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The Effect of Clomiphene Citrate Dose and Initiation Day on Endometrial Thickness, Follicular Recruitment and Clinical Pregnancy Rates

Objective: To evaluate whether clomiphene citrate (CC) dose and initiation day affects endometrial thickness (EMT), follicular number, and pregnancy outcomes in CC/intrauterine insemination (IUI) cycles.

Methods: Retrospective cohort study of 2453 CC/IUI cycles at an academic fertility center between 12/2003-12/2015. 1051 women undergoing a 5-day course of CC (25-150 mg) initiated on different cycle days (CD2–6) were analyzed. Mixed random and fixed effects generalized linear models were fit.

Result(s): Mean (SD) age, BMI, and day-3 FSH at first cycle were: 33.5 (4.3) years, 24.5 (4.7) Kg/m², and 7.1 (2.8) IU/L, respectively. Higher CC doses initiated at later cycle days were associated with a thinner EMT. In patients with later CC starts (CD4 or CD5), the EMT became thinner as the dose increased. Lower CC Dose ($p=0.0098$), earlier initiation day ($p=0.0109$), as well as lower BMI ($p=0.0002$), were associated with recruitment of a higher number of pre-ovulatory follicles ≥ 13 mm. A significant interaction between CC dose and BMI was found when Clinical Pregnancy Rate (CPR; $p=0.02$) and early pregnancy viability ($p<0.0001$) were analyzed. Specifically, CC dose related positively with CPR and viability in patients of normal weight (BMI <25), whereas the opposite was noted among patients with BMI ≥ 25 . Initiation day did not have a significant effect on CPR.

Conclusion(s): Higher doses of CC (100 or 150 mg) and administering CC earlier (on CD2 or CD3) might attenuate its negative effect on EMT. Lower CC doses, and earlier initiation day, as well as lower BMI were associated with increased recruitment of pre-ovulatory, albeit likely clinically non-significant, follicles. The effect of CC dose on CPR is modified by BMI, with higher doses associated with higher CPR among patients with normal BMI, and the opposite effect among patients with higher BMI .

THE BMI effect is an ASSOCIATION, the finding does not imply causality. WE should not overstate our findings.

A sensitivity analysis excluding pts with PCOS, especially obese ones would help clarify.

Now that it is clarified by excluding PCOS patients in sub-analysis, I think we can say it. Let me know what you think.