

Factors Related to Post-Natal Depression in Australian Women with Epilepsy

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ABSTRACT

We explored the possibility that certain factors that applied during pregnancy might have influenced the occurrence of depression in the year following pregnancy in a cohort of informed consenting Australian women with epilepsy drawn from the Raoul Wallenberg Australian Register of Antiepileptic Drugs in Pregnancy (RWAPR). The women involved in 29 of 224 consecutive pregnancies (12.9%) followed to 12 months postpartum reported having experienced depression and /or anxiety in the post-natal period. Ten of the 29 had received antidepressant medications. Compared with the 195 pregnancies where there was no post-natal mood disorder, the factors statistically significantly associated with post-natal depression included (i) experiencing depression during or before pregnancy, particularly if that depression was untreated, (ii) not taking folate in preparation for pregnancy, (iii) not breastfeeding, and (iv) having epileptic seizures during labour. Seizures occurring in later pregnancy and after delivery showed non-statistically significant associations with the depression, but antiepileptic drug therapy had no significant effect. These findings suggest that treatment of depression during pregnancy might decrease the risk of post-natal depression in women with epilepsy.

KEYWORDS

Antiepileptic drugs, Breast Feeding, Depression, Epilepsy, Pregnancy

INTRODUCTION

There is substantial recent interest in depression occurring both during pregnancy, and in the postpartum period, in women in general. The disorder is not infrequent [1] and in high income countries has been reported to affect 6.9% to 12.9% of women in the postnatal period [2]. Recent evidence suggests that depression associated with the postnatal period frequently begins during pregnancy, and is underdiagnosed during that period [3]. There is substantial evidence that postnatal depression, if untreated, may produce a risk of significant and long ranging adverse outcomes for both mother and baby [4-6]. These hazards include low birth weight, impaired infant-mother bonding, reduced likelihood of breastfeeding, and long-term neurodevelopmental consequences for the child. There may also be long-term damage to maternal self-esteem, family relationships and to a woman's confidence in her ability to have another child, aspects that are more difficult to quantify. However, relatively little appears to have been published on the issue of postnatal depression as it occurs in the special situation of the woman with epilepsy.

The Raoul Wallenberg Australian Register of Antiepileptic Drugs in Pregnancy (RWAPR) was set up 20 years ago with the primary purpose of investigating relationships between intrauterine exposure to these drugs (AEDs) and foetal malformation. Information concerning various items of potential relevance to this purpose has been recorded in the Register, though specific enquiry concerning the presence or absence of post-natal depression was made routinely only for pregnancies that were enrolled after December 2015. The material in the RWAPR concerning the latter subset of pregnancies has been analysed in the present paper in relation to factors, including antiepileptic drug therapy,

that seemed potentially relevant to the occurrence of this particular mood disorder in women with epilepsy.

MATERIALS AND METHODS

The Pregnancy Register

Fuller details of the RWAPR's aims, recruitment policies and methods have been published elsewhere [7,8]. In brief, pregnant women, mainly those with epilepsy, who know of the existence of the Register through various means may elect to become enrolled in it after telephone discussion with the Register's staff. If such women decide to enrol, and provide informed consent, all further contact between them and the RWAPR is by telephone, with interviews at the time of recruitment, at seven months of pregnancy, within the first month after childbirth, and a year later.

At the time of each interview, relevant details are recorded in a standard pro-forma and the data stored in two Microsoft Access databases, one for the women's names and contact details, the other for clinical details concerning the current and any previous pregnancies, and aspects of maternal health including, after 2015, the presence of pre-existing and post-natal psychological symptoms, in particular anxiety and depression. No specific interview questioning such as that used for the Edinburgh Postnatal Depression Scale scoring was employed. Any foetal malformations that occurred were categorised in terms of the Victorian Birth Defect Classification [9]. Epileptic seizure occurrence details depended on information provided at times of interview, as seizure diary keeping proved impracticable over the durations of the individual pregnancies. The accuracy of health-related information supplied by the enrolled women was confirmed by their treating medical practitioners, but RWAPR personnel did not attempt to manage or provide advice on the women's epilepsy therapy during pregnancy.

Throughout its existence, the RWAPR has been housed in various institutions in Melbourne (St Vincent's Hospital, Monash University, the Royal Melbourne Hospital), depending on the current institutional affiliations of those involved in its operation. The Research Ethics Committees of the Royal Melbourne Hospital provided ethics oversight for the study reported here.

The Pregnancies Studied

After excluding pregnancies in AED-treated women who did not suffer from epilepsy, the material available for the present study comprised 224 pregnancies, all of which had been recruited after the end of 2015 and followed to the end of their first post-natal year before December 2018. The information regarding post-natal depression or other mood disorder was obtained at the early post-natal interviews or, retrospectively, at the end of the first postnatal year interviews. The postnatal mood disorders were recorded as instances of depression, some with an admixture of anxiety, or as anxiety alone. Both depression and anxiety had been present in some of these pregnancies at their times of enrolment in the RWAPR or before giving birth. Some instances of early pregnancy anxiety later developed postnatal depression. If this occurred, for the purposes of the present analysis the pre-existing anxiety was taken as probably a manifestation of depression.

