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CLINICAL MANAGEMENT OF ANTIEPILEPTICS DURING PREGNANCY

Lea Karabegovic (Kathleen Job, PhD)
Department of Pediatrics, Division of Pediatric Clinical Pharmacology, University of Utah School of Medicine

Background

With over 65 million afflicted worldwide today, epilepsy is one of the most common neurological diseases known [1]. Epilepsy is especially of concern during pregnancy. Risks associated with maternal epilepsy include fall secondary to epileptic events and miscarriage, among others. However, some antiepileptic drugs (AEDs) are known to cause teratogenic outcomes. As such, it is recommended that women be appropriately counseled and treated for epilepsy [2]. The American Academy of Neurology (AAN) and American Epilepsy Society (AES) introduced new guidelines for the clinical management of epilepsy during pregnancy in 2009 [3]. The AEDs with the most likely safe outcomes in pregnancy included carbamazepine and lamotrigine, whereas it was recommended that the use of valproate and phenytoin be avoided [3, 4].

Aims and Methods

The aim of this study was to determine AED prescription patterns for a pregnant population, and whether the published guidelines were followed, using a retrospective chart review. The data included demographic and drug prescription information for a set of pregnant women exposed to at least one AED at an Intermountain Healthcare facility between January 1, 2006 and December 31, 2016. The data was separated so as to include each pregnancy as a separate point (even though a single patient may have had several pregnancies during which she was exposed to an AED). The time-stamped “Drug Administration Date” information was used to further separate the data by the trimester during which the AED exposure event occurred. Excel software was then used to determine trends in AED prescription, both in pregnancy as a whole, as well as across trimesters.

Results

The results of the study were based on a total of 201 pregnancies exposed to a total of 251 AEDs at some point during pregnancy. Clonazepam was the most commonly prescribed AED, with lamotrigine closely following. A summary of AED prescription patterns throughout pregnancy and by trimester can be found in Figure 3 (below). The general prescription patterns were found to be similar throughout all ten years included in this study—which included dates both before and after the AAN and AES guidelines were published. One concerning incidence of valproate use in the first trimester was included, and about 5% of all pregnancies in this study were exposed to phenytoin.

AED Prescribed	All Pregnancies: N (%)	1st Trimester N (%)	2nd Trimester N (%)	3rd Trimester N (%)
Phenobarbital	7 (2.8%)	1 (1.3%)	2 (2.2%)	4 (4.9%)
Phenytoin	12 (4.8%)	1 (1.3%)	10 (10.8%)	1 (1.2%)
Fosphenytoin	3 (1.2%)	-	2 (2.2%)	1 (1.2%)
Clonazepam	66 (26.3%)	24 (31.2%)	25 (26.9%)	17 (21.0%)
Carbamazepine	13 (4.8%)	2 (2.6%)	3 (3.2%)	8 (9.9%)
Oxcarbazepine	4 (1.6%)	1 (1.3%)	2 (2.2%)	1 (1.2%)
Valproic	1 (0.4%)	1 (1.3%)	-	-
Tiagabine	1 (0.4%)	-	-	1 (1.2%)
Lamotrigine	63 (25.1%)	20 (26.0%)	17 (18.3%)	26 (32.1%)
Gabapentin	31 (12.4%)	11 (14.3%)	11 (11.8%)	9 (11.1%)
Levetiracetam	33 (13.1%)	10 (13.0%)	15 (16.1%)	8 (9.9%)
Zonisamide	5 (2.0%)	1 (1.3%)	2 (2.2%)	2(2.5%)
Pregabalin	7 (2.8%)	3 (3.9%)	1 (1.1%)	3 (3.7%)
Lacosamide	5 (2.0%)	2 (2.6%)	3 (3.2%)	-
Total Prescriptions:	251	77 (*30.7%*)	93 (*37.1%*)	81 (*32.2%*)

Table 1: Antiepileptic Drug Prescription Throughout Pregnancy and By Trimester. A total of 251 prescriptions (or AED exposures) occurred between the 201 pregnancies included in the study. The number of patients prescribed an AED was similar across all trimesters. Clonazepam and lamotrigine were consistently the most commonly prescribed AEDs, both within and across the three trimesters.

Summary and Future Directions

Though the AAN and AES guidelines were followed in the treatment of the majority of the pregnancies, incidents of valproate and phenytoin prescriptions are concerning. The single exposure of valproate and the majority of the phenytoin exposures occurred in the years after 2009, when the use of these two drugs during pregnancy were specifically advised against. This suggests that providers are not aware of the guidelines, or have not implemented these suggestions into their practice. It also leads to questions of whether medication decisions were guided by patients or physicians. Future studies should also look into why clonazepam exposure was greater than what was anticipated, and whether this may have had any association with the treatment of non-epileptic conditions.

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