Reliability Key to Contraception for Epileptic Women

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

All women of childbearing age—including those who have epilepsy—should be offered a prescription for emergency contraception.

The intrauterine device (IUD) and the depot medroxyprogesterone acetate (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. The depot medroxyprogesterone acetate (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."

The second choice for women on the CYP450-enhancing drugs would be higher-dose oral contraceptives. No OC on the market is "high dose." "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 DPMA shot reliably suppresses ovulation," Dr. Davis said. "This is an important consideration for seizure frequency that's responsive to fluctuations in the menstrual cycle."

All women of childbearing age—including those with epilepsy—should be offered a prescription for emergency contraception, Dr. Davis said. No studies have assessed any possible interactions with AEDs, but "there's no downside to giving it," she said.

"Give it anyway. It doesn't interrupt an established pregnancy. There's no harm in giving it and you might prevent something that would be good to prevent." ■

No Need for 24-Hour Fast Before Introducing Ketogenic Diet in Children

NEW ORLEANS — A gradual induction of the ketogenic diet that spares children the need to fast is just as effective in seizure reduction as the traditional protocol, Christina Bergqvist, M.D., said at the annual meeting of the American Epilepsy Society.

The gradual induction protocol is also easier on children and their families, and is associated with fewer adverse events. Many families are put off by the idea of 24-48 hours of fasting, said Dr. Bergqvist of the Children's Hospital of Philadelphia.

"The management of this diet has changed very little since it was invented about 84 years ago," she said in an interview. "For some families, who are already dealing with intractable seizures, the idea of putting their child through the fasting and the adverse events that go along with it is enough for them to decide against it."

Dr. Bergqvist randomized 48 children with intractable seizures to either the standard fasting or gradual induction approach. The children were aged 1-14 years (median age 5 years). They had not responded to a median of eight antiepileptic drugs. Half of the group had generalized seizures, and half had partial seizures.

Each group began the study with a day of regular meals. The standard induction group then had a 24-hour fast, followed by 4 days of full ketogenic diet meals (90% fat) of increasing calorie amounts (33% of normal daily calories on day 1, 67% on day 2, and then 100% of daily calorie intake).

The gradual induction group had a day of regular meals followed by 4 days of gradually increased fat intake: 50% of calories from fat, 69% from at, 82% from fat, and, finally, standard ketogenic meals of 90% calories from fat.

Ketosis was measured by whole blood levels of -hydroxybutyrate (BHB). BHB levels increased more rapidly and to a higher degree in the standard induction group, from about 1 mol/L on day 1 to 4.5 mol/L on day 3. Thereafter, BHB remained around 5 mol/L. The BHB level rose more slowly in the gradual induction group, not reaching 4 mol/L until day 5 and reaching 5 mol/L by day 6.

Dr. Bergqvist said she considers BHB a more accurate measurement of ketosis than urinary acetoacetate, the level of which can be affected by dehydration. Additionally, she said, BHB is thought to have a significant impact on seizure reduction. Animal studies have shown that BHB potentiates the production of the neurotransmitter -aminobutyric acid. At 3 months' follow-up, during which the children maintained the full ketogenic diet, there was no significant difference in seizure reduction between the two groups. In the standard induction group, 58% of patients had a seizure reduction of greater than 50%, and 21% were seizure free. In the gradual induction group, 67% of patients had a seizure reduction of greater than 50% at 3 months, and 21% were seizure free.

Dr. Bergqvist is still evaluating the adverse events but did say that hypoglycemia, nausea, vomiting, diarrhea, and lethargy were less frequent and less severe with gradual induction.

"Because these side effects can be pretty significant for some children, everybody has to start the diet as an inpatient, and usually only large university medical centers can offer it," she said. "But based on the results of this study, it's possible that we could adjust the protocol, and if the side effects were less severe, maybe the diet could be more widely offered." ■

Children With Myoclonic-Astatic Epilepsy Appear Highly Responsive to Ketogenic Diet

NEW ORLEANS — The ketogenic diet appears to be especially effective for reducing seizures in children with myoclonic-astatic epilepsy of Doose, Linda C. Laux, M.D., reported in a poster at the annual meeting of the American Epilepsy Society.

"The diet is a particularly efficacious treatment modality for this particular epilepsy syndrome," said Dr. Laux of Northwestern University, Chicago. "It should be considered early in the course of therapy for children with myoclonic-astatic epilepsy."

Six of 10 children became free of seizures after an average of 12 months on the ketogenic diet.

DR. LAUX

Myoclonic-astatic epilepsy (MAE) usually begins before 5 years of age in developmentally normal children. It includes a mixture of generalized seizures including myoclonic-astatic, atonic-astatic, myoclonic, absence, generalized tonic-clonic, and tonic vibratory seizures. These seizures are often difficult to control, and cognitive outcome is variable. An EEG typically shows irregular fast spike-and-wave discharges with a monomorphic 4- to 7-Hz parasagittal rhythm.

Dr. Laux presented the results of a retrospective chart study of 28 pediatric patients who were placed on the ketogenic diet over a 2-year period. Of the group, 10 had both a clinical and an EEG-aided diagnosis of MAE, 2 had cryptogenic localized epilepsy, and 16 had symptomatic generalized epilepsy (including Lennox-Gastaut syndrome periodic spasms, diffuse encephalopathy with multifocal seizures, severe myoclonic epilepsy of infancy, and generalized epilepsy not otherwise specified).

To be included in the review, patients in the study group had to be on the diet for at least 6 months; the average duration of the diet was 12 months. The best outcomes were seen in those with MAE: Six became seizure free, one had a reduction in seizure frequency of greater than 90%, and three had reductions of 50%-90%.

Children with the other epilepsies did much worse. Among those with localized epilepsy, one became seizure free, but six had a seizure reduction of less than 50%. Among those with generalized epilepsy, two had a reduction of 50%-90% and five had a reduction of less than 50%.

Both of the children with spasms and two with localization-related epilepsy had seizure reductions of less than 50%. ■