Low-Dose Continuous OC Found Effective in Two Studies

BY BOB BABINSKI
Contributing Writer

Two studies demonstrated a positive response to an investigational low-dose continuous oral contraceptive in terms of suppression of ovulation and premenstrual symptoms and return to normal ovulation, researchers reported at the joint annual meeting of the American Society for Reproductive Medicine and the Canadian Fertility and Andrology Society.

Both studies were sponsored by Wyeth, which has submitted the contraceptive for approval by the Food and Drug Administration. If approved, the contraceptive would be marketed under the trade name Lybrel.

The oral formulation of 20-mcg ethinyl estradiol and 90-mcg levonorgestrel is designed to be taken daily with no hormone-free intervals. One study, involving 37 women aged 18-35 years, showed complete inhibition of ovulation in all women while on the oral formulation.

"We showed that none of the subjects developed follicles equal to or greater than 10 mm during treatment," said study investigator Susan A. Ballagh, M.D., of CONRAD Clinical Research Center at Eastern Virginia Medical School, Norfolk. "We used a very conservative measure to show there was no ovulation."

Participants followed the continuous oral contraception (COC) regimen for 84 days, using three pill-pack segments.

After discontinuation of contraception, the time to return to normal ovulation—defined as serum progesterone levels greater than 5 ng/mL—was a mean of 20 days. A total of 95% of subjects ovulated within 25 days after discontinuation.

'Almost all the response occurred right away. That's fast.'

DR. FREEMAN

The study did not include women unable to meet the compliance demands of the program, and Dr. Ballagh said that's an element that will have to be explored in a future study.

"Our next question is, when women are taking the pills in less controlled circumstances, does this COC formulation in fact lead to less chance of them becoming pregnant," she said. "Patient failure rates of pills in common use is estimated to be at least 3%, and some have recently suggested that it may be as high as 7%."

The second study found that the same COC regimen significantly alleviated premenstrual symptoms.

A total of 278 women with a history of cycle-related symptoms or dysmenorrhea were monitored during three cycles of the COC regimen, with no pill-free interval. The subjects maintained a daily diary, rating mood, behavior, pain, and physical symptoms using the Penn Daily Symptom Rating scale. Two-thirds of the women improved their scores by 50% in the first 28-day cycle (one pill pack). In addition, work productivity was improved.

"What impressed me the most was the very immediate response of the first cycle and the strong response at end point," said lead investigator Ellen Freeman, Ph.D., of the University of Pennsylvania in Philadelphia. "Almost all the response occurred right away. That's fast. Secondly, I was surprised that all four of the symptom subscales seemed to respond similarly."

The study, which was not placebo-controlled, shows the impact of the COC on PMS symptoms to be more effective than what has been reported with selective serotonin reuptake inhibitors.

"SSRIs don't appear to reduce the symptoms to their postmenstrual level for women overall, which is what is considered the normal asymptomatic level. This data suggest this therapy does, but that has to be confirmed with a placebo-controlled study," said Dr. Freeman. ■

Oral Contraceptives Could Lessen Premenstrual Worsening of Depression

ATLANTA — The use of oral contraceptives appears to decrease the premenstrual worsening of depressive symptoms, Hadine Joffe, M.D., said at the annual meeting of the American Psychiatric Association.

In preliminary research, the use of augmentation with oral contraceptive pills was evaluated in women who already take antidepressants but experience worsening symptoms during the luteal phase of the menstrual cycle, said Dr. Joffe, a psychiatrist at Massachusetts General Hospital, Boston.

The 17 women who completed the study reduced their depression scores during the premenstrual phase on the Daily Record of Severity of Problems Scale from a median score of 58 to a median score of 35.3. In addition, their Montgomery-Asberg Depression Rating Scale scores improved from a median of 20 to a median of 4.

A total of 26 women, aged 18-45 years, were randomized to a double-blind treatment with an oral contraceptive that contained drospirenone and ethinyl estradiol (Yasmin). One group received additional ethinyl estradiol on days 22-28, which is the typical placebo week of the oral contraceptive pills.

