Seizure 28 (2015) 39–45

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

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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ARTICLE INFO

Article history:
Received 3 November 2014
Received in revised form 6 February 2015
Accepted 10 February 2015

Keywords:
Perinatal
Seizure
Psychiatry
Antiepileptic drugs
Antidepressants
Postnatal

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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http://dx.doi.org/10.1016/j.seizure.2015.02.016
1059-1311/

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