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Contraceptive Steroids Influence the Hemostatic Activation State in Healthy Men

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Hormonal contraception for men requires administration of testosterone and gestagens. The effects of a long-acting testosterone ester and 2 different progestins on hemostatic activation parameters were studied in relation to cardiovascular risk. In phase 1, 7 healthy men aged 28-38 years received a single intramuscular injection of 200 mg norethisterone-enanthate (NET-EN) on Day 0. Plasma samples were obtained on Days 0, 14, 41, and 84. In phase 2, 3 groups of 14 healthy men aged 18-45 years received four injections (every 6 weeks) of 1000 mg testosterone undecanoate (TU), plus daily oral placebo or daily oral levonorgestrel (LNG, 250 µg); or four injections (every 6 weeks) of NET-EN. Treatment lasted 24 weeks. Plasma samples were obtained at weeks 0, 16, 24, and 52. All samples were assayed for levels of coagulation factors VIIc, VIIa, XIIc, and XIIa; prothrombin fragment F1+2 (F1+2); antithrombin; plasmin-α_2-antiplasmin-complex (PAP); and fibrinogen. NET-EN alone led to a depletion of sexual hormones and a marked shift in hemostatic parameters with increasing levels of FXIIc, fibrinogen, antithrombin, and F1+2, whereas FVIIc and FVIIa levels decreased. PAP levels increased significantly. Opposite effects were seen in the TU/placebo group, with a significant down-regulation of fibrinolysis and the hemostatic turnover rate. Testosterone effects were attenuated by additional administration of gestagens. The effect of hormonal male contraception using long-acting testosterone esters with or without gestagens was significantly measurable within the hemostatic system. Down-regulation of the hemostatic system with testosterone alone may indicate an antithrombotic effect, whereas clinical consequences of an additional gestagen compound cannot be derived.

Key words: Cardiovascular risk, gestagens, hemostasis, hormonal male contraception, testosterone

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