been gathered from epilepsy centers or the general population [18,19]. These disorders are among the strongest predictors of quality of life in people with epilepsy and related to poor seizure control, AED side effects, cognitive complaints, suicidal ideation and high economical costs for the society [20–22].

Psychiatric implications of epilepsy in pregnancy have received little attention. The challenges related to preventing epileptic seizures and teratogenic effects of antiepileptic medication probably overshadow concerns about psychiatric symptoms. However, psychological health is of vital importance for the mother in order to maintain care for herself and her children. Health personnel should therefore be aware of the frequency, warning signs, consequences and treatment options of psychiatric disorders during pregnancy in patients with epilepsy.

2. Methods

We searched the Cohrane library, the TOXNET (DART), the LactMed, and the PubMed databases using combinations of the keywords: ‘‘epilepsy’’, ‘‘postpartum’’, ‘‘depression’’, ‘‘fear of birth’’, ‘‘anxiety’’, ‘‘pregnancy’’, ‘‘SSRI’’, ‘‘SNRI’’ and ‘‘peripartum’’. Based on title or abstract, we selected all English language original articles concerning psychiatric disease in patients with epilepsy during pregnancy or in the postpartum period. A selection of papers concerning peripartum psychiatric disease in general as well as psychiatric disease in epilepsy was also included.

3. Results: peripartum psychiatric disorders in epilepsy

3.1. Background factors

Pregnant women with epilepsy (WWE) are sociodemographically and psychosocially different from other pregnant women. This should be accounted for when interpreting data and making treatment decisions. In two Norwegian population-based studies of social aspects in pregnant WWE, women taking AEDs had a high frequency of low education, low income, and unemployment due to disability. Four percent were single mothers [23]. More than 20% reported previous sexual and/or physical abuse, and 1 in 4 stated that the pregnancy was unplanned [24].

3.2. Frequency

Five studies have investigated peripartum depression in WWE (Table 1). General anxiety was included in one study and fear of birth was investigated in another study. There were no studies examining treatment effects or consequences for child outcome.

Turner et al. found the point prevalence of depression 5–8 weeks postpartum to be more than 3 times higher than in healthy control women in two studies [25,26]. After an initial evaluation with the Edinburgh Postpartum Depression Score (EPDS), the final diagnosis of postpartum depression was done after an unblinded clinical psychiatric interview that raised the percentage of affected women with 6% in the epilepsy group, but did not change the prevalence in the control group. Possibly, EDPS is less sensitive for depression in WWE than in other women. Alternatively awareness of the epilepsy group affected the prevalence ratings. Strengths of these studies included a validated epilepsy diagnosis, prospective follow up, and detailed clinical information.

In a prospective uncontrolled patient cohort from a tertiary epilepsy center, Galanti et al. found depression in 25% of epilepsy patients 12 weeks postpartum [27]. In a population-based Norwegian cohort including more than 100,000 pregnancies, 0.7% from WWE, Reiter et al. found that self-reported symptoms of depression and/or anxiety were almost doubled in the epilepsy cohort that used AEDs (Table 1) [23]. However, the frequencies of a diagnosis of depression and anxiety were similar among women with and without epilepsy, possibly pointing to underacknowlegement of psychiatric symptoms in WWE. In a study by Bjørk et al., the same cohort was followed throughout pregnancy until 3 years after delivery using a diagnostic screening tool for depression and anxiety [24]. Peripartum period-prevalence of depression was higher in women with AED treated epilepsy than in women without epilepsy (32 vs. 19%) and in women with other chronic disease (23%). Point prevalence was higher at all time points. Significantly fewer of depressed WWE used antidepressive medication during the pregnancy compared to women without epilepsy and to women with other chronic diseases (4.6 vs. 13.2 and 15.5% respectively). An attempt to reduce total drug load in pregnancy might explain why AED treated WWE seldom used antidepressants. However, those who did not use AED during pregnancy had an even lower frequency of antidepressants (2.6%). Hence, less use of medication against depression could not be explained by concomitant AED medication [24]. Bjork et al. also found that the point prevalence of general anxiety symptoms 6 months after delivery was 10% in WWE, 5% in women without epilepsy, and 7% in women with other chronic disease [24]. Strengths of these two studies include a less selected epilepsy cohort and a long follow-up period. Methodological weaknesses are self-reported diagnosis of epilepsy and lack of a clinical psychiatric evaluation.

