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Modification of fibrinolytic potential after cessation of combined hormonal contraceptives

Hemostatis, transfusion medicine, vascular, laboratory medicine

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INTRODUCTION

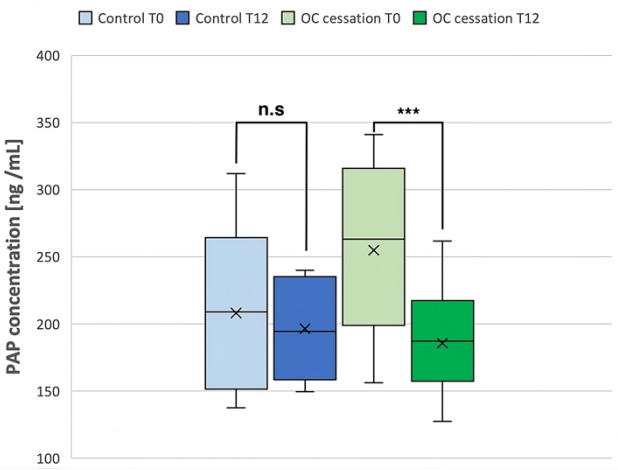
Combined oral contraceptives (OCs) are known to contribute to a procoagulant state by increasing clotting factor production and decreasing levels of hemostatic inhibitors. Such effects can result in venous thromboembolism (VTE) and persist even after treatment discontinuation. To date, modification of fibrinolytic biomarkers has been observed in disease but specific data on fibrinolysis in OC users is limited. Therefore, we aimed to determine whether plasmin generation (PG) is elevated in OC users and assess the time needed for fibrinolytic biomarkers to normalise after OC cessation.

METHODS

In a monocentric, observational study cohort of adult women, platelet-poor plasma was collected from an OC cessation group (n=66) and a control group (n=28) of women using progestin-only pills or an intrauterine device at T0 (the date of OC cessation) and T12 (12 weeks later). Twenty individuals with OC cessation presenting with the highest modifications of thrombin generation (TG) parameters between T0 and T12 were selected and compared to five controls. Fibrin clot degradation was evaluated using a) a PG assay recording endogenous plasmin potential (EPP; nM*min), Peak (nM), and time to peak (ttPeak; min) (Synapse Research Institute, Maastricht, Netherlands), and b) plasmin α2-antiplasmin complex concentration (PAP, ng/mL) by ELISA (Technozym®, Technoclone, Austria).

RESULTS

At T0, Peak plasmin from OC cessation samples was significantly higher than in controls (p=0.002). However, at T12, OC cessation EPP and Peak were comparable to controls. Overall, we observed a statistically significant decrease in EPP (p=0.005) and Peak (p<0.001) between T0 and T12 in OC cessation samples. In comparison, no differences were noted in EPP and Peak in control samples. TtPeak in OC cessation samples at T0 and T12 were similar and higher than controls at both time points (T0, p=0.005; T12, p=0.004). PAP complex concentrations decreased significantly with OC cessation between T0 and T12 (p<0.001, see Fig.1). This change was not observed in controls (p=0.761).



CONCLUSION

Compared to controls, women taking OCs exhibited enhanced fibrinolytic activity, reflected by high PG and PAP complex levels, linked to a procoagulant state during OC use. These levels decreased significantly 12 weeks after OC cessation.

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