ISGE
GYNECOLOGICAL ENDOCRINOLOGY
THE 18TH WORLD CONGRESS
7-10 MARCH 2018 FLORENCE, ITALY

Effect of two ethinyl estradiol and drosperinone containing combined oral contraceptives on whole blood clot viscoelasticity

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Context
Combined oral contraceptive (COC) use is indisputably associated with increased risk of venous thrombosis (VT). Lowering the doses of ethinyl estradiol (EE) has decreased the risk of VT. EE in combination with the fourth-generation progestin Drosperinone (DRSP) is some of the most commonly used COC formulations globally, since it is prescribed not only for its contraceptive properties but also for non-contraceptive uses like treatement of acne vulgaris, endometriosis as well as dysmenorrhea and menstrual cramps. DRSP-use poses a 6-fold increased risk of VT compared to non-users and double the risk of VT compared to second generation progestins.
Objective
To evaluate the impact of two COC formulations (both containing EE at different concentration of 20?g and 30?g respectively and DRSP at the same concentration of 3mg) on whole blood clot formation compared to the control group using no COCs.
Methods
Viscoelastic measurements were taken using thromboelastography (TEG). A volume of 340?L of whole blood was pipetted into a TEG cup. Subsequently 20?L of CaCl2 was added to overturn the effect of sodium citrate. The samples were then placed into a Thromboelastograph 5000 Hemostasis Analyzer System for to analyse clot kinetics.
Patient(s)
A total of 75 healthy females between the age of 18 and 30 were recruited, all none smokers and not using any chronic medication (other than the COCs for the test groups). For the control group 25 females were included that did not use any hormonal contraceptive. For the two COC test groups 25 females were included respectively.
Intervention(s)
No interventions were followed in this study.
Main Outcome Measure(s)
Seven parameters relating to the viscoelastic properties of whole blood clots were measured for the control and two test groups.
Result(s)
Both test groups exhibited a decreased reaction time and increased thrombin burst related to EE concentration compared to the control group. Both test groups did not have a significant impact on the stiffness and strength of the whole blood clots compared to the control group.
Conclusions

A combination of EE and DRSP decreases the initiation time of whole blood clot formation and is associated with an elevated thrombin burst which is related to the concentration of EE in the formulation. This could possibly explain the increased risk of VTE associated with these formulations.

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