Infertility & Reproduction Health Center

Study: Infertility Treatments No Help

Drug Treatment and Intrauterine Insemination May Not Work When Used Separately

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Aug. 7, 2008 -- Two common infertility treatments do not improve fertility, according to a study conducted in the U.K.

Researchers compared drug treatment to induce ovulation with no treatment; they also compared intrauterine insemination -- in which the sperm are placed inside the uterus to facilitate fertilization -- with no treatment. They only studied couples with unexplained infertility, only one of many reasons for failing to conceive.

"What we found is that neither of these popular and commonly used treatments offered a higher birth rate than no treatment at all," says Siladitya Bhattacharya, MD, a professor of reproductive medicine at the University of Aberdeen in Scotland and the study's lead author. "What we've shown is that neither of these first-line treatments is better than [the couples] trying themselves."

The rate of live births was 17% for the no-treatment group, 14% for the medication group, and 23% for the insemination group. "There were no significant differences between them," Bhattacharya tells WebMD.

But U.S. fertility experts who reviewed the study for WebMD say the findings probably have little relevance for infertile couples with unexplained infertility in the U.S. because the two infertility treatments -- each compared singly to no treatment in the U.K. study -- are typically used in combination here. The dose of medication used in the U.K. study is also much lower than what is typically prescribed in the U.S.

Infertility Treatments Fall Short

Bhattacharya and his colleagues recruited 580 infertile women, average age 32, from five hospitals in Scotland, randomly assigning them to one of three groups:

- The medication group took a 50 milligram oral dose of Clomid. If that overstimulated the ovaries, the dose was dropped to 25 milligrams. They were given advice about the best times to have intercourse.
- In the intrauterine insemination group, women monitored their hormone levels and when they were ideal, the sperm were placed inside the uterus to facilitate fertilization.
- The no-treatment group was given general advice about the need to have intercourse regularly during the six-month study.

All the women had been trying unsuccessfully to become pregnant naturally for at least two years. All had unexplained infertility, a condition in which doctors are unable to find any abnormalities after doing tests such as semen analysis, evaluating the fallopian tubes, or ovulation. About one in seven couples are infertile, with about one-quarter of those experiencing unexplained infertility, according to the researchers.

Comparing Infertility Treatments
At the study's end, 32 women (17%) in the no-treatment group had given birth, compared to 26 (14%) in the medication group and 43 (23%) in the insemination group.

More women who got either the insemination or the medication found the process more acceptable than those who got no treatment, the researchers found.

Bhattacharya believes his team is the first to compare the treatments in this way. "Most people have compared treatment A with treatment B."

"Although it may seem a bit counterintuitive, this is the one area of medicine where doing nothing could be as effective as going for any of these treatments," he says.

The researchers write that the findings challenge current practice in the U.K., with recommendations now favoring what they found ineffective -- insemination without stimulation by a medication and lower doses of the ovulation-inducing medication to decrease the risk of multiple pregnancies.

The study is published in Online First at bmj.com.

**Infertility Treatments: Second Opinion**

In an editorial accompanying the study, experts from the Assisted Conception Unit at Guy's and St. Thomas' Hospital NHS Foundation Trust in London write that treatment should be individualized, taking into account the woman's age, the duration of infertility, and other factors.

While U.S. experts point out that they generally use ovarian stimulation and intrauterine insemination in combination, the editorial authors point to a study, published in *The Lancet* in 2006, that questions the benefit of even the combination treatment compared with no treatment.

They conclude that the generally higher-tech option, in vitro fertilization -- in which eggs and sperm are fertilized in the lab, and then the embryo is implanted in the uterus -- may be the most cost-effective option.

Treatment approaches differ in the U.K. and U.S., says Donna Session, MD, chief of the division of reproductive endocrinology and fertility and associate professor of obstetrics and gynecology at Emory University School of Medicine in Atlanta. "In the U.S., generally higher doses [of Clomid] are used, typically 100 milligrams a day." And medication and insemination are typically combined.

"If anything, the take-home point from this study is, in the group where they did insemination alone -- without any fertility drug -- there wasn't a significant increase in pregnancy," she tells WebMD. "Just doing insemination alone is probably not going to really increase a person's chance of pregnancy."

Individualizing treatment recommendations is important, she says, taking into account a woman's age and other factors such as "ovarian reserve" testing to evaluate the quality of the ovaries and how likely a woman is to become pregnant.

"If you have a patient with good results on the ovarian reserve testing, then expectant management [no treatment] might be something the patient might desire," she says.

The results particularly don't apply to U.S. women if they are treated by a fertility specialist, says Tracey Telles, MD, chief of reproductive endocrinology and infertility at the Kaiser Permanente Diablo Service Area in Walnut Creek, Calif. "In the United States, the indication of unexplained infertility is definitely managed more aggressively than it was in this study."

But the less aggressive, less expensive fertility treatments are worth a try in some women, says Mousa Shamonki, MD, director of in vitro fertilization and assisted reproduction at the University of California Los Angeles Medical Center. For unexplained infertility, the lower-tech options
include those evaluated in the U.K. study and also injections of hormones combined with intrauterine insemination, he says.

For other types of fertility problems -- other than unexplained infertility -- Clomid alone may work, Shamonki says. "Clomid works well for women who aren't ovulating [regularly]," he says, such as women with polycystic ovary syndrome. PCOS is a leading cause of female infertility.

Insemination alone may work for couples who have mild male-factor infertility or who have a history of cervical surgery, he says.

If none work, IVF techniques can be tried, he says; if couples are running out of time, they may opt to get more aggressive more quickly.

Psychologically, couples can find waiting frustrating, says Michael Diamond, MD, professor of obstetrics and gynecology at Wayne State University, Detroit. "Usually after a year of trying and not succeeding, the last thing a couple wants to hear is 'Go home and try again.'"