New Spermicide Matches Nonoxynol-9 in Efficacy

ARTICLES BY BRUCE K. DIXON
Chicago Bureau

LA JOLLA, CALIF. — The new spermicidal microbicide BufferGel, when used with a diaphragm, is a safe, acceptable contraceptive with efficacy that is noninferior to the Gynol II–diaphragm combination, according to a phase III multicenter study.

"These important findings demonstrate that a new spermicide and potential microbicide works as well as the currently marketed nonoxynol-9–based product," Dr. Kurt T. Barnhart said in an interview. "The advantages of this new product, the first nonsurfactant spermicide demonstrated to work in decades, is that it is potentially safer than N-9 and may also prevent HIV transmission," said Dr. Barnhart, who is director of clinical research for the department of obstetrics and gynecology at the University of Pennsylvania in Philadelphia.

'Differences were within 6% ... , so we can say these two products are noninferior to each other.'

DR. BARNHART

Whereas N-9 is a surfactant that indiscriminately disrupts epithelial cell membranes and kills sperm before they can enter the uterus, BufferGel is a nondetergent agent that keeps the pH in the vagina acidic instead of raising it to neutrality when sperm are introduced, Dr. Barnhart said at the annual meeting of the Association of Reproductive Health Professionals.

"By keeping those natural defenses acidic, BufferGel is toxic to both sperm and some microbes, including HIV, though the phase II-III HIV arm of the trial is still underway in Africa," he explained.

These new findings emerged from an 11-center noninferiority trial stemming from the hypothesis that BufferGel is noninferior to Gynol II when both compounds are used with a diaphragm, with noninferiority being defined as within 6% of each other in terms of contraceptive efficacy.

This was a two-part trial: Study 1 was a double-blind, randomized, direct comparison of the two preparations. A total of 621 women used BufferGel and 300 received Gynol II. After completing six cycles, they could elect to continue for an additional six cycles as part of an open-label BufferGel study (study 2), and 234 did so. Of those, 63 discontinued before 6 months elapsed.

Study 1 showed the two compounds to be comparable in virtually all respects. "All the differences favor BufferGel, but those differences were within 6% of each other, so we can say these two products are noninferior to each other," said Dr. Barnhart. About the same percentage (3%) in each group thought adverse events warranted discontinuation, Dr. Barnhart said.

At cycle six, 68% of BufferGel users and 70% of Gynol II users said they would definitely or probably use the product if available, while 54% of BufferGel users and 57% of Gynol II users preferred the system to condoms.

BufferGel's typical use pregnancy rate was 10% in this study sponsored by the National Institute of Child Health and Development Clinical Trials Network. ■

Unfulfilled Sterilization Requests Linked to Low Contraceptive Use

LA JOLLA, CALIF. — Women who request sterilization but do not undergo the procedure may be at high risk for contraceptive nonuse and repeat pregnancy, according to a descriptive pilot study conducted in Chicago.

University of Illinois researchers recruited a total group of 103 postpartum patients, predominantly African American and Latino women; 29 of these patients did not request sterilization. Of the 74 who did request sterilization, 34 failed to undergo the procedure, said Dr. Melissa Gilliam, now section chief of family planning and contraceptive research at the University of Chicago.

'We have to realize that these women are at risk for repeat pregnancies.'

DR. GILLIAM

Women who requested sterilization were more likely to be of lower gravidity, to have a preexisting medical condition, to have a history of pregnancy while using birth control, and to be younger at first pregnancy, Dr. Gilliam said at the annual meeting of the Association of Reproductive Health Professionals.

Reasons for not choosing sterilization included fear of the procedure or of anesthesia, the existence of a medical condition, institutional logistics, and poor birth outcome, Dr. Gilliam explained.

"At discharge, one-quarter of women in the unfulfilled sterilization group were more likely to be using no method of contraception and have no plan for future contraceptive use, and those who chose a method were likely to be dissatisfied with it.

"In the cohort that had not requested sterilization, all but 4% were satisfied with the contraceptive choice they had made—chiefly IUDs—suggesting that they were counseled for reversible contraception," she said.

However, more than 30% of the women said that they had received no predischarge counseling about reversible contraceptives, Dr. Gilliam noted.

