Encourage Healthy BMI in Patients Before IVF

Study of 5,800 IVF cycles shows a trend toward decreasing success rates with increasing BMIs.

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PHILADELPHIA — Patients considering in vitro fertilization should be encouraged to aim for a healthy body mass index before they start treatment, results of a large retrospective study suggest.

"There was a trend toward decreasing success rates with increasing BMIs," reported lead investigator David Ryley, M.D., of Beth Israel Deaconess Medical Center, Boston, and Boston IVF, a private fertility clinic.

The study reviewed more than 5,800 fresh, non-donor in vitro fertilization (IVF) cycles at Boston IVF in which the patient's BMI had been recorded, he reported at the annual meeting of the American Society for Reproductive Medicine.

Patients were divided into five groups according to BMI: under 20 kg/m^2, 20-24.9 kg/m^2, 25-29.9 kg/m^2, 30-34.9 kg/m^2, and more than 35 kg/m^2. Women with a BMI of more than 40 kg/m^2 are not allowed to undergo IVF at the center, he said.

There was no difference between the groups with respect to the number of mature follicles, number of oocytes retrieved, number of mature oocytes, the number of cycles per patient, and the number of embryos transferred. Still, patients in the highest BMI category had a significantly lower implantation rate and clinical pregnancy rate, compared with the other BMI groups.

Although the clinical pregnancy rate ranged from about 27% to almost 33% in the lower BMI categories, it was not quite 22% in the highest BMI category.

Similarly, the implantation rate ranged from 18% to 20% in the lower BMI categories, but it was only 13% in the highest BMI category.

Unlike previous published studies on this topic, the current study did not find an association between extremely low BMI and poor IVF success rates, Dr. Ryley said.

Although the clinical pregnancy rate ranged from 27% to almost 33% in the lower BMI categories, it was not quite 22% in the highest BMI category.

"The best data in the literature suggest that severely low BMIs under 20, or under 18, affect the hypothalamic-pituitary axis, such that patients have irregular menstrual cycles and, therefore, have an impaired chance of fertility," he told this newspaper. "But in our study the patients with the lowest BMIs actually had the highest pregnancy rates—although the difference was only significant when compared with the highest BMI category."

The study's findings are consistent with other reports of how excess weight can impact hormonal balance and the quality of oocytes and embryos, he said. Weight loss can often correct problems such as hyperinsulinemia and polycystic ovarian syndrome, which can in turn increase fertility.

But physicians should also know how to manage an IVF cycle in an overweight patient who has not lost weight.

"We know that patients with high BMIs require higher doses of medications, particularly gonadotropins, to stimulate folliculogenesis, and they often require longer cycles," Dr. Ryley said. "By increasing the doses of these medications, you can often get an adequate number of oocytes. However, in many of these patients, hormonal imbalances may have a deleterious effect on the quality of oocytes you get." ■

Single-Dose Letrozole Equal to Multiple-Dose Regimen in IUI

PHILADELPHIA — Patients with unexplained infertility who undergo ovarian stimulation before intrauterine insemination have comparable pregnancy rates and side effects when treated with a single 25-mg dose of letrozole, compared with five daily doses of 5 mg each, Marinko M. Biljan, M.D., reported.

"A single dose may be more practical and convenient for patients," commented Dr. Biljan, medical director of the Montreal Fertility Centre, who reported his findings during the annual meeting of the American Society for Reproductive Medicine.

Letrozole, an aromatase inhibitor, was originally used for ovarian stimulation in infertility patients who responded poorly to clomiphene citrate or gonadotropin stimulation.

Dr. Biljan's previous work in this area has shown that, even in good responders to gonadotropins, letrozole used in combination with gonadotropins can reduce gonadotropin requirements by up to 50%.

Letrozole is considered by some specialists to be as effective as and possibly even superior to clomiphene for most patients undergoing intrauterine insemination (IUI).

But the traditional 5-mg dose starting at day 3 of the menstrual cycle and given through day 7 is often impractical, said Dr. Biljan, who now has experience with approximately 2,000 letrozole cycles.

"Patients would call us up and say they forgot their dose yesterday and [ask] should they take two doses today? It was becoming a problem," he said.

