In male patients who suffer from idiopathic male infertility, does clomiphene improve fertility rates?

**Bottom line**
Probably not. In male patients with idiopathic infertility, clomiphene citrate alone has not been shown to be effective in improving fertility rates. (SOR: B, based on a single RCT.) Clomiphene and vitamin E together may improve male fertility and increase pregnancy rates. (SOR: C, based on a single small RCT.)

**Evidence summary**

**Clomiphene no better than placebo**
A multicenter, double-blind, placebo-controlled study compared clomiphene citrate versus placebo for the treatment of idiopathic male infertility.¹ To be included, couples attempted conception for at least 12 months without success, male partners were diagnosed with idiopathic deficient sperm quality or motility, and female partners had no demonstrable cause of infertility.

In the selected 142 couples, male partners were randomized to 25 mg clomiphene citrate or placebo daily for 6 months. All subjects were initially given a 2-month supply of tablets and were seen for at least 2 additional visits during the 6 months of treatment for semen analysis and inquiry regarding pregnancy. Subjects returned for 1 additional visit 3 months after treatment ended. Thirty-five couples discontinued therapy before completing the treatment regimen, primarily due to frustration or interest in pursuing other methods of assisted reproduction, and 24 couples were lost to follow-up. The final evaluation included 1,308 couple-months.¹

In total, 18 pregnancies were achieved. Two pregnancies occurred prior to the day of first-tablet intake and were excluded. No difference was noted in pregnancy rates between the clomiphene and placebo groups (RR=1.3; 95% CI, 0.4–4.1).¹

**Clomiphene plus vitamin E increased fertility**
A prospective, double-blind, RCT compared clomiphene citrate plus vitamin E with placebo for idiopathic male infertility.² The study included 60 clinically infertile men between 20 and 40 years of age. A minimum of 1 year of unprotected sex without conception was required for enrollment. Exclusion criteria included diminished testicular volume, varicocele, or abnormal follicle-stimulating hormone (FSH) levels. Couples in which the female partner was found to be infertile (demonstrated anovulation, abnormal FSH and prolactin levels, and other physiologic factors) were excluded.

Patients were randomly assigned to receive either placebo (n=30) or combination of clomiphene citrate (25 mg/d) and vitamin E (400 mg/d; n=30). Treatment was continued for 6 months.²

The cumulative number of pregnancies in the treatment group (11 pregnancies) was statistically higher than that of the placebo group (4 pregnancies; OR 3.76; 95% CI, 1.03–13.64; NNT=4.2).²

**Recommendation**
The National Collaborating Centre for Women’s and Children’s Health recommends against giving men with idiopathic semen abnormalities antiestrogens, gonadotrophins, androgens, bromocriptine, or kinin-enhancing drugs, due to lack of proven efficacy (based on either evidence from systematic review and meta-analysis of randomized trials or from at least 1 randomized controlled trial).³

---

**REFERENCES**