

Antiepileptics May Hinder Oral Contraception

BY HEIDI SPLETE

FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF NEUROLOGY

TORONTO — A standard dose of the antiepileptic drug carbamazepine allowed ovulation and the potential for pregnancy in women using low-dose birth control in a small randomized, double-blind study of healthy women without epilepsy.

The key clinical implication of the findings is that women us-

ing antiepileptic drugs who wish to avoid pregnancy should take additional birth control measures, according to Dr. Anne Davis of Columbia University in New York.

"We were very surprised to see that half of the women who took the [carbamazepine] ovulated," placing them at an obvious increased risk for pregnancy, she said in an interview.

Clinicians have suspected that oral contraceptives are not ful-

ly effective in women who take antiepileptic medications, Dr. Davis and colleagues said in a poster.

But case reports of breakthrough bleeding in epileptic patients were not enough to establish a causal relationship between the antiepileptic drug carbamazepine and the loss of effectiveness from low-dose oral contraceptives, the researchers said.

In this study, the researchers randomized 24 women, aged 18-35 years, with regular menstrual cycles to receive a low-dose birth control pill containing 20 mcg of ethinyl estradiol and 100 mcg of levonorgestrel for 4 months. In addition, the women took either 600 mg of carbamazepine or a matching placebo daily for 2 months.

Breakthrough bleeding was more frequent in the carbamazepine group, with a median of 7 bleeding days, compared with zero bleeding days in the placebo group. At least 3 days of breakthrough bleeding occurred in 8 of 10 carbamazepine cycles, compared with 2 of 10 placebo cycles.

VITALS

Major Finding: Half of healthy women taking the antiepileptic carbamazepine ovulated despite taking a low-dose oral contraceptive.

Data Source: A randomized, double-blind crossover study of 24 healthy women aged 18-35 years.

Disclosures: Dr. Davis has received personal compensation from Bayer Pharmaceuticals and Schering Plough for participating on their advisory boards.

In addition, progesterone levels greater than 3 ng/mL (suggestive of ovulation) occurred in five of the carbamazepine cycles, compared with one of the placebo cycles. Three women in the carbamazepine group showed increased levels of progesterone during week 1 of a cycle, immediately after the placebo pills in the oral contraceptive pack.

The differences between the groups fell short of statistical significance, in part because only 10 of the 24 women completed the entire study.

Of the women initially randomized, two in the carbamazepine group and one in the placebo group did not take the drug. Five women in the carbamazepine group discontinued due to reversible side effects,

and three women in the placebo group discontinued for reasons unrelated to the medication. One patient in the placebo group discontinued due to an adverse event, and samples were lost for one patient in each group, leaving four carbamazepine patients and six placebo patients in the final analysis.

Despite the study's small size, the results show that the known pharmacokinetic effect of carbamazepine on contraceptive steroids has a clinically significant effect, Dr. Davis said.

"If a woman is taking carbamazepine, and she needs birth control, a low-dose pill is not going to be effective," Dr. Davis noted. "I think the next question is to figure out what will be effective for women in that situation." ■



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Progesterone levels suggestive of ovulation occurred in five of the carbamazepine cycles, compared with one placebo cycle.

Long-Acting Implants Are the Frontier for Contraception

BY SHERRY BOSCHERT

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

SAN FRANCISCO — Fifty years after the introduction of oral contraceptives, physicians are looking to long-acting removable contraceptives to provide the next leap forward in preventing unintended pregnancy.

Three themes emerged in interviews with multiple physicians who gave separate presentations on contraception in sessions at the annual meeting of the American College of Obstetricians and Gynecologists.

First, nothing in the future of contraception is likely to match the revolutionary impact of oral contraception. Second, the great advances in contraception over the last half-decade still are accompanied by an unacceptably high rate of unintended pregnancies. And third, when asked to imagine what contraception might look like 50 years from now, most physicians looked to greater use of long-acting removable contraception (LARC) such as intrauterine devices (IUDs) or implants.