Inspired by a pilot study of 7 patients who were treated with a single dose of letrozole and had similar responses to historical controls, Dr. Biljan launched his prospective, double-blind, randomized trial of 20 patients. The patients, all under age 40, had at least 12 months of unexplained infertility; they all had ovulatory cycles, patent tubes, and normal sperm parameters in their male partners.

The women in the study were randomized to receive either one 25-mg tablet of letrozole on day 3 of their menstrual cycle and a placebo pill on each of the next 4 days, or five daily tablets of 5-mg letrozole each.

"We were petrified of the possible side effects of such a large, single dose of letrozole, but in fact, there were actually more side effects reported in the women who took the smaller daily doses, although the difference was nonsignificant," Dr. Biljan said.

A baseline transvaginal ultrasound scan was performed between days 1 and 3, along with a baseline blood test. These tests were repeated on day 9, after which daily scans were performed until the largest follicle reached a diameter of 18 mm.

Ovulation was then triggered with 10,000 U of β-hCG, and IUI was performed 36 hours later.

In addition to a similar rate of side effects, both groups had similar serum FSH and estradiol levels, similar numbers of follicles, and similar endometrial thicknesses.

Pregnancy rates were also similar, with two pregnancies in the single-dose group and one in the multi-dose group; this difference was not statistically significant.

Although he did not present the figures at the meeting, Dr. Biljan noted that he has now doubled the number of patients in his study and has achieved the same results. ■

Acupuncture in IVF Linked to Lower Miscarriage and Ectopic Rates

PHILADELPHIA — Women who receive acupuncture during the stimulation phase of an in vitro fertilization cycle and again immediately after embryo transfer have a higher live-birth rate than do controls, according to the first acupuncture study with this end point.

"Other studies have looked at pregnancy rates, but what is really important is whether or not there is a baby," said Paul C. Magarelli, M.D., who reported his findings at the annual meeting of the American Society for Reproductive Medicine.

The retrospective study included 131 women who were undergoing standard in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI). All of these women were considered good prognosis candidates for IVF/ICSI and were given the choice of having acupuncture.

A total of 83 women declined (controls) and 48 accepted.

There were no significant differences between the two groups in terms of infertility diagnoses, demographics, and treatment protocols, except that sperm morphology was slightly better in the partners of women receiving acupuncture (7.3% vs. 5.9 % normal forms with strict criteria evaluation), and the average uterine artery pulsatility index was lower in the acupuncture group (1.57 vs. 1.72), said Dr. Magarelli of the department of ob.gyn. at the University of New Mexico, Albuquerque.

The study found that pregnancy rates per embryo transfer were not significantly different between the two groups (50% in the acupuncture group and 45% in controls).

The miscarriage rate was almost halved in the acupuncture group (8% vs. 14%).

In addition, the rate of ectopic pregnancies was significantly lower in the acupuncture group—0 of 24 pregnancies (0%) vs. 2 of 37 pregnancies (9%), said Dr. Magarelli, who is also in private practice in Colorado Springs and Albuquerque.

Thus, the live-birth rate per IVF/ICSI cycle was significantly higher in the acupuncture group than in controls (21% vs. 16%).

"The live-birth rate per pregnancy is an even more telling number, since some cycles get cancelled. There was a 42% live-birth rate per pregnancy in the acupuncture group, compared to a 35% rate in the nonacupuncture group," Dr. Magarelli said in an interview with this newspaper.

"We believe that what we are doing is improving the uterine environment such that implantation is improved," he added.

The study used two acupuncture protocols.

The Stener-Victorin electrostimulation protocol—which has been shown to reduce high uterine artery blood flow impedence, or pulsatility index (Hum. Reprod. 1996;11:1314-7)—was used for eight treatments during ovarian stimulation.

The second acupuncture technique—the Paulus protocol, which has been associated with improved pregnancy rates (Fertil. Steril. 2002;77:721-4)—was used within 24 hours before the embryo transfer and 1 hour after.

"This protocol has demonstrated reductions in uterine contractility, so by relaxing the uterus before the embryo transfer and immediately after, we felt we were setting up a better environment for implantation," Dr. Magarelli said. ■