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An educational intervention on drug interactions and contraceptive options for epilepsy patients: a pilot randomized controlled trial☆

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Abstract

Objective: This pilot study investigates whether an educational handout could increase short-term information retention about drug interactions between antiepileptic drugs (AEDs) and hormonal contraceptives among female epilepsy patients of reproductive age.
Study design: This is a pilot randomized controlled trial of an educational intervention among reproductive-age women with epilepsy in an academic neurology clinic. Investigators measured knowledge before and after participants received either usual care or the educational handout. The 10-question test assessed increased knowledge of which AEDs affected efficacy of certain hormonal contraceptives and was assessed by calculating the improvement in score between the pretest and posttest. The educational handout included the names of AEDs that have drug interactions with certain contraceptives and the efficacy of the contraceptives.
Results: A total of 42 epilepsy patients participated in this study. Fourteen participants were taking AEDs that are enzyme p450 inducers and 13 participants were taking Lamotrigine. Twenty women were randomized to receive the educational handout and 22 women were randomized to usual care. We found no statistical difference in the groups with regard to age, ethnicity or level of education. We found a significantly higher improvement in quiz scores in the educational handout group (3.65 point increase) compared to the usual care group (0.68 point increase) as calculated by the Student's two-sample t test ($p<.001$).
Conclusions: An educational handout on drug interactions and contraceptives resulted in increased short-term information retention on this topic among reproductive-age female epilepsy patients.
Implications: This pilot study highlights the need for further larger studies to evaluate the impact of educational interventions on improving patient knowledge about the drug interaction of AEDs and hormonal contraceptives.

Keywords: Epilepsy; Contraception; Counseling; Drug interactions

1. Introduction

There are an estimated 1 million women with epilepsy in the United States with a cumulative incidence of 1.7% in women by age 50 years [1,2]. Hormonal contraceptives can interact with antiepileptic drugs (AEDs) in a variety of ways. Many AEDs such as oxcarbazepine, carbamazepine, topiramate and phenytoin can induce enzymes in the liver that increase the metabolism of hormonal contraceptives that can lead to unintended pregnancy [3]. Unintended pregnancy should especially be avoided in women with epilepsy because of the risk of birth defects with use of several of the AEDs [4]. Lamotrigine is an AED frequently used in reproductive-age women because it is less teratogenic than alternative AEDs. However, combined oral contraceptive can affect the metabolism of Lamotrigine reducing the concentration and potentially causing increased seizure activity [4].

The few small cross-sectional descriptive studies looking at contraceptive use in women with epilepsy found at women on

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AEDs do not have adequate knowledge of hormonal contraception/AED interactions and feel that they are receiving insufficient counseling [1,5–7]. Looking at what methods of contraception women with epilepsy use, a small study in urban medical center showed that, of 58 women at risk for pregnancy, 10 women (17%) used sterilization and 13 women (22%) used hormonal methods (9 oral contraceptive pills, 3 patch, 1 depot medroxyprogesterone acetate) [1]. We could find no published reports on interventions that address the issues of improving patient knowledge or improving use of highly effective methods of contraception. Specifically, there has not been a study on an educational intervention about the interaction between hormonal contraceptives and AEDs. The goal of this study was to assess the efficacy of an educational handout for participants on the ways AEDs and hormonal contraceptives may interact to alter effectiveness of the medications.

2. Materials and methods

This study was approved by the University of California, San Diego, Human Research Protection Program. Women of reproductive age (18–45 years old) presenting to an outpatient neurology clinic at an academic medical center in San Diego for follow-up epilepsy care were approached to participate in this study. The neurology staff performed eligibility screening and notified the study team member when there was a potential qualifying participant interested in study participation. The study team member screened for inclusion and exclusion criteria prior to consenting eligible participants. Inclusion criteria were sexually activity with a male, taking at least one AED and English speaking. Women were excluded if they were currently pregnant, were attempting pregnancy or had a history of hysterectomy, bilateral oophorectomy or sterilization procedures. Once enrolled in the study, participants were allocated to either the intervention arm or control arm. Randomization was 1:1 and included a block size of 6. Randomization was computer generated and stratified by clinic location. One clinic was in an urban setting and the other clinic was in a suburban setting. The randomization allocation assignments (handout or usual care arm) were prepared by a statistical service. The assignments were sealed in sequentially numbered, opaque envelopes. After participants were consented, the study team member opened the envelope and allocated the participant to the arm of the study indicated in the envelope.

All participants completed a preintervention knowledge examination (pretest) in their patient examination room. With a study team member in the room to ensure no outside information resources were used, participants had approximately 5 min to complete the pretest before it was collected. The 10-question pretest assessed patient knowledge of which AEDs were known to interact with contraceptive methods, patients' knowledge of rates of unexpected pregnancy and efficacy of different contraceptive methods (Appendix Fig. 1). The maximum score on this test was 10 with each correct answer given one point. The pre-test questions were adapted with permission from studies by Pack et al. and Eisenberg et al. [1,8] participants also received a preintervention contraceptive questionnaire. This questionnaire included contact information, demographics and pregnancy history. The questionnaire was adapted from the Center for Disease Control and Prevention's Behavioral Risk Factor Surveillance System [9]. After completing the pretest and contraceptive questionnaire, participants randomized to the intervention arm received the educational handout (Appendix Fig. 2). These participants had until the end of their appointment with the neurologist to read and review the handout before it was collected by a study team member. Participants randomized to the control group did not receive the handout and proceeded to their scheduled appointment with the neurologist. All participants completed a posttest after their neurology appointment. The posttest consisted of the same questions as the pretest but with the answer choices scrambled. Finally, all participants also completed a postintervention contraception questionnaire capturing information about counseling and contraceptive plans. Participants were compensated with a gift card after completion of the postintervention contraception questionnaire.

We considered a difference in score of 20% (2 points) to be clinically meaningful. Assuming a standard deviation of 2, the number of participants needed in each treatment arm for a power of 0.80 with an α equal to 0.05 was 17. We needed 42 total participants to account for 20% potential participant discontinuation.

Descriptive statistics were used to report participants' demographic characteristics and baseline knowledge test scores. Intervention vs. control group differences on demographics and baseline variables were assessed using χ^2 tests. Separate exploratory two-way (study assignment×subject characteristic) analyses of variance examined whether the effects of the intervention on contraceptive knowledge were moderated by the following subject characteristics: baseline knowledge of hormonal contraceptives/AED interactions, age and education. Point estimates of continuous variables are reported in the form of mean and standard deviation or median and interquartile range (IQR) by specifying the first and third quartiles.

3. Results

A total of 42 epilepsy patients participated in this study. Twenty women were randomized to receive the educational handout and 22 women were randomized to usual care. Fourteen participants were taking AEDs that are enzyme p450 inducers and 13 participants were taking Lamotrigine.

We found no statistically significant difference in demographic background among the women who received the interventional handout and participants that received usual care, as shown in Table 1. The two groups also had similar rates of any contraceptive use, with 10 in the control group and 9 in the intervention group using contraceptives.

We found no statistically significant difference in baseline level of knowledge between the educational handout group