Comparative Effects of a 91-Day or a 28-Day Combined Oral Contraceptive on Adolescent Bone Mineral Density

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CONTEXT: Although combined oral contraceptives (COCs) have been hypothesized to interfere with skeletal growth and development in adolescents, studies are limited.

OBJECTIVE: To assess changes in lumbar spine bone mineral density (BMD) in a 91-day extended-regimen (ER) COC and a 28-day COC treatment group, compared to a control group (no COC).

METHODS: Phase 2, multicenter, open-label, randomized, controlled study.

PATIENTS: Healthy adolescent postmenarcheal females 12-18 years old.

INTERVENTIONS: Participants were randomized to a 91-day levonorgestrel (LNG)/ethinyl estradiol (EE) ER (84 days' LNG 150mcg/EE 30mcg + 7 days' EE 10mcg [LNG/EE ER], or a 28-day LNG/EE regimen (21 days' LNG 100mcg/EE 20mcg + 7 days' placebo [LNG/EE 21/7] for 12 months. Participants not seeking hormonal contraception were enrolled as controls.

MAIN OUTCOME MEASURES: Mean percent change in lumbar spine BMD from baseline to 12 months of active treatment as determined by dual energy X-ray absorptiometry (DXA), compared with mean percent change in lumbar spine BMD of controls. Noninferiority of each COC group to the control group would be met if the upper bound of the 2-sided 95% CI for the treatment difference was <3%.

RESULTS: Of 1361 adolescents randomized/enrolled, 829 were included in the primary analysis. Mean percent changes from baseline in lumbar spine BMD were +2.26% (LNG/EE ER), +1.45% (LNG/EE 21/7), and +2.50% (controls). Noninferiority of LNG/EE ER and LNG/EE 21/7 to controls was met. Treatment differences were statistically significant between LNG/EE 21/7 and controls (1.05%; 95% CI, 0.61%, 1.49%) but not between LNG/EE ER and controls (0.23%; 95% CI, -0.20%, 0.67%).

CONCLUSION: Compared with controls, bone accrual was statistically significantly lower among LNG/EE 21/7 users but not among LNG/EE ER users. Observed differences were not considered clinically meaningful.

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