3.3. Fear of childbirth

Severe fear of childbirth is experienced by 5–6% of women in general during pregnancy and includes fear of pain, incapacity to give birth, losing control, parenting capacity, concerns about the health of the baby, as well as delivery complications [29–32]. The condition is related to previous psychiatric disease, sexual abuse, requests for caesarian section, previous complicated deliveries, and low partner support [30,31,33]. Psychotherapeutic interventions have proved effective and represent first line therapy [30,33].

No difference in fear of birth frequency diagnosed with the Wilma Delivery Expectancy Questionnaire was found in 50 previous psychiatric healthy WWE and 50 matched controls (54 vs 52% respectively) [28]. However, nulliparous WWE reported a significantly higher mean score than controls. Strengths of the study included a validated diagnosis of epilepsy and available clinical epilepsy information. However, as only psychiatric and somatic healthy women were included, the generalizability to epilepsy populations is uncertain.

3.4. Risk factors

Galanti et al. reported that AED polytherapy, multiparity and tonic clonic seizures during the postpartum period were related to

Table 1
Point prevalence of postpartum depression (PPD) during and after pregnancy in women with AED treated epilepsy.

Author	Population	Epilepsy type	Number	Diagnostic tool	Time of assessment	Results
Turner et al. [25]	Epilepsy clinic	Generalized 51% Focal 49% (77% symptomatic)	Epilepsy: 35 Controls: 35 Psychiatric healthy, educated women	EDPS >9 Clinical interview	5–8 weeks postpartum	PPD epilepsy: 35% Controls: 11% EDPS: Epilepsy 29% Controls 11%
Turner et al. [28]	Epilepsy clinic	Generalized 45% Focal 55% (33% symptomatic)	Epilepsy: 35 Controls: 35 Psychiatric healthy, educated women.	EDPS >9 Clinical interview	5–8 weeks postpartum	PPD epilepsy: 39% Controls: 12%
Galanti et al. [27]	Tertiary epilepsy center	30% generalized (18% juvenile myoclonic epilepsy) 63% focal	56 Epilepsy	BDI ≥ 12	Within 12 weeks postpartum	PPD 25%
Reiter et al. [23]	Population based cohort	52.5% focal, 25% primary generalized (15% juvenile myoclonic epilepsy)*	Epilepsy 329 pregnancies Reference: 106,224 pregnancies	SCL-5 mean > 1.75	Gestational week 13–17	2nd trimester depression/anxiety Epilepsy 19% Reference cohort: 11%
Bjørk et al. [24]	Population based cohort	52.5% focal, 25% primary generalized (15% juvenile myoclonic epilepsy)*	Epilepsy 319 pregnancies Reference: 98,282 pregnancies	SCL-8 mean > 1.75	Gestational week 30 6 months postpartum	3rd trimester depression Epilepsy: 17% Reference: 9% PPD: Epilepsy: 16% Reference: 10%

EDPS: Depression diagnosed by the Edinburgh postnatal depression scale.
BDI: Depression diagnosed by the Beck depression inventory.
SCL-5: Hopkins symptom checklist 5 item (3 questions concerning depression, 2 concerning anxiety.
SCL-8: Hopkins symptom checklist 8 item (4 questions concerning depression).
* Based on hospital records from a subcohort ($n = 40$).

depression [27]. Lamotrigine was not associated with reduced risk compared to other AEDs. On the contrary, depression rates were numerically higher in lamotrigine treated groups, independent of former episodes of major depression. The authors concluded that mood-stabilizing AEDs did not reduce the risk of postnatal depression [27]. In contrast, Turner et al., did not find significant associations between postpartum depression and any risk factors, possibly due to low power [25,26].