Data Analysis

Data for the pregnancies were transferred from the RWAPR database to a Microsoft Excel spreadsheet and analysed using conventional simple statistical techniques, mainly confidence interval methods, after employing logistic regression to identify data items from the RWAPR that seemed worth further evaluation.

RESULTS

Postnatal depression, as distinct from continuing prenatal depression, was reported in 29 of the 224 pregnancies studied (12.9%). The symptom occurred in 12 of the 87 first pregnancies (13.8%) and in 12 of the 106 women with previous completed pregnancies (11.3%; Odds Ratio 1.253, 95% C.I. = 0.568, 2.765). In the present dataset, antidepressant medication had been taken in 10

of the 29 postnatal depression pregnancies (34.5%).

Twelve women had two separate pregnancies, none involving postnatal depression, among the 224 pregnancy dataset, with the remaining 200 women having one pregnancy each. There was record of a past history of postnatal depression in 5 of the 106 women who had previous completed pregnancies. None of this 5 had postnatal depression in the pregnancy here considered. These numbers are too small to safely exclude the possibility that some women with epilepsy may have an inherent tendency to develop postnatal depression.

Multiple variable logistic regression was employed to detect items recorded in the RWAPR that might be related to the occurrence of this post-natal depression, sequentially stripping variables from the regressions until they became statistically significant. The resultant findings made it sufficiently unlikely that any of the following factors contributed to the occurrence of postnatal depression and they were not pursued further, viz. maternal age in pregnancy, maternal age at onset of seizure disorder, having generalised or having focal epilepsy, having a pre-existing physical illness at recruitment into the study, taking various antiepileptic drugs in their doses prescribed at enrolment or prescribed in their third trimesters, taking antidepressant drugs, experiencing seizures in the year before pregnancy, the baby's birth weight, and giving birth to a malformed baby. The variables in the regressions comprising dosages of the individual major antiepileptic drugs, and the use of the uncommonly employed antiepileptic drugs collectively, never achieved P values below 0.48 (that for valproate) and therefore disappeared early in the variable stripping process. Certain other variables considered in the regression also seemed unlikely to play any role in relation to postnatal depression, but it seemed useful to include them in the data of Table 1 to provide perspective for the roles of the several variables which appeared to influence the occurrence of the depression. The variables in the regression associated with a statistically significantly increased hazard of postpartum depression were (i) pre-existing depression at entry into the study, in particular pre-existing depression that was untreated (treated pre-existing depression did not show a statistically significant effect), (ii) not taking folate before the onset of pregnancy, and (iii) seizures occurring during labour. Seizures occurring in the final two months of pregnancy and postpartum seizures showed non-statistically significant increased hazards of postnatal depression. In contrast, breastfeeding was associated with a statistically significantly decreased hazard of postnatal depression.

Postnatal depression occurred in 15 of 69 pregnancies (21.7%) where depression with or without anxiety had existed in the same pregnancy at enrolment, and in 14 of 155 pregnancies (9.0%) where it had not (O.R. = 2.798, 95% C.I. = 1.344, 5.823). The hazard was 2 in 14 (14.3%) when the pre-enrolment depression had been treated, and 13 in 55 (23.6%) when the pre-enrolment depression was not treated (O.R. = 0.539, 95% confidence interval = 0.106, 2.734).

DISCUSSION

The present study, based on material in a database constructed to investigate a different though not necessarily unrelated matter, viz. foetal malformation, contained few pregnancies in women who did not have epilepsy. Consequently, it was not feasible to investigate whether the incidence and character of postnatal depression in women with epilepsy differed from that in women who did not have epilepsy but who took antiepileptic drugs. However, the reported incidence of postnatal depression in the present study of women with epilepsy (12.9%) was consistent with the 6.9% to 12.9% population rate reported by Stewart and Vigod [2], and the described Australian rate of 16% [10].

The findings of the present study have been derived from a comparatively small subset (some 11.4%) of all the pregnancies in the RWAPR that have been followed to one year post-partum. As well, the pregnancies studied have, as it were, been selected by the women involved in them, and may not necessarily be representative of the whole population of pregnant Australian women with epilepsy. Nevertheless, some statistically significant information has emerged

Table 1: Variables influencing the occurrence of postnatal depression. Statistically significant variables are shown in bold type

