



Counseling by epileptologists affects contraceptive choices of women with epilepsy



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ABSTRACT

Introduction: There are several important interactions between antiepileptic drugs (AEDs) and hormonal contraception that need to be carefully considered by women with epilepsy (WWE) and their practitioners. Many AEDs induce hepatic enzymes and decrease the efficacy of hormonal contraception. In addition, estrogen-containing hormonal contraception can increase the metabolism of lamotrigine, the most commonly prescribed AED in women of childbearing age. The intrauterine device (IUD) is a highly effective form of reversible contraception without AED drug interactions that is considered by many to be the contraceptive of choice for WWE. Women with epilepsy not planning pregnancy require effective contraceptive counseling that should include discussion of an IUD. There are no guidelines, however, on who should deliver these recommendations. The objective of this study was to explore the hypothesis that contraceptive counseling by a neurologist can influence the contraceptive choices of WWE. In particular, we explored the relationship between contraceptive counseling in the epilepsy clinic and the likelihood that patients would obtain an IUD.

Methods: We conducted a retrospective chart review of female patients age 18–45 seen at our institution for an initial visit between 2010 and 2014 to ascertain the type of contraceptive counseling each patient received as well as AED use and contraceptive methods. Patients who were pregnant or planning pregnancy at the first visit were excluded from further analyses as were patients with surgical sterilization. We also examined a subgroup of 95 patients with at least 4 follow-up visits to evaluate the efficacy of epileptologists' counseling. Specifically, we looked at the likelihood a patient obtained an IUD based on the type of counseling she had received. Fisher exact tests assessed associations between counseling type and whether patients had obtained an IUD.

Results: Three hundred and ninety-seven women met criteria for inclusion. Only 35% of female patients were counseled about contraception at the first visit. If women were not counseled at the first visit, they were unlikely to be counseled at subsequent visits; only 37% had ever received counseling by their fourth visit. Of the 95 patients who completed 4 visits, 28.4% were counseled about an IUD as an optimal contraceptive choice, 38.9% were generally counseled about contraceptive interactions, and 32.6% were not counseled about contraception. Women with epilepsy who received IUD-specific counseling were significantly more likely to switch to an IUD (44.4%) compared with women who received no contraceptive counseling (6.5%; $p = 0.0009$). Women with epilepsy who received IUD-specific counseling also tended to switch to an IUD more often than those women receiving general counseling about AEDs and contraceptive interactions (18.9%; $p = 0.027$). There was no significant difference in the likelihood of acquiring an IUD between the general counseling and no counseling groups.

Conclusions: Contraceptive counseling by epileptologists and specific mention of an IUD is significantly associated with patient selection of an IUD as a contraceptive method. This suggests that neurologists can play an important role in patients' contraceptive choices.

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Abbreviations: AED, antiepileptic drug; CDC, Center for Disease Control; COC, combined oral contraceptive pills; EI-AED, enzyme-inducing antiepileptic drug; IUD, intrauterine device; SHBG, sex hormone-binding globulin; WHO, World Health Organization; WWE, women with epilepsy.

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1. Introduction

1.1. Antiepileptic drugs and hormonal contraception

Epilepsy affects 0.5–1% of the population, and 33% of these individuals are women of childbearing age [1]. It is critical that women with epilepsy (WWE) plan their pregnancies in advance in order to minimize the teratogenic risk of antiepileptic drugs (AEDs) and optimize seizure control

prior to getting pregnant. Thus, understanding and obtaining an optimal form of contraception is an important part of their health management early in their care.

Obtaining appropriate contraception is complicated for WWE given the bidirectional interactions between hormonal contraceptives and the majority of AEDs. Enzyme-inducing AEDs (EI-AEDs) including carbamazepine, perampanel, phenobarbital, phenytoin, and primidone are potent inducers of hepatic P450 microsomal enzymes. In addition, they may increase sex hormone-binding globulin (SHBG) production. Both mechanisms result in decreased bioactive sex hormone levels and reduce the effectiveness of hormonal contraception [2]. Clobazam, eslicarbazepine, felbamate, lamotrigine, oxcarbazepine, and topiramate induce P450 enzymes to a lesser degree but may also decrease sex steroid concentrations and the efficacy of hormonal contraception [2,3].

Estrogen-containing contraceptives such as the combined oral contraceptive pills (COC), the vaginal ring, and patch enhance the glucuronosyltransferase system resulting in increased metabolism and lower serum concentrations of glucuronidated drugs including lamotrigine and valproic acid [4–6].

1.2. Contraceptive recommendations for WWE

According to consensus statements from a World Health Organization (WHO) working group and the Center for Disease Control (CDC), combined oral contraceptive pills and progesterone only pills, as well as contraceptive patches and vaginal rings are not recommended as first-line contraception in women taking EI-AEDs [2,7].