We found that the risk of peripartum depression and/or anxiety was highest in patients that used AEDs, especially in polytherapy users [24]. Patients with high AED doses and/or plasma concentrations had higher risk than those with lower doses and/or plasma concentrations. No risk-reducing effect was found for any specific AED. A subgroup with high seizure frequency during pregnancy had the highest risk of peripartum depression and/or anxiety (Fig. 1). Long-term outcome was less favorable for WWE with a history of anxiety and/or depression or previous sexual/physical abuse, but prognosis was otherwise similar between groups. For WWE it was less common that depressive symptoms in the peripartum period represented the first depressive episode. The association between peripartum depression and/or anxiety and psychosocial risk factors was similar in WWE, women without epilepsy, and women with other chronic diseases [24].

Fear of birth was related to high seizure frequency. WWE were more often afraid of congenital malformations, while the control women more frequently feared pain during labor [28].

4. Discussion and recommendations

4.1. Risk mechanisms

Peripartum depression in WWE is most frequent early in pregnancy and 0–12 weeks postpartum. This is in line with studies of women without epilepsy [3,4]. In women without epilepsy, there may be a subset of postpartum depressions that are specifically linked to childbirth, perhaps hormonally mediated. However, the majority probably reflects a general psychological or biological vulnerability to depression where childbirth represents a triggering stressor [5]. In WWE, pregnancy related psychiatric distress is highly associated with the disease and its treatment. Treatment-resistant epilepsy particularly carries a high risk for postpartum depression [24,27,28]. As previous psychiatric disease is strongly related to depression and anxiety in pregnancy [34,35], and WWE more often have a history of such disorders [23], these women are already vulnerable. Outside of pregnancy, interictal depression in epilepsy has a multifactorial etiology including underlying neurobiological pathophysiology, psychosocial factors, AED side effects, and health risk behaviors [20,22]. These mechanisms probably operate also in pregnancy.

4.2. Child care

When caring for an infant, the unpredictability of seizures, accompanying sense of vulnerability and fear of causing harm to