At 6 months after discharge, she said, the data showed that women who did not undergo sterilization after having requested it were still not using a contraceptive and in some cases had become pregnant.

At 1 year, of the 34 women who had requested but did not undergo postpartum sterilization, 8 had undergone sterilization, 6 were pregnant, 2 were lost to follow-up, and the rest were using some type of contraceptive, primarily Depo-Provera (7) or condoms (3).

Dr. Gilliam believes that women often seek sterilization because they have gotten pregnant while on the birth control pill and now want control over their own fertility.

"And for many women, this can be quite hard to achieve," she said. "We have to realize that these women are at risk for repeat pregnancies and that they experience difficulties dealing with contraception post partum," she said in an interview. ■

Levonorgestrel IUS Gets High Marks in U.S. Multicenter Study

LA JOLLA, CALIF. — American women and their physicians have given thumbs up to the levonorgestrel-releasing intrauterine system. The verdict came in a 29-center open-label trial, the first big test for the system in the United States, Dr. Jeffrey T. Jensen said in a poster presentation at the annual meeting of the Association of Reproductive Health Professionals.

The levonorgestrel-releasing intrauterine system (LNG IUS), a T-shaped polyethylene frame with a steroid reservoir, is marketed as Mirena and was approved by the Food and Drug Administration in 2000 for intrauterine contraception for up to 5 years.

Mirena was launched by Berlex in the U.S. market the following year; whereas it is approved in other countries for a number of indications, such as heavy uterine bleeding and endometrial hyperplasia, its sole U.S. indication is for intrauterine contraception.

"This study was done to gain experience for U.S. clinicians leading to the marketing of this very important and significant device," said Dr. Jensen, who is an adviser to Berlex, which provided funding for this study.

"We waited many years for the levonorgestrel-releasing intrauterine system," said Dr. Jensen, expressing the hope that the LNG IUS will soon receive FDA approval for additional indications.

In this 29-center study, 509 women met the eligibility criteria for inclusion in the intention-to-treat analysis. All but 2 of the women had successful IUS insertions, and 402 women completed the 1-year study. The mean age of participants was 32, and over half were white. All but 37 of the women had had more than a single prior delivery, and the average uterine cavity size was 7.8 cm.

Among the study findings were the following:

► Device insertion was successfully carried out on the initial visit 96% of the time.

► Investigators rated 92% of insertions as "easy," while 68% of subjects reported "mild" or "no" pain at insertion.

► Based on a 7-point scale from very "dissatisfied" to "very satisfied," 95% of subjects and 91% of providers rated the adequacy of product information at 6 or 7.

► More than four-fifths of subjects were "very satisfied" with the LNG IUS. Reasons for liking the product included ease of use, contraceptive reliability, and acceptable changes in bleeding patterns.

► The vast majority of investigators stated that between one and five insertions are necessary to feel comfortable with Mirena insertion.

"The reasons for noninsertion included cervical stenosis in one woman and a uterine cavity less than 6 cm in the other," said Dr. Jensen, who is Leon Speroff professor of obstetrics and gynecology at the Oregon Health and Science University, Portland.

About half the women received premedication with ibuprofen, and only 6% of the subjects required cervical dilation, half as a planned portion of the insertion and half after difficulty with passing the device, he said.

Continuation rates at 3, 6, and 12 months were 95%, 87%, and 79%, respectively. Most discontinuations were due to adverse events, including complications with the device. There were 26 incidents of expulsion or accidental removal and no cases of perforation.

Bleeding results were similar to those in published international studies, Dr. Jensen said.

When the bleeding experience was divided into 90-day treatment intervals, the number of bleeding and spotting and bleeding-only days decreased throughout the study, with about 15% of subjects reporting amenorrhea and only 14% reporting spotting at the end of the 12-month period.

"Most women given the option of continuing with the device, which received FDA approval during the course of the study, opted to do so," Dr. Jensen said.

Discussant Dr. David A. Grimes agreed that American women and their physicians have looked forward to Mirena's approval for a long time.

"Women deserve this product, and they now have it," said Dr. Grimes, who disclosed that he serves on the Berlex speaker's bureau. Although the study provided no surprises, it showed the product to be effective, safe, and well tolerated, said Dr. Grimes, who is vice president of biomedical affairs for Family Health International. ■