

IUD Advocated for Women Using Antiepileptics

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

NEW ORLEANS — The best contraceptive choices for women on antiepileptic medications are probably a progesterone-eluting intrauterine device or intramuscular medroxyprogesterone, with the higher doses of oral contraceptives running in second place, Anne Davis, M.D., said at the annual meeting of the American Epilepsy Society.

Some antiepileptic drugs—carbamazepine, oxcarbazepine, phenytoin, barbiturates (phenobarbital, me-

phobarbital and primidone), and topiramate—enhance the P450 cytochrome enzyme system. "This decline potentially decreases the effectiveness of hormonal methods of contraception," said Dr. Davis of Columbia University, New York.

The intrauterine device (IUD) and the depot medroxyprogesterone acetate (DMPA) (Depo-Provera) injection are not as prone to these drug interactions. The progesterone-eluting IUD thickens cervical mucus, impairs sperm movement, suppresses endometrial development, and has a slight anovulatory effect. DMPA suppresses ovulation and its progesterone content protects its effect from

alterations in the enzyme system, Dr. Davis said.

In addition, the high progesterone content might have antiseizure properties. "This is a little bit of a teaser, something that's out there in the literature. Progesterone decreased seizure frequency in animal models, and DMPA decreased seizure frequency in women with intractable epilepsy. It's a tantalizing thing, but there's too little information out there to make any conclusions."

The second choice for women on the CYP450-enhancing drugs would be higher dose oral contraceptives. "It's a little misleading to actually call

some oral contraceptives 'high dose,' because everything these days is really low dose," she said. "What we're really talking about is differentiating between medium dose, low dose, and very low dose."

Experts have said that oral contraceptives containing 50 mcg estrogen are probably the most effective for these women. "But there are no real data to back that up," Dr. Davis said. The contraceptive patch and vaginal ring are comparable in estrogen dose with the 50-mcg pill.

The lower-dose pills are much more prone to failure in these women, as are progesterone-only pills. Neither the six-rod implant currently available nor the soon-to-be-approved single rod implant (Implanon) are good choices for this population, as they are both progesterone-only methods.

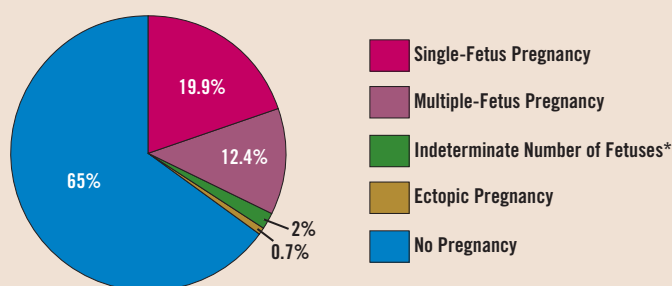
Some women may want to consider a barrier method, since this alleviates the concern of failure due to drug interaction. However, the failure rates of barrier methods are so much higher than those of hormonal methods that the chance of pregnancy is vastly increased, even taking into consideration drug interaction failures.

Even women taking medications that don't increase contraceptive failure may have special contraceptive considerations, Dr. Davis said. Numerous studies point to valproate's teratogenicity. Women on this drug who want to conceive may consider switching to another effective drug. If pregnancy is not in the cards for them, sterilization may be a viable alternative.

Women with catamenial epilepsy should use a form of birth control that reliably suppresses ovulation. DMPA is a good choice for this population. "Unlike the amenorrhea produced by the progesterone IUD, where they are still ovulating, the DMPA shot reliably suppresses ovulation," Dr. Davis said. "This is an important consideration for seizure frequency that's responsive to fluctuations in the menstrual cycle."

DATA WATCH

Outcomes of Assisted Reproductive Technology Cycles



* Number of fetuses not known because the pregnancy ended in an early miscarriage.

Note: Based on 85,826 ART cycles in 2002 that used only fresh embryos from nondonor eggs or, in a few cases, a mixture of fresh and frozen embryos from nondonor eggs.

Source: Centers for Disease Control and Prevention

KEVIN FOLEY, RESEARCH/DESIGN

Review of 28 Studies Links HT to Higher Stroke Risk

BY HEIDI SPLETE
Senior Writer

Hormone therapy is associated with a significantly increased risk of stroke, based on studies involving nearly 40,000 patients.