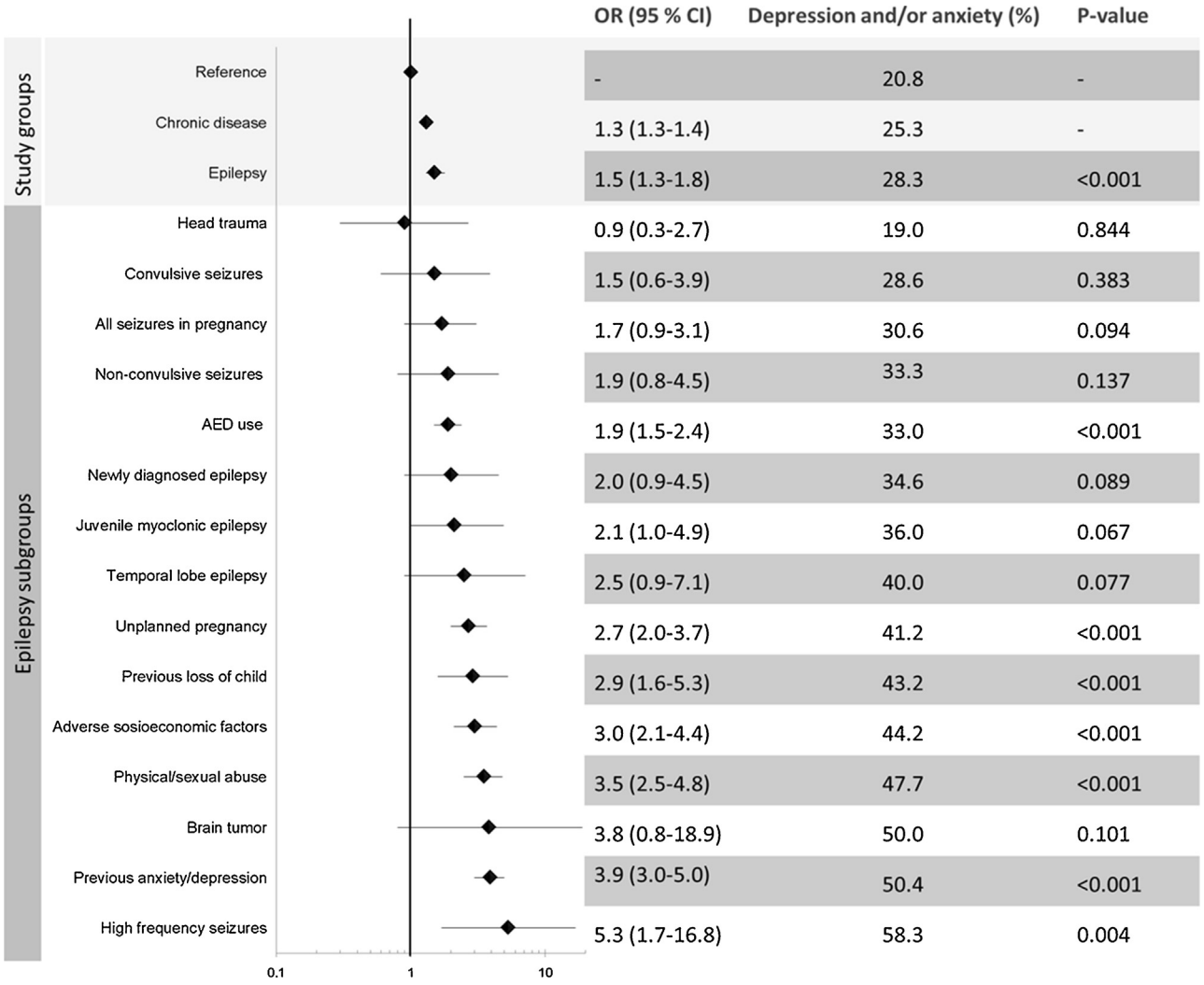

Fig. 1. Risk of peripartum depression and/or anxiety shown as unadjusted odds ratios with confidence intervals in epilepsy subgroups with various risk factors. Source: Printed with the kind permission of Epilepsia and Wiley. Copyright John Wiley and Sons 2014©.

the child are significant sources of anxiety. These fears can include dropping the child due to myoclonic jerks or tonic clonic seizures, or leaving the child unsupervised during a generalized seizure and in the postictal period. In a survey of child care issues in mothers with epilepsy, going outdoors and bathing the child were rated as especially problematic [36]. Such fears are not unfounded. In a group of 28 mothers with severe epilepsy that had not received child-care advice before delivery, unfortunate events caused by maternal seizures happened to 32% of their children during the first year [37]. This included two near-drowning accidents and 6 child droppings (one fatal). Inappropriate handlings of the child during non-convulsive seizures, were also seen. The majority of the incidents were preventable. In a control group of mothers with epilepsy that had received advice on safe child care, unfortunate events were very rare [37]. In order to prevent unnecessary anxiety, child-expecting parents with epilepsy should be advised on safe child care (Table 3) [38] and reassured that if such measures are undertaken, harm to the child due to parent seizures is unlikely. Also, such information should be conveyed to patients with controlled epilepsy. Especially in the puerperium, parents with a former controlled epilepsy can experience recurrence of seizures and myoclonic jerks [37,38]. Since following advice often requires the presence of another person, single mothers can be especially vulnerable for anxiety related to the child care situation. Single motherhood is common in epilepsy populations [23], and such women need extra support (Table 2).