The statements mention that depot medroxyprogesterone and the levonorgestrel implant can be considered in women taking EI-AEDs; however, contraceptive failure has been reported when the levonorgestrel implant was used in combination with EI-AEDs [2,7].

These statements from the WHO working group and the CDC as well as other authors also recommend against combining lamotrigine and estrogen-containing birth control methods (COCs, orthoevra patch, and nuva ring) because of the risk of loss of seizure control [2,7]. While, in practice, fluctuations in lamotrigine levels can be avoided by an experienced neurologist or epileptologist, it is preferable to avoid this variability.

An intrauterine device (IUD) is recommended as the contraceptive of choice for WWE [3,8,9]. The IUD avoids all of the above drug–drug interactions between contraception and AEDs. Additionally, the IUD is an exceptionally effective form of contraception with a failure rate of 0.2–0.8% per year, which is superior to most hormonal contraceptive methods and nonhormonal barrier methods such as male condoms which with ‘typical use’ have a failure rate of 18% [10]. While it was once thought that the IUD could only be used after childbirth, the IUD is now recommended as a first-line contraceptive choice for teenage girls by the American Academy of Pediatrics [11]. The IUD does not require consistent compliance as is needed with barrier methods or the depot medroxyprogesterone injection. The copper IUD is approved for 10 years, and the 52-mg and 13.5-mg levonorgestrel IUDs are approved for 5 and 3 years, respectively. Both the copper and levonorgestrel-containing IUDs can be considered for WWE. The progestin, levonorgestrel, in the levonorgestrel IUD, is thought to exert its effect locally and not be subject to drug–drug interactions. In one study of 56 women using the 52-mg levonorgestrel-containing and EI-AEDs, the failure rate was 1.1% per year [12].

1.3. Contraceptive counseling

Counseling WWE about drug interactions and contraception is necessary to prevent unintentional pregnancy and avoid breakthrough seizures. However, there are no guidelines stating who is responsible for relaying this critically important information to the patient. The aim of the current study was to document the current contraceptive counseling practices of epileptologists at our institution and to investigate whether counseling by a neurologist was effective in influencing the contraceptive

choices of WWE. In particular, we chose to focus on the association between epileptologists' counseling and patient selection of an IUD, the most efficacious form of reversible birth control.

2. Methods

All study procedures were approved by the Northwestern University Institutional Review Board. The study patients were women of child-bearing age (18–45 years) seen as new patients in the Northwestern University epilepsy clinic from 2010 to 2014. This cohort was selected from all patients seen in our epilepsy clinic by Electronic Data Warehouse (EDW) using the search terms “new patient”, “female”, “2010 to 2014”, and age “18 to 45”. Data were extracted by manual chart review for each patient from the first visit and up to 4 subsequent visits depending on the number of follow-up appointments the patient attended. The electronic medical record included a new patient intake form with information regarding the patient's sexual and reproductive history, plans for pregnancy, current medications, and birth control which was used as an adjunct to the information documented in the visit progress note. Patients were excluded based on information documented in the first visit progress note or intake form. The exclusion criteria included the following: surgical sterilization, current pregnancy, or currently trying to become pregnant (Fig. 2.1.1).

For each visit, AED use and contraceptive methods as well as counseling by the epileptologist were recorded as documented in the patient's visit progress note. Counseling documentation was placed into 1 of 3 groups: no counseling, general counseling, or IUD counseling.

“No counseling” – the physician did not document the occurrence of counseling during the visit about interactions between AEDs and contraceptives nor did the physician select “counseled about contraceptive drug interactions” from the discussion dropdown menu in the epilepsy template.

“General counseling” – physician documented discussion about contraception interactions in the visit note without specific mention of an IUD, or “counseled about contraceptive drug interactions” was selected from the discussion dropdown menu in the epilepsy template.

“IUD counseling” – physician documented in the visit note that an IUD was mentioned to the patient during contraceptive counseling.

A subgroup of female patients who had 4 visits at the epilepsy clinic between 2010 and 2014 was used to investigate the effectiveness of the current contraceptive counseling practices (Fig. 2.1.1). These women were divided into 3 groups based on the type of counseling they received at visit 1 or 2 as described above. The outcomes at visit 4 were documented as 1) changed to an IUD or 2) did not change to an IUD. Women who already had IUDs at the first visit were excluded from this efficacy cohort.

3. Statistical analysis

The presence or absence of counseling was documented for each visit and is presented using descriptive statistics. Fisher exact tests with 2x2 contingency tables were used to test the hypothesis that counseling type (no counseling, general counseling, or IUD counseling) was associated with patients' selection of an IUD for contraception. After Bonferroni correction for multiple comparisons a p value of <0.0125 was used to determine statistical significance.

4. Results

4.1. Patient population

Three hundred and ninety-seven new female patients seen in our epilepsy clinic between 2010 and 2014 met criteria for inclusion in

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