Model suggests lowering hormone doses in contraceptives

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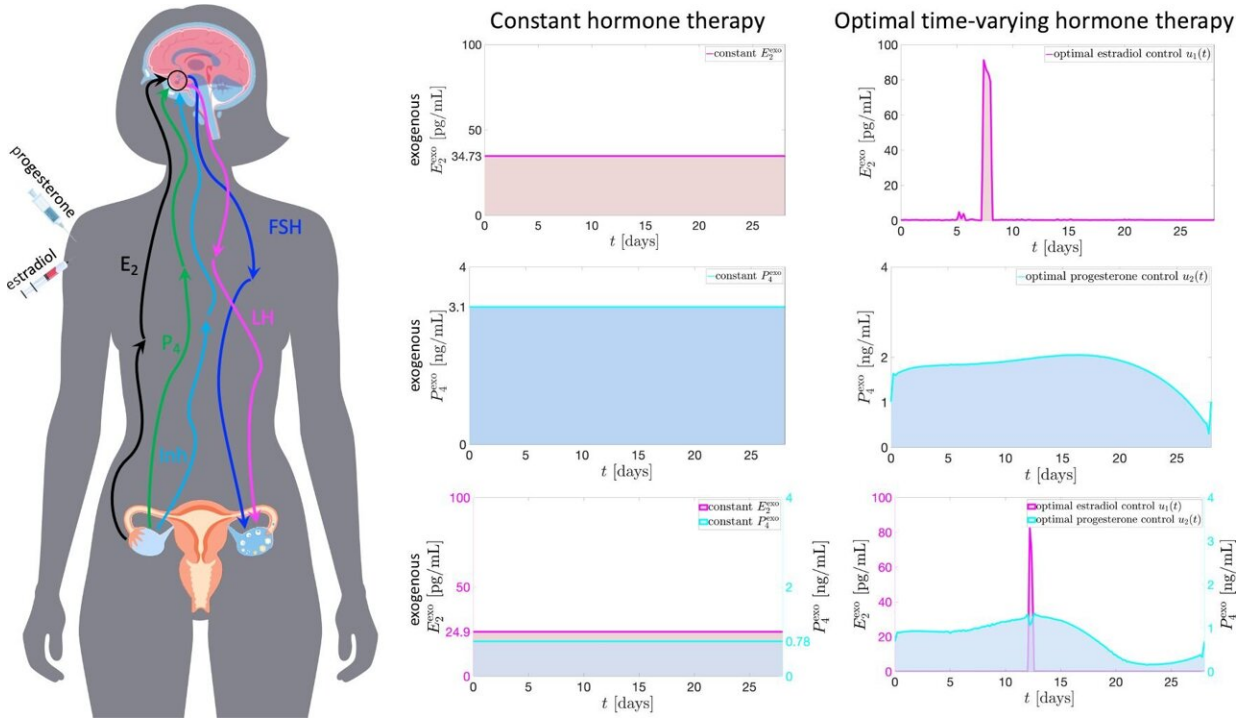

Constant dosage and nonconstant dosage comparison. The shaded regions in Panels (A), (C), and (E) indicate the minimum total constant dosage of exogenous estrogen and/or progesterone over 28 days that lowers maximum P4 concentration to 4.99 ng/mL. The shaded region below u1 (area under the curve or AUC) in Panel (B) is the total nonconstant dosage of exogenous E2 which suppresses the P4 level to 4.43 ng/mL, a reduction by about 92% of the total dosage in (A). Panel (D) illustrates the total nonconstant dosage of exogenous P4 that reduces maximum P4 to 4.66 ng/mL, a reduction by about 43% of the total dosage in (C). Panel (F) shows the combined nonconstant doses of exogenous E2 and P4 that gives a maximum P4 level of 4.31 ng/mL. Credit: Gavina et al.,

The dosage of hormones in common contraceptives could be reduced by as much as 92% and still effectively suppress ovulation, according to a computational model described this week in *PLoS Computational Biology* by Brenda Lyn A. Gavina, Ph.D. student at the University of the Philippines Diliman, and her collaborators.

A normal menstrual cycle involves multiple phases which are regulated by the endocrine system and influenced by levels of various hormones. The most contraceptive approaches, including pills, injectables and implants, involve the administration of exogenous estrogen and/or progesterone to block ovulation—the phase of the cycle in which an egg is released into the uterus.

In the new study, researchers used data on hormone levels in 23 women aged 20 to 34 with normal menstrual cycles. The team developed computational models depicting the interactions between various hormone levels as well as the impacts of exogenous hormones.

The model provided evidence that it is possible to reduce the total dose by 92% in estrogen-only contraceptives, or the total dose by 43% in progesterone-only contraceptives, and still prevent ovulation.

By combining estrogen and progesterone, the doses of each hormone could be reduced even further. In addition, the model showed the importance of timing the hormones during the cycle, pointing toward ways that exogenous estrogen and progesterone could be given during only certain phases of the menstrual cycle rather than at steady constant doses.

"These results may give clinicians insights into optimal dosing formulations and schedule of therapy that can suppress ovulation," the authors say.

More information: Toward an optimal contraception dosing strategy, *PLoS Computational Biology* (2023). DOI: 10.1371/journal.pcbi.1010073

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