4.3. AED treatment

AED therapy was associated with peripartum depression in WWE in three studies, and AEDs assumed to be "mood stabilizing" did not reduce the risk [23,24,27]. Co-morbidity associated with prescription of AEDs with psychotropic properties represents

Table 2
Safe child care advise.

Child care safety issues
Maximize opportunity for bonding, but minimize risk
Avoid exhaustion. Share care at night
Breastfeed/bottle feed on floor
Use safe baby/childrens chair
Change on floor
Never bath child alone
Carrry child in secure carrycot up and down stairs
Contain child by safety gates, playpen, harness etc.
Make kitchen completely safe
Use dead man's handle on prams
Teach older children what to do during seizures

Source: Adapted from Fox et al. [38].

potential selection bias, though the results were independent of a former psychiatric history. Also, it is difficult to fully account for the relationship between AED therapy and severity of epilepsy, as exemplified by the strong association between seizure frequency and peripartum psychiatric symptoms.

In terms of *side effects*, the same AED may exhibit both positive and negative psychotropic effects [39]. Carbamazepine, valproate, oxcarbazepine, lamotrigine and pregabalin are believed to have positive psychotropic effects, while phenobarbital, phenytoin, vigabatrin, levetiracetam, topiramate, tiagabine, zonisamide and felbamate are suspected to affect mood in a negative way [20,39]. Anxiety can emerge after discontinuation of an AED with anxiolytic properties [39]. However, observed positive effects on mood in relation to anticonvulsant treatment do not necessarily mean that such AEDs also have a therapeutic effect on depression or anxiety disorders in people without epilepsy. Hard evidence for a positive effect of AEDs on psychiatric disease only exists from trials on patients with psychiatric disease without epilepsy [40]. In epilepsy, underlying etiology and the spectrum and symptoms of mood disorders can be different compared to other populations [22]. Patients often have complicating factors such as AED polytherapy and cognitive dysfunction. Add-on therapy with AEDs with positive psychotropic effects were claimed to have some effect on psychiatric symptoms in a recent review, but not more useful than antidepressive medication or psychotherapy [41]. Due to the negative associations between polytherapy and depression, we do not recommend to treat depression or anxiety in relation to pregnancy by add-on therapy with AEDs.

4.4. Antidepressive medication

A recent Cochrane review regarding treatment for moderate postnatal depression in women without epilepsy favored selective serotonin re-uptake inhibitors (SSRIs) over placebo in terms of response and remission rates [2]. Maternal side effects were frequently reported. There was insufficient evidence to conclude whether antidepressant or psychosocial treatments were more effective. There were little data on potential effects on the mother–child relationship [2].

Even though there are few methodologically adequate studies on the efficacy of antidepressants in epilepsy, it is assumed that depressive symptoms in patients with epilepsy outside of pregnancy respond well to treatment with SSRIs and selected serotonin-norepinephrine reuptake inhibitors (SNRIs) [20]. Worsening of seizures with initiation of a SSRI is rarely seen [20,39,40]. In patients with concomitant AED use, citalopram, escitalopram and venlafaxine are theoretically favorable to drugs that inhibit cytochrome P450 (CYP) enzymes [40]. Conversely, serum levels of most SSRIs and SNRIs can be reduced by CYP inducers such as carbamazepine and phenytoin, and increased by CYP inhibitors such as valproate [21,39,40]. Escitalopram, sertraline and venlafaxine are documented as effective for certain anxiety disorders in patients without epilepsy, while other conditions respond better to cognitive behavioral therapy (CBT), or CBT in combination with antidepressants [21].