	Postnatal Depression		O.R.	95% C.I.
	<i>Absent</i>	<i>Present</i>		
	N=195	N=29		
Earlier depression / anxiety	27.7%	51.7%	2.800	1.266, 6.193
- Treated	6.2%	6.9%	1.170	0.240, 5.325
- Untreated	21.3%	44.8%	2.960	1.320, 6.637
Folate before pregnancy	77.4%	58.6%	0.413	0.183, 0.930
Folate during pregnancy	93.8%	96.3%	0.556	0.147, 2.106
Unassisted birth	44.1%	31.0%	0.570	0.247, 1.136
Caesarean section	47.2%	44.8%	0.910	0.415, 1.992
Breast feeding	55.9%	31.0%	0.355	0.134, 0.819
Illness in late pregnancy	19.0%	3.5%	0.152	0.028, 1.157
Seizures in pregnancy	41.0%	44.8%	1.168	0.533, 2.562
- in late pregnancy	15.9%	24.1%	1.683	0.533, 2.562
- in labour	2.1%	10.3%	5.510	1.167, 26.010
- post-partum	21.0%	34.5%	1.977	0.854, 4.578

from the present analysis of the available pregnancies. Certain variables that might have played a role in relation to postnatal depression in the pregnancies were found unlikely to have done so, e.g. having a malformed or low birth weight baby, undergoing Caesarean section, being exposed to anti-depressant or antiepileptic drugs in pregnancy, and having seizures occurring at any stage during pregnancy. Hahn-Holbrook *et al* [10] obtained a similar finding in relation to Caesarean section in pregnant women in general.

Suicidal ideation is more common in pregnant and postpartum women than in the general population [11,12]. This hazard should always be considered, and the patient be questioned about the distressing topic of any thoughts such as wishing that the baby had never been born. A recent epidemiological study suggests that suicidal ideation in this situation often does not meet the criteria for a diagnosis of major depression, but emphasises that the stress-diathesis model shows susceptibility to suicidal behaviour is increased independently of the presence of a depressive disorder [11]. We are not aware of any instances of suicide in the present series of cases, but it is possible that such events could have occurred, because the women involved would not have been available for the one-year follow-up interview and, being regarded as instances of loss of contact after the postnatal interview, would not have been included in the population studied.

The finding that depression and/or anxiety that was present at enrolment in the Register tended to be associated with subsequent postnatal depression has been recorded previously in relation to pregnant women in general [12, 13]. What is perhaps more unexpected is that this association was found in the present study only in the case of pre-existing mood disorder that was not treated, and not if the disorder had been treated with antidepressants. This finding raises the possibility that the incidence of postnatal depression might be reduced if mood disorders present in the earlier part of pregnancy were more often treated with appropriate therapeutic agents. Unfortunately, evidence is beginning to appear that intrauterine exposure to antidepressant drugs may increase the hazard of foetal malformation [14], so that the maternal benefits derived from such treatment might be offset by foetal morphological disadvantages. More relevant information is needed regarding the balance between maternal advantage and foetal disadvantage in this situation before any soundly based recommendation can be justified.

There seems no obvious reason why not taking folate prior to pregnancy should have been associated with an increased chance of postnatal depression. One could speculate that women with a pre-existing mood disorder might have been reluctant, or been too inert, to take a potentially beneficial therapeutic agent before becoming pregnant, but the present study can provide no evidence that this was the case.

The correlation found between not breastfeeding and suffering postnatal depression has been noted previously in women who did not have epilepsy [3] and might be explained to an extent by women having a sense of failure and guilt from being unable or unwilling to breastfeed. Equally, it might be attributed to the depression resulting in failure to cope with breastfeeding.

The occurrence rates of epileptic seizures over the whole length of pregnancy did not correlate with the occurrence of postnatal depression, but the rates for seizures in the final two months of pregnancy, during labour, and postnatally tended to do so, with seizures occurring during labour having a statistically significant effect. This finding raises at least two possibilities. Having uncontrolled seizures close the time of birth might undermine the woman's confidence in her ability to manage a baby and lead to reactive depression and anxiety. An association between emotional distress in labour and postnatal depression in women in general has been reported previously [13]. It is also possible that, particularly if seizures occurred during labour, antiepileptic drug doses may have been increased at that time (this would not be recorded in the RWAPR data). With higher circulating drug concentrations in the early postpartum period, a time when the raised drug clearances of pregnancy are falling progressively, a failure to adjust drug dosages downwards at appropriate times might have resulted in maternal and perhaps infant over-sedation, with consequent maternal mood alterations.

CONCLUSIONS

Evaluation of a larger set of pregnancies is desirable to provide additional relevant information regarding postnatal depression in Australian women with epilepsy. However, the overall findings of the present analysis suggest that the situation regarding postnatal depression in these women probably does not differ substantially from that which applies in the wider general population of pregnant women. Nevertheless, the present study does suggest the desirability of recognising and then treating depression during pregnancy in women with epilepsy, and the need to watch women with epilepsy closely for evidences of depression during their postnatal weeks, particularly if they have experienced seizures in the immediate perinatal period, and the importance of assessing whether the doses of the antiepileptic medications they are taking in their early postnatal weeks may be producing drug concentration-related unwanted effects on their mood.

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DISCLOSURE OF CONFLICT OF INTEREST

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