Effect of clomiphene citrate on endometrial thickness, ovulation, pregnancy and live birth in anovulatory women: systematic review and meta-analysis


Abstract:

ABSTRACT Objectives: To compare the impact of clomiphene citrate (CC) vs other drug regimens on mid-cycle endometrial thickness (EMT), ovulation, pregnancy and live birth rates in women with World Health Organization (WHO) group II ovulatory disorders. Methods: We searched MEDLINE, EMBASE, Scopus, Web of Science, The Cochrane Central Register of Clinical Trials (CENTRAL) and the non-MEDLINE subset of PubMed from inception to December 2016 and cross-checked references of relevant articles. We included only randomized controlled trials (RCTs) comparing CC used alone vs other drug regimens for ovulation induction in women with WHO group II anovulation. Outcomes were mid-cycle EMT, ovulation, pregnancy and live birth rates. We pooled weighted mean differences (WMD) with 95% confidence intervals (CI) for continuous variables (EMT) and risk ratios (RR) with 95% CI for binary variables (ovulation, pregnancy and live birth rates). Results: We retrieved 1718 articles of which 33 RCTs (4349 women, 7210 ovulation induction cycles) were included. In 15 RCTs that compared CC with letrozole, EMT was lower in the CC group (1957 women, 3892 cycles; WMD, −1.39; 95% CI, −2.27 to −0.51; I² =100%), ovulation rates after CC and letrozole were comparable (1710 women, 3217 cycles; RR, 0.97; 95% CI, 0.90 to 1.04; I² =47%), while CC led to a lower pregnancy rate (1957 women, 3892 cycles; RR, 0.78; 95% CI, 0.63 to 0.95; I² =43%) and a lower live birth rate (RR, 0.70; 95% CI, 0.49 to 0.98; I² =35%). In two RCTs that compared CC with CC plus metformin, EMT, ovulation and pregnancy rates were comparable (101 women, 140 cycles; WMD, 0.23; 95% CI, 0.92 to 0.45; I² =78%; RR, 0.84; 95% CI, 0.67 to 1.06; I² =0%; and RR, 0.79; 95% CI, 0.33 to 1.87; I² =0%). In three studies that compared CC with CC plus N-acetyl cysteine (NAC), EMT was lower in the CC group (340 women, 300 cycles; WMD, −1.51; 95% CI, −1.98 to −1.04; I² =45%). In two studies that compared CC with CC plus nitric oxide (NO) donor, EMT was lower in the CC group (120 women, 304 cycles; WMD, −1.75; 95% CI, −2.08 to −1.41; I² =0%). Compared with CC plus NO donor or NAC, CC showed statistically significant lower ovulation and pregnancy rates. Compared with tamoxifen in three studies, CC showed a tendency towards lower EMT (571 women, 844 cycles; WMD, −1.34; 95% CI, −2.70 to 0.01; I² =96%) with comparable ovulation and pregnancy rates. Conclusions: In women with WHO group II ovulatory disorders, ovulation induction with CC might result in lower EMT than other ovulation induction regimens. Whether the lower EMT caused the lower pregnancy and live birth rates remains to be elucidated. Letrozole seems to be beneficial for these women. However, our findings should be interpreted with caution as the quality of evidence was very low. Copyright © 2017 ISUOG. Published by John Wiley & Sons Ltd.

Keywords:

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