4.5. Antidepressants in pregnancy

Risks of adverse events related to antidepressants in pregnancy have been widely studied. Both SSRIs and tricyclic antidepressants pass via the placenta in considerable amounts. SSRIs are assumed to be least harmful, and have in later years been extensively prescribed in pregnancy [42]. There is concern that in utero exposure may cause offspring adverse effects, especially cardiac defects, respiratory distress, and low birth weight. However, studies report conflicting results, probably due to the many confounders related to psychiatric disease [43]. Several register-based clinical studies and preclinical data show a low but significant risk of persistent pulmonary hypertension, and an increased risk of transient sleep-pattern disruption and transient neonatal jitteriness and irritability [43,44]. Regarding long-term offspring effects, some studies have found increased risk of cognitive, behavioral and developmental problems, even after adjusting for maternal mood disorders. A recent review concluded that non-pharmacological treatment is recommended as first line therapy in pregnancy. However, it is not always a viable option. Due to potentially serious consequences of maternal depression, the need to initiate effective, rapid-onset therapies must be weighed against the possible teratogenic potential of SSRIs [43]. In WWE, an individual cost-benefit evaluation is especially important, as there are no data regarding consequences of combining AEDs with SSRIs in pregnancy.

4.6. Antidepressants and breastfeeding

Antidepressants are lipid soluble and excreted in breast milk [2], but the degree of exposure for the child is considerably lower than in utero. Some case reports have described adverse events such as sedation, poor feeding and disturbed sleep. There is no evidence of long term adverse effects of antidepressants via breast milk, but studies are lacking. Drug concentrations can accumulate in premature or sick babies with compromised kidney and liver function [45], and also with the tricyclic antidepressant doxepin. Significant drug infant levels are more likely with the SSRIs fluoxetine and citalopram, than for paroxetine, sertraline and escitalopram, and lower with the SNRI devenlafaxine than for venlafaxine [46]. Information on infant drug exposure is sparse for some agents and long term data exist only for a few antidepressants, mainly SSRIs. Before initiating antidepressive treatment in the postpartum period, we recommend consulting the LactMed database which offers monthly updates on lactation safety [46]. If the mother was successfully treated with an antidepressant during pregnancy, or if other antidepressants have been ineffective, changing medications during breastfeeding is not recommended [46]. Medication discontinuation could lead to relapse. Due to the many maternal and offspring benefits, breastfeeding should generally be encouraged also in women with medically treated postnatal depression [47], but individual risk-benefit assessments is necessary. The infant should be monitored for adverse side effects, especially if antidepressants are taken together with AEDs. Breastfeeding should be performed before rather than after dose intake. If adverse effects are suspected, antidepressive - and antiepileptic drug concentrations should be measured in the infant, and mixed nutrition with formula milk may be considered. Mothers taking an SSRI during pregnancy and postpartum may need additional support to succeed with breastfeeding [46].

4.7. Electroconvulsive therapy (ECT)

There are several case reports on successful treatment with ECT in patients with epilepsy and psychiatric disease [48], and ECT is not contraindicated in epilepsy outside pregnancy. However, there are also reports that describe ECT-induced status epilepticus [49–51]. A review found evidence for efficacy in treating severe psychiatric illness during pregnancy in patients without epilepsy [52]. Possibly ECT-related adverse effects were noted for 5.3% of the mothers and 3.2% of the children. Transient fetal bradyarrhythmias and uterine contractions were among the most frequent complications, but one fetal death after ECT induced status epilepticus was also reported [52]. However, long-term effects on offspring after ECT in pregnancy are not known. In our opinion,

Table 3
Recommendations for management of women with epilepsy in the peripartum period.

