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Ovulation Induction in Women Undergoing Intrauterine Inseminations with Donor Sperm: Letrozole or Clomiphene Citrate?

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Background: Ovulation induction (OI) with Letrozole (LET) or Clomiphene Citrate (CC) is widely used in Intrauterine Insemination (IUI) cycles for various indications, such as unexplained infertility, anovulation due to Polycystic Ovarian Syndrome (PCOS), or in women undergoing Donor sperm IUI (DS-IUI). However, the issue surrounding which is the optimal oral drug for OI remains unresolved, and results vary significantly between studies. We decided to compare the efficacy of LET and CC in a specific population of women with no history of infertility undergoing DS-IUI. **Material and Methods:** We performed a retrospective cohort study at Ovo clinic (University-affiliated private IVF clinic) between January 2011 and June 2014. All women ≤ 40 years with regular menstrual cycles and no history of infertility who underwent DS-IUI for absence of a male partner (single women and same-sex couples) and azoospermia were included. Patients with PCOS according to the Rotterdam criteria were excluded. All women had ovarian reserve testing (FSH, antral follicle count, AMH) and at least one patent tube. The choice of OI protocol (LET 5 mg, cycle day 3-7 Vs CC 100 mg, cycle day 3-7) was based on the physician's discretion, and only the first three treatment cycles were analyzed for each patient. Ultrasound monitoring of follicular growth was started on cycle day 9, and when a leading follicle ≥ 17 mm was noted, ovulation was triggered with recombinant hCG and DS-IUI performed approximately 36 hours later. Our primary outcomes were live birth rate (LBR) per started cycle and cumulative LBR. Secondary outcomes were clinical pregnancy rate per started cycle (CPR) (fetal heartbeat at 7 weeks), twin pregnancy rate, miscarriage rate and cycle cancellation rate.

Results: In total, 590 DS-IUI cycles in 257 women were included: 269 LET cycles in 112 women, and 321 CC cycles in 145 women. The two groups were comparable for age, Body Mass Index, ovarian reserve and number/mobility of inseminated sperm. There were no differences in LBR (11.5% (31/269) vs 16.5% (53/321), $p=0.08$), cumulative LBR (27.7% (31/112) vs 36.6% (53/145), $p=0.13$), CPR (17.1% (46/269) vs 21.5% (69/321), $p=0.18$), twin pregnancy rate (8.7% (4/46) vs 11.6% (8/69), $p=0.6$), miscarriage rate (21.7% (10/46) vs 21.7% (15/69), $p=1$) and cycle cancellation rate (3% (8/269) vs 2.8% (9/321), $p=0.9$) between LET and CC, respectively. **Conclusion:** For women with regular menstrual cycles and no history of infertility undergoing DS-IUI, OI with LET or CC leads to similar outcomes. Therefore, other factors, such as side effects, tolerance, price and availability, should be taken into account when choosing one drug over the other. In Canada, CC is less expensive than LET and thus should be the preferred treatment for these patients.