"The Pill is still one of the most important inventions ever, in terms of advancing not just women's health care but also women's rights and the ability for women to be in the workforce and to contribute in more ways that they want as members of society," said Dr. Sarah Prager

of the University of Washington, Seattle.

Long-acting removable contraception is the wave of the future, she said, because once the devices are inserted, they don't require patient participation in contraception, which has been one of the major stumbling blocks in contraceptive failures.

The next 50 years probably will see improvements in long-acting removable contraceptives, Dr. Prager added. "Our longest-acting LARC method only lasts for 10-12 years," she noted.

Dr. Joseph Anthony Ogburn of the University of New Mexico, Albuquerque, shared the same vision for the future. "We did better than we did in the past, but we have great room for improvement," he said. Approximately half of U.S. pregnancies are unintended, giving the United States the worst unintended pregnancy rate among developed countries.

Only about 1%-2% of U.S. women on contraception use an IUD, and less than 1% have a contraceptive implant. "If we could increase those numbers significantly, I think we could have a dramatic impact on the unintended pregnancy rate," he said. Advances in the next 50 years probably will entail tweaking existing long-acting removable contraceptives to make them more acceptable.

But "I don't see anything as revolutionary as the Pill coming along any time in my lifetime," he added.

Dr. Pouri Bhiwandi was more enthusiastic. "It's a very, very exciting time for all of contraception," said Dr. Bhiwandi,

an ob.gyn. in Raleigh, N.C., and an international consultant in women's health. "We have so many choices today, which we've never had before."

Since the first oral contraceptive was approved in 1960, women's options grew with approval of more than 40 birth control pills and the development of other forms of hormonal contraception in transdermal patches, the vaginal ring, implants, and intrauterine devices (IUDs).

Modifications in dosing since the first oral contraceptives, which contained nearly four times the amount of estrogen and nearly 10 times the amount of progesterin as today's formulations, have made the Pill safer and more acceptable, as have the development of newer estrogens and progestones, she added. Newer regimens mean women no longer have to bleed while on hormonal contraception.

On the horizon are "exciting possibilities" for new products in barrier contraception that are both spermicidal and microbicidal to prevent sexually transmitted infections, plus "a whole range of new IUDs, a 1-year vaginal ring with a new progestin, and other products, Dr. Bhiwandi said.

The U.S. should emulate Europe, where longer-acting methods of birth control, including IUDs and contraceptives are much more prevalent, said Dr. Andrew Kaunitz, professor of ob.gyn. at the University of Florida, Jacksonville.

Although U.S. clinical trials report a failure rate of 1%-2% with oral contra-

ceptive use, in "typical practice" it's much higher, Dr. Kaunitz said—around nine women per 100 couples annually have unintended pregnancies on the Pill. "That's too high," he said.

Dr. Bliss Kaneshiro of the University of Hawaii, Honolulu, noted that long-acting contraceptive devices are expensive and not always covered by insurance. "One of the big challenges, I think, is cost," she said. "Our challenge for the next 50 years is improving access to those good contraceptive methods."

Dr. David Plourd of the Naval Medical Center, San Diego, said he hopes to see more options in long-acting removable contraceptives in the next 50 years, such as "a flexible IUD, not the semi-rigid T-shaped ones we have currently."

The development of contraception methods targeted to men should play more of a significant role, he added.

Dr. Kaunitz disclosed financial relationships with Teva Pharmaceuticals, Bayer, Ortho (Johnson & Johnson), Merck, Procter & Gamble, Becton Dickinson, Sanofi-Aventis, and Medical Diagnostic Laboratories. Dr. Ogburn has been a consultant for Organon/Schering-Plough. Dr. Bhiwandi disclosed financial relationships with Teva Pharmaceuticals, Warner Chilcott, Boehringer Ingelheim, and Watson Pharmaceuticals. Dr. Plourd has been a speaker for Merck, Novartis, Sanofi-Aventis, Graceway, and Warner Chilcott.

Dr. Prager and Dr. Kaneshiro said they have no conflicts of interest. ■