

Clinical

Doxycycline does not reduce unscheduled bleeding and spotting

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By Victoria Stern

NEW YORK (Reuters Health) - Doxycycline, taken with a continuous oral contraceptive pill, does not decrease unscheduled bleeding and spotting episodes, according to a study in the June issue of *Obstetrics & Gynecology*.

In the 1980s, researchers discovered that the common antibiotic doxycycline also inhibits matrix metalloproteinases (MMPs), which are known to play a role in endometrial bleeding. Progesterone has been shown to regulate MMP activity as well. Upregulation of MMPs has been associated with unscheduled bleeding, while inhibition of MMPs is associated with decreased endometrial bleeding.

But when Dr. Bliss Kaneshiro, from the University of Hawaii, and colleagues conducted a randomized trial with 66 women, they found no difference between doxycycline and placebo in unscheduled bleeding.

All of the women were initiating treatment with a continuous oral contraceptive (20 mcg ethinyl estradiol/90 mcg levonorgestrel). For 84 days, the women also took either doxycycline (100 mg) or placebo twice a day for 5 days at the onset of each bleeding or spotting episode. For the final 28 days of the study, participants took only the oral contraceptive.

During the 84-day treatment period, Dr. Kaneshiro and her group found no significant differences in bleeding or spotting days or in duration of the longest bleeding or spotting episode between doxycycline and placebo.

In addition, there was no significant difference between doxycycline and placebo in the average number of bleeding days or in bleeding patterns over time.

Women in the placebo group (vs. the doxycycline group) were more likely to have either no bleeding (18.2% vs 3.0%) or more than four episodes of bleeding (36.4% vs. 24.2%).

The investigators found no differences in the side effects profiles or major adverse outcomes reported in either group.

Dr. Kaneshiro and colleagues suggest several reasons why doxycycline might have failed. For instance, they say, once endometrial degradation begins, it is not possible to halt the cascade and so perhaps women need to take doxycycline earlier, when MMP levels are very low.

Or perhaps the oral contraceptive dose or type of progestin used is not sufficient to stop bleeding, said Dr. Leslie Miller, from the University of Washington. Dr. Miller, who was not involved in the study, published a paper in 2003 showing better suppression of bleeding with higher levonorgestrel doses.

The authors acknowledge that a different dose or dosing frequency might be needed to inhibit MMP in the endometrium -- although without biopsies, ultrasound, or drug serum levels, this is all speculation, Dr. Miller said.

The study was supported by Wyeth Pharmaceuticals, which manufactures Lybrel, the continuous birth control pill used in the trial.

http://journals.lww.com/greenjournal/Fulltext/2010/06000/Treatment_of_Unscheduled_Bleeding_in_Continuous.8.aspx

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