A review of 28 studies ranging in size from 59 to 16,608 adults and with follow-up times of 0.7-6.8 years showed a significant association between HT use and an increased risk of total stroke, with an odds ratio of 1.29. The review supports previous studies that showed an association between increased risk of stroke and hormone therapy, reported Philip Bath, M.D., and Laura Gray of the University of Nottingham, Nottingham, England (BMJ [Epub ahead of print], January 2005. Article DOI number: 10.1136/bmj.38331.655347.8F. Available from: www.bmj.com.).

Twelve studies included women taking estrogen only; 16 included women taking estrogen plus progesterone. The average ages ranged from 55 to 71 years, and three studies of estrogen combined with progesterone included men. All but five studies were placebo-controlled, and 11 small trials recorded no stroke events.

Overall, 2% of patients randomized to no HT suffered strokes, but the risk of stroke among women randomized to HT increased 29%, primarily because of the increase in ischemic stroke.

In addition, the severity of stroke increased with HT use; the chance of a poor functional outcome, defined as either death or disability and dependency, was 56% higher among women randomized to HT.

In particular, HT use was associated with a significant increase in the risk of ischemic stroke in 16 studies (OR 1.29). HT use also was significantly associated with an increased risk of nonfatal stroke in 21 studies (OR 1.23), and with an increased risk of stroke leading to death or dependency in 14 studies (OR 1.56).

HT was not significantly associated with hemorrhagic stroke or transient ischemic attacks in 17 studies and 22 studies, respectively. However, none of the studies showed any association between HT and a reduction of stroke risk, despite data from previous observational studies suggesting a protective effect of HT against cerebrovascular events.

The investigators suggested that phytoestrogens, which were not included in these studies, may have yielded different results.

They also noted that the estrogen dose in several trials was higher than the standard starting doses of conjugated equine estrogen and estradiol in Great Britain, 0.625 mg and 1 mg, respectively, and studies of lower doses may yield different results.

Enterococcus Behind Many UTIs in Elderly; Tx Resistance Rises with Age

SAN FRANCISCO — The culprit behind most noncomplicated urinary tract infections in outpatients—*Escherichia coli*—plays less of a role as patients age, a study of 2,751 urine cultures showed.

Other pathogens, particularly enterococcus, played a greater role in urinary tract infections (UTIs) in older patients, and the rates of antibiotic-resistant enterococcus increased in older patients, David J. Blehar, M.D., said at the annual meeting of the American College of Emergency Physicians.

The prospective study of serial cases from 80 outpatient offices and four emergency departments divided adult patients into five age groups and looked at the pathogens responsible for UTIs and their susceptibility to antibiotic treatment.

In the youngest group, 18- to 40-year-olds, *E. coli* caused more than 75% of UTIs, a finding similar to previous estimates that *E. coli* causes 75%-90% of UTIs overall. The role of *E. coli* fell with increasing age, however, with a proportional increase in other pathogens. In patients older than 80 years, *E. coli* accounted for fewer than half of UTIs, but enterococcus caused up to 20% of UTIs, said Dr. Blehar of the University of Massachusetts, Worcester.

The study looked at rates of resistance to four antibiotic therapies. Although trimethoprim/sulfamethoxazole

(TMP/SMX) is the formal first-line drug therapy for noncomplicated UTI, guidelines suggest substituting a fluoroquinolone in areas where rates of *E. coli* resistance to TMP/SMX exceed 10%-20%. Dr. Blehar's institution and others have adopted the fluoroquinolone levofloxacin as first-line therapy for noncomplicated UTIs. The study also looked at ceftriaxone and ampicillin resistance.

E. coli generally maintained susceptibility to the various antibiotics across age groups, except for a statistically non-significant trend toward greater resistance to TMP/SMX with increasing age. Pathogen resistance to ceftriaxone or ampicillin also held steady across age groups.

While *E. coli* resistance rates to levofloxacin remained low across age groups, enterococcus resistance rates climbed with age. In patients aged 70 years or older, 22% of enterococci were resistant to levofloxacin, and 38% of enterococci showed resistance to levofloxacin in patients aged 80 years and older.

"Urine Gram stain is not a routine study done in our institution, but it may be warranted in this subset of patients to aid in the work-up of UTI," Dr. Blehar said. "If gram-positive UTI is identified, we would add additional coverage for enterococcus."

—Sherry Boschert