Clomiphene citrate (CC) as a usual first choice for ovulation induction in polycystic ovary syndrome (PCOS) exerts its effect by long-term estrogen-receptor binding. Despite a high success rate of CC-induced ovulation, the overall conception rate is low. A widely accepted explanation for this discrepancy goes back to the anti-estrogenic properties of CC which shows to have intrinsic negative influence on the synchronization of glandular development and stromal maturity of endometrium, the properties of cervical mucus and uterine blood flow.

Clomiphene citrate (CC) as a usual first choice for ovulation induction in polycystic ovary syndrome (PCOS) exerts its effect by long-term estrogen-receptor binding. Despite a high success rate of CC-induced ovulation, the overall conception rate is low. A widely accepted explanation for this discrepancy goes back to the anti-estrogenic properties of CC which shows to have intrinsic negative influence on the synchronization of glandular development and stromal maturity of endometrium, the properties of cervical mucus and uterine blood flow.

In this randomized, double blind, placebo-controlled study, a total of 154 eligible patients (77 in each group) were enrolled during 2009-2013. Patients were randomly assigned to receive CC plus EE or CC plus placebo. Uterine artery pulsatility index (PI) and endometrial thickness were measured on the day of human chorionic gonadotropin administration.

Of the 154 enrolled patients, a total of 59 patients' treatment cycles were cancelled before human chorionic gonadotropin (hCG) is given and these patients were excluded. Both groups were comparable in regards to mean age, body mass index, infertility duration and basal hormone levels. The women used EE and CC combination, had significantly thicker endometrium (9.7± 2.1 vs. 8.9± 1.6 mm, P = 0.036) and lower values for the PI of both uterine arteries compared with placebo-CC controls (P = 0.027; P = 0.001). Furthermore, statistically significant differences were found between the groups with respect to clinical pregnancy (28.9% vs. 10%, P = 0.019). The miscarriage rate was not statistically significant between groups.

This finding is close to the estimate of one study, reported a higher ongoing pregnancy rate for patients with unexplained infertility when CC is used in combination of EE. Similarly, another study reported that adding EE creates a desirable endometrial response even with very low doses. In these two studies no significant differences in PI values were noted. The noticeable rate of pregnancy in our study might be associated with endometrial thickness and uterine artery PI improved with estrogens that enhanced embryo implantation. There is little empirical evidence regarding the relationship between endometrial and uterine blood flow and pregnancy after IUI.