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Simvastatin Appears Safe and Effective for PCOS Patients

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March 25, 2005 (Los Angeles) — Simvastatin decreased serum testosterone and normalized gonadotropin levels in women with polycystic ovary syndrome (PCOS), according to a presentation here yesterday by Antoni J. Duleba, MD, at the 52nd annual meeting of the Society for Gynecologic Investigation.

"To my knowledge, this is the first study showing that you can use a statin safely in the presence of birth control pills in PCOS patients. So there is no risk of pregnancy, yet the statin will improve lipid levels and the level of testosterone," Dr. Duleba, from the Yale University School of Medicine in New Haven, Connecticut, and lead investigator of the study, told Medscape.

Approximately 5% to 7% of women of reproductive age have PCOS, which is characterized by high levels of serum testosterone, an elevated luteinizing hormone (LH) to follicle stimulating hormone (FSH) ratio, and symptoms such as hirsutism and infertility.

The investigators hypothesized that statins would be beneficial in treating PCOS because experiments in culture had shown that a statin limited proliferation of theca-interstitial cells of the ovary, reduced sex steroid production, and minimized oxidative stress. PCOS is also associated with dyslipidemia and systemic inflammation (as measured by C-reactive protein), conditions that statins also improve, according to previous research.

The study was conducted at the Poznan University of Medical Sciences in Poland. All participants provided informed consent using procedures approved by the Yale University Human Investigations Committee. Potential study subjects were excluded if they had been treated with oral contraceptives or any other hormones within three months prior to the study. Four of the 54 potential study subjects refused to participate, and the investigators excluded two ineligible women.

Among the participants, the mean age was 24.2 ± 3.5 years. Subjects randomized to the statin group (n = 24) received 20 mg of simvastatin daily plus an oral contraceptive pill (OCP) containing ethinyl estradiol (20 µg) and desogestrel (150 µg). The control group (n = 24) received OCP alone. Hormone, glucose, insulin, and lipid levels were measured at baseline and after 12 weeks of therapy.

Randomization successfully structured the statin and OCP groups with comparable baseline body mass index ([BMI] mean, 22.4± 3.5 kg/m^2), serum testosterone, LH, FSH, insulin (both fasting and two hours after oral glucose challenge), and lipid levels.

The primary outcome measure was change in serum testosterone. The mean testosterone decrease was 34.6 ng/dL in the statin group (41%) compared with 10.9 ng/dL in the OCP group (14%). The between-group difference was statistically significant (P = .006).

Simvastatin was also associated with significant declines in serum LH, FSH, dihydroepiandrosterone sulfate (DHEAS, an adrenal steroid), and lipid levels. LH levels decreased significantly more in the statin group than in the OCP group (43% vs 9%, respectively; P = .02), as did the LH:FSH ratio (41% vs 12%; P = .02). DHEAS declined by 26% in the statin group and by 28% in the OCP group.

Total cholesterol level decreased 10% and LDL cholesterol level decreased 24% in the statin group compared with 8% and no change in the OCP group, respectively (P < .01 for both). Triglyceride levels did not significantly change in the statin group but increased by 21% in the OCP group.

Insulin sensitivity did not improve in either group and BMI in both groups remained essentially the same during the course of the study.

All 48 women completed the three-month initial phase of the trial, perhaps because there were no important adverse events. "We deliberately started at a low dose (20 mg of simvastatin) because we didn't want side effects. No patient experienced muscle pains or other significant side effects," Dr. Duleba said.

The study was too short to evaluate clinical end points such as resolution of hirsutism. Study subjects continue to participate; each has crossed over to the opposite treatment group for another three-month study period.

Participants were all young women, none of whom were interested in getting pregnant. "Clearly, if they want to get pregnant, statin treatment should be interrupted, because we want to get assurance of safety." Dr. Duleba said. "I would not recommend statins while attempting pregnancy or during pregnancy. Statins are labeled as category X medications by the FDA."

In fact, Dr. Duleba stated that most participants were not concerned with fertility issues at all, but that they wished to protect themselves from cardiovascular risk factors that their female relatives had.

Although testosterone levels decreased in women in the statin group, Dr. Duleba cautioned that serum testosterone itself is not a clinical end point. "We don't have enough data to recommend use of a statin only to treat androgenemia in PCOS patients yet. We know we are not going to hurt them, and if anything we are likely to help their hormonal profile and improve their dyslipidemia."

This study was funded by the Yale University School of Medicine. Organon, Inc., provided the oral contraceptive (Marvelon), and Polfa, a Polish pharmaceutical company, provided simvastatin to study participants at no cost.

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