## Vitamin Therapy Failed to Reduce Preeclampsia

## BY DOUG BRUNK

SAN DIEGO — Antioxidant vitamins C and E given prior to 17 weeks' gestation in nulliparous, low-risk women do not reduce the frequency of serious maternal and perinatal complications associated with pregnancy-related hypertension.

Nor do the vitamins reduce the diagnosis of preeclampsia, according to findings from a 5-year study of more than 10,000 women conducted by the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, Bethesda, Md.

In the randomized, placebo-controlled, double-blinded trial of low-risk nulliparous women, Dr. James M.



Vitamins C and E did not reduce complications associated with pregnancy-related hypertension.

## DR. ROBERTS

Roberts and his colleagues at 16 centers in the United States allocated 10,154 women to daily treatment with 1,000 mg vitamin C and 400 IU vitamin E or placebo at 9-16 weeks' gestation.

The primary outcome was severe pregnancy-related hypertension (defined as a systolic blood pressure greater than 160 mm Hg or a diastolic pressure greater than 110 mm Hg), or mild pregnancy-related hypertension (defined as a blood pressure reading of greater than 140/90 mm Hg), with at least one of the following: renal or hepatic dysfunction, thrombocytopenia, eclampsia, indicated preterm delivery prior to 32 weeks' gestation, small for gestational age infant, stillbirth, or neonatal death up to discharge, Dr. Roberts explained at the annual meeting of the Society for Maternal-Fetal Medicine.

Dr. Roberts, professor of obstetrics, gynecology, and reproductive sciences at the Magee-Womens Research Institute at the University of Pittsburgh School of Medicine, reported that the women had a mean age of 24 years, their mean prepregnancy body mass index was 25 kg/m<sup>2</sup>, 16% were smokers, 44% entered the trial by 13 weeks' gestation, and 77% entered the trial taking multivitamins.



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Pregnancy outcome data were available on 9,969 women (4,993 in the vitamin treatment group and 4,976 in the placebo group). There were no significant differences between the treatment and control groups in terms of hypertension as a composite outcome (6.1% vs. 5.8%, respectively) or in the incidence of preeclampsia (7.2% vs. 6.7%). The only difference in outcomes be-

tween the two groups was observed in

the rate of gestational hypertension, which was 2.6% higher in the treatment group, compared with controls, though this difference was not statistically significant. Failing that, "everything was identical between the two groups," including rates of admission to the neonatal intensive care unit, respiratory distress syndrome, and sepsis, Dr. Roberts said. "Why doesn't antioxidant therapy re-

duce the frequency of preeclampsia or

adverse outcomes?" he asked. One possibility is that not all women develop preeclampsia due to the same linkage between reduced placental perfusion and abnormal implantation. It may be that only a subset of women benefit from treatment to reduce oxidative stress. "This is an important possibility that we will be testing in another part of this study." Dr. Roberts reported having no conflicts of interest to disclose.



## Important Safety Information

ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA.

Three independent, case-controlled studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incident rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer-reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade.

The three case-controlled studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be re-assessed, on at least a semiannual basis, to determine the need for continued therapy. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or reoccurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equi-estrogenic doses.

Other warnings include: induction of malignant neoplasms, gallbladder disease, effects similar to those caused by estrogen-progestogen oral contraceptives (such as thromboembolic disease, hepatic adenoma, elevated blood pressure, worsening of glucose tolerance), hypercalcemia, and rarely, trauma induced by the Vagifem<sup>®</sup> applicator.

In a placebo-controlled clinical trial, the most commonly reported adverse events included: headache (9%), abdominal pain (7%), upper respiratory tract infection (5%), genital moniliasis (5%), and back pain (7%).

The use of Vagifem<sup>®</sup> is contraindicated in women who exhibit one or more of the following: known or suspected breast carcinoma, known or suspected estrogen-dependent neoplasia (