Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin on urinary incontinence. JAMA. 2005;293:935–948.

FAST TRACK

Estrogen, with or without progestin, worsened incontinence or raised risk

Q Does HRT diminish urinary incontinence?

A Not at all. On the contrary, it increases the risk among continent women and worsens symptoms in incontinent ones, according to a study of Women's Health Initiative (WHI) participants.

EXPERT COMMENTARY

Based on weak evidence, some experts have recommended hormone replacement therapy (HRT) as initial treatment of urinary incontinence in hypoestrogenic menopausal women. In fact, HRT has been used for this indication for several decades, mainly because there are estrogen receptors on urinary tract tissues.

This substudy of the WHI involving 27,347 women contradicts the longstanding practice of prescribing HRT for urinary incontinence: Both conjugated equine estrogen (CEE) and CEE with medroxyprogesterone acetate (MPA) stimulated new symptoms or aggravated existing ones.

How these data stack up

These findings are consistent with those of the Heart and Estrogen/Progestin Replacement Study (HERS),[1] but contradict small observational studies. In addition, a large cross-sectional investigation of osteoporotic fractures had found estrogen use in postmenopausal women to be associated with almost double the risk of daily urinary incontinence—though these findings did little to change clinical practice.[2]

Major advantages of the WHI study are its large size and great statistical power. Since medications were not prescribed for therapy and since this was a blinded study, the placebo effect was also neutralized. Participants were followed over 3 years.

Unfortunately, the study provides no information for women below the age of 50.

What about other HRT formulations?

Only 1 dose of CEE with and without a single dose of MPA was utilized, although the authors cite an observational study[3] of different formulations of estrogen-progestin and estrogen alone that "suggested an increased risk" of urinary incontinence with HRT. The authors also note that theirs is the first randomized trial to demonstrate that estrogen alone increases urinary incontinence.

The bottom line

Without any convincing evidence to the contrary, clinicians should avoid prescribing estrogen—with or without a progestin—to prevent or treat urinary incontinence in menopausal women.

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Sanchez-Ramos L, Kaunitz AM, Delke I. Progestational agents to prevent preterm birth: a meta-analysis of randomized controlled trials. Am J Obstet Gynecol. 2005;105:273–279.

Q Do progestational agents prevent preterm birth?

A Yes. Using 17 α-hydroxyprogesterone caproate reduced the rate of preterm birth and low-birthweight infants. Women with a history of preterm birth should be offered weekly injections to minimize their risk. A dose of 250 mg of 17 α-hydroxyprogesterone caproate should be given from approximately 20 to 34 weeks of gestation as weekly 1-mL intramuscular injections.

FAST TRACK

The preterm delivery rate was 26.2% with progestational agents and 35.9% with placebo

EXPERT COMMENTARY

Great progress has marked many medical problems in recent years, but premature delivery is not one of them. Rather, the rate of preterm birth, defined as delivery at less than 37 weeks of gestation, rose to 12.3% in 2003, continuing its steady increase in the United States since the mid-1900s.[1] This lack of progress has stimulated renewed interest in the use of progestational agents to prevent premature delivery.

Why do the study now?

Previous metaanalyses were inconclusive. There were statistical flaws, and the analyses did not include 2 studies from 2003. In this analysis, Sanchez-Ramos and colleagues followed guidelines for metaanalyses and systematic reviews of randomized controlled trials defined by the Quality of Reporting of Meta-Analyses conference.[2]

In addition, they included only trials that:

- evaluated the efficacy of progestational agents to prevent preterm birth in women at elevated risk,
- assigned patients to either a progestational agent or placebo, and
- clearly defined preterm birth.

Ten studies met the criteria, including a randomized trial of 463 subjects from 2003.[3]

The findings

There was a significant reduction in the rate of preterm delivery in women who received progestational agents, compared with placebo (26.2% versus 35.9%; odds ratio 0.45, 95% confidence interval, 0.25–0.80). This reduction was observed not only in studies assessing 17 α-hydroxyprogesterone caproate, but also in investigations of other progestational agents such as allylestrenol.

Overall, women who received progesterone had lower hospitalization rates for threatened preterm labor and fewer infants weighing less than 2,500 g, compared with women taking placebo.

A possible exception: multiple gestation. Only 1 of the RCTs in this analysis included multiple gestations, and that trial failed to show a reduction in preterm births.

Limitations of the analysis

The 10 RCTs included in the metaanalysis had generally modest numbers of patients and outcome events, so there was not enough statistical power to make precise estimates of incidence and to detect significant and clinically important differences in some outcome variables, such as perinatal mortality.

Overall, however, the metaanalysis was well performed and reached the same conclusion as the most recent and largest randomized trial[3]: Progesterone effectively prevents preterm delivery. ■

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