Recommendations	
Pre-pregnancy planning	Optimize AED and antidepressive drug treatment with as few drugs in as low doses as possible. Maintain seizure control.
Notice risk factors	Previous psychiatric disease, previous sexual/physical abuse, AED polytherapy, high seizure frequency and adverse psychosocial factors increase the risk of peripartum depression and anxiety.
Symptom screening	Screen for symptoms of anxiety and depression before, during and after pregnancy
Swift treatment	Treatment for peripartum psychiatric disease should not be delayed.
Multidisciplinary approach	Neurologist, obstetrician, psychiatrist, general practitioner and community midwife/nurse should work together
Non-pharmacological treatment	Psychotherapy is recommended for mild to moderate depression and anxiety during pregnancy and breastfeeding
Antidepressive treatment	If indicated, SSRIs without a pro-convulsive effect or AED interaction are preferred
Measure serum concentrations	Serum levels of AEDs and antidepressive drugs can change due to interaction and metabolic changes in pregnancy and should be measured
Avoid electroconvulsive therapy	ECT should not be used in pregnancy in women with epilepsy
Child care advise	Advise expecting parents with epilepsy on safe child care
Monitor child	If AEDs and/or antidepressive medications are used during breastfeeding: monitor child for side effects

AED, antiepileptic treatment; SSRI, selective serotonin reuptake-inhibitors; ECT, electroconvulsive therapy.

ECT during pregnancy in patients with epilepsy should be regarded as experimental therapy, and is not recommended.

4.8. Recommendations for peripartum depression in WWE

Peripartum psychiatric symptoms are associated with high seizure frequency and AED use. Therefore the primary aim should be seizure control with as few AEDs with the lowest possible dose. This is in line with the recommendations for avoiding teratogenic effects by in utero exposure to AEDs [38,53] and SSRIs [43]. Testing of a new antidepressant during pregnancy is not advisable if a previously used substance has been effective, as the child's outcome after exposure to multiple antidepressants in pregnancy is unknown [43]. Pregnancy planning is therefore important to optimize AED and antidepressive treatment before conception. It has been shown that pre-conception planning leads to less use of AED polytherapy, less switching between drugs and better seizure control during pregnancy compared to unplanned pregnancies [54]. In non-pregnant epilepsy patients it is recommended to screen for psychiatric comorbidities and suicidal ideation before starting treatment with AEDs as well as during drug titration and change [20]. Such surveillance should be intensified throughout pregnancy and in the postpartum period. A positive effect of postpartum depression prevention has been shown in high risk populations [55]. These findings probably apply also to epilepsy populations. Patients at risk of psychiatric disease should be followed up closely. The general practitioner, obstetrical unit, community midwife/nurse, and other health personnel caring for the woman should be alerted. In case of depression, anxiety or other psychiatric symptoms, swift referral to a psychiatrist for further treatment should be considered. Since some psychoactive medications reduce the seizure threshold, AEDs may influence psychiatric symptoms and both AEDs and antidepressants potentially affect pregnancy outcome, a multidisciplinary approach is highly recommended. The possible impact of AED treatment combined with antidepressive treatment during pregnancy and lactation on offspring development is not studied. Caution is therefore warranted. There is no strong evidence that favors the superiority of antidepressive drug treatment over psychotherapy [2,5]. In our opinion, psychotherapy is the first line treatment for mild to moderate depression in pregnant or breastfeeding WWE. If co-therapy with antidepressants is necessary, a SSRI without AED interaction should be chosen. Drug clearance can increase during pregnancy for both AEDs and SSRIs and these drug types may interact [40,43]. Clinical effect and maternal serum levels of both AEDs and antidepressants should therefore be monitored and the doses adjusted accordingly (Table 3) [40].

5. Conclusions

WWE often have depression and anxiety during and after pregnancy. This risk is related to a combination of epilepsy severity, AED treatment, adverse psychosocial factors, and a previous history of psychiatric disease or sexual/physical abuse. Psychiatric disorders are undertreated during pregnancy. Health personnel should always include an evaluation of psychiatric disorders in pre-pregnancy planning, during pregnancy, and in postpartum consultations. Parents with epilepsy should be advised on safety issues in child care. Single parents may need extra support. As the consequence of combining AEDs and antidepressive drugs on child outcome is unknown, non-pharmacological treatment options are recommended as first line therapy during pregnancy and breastfeeding. A multidisciplinary approach is advisable.

Conflict of interest statement

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