

AMIGOS: Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation

BACKGROUND:

The standard therapy for women with unexplained infertility is gonadotropin or clomiphene citrate. Ovarian stimulation with letrozole has been proposed to reduce multiple gestations while maintaining live birth rates.

METHODS:

We enrolled couples with unexplained infertility in a multicenter, randomized trial. Ovulatory women 18 to 40 years of age with at least one patent fallopian tube were randomly assigned to ovarian stimulation (up to four cycles) with gonadotropin (301 women), clomiphene (300), or letrozole (299). The primary outcome was the rate of multiple gestations among women with clinical pregnancies.

RESULTS:

After treatment with gonadotropin, clomiphene, or letrozole, clinical pregnancies occurred in 35.5%, 28.3%, and 22.4% of cycles, and live birth in 32.2%, 23.3%, and 18.7%, respectively; pregnancy rates with letrozole were significantly lower than the rates with standard therapy (gonadotropin or clomiphene) ($P=0.003$) or gonadotropin alone ($P<0.001$) but not with clomiphene alone ($P=0.10$). Among ongoing pregnancies with fetal heart activity, the multiple gestation rate with letrozole (9 of 67 pregnancies, 13%) did not differ significantly from the rate with gonadotropin or clomiphene (42 of 192, 22%; $P=0.15$) or clomiphene alone (8 of 85, 9%; $P=0.44$) but was lower than the rate with gonadotropin alone (34 of 107, 32%; $P=0.006$). All multiple gestations in the clomiphene and letrozole groups were twins, whereas gonadotropin treatment resulted in 24 twin and 10 triplet gestations. There were no significant differences among groups in the frequencies of congenital anomalies or major fetal and neonatal complications.

CONCLUSIONS:

In women with unexplained infertility, ovarian stimulation with letrozole resulted in a significantly lower frequency of multiple gestation but also a lower frequency of live birth, as compared with gonadotropin but not as compared with clomiphene.