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Estetrol Combined with Drospirenone: A New Oral Contraceptive With a Favorable Hemostatic Profile

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assessing the longitudinal effect of changes in branch-specific contraceptive policy on rates of: longer-acting (depot-medroxyprogesterone, implant, and intrauterine) contraception use at six months on active duty; and childbirth during the first 24-months of active duty. Multivariable Logistic (contraception use) and Cox (time to childbirth) Regression models were used to compare outcomes before and after the intervention, between the service making the intervention and the other three branches, and the interaction between these variables. IRB approved.

RESULTS: Group contraceptive education emphasizing implantable and intrauterine methods followed by individual contraceptive consultation with a provider for all female, Navy basic trainees increased longer-acting method use (11.8% to 24.3%, Interaction Term OR: 2.14 (95% CI: 1.92-2.39), $P<.001$) and decreased childbirth rates (7.5% to 6.3%, HR: 0.86 (0.76-0.88), $P=.015$). Restricting time away from training for implant or intrauterine method insertion during Marine Corps basic training and providing education emphasizing use of depot-medroxyprogesterone for menstrual control decreased overall longer-acting method use (16.2% to 10.0%, OR: 0.43 (0.38-0.49), $P<.001$) and increased childbirth rates (8.0% to 9.7%, HR: 1.24 (1.02-1.51), $P=.027$). Allowing contraceptive implant placement during basic training increased use of longer-acting contraception among Air Force recruits 4.4% to 6.9%, OR: 1.31 (1.14-1.51), $P<.001$).

CONCLUSION: Branch-specific changes in military contraceptive policy significantly impact contraceptive use and childbirth rates among junior enlisted.

Financial Disclosure: The authors did not report any potential conflicts of interest.

5:10 PM–5:20 PM

Estetrol Combined with Drospirenone: A New Oral Contraceptive With a Favorable Hemostatic Profile [20OP]

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Guillaume Chatel, PhD, and Jean Michel Foidart, MD, PhD

INTRODUCTION: Estetrol (E4) is a natural human estrogen with selective action in different tissues. A combined oral contraceptive (COC) with E4 15 mg and Drospirenone (DRSP) 3mg is in Phase 3 trials. Here, we report its effects on hemostatic markers.

METHODS: In this IRB-approved, randomized, open-label study, women received E4 15 mg/DRSP 3mg ($n=38$), ethinyl-estradiol (EE) 30 mcg/Levonorgestrel-(LNG) 150 mcg ($n=29$) or EE-20 mcg/DRSP-3 mg ($n=31$). We compared changes of hemostasis parameters between baseline and cycle 6 with a $P<.05$ considered significant.

RESULTS: Pro-coagulant factors increased similarly in E4/DRSP, EE/LNG and EE/DRSP users for fibrinogen (+10%, +5% and +16%, respectively) and prothrombin (+7%, +13% and +7%, respectively). Anti-coagulant factors decreased significantly less with E4/DRSP and EE/LNG compared to EE/DRSP for Protein S activity (-4%, -5% and -30%, respectively) and free Protein S antigen (+5%, -3%; and -23%, respectively). The fibrinolysis marker, tissue-plasminogen activator, changed significantly more favorably with E4/DRSP than EE/LNG or EE/DRSP (-7%, -33% and -40%, respectively). Prothrombin fragment 1+2, a marker of ongoing coagulation, changed significantly less with E4/DRSP than other COCs (+23%, +71% and +64%, respectively). Endogenous thrombin potential (ETP) activated protein C resistance (APCr) increased significantly with EE/LNG (+78%) and EE/DRSP (+121%) compared to E4/DRSP (+3.0).

CONCLUSION: Coagulation parameter changes over 6 months demonstrate mostly similar changes for E4/DRSP and EE/LNG, both of which are less thrombogenic than EE/DRSP. For some

factors, primarily anticoagulant and fibrinolysis markers, ETP-APCr, and prothrombin fragment 1+2, E4/DRSP is more favorable than EE/LNG. The differences between E4/DRSP and EE/DRSP demonstrate that the choice of estrogen is important when considering thrombosis risk.

Financial Disclosure: Jan Rosing disclosed the following—Mithra Pharmaceuticals, Liege: Consultant/Advisory Board, Speaker/Honoraria includes speakers bureau, symposia, and expert witness; Pantarhei Bioscience, Zeist: Consultant/Advisory Board. Maud Jost disclosed the following—Mithra Pharmaceuticals: Employment. Virginie Kinet disclosed the following—MITHRA PHARMACEUTICALS: Employment. Guillaume Chatel disclosed the following—Mithra Pharmaceuticals: Employment. Jean Michel Foidart disclosed the following—Mithra: Consultant/Advisory Board, Speaker/Honoraria includes speakers bureau, symposia, and expert witness. Mitchell Creinin did not report any potential conflicts of interest.

5:20 PM–5:30 PM

Efficacy of the 1-Year Segesterone Acetate/Ethinyl Estradiol Contraceptive Vaginal System [21OP]

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INTRODUCTION: A novel, ring-shaped, contraceptive vaginal system (CVS) containing segesterone acetate (SA), also known as Nestorone®, and ethinyl estradiol (EE) is designed to last 1 year (13 cycles), delivering an average of SA 0.15/EE 0.013 mg/day. Efficacy was evaluated in 2 multicenter, 1-year, open-label studies (one at 15 US sites; one at 5 US/7 international sites).

METHODS: Women (18-40 yrs) used the CVS for 21 days/cycle followed by having it out for 7 days. Women were not to remove the CVS for >2 hours during the 21 days of use. The primary efficacy outcome was the Pearl Index (PI) for women ≤ 35 years of age, excluding cycles with adjunctive contraception. Secondary outcomes included the PI for subgroups and intention-to-treat Kaplan-Meier life-table analyses.

RESULTS: Of 2265 participants analyzed, 1303 (57.5%) completed. The primary PI was 2.98 (95% CI [2.13-4.06]). The PI was 2.10 (95% CI [1.37-3.06]) in women who followed use instructions versus 5.89 (95% CI [3.46-9.27]) for women who documented removals >2 hours ($P=0.0024$). Significantly higher PIs were also observed in subgroups by age (18-19 yrs vs ≥ 36 yrs), parity (≥ 1 vs 0), race (Black vs white), ethnicity (Hispanic vs non-Hispanic), and site (non-Europe vs Europe), but not by BMI. Life-table analyses revealed the CVS is 97.3% effective in preventing pregnancy. Pregnancies did not increase across cycles.

CONCLUSION: The SA/EE CVS is an effective 1-year, procedure-free contraceptive controlled by women that can help address an unmet worldwide contraceptive need. Counseling to ensure correct use is essential for optimizing efficacy.

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