To be eligible for the 2-month study, women had to have regular 25- to 35-day menstrual cycles, a depressive disorder, and stable use of an antidepressant for 2 months or more. In addition, all participants completed a run-in tracking month before starting the oral contraceptive pill. Depressive symptoms were found to be present only during the premenstrual phase. Of the women included in the study, 82% had major depression, 12% had minor depression, and 6% had dysthymia.

The oral contraceptive pills were well tolerated. There seemed to be no difference between women who received the additional ethinyl estradiol during days 22-28 of their cycles and those who received placebo during that time. The study was sponsored by the National Alliance for Research on Schizophrenia and Depression. Berlex, which manufactures Yasmin, provided product support.

—Mary Ellen Schneider

Continuous OCs Suppress Ovulation Better Than Standard OCs

BY BOB BABINSKI
Contributing Writer

MONTREAL — Continuous oral contraceptive regimens suppress ovulation better than do conventional 21-day regimens, according to research presented at the conjoint annual meeting of the American Society for Reproductive Medicine and Canadian Fertility and Andrology Society.

This effect of continuous oral contraceptives (COCs) has not been previously reported, said Roger Pierson, Ph.D., explaining that COCs have been promoted primarily for their ability to eliminate cyclic bleeding and premenstrual symptoms.

'The side effect of not bleeding is much more effective contraceptive control.'

DR. PIERSON

"The side effect of not bleeding is more effective contraceptive control," said Dr. Pierson, professor of obstetrics, gynecology, and reproductive sciences at the University of Saskatchewan, Saskatoon.

In his single-center, randomized, open-label trial which was sponsored by the Canadian Institutes of Health Research, Dr. Pierson compared two different formulations of traditional 21-day oral contraceptive (OC) regimens with the same formulations given continuously for 28 days per cycle.

Women took the pills for three cycles. Transvaginal ultrasonography was used to monitor follicular development once weekly for the first 3 weeks of the study, then every third day until the end of the third cycle.

The nine women on the 28-day regimen of 30-mcg ethinyl estradiol/150-mcg levonorgestrel and the 11 women on the 28-day regimen of 35-mcg ethinyl estradiol/250-mcg norgestimate showed less follicular development than did those given the traditional 21-day regimens of both formulations (8 women in each group).

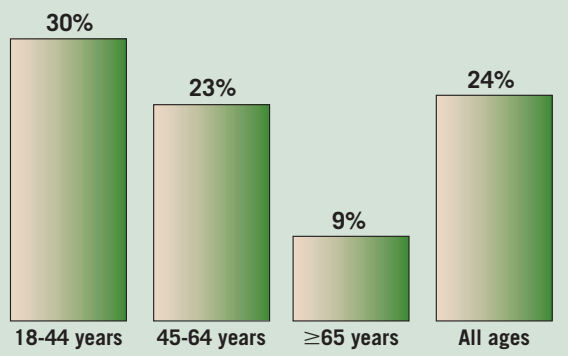
Those on the continuous regimen had no dominant follicles and no ovulations. Those on the standard regimens produced a total of eight dominant follicles, two of which ovulated. The time to return to normal ovulation during the first cycle after contraceptive discontinuation was measured in the conventional OC and COC groups and compared with historical data for ovulation after discontinuation of other forms of contraception.

Follicles developing after discontinuation of COCs took about 5 days longer to ovulate than did follicles developing after discontinuation of OCs. Time to ovulation for both OC groups was longer than in natural cycles. In addition, serum estradiol 17-β at a follicular diameter of 18 mm was significantly higher after discontinuation of OCs, compared with natural cycles. Dr. Pierson said the delayed return to normal ovulation was not significant, but noted the study's short length. ■

Kate Johnson of the Montreal Bureau contributed to this report.

DATA WATCH

Younger Women Are More Likely to Delay or Forgo Needed Health Care Because of Cost



Note: Based on a national survey of 2,766 women conducted from July 6 to Sept. 26, 2004.
Source: Kaiser Family Foundation

KEVIN FOLEY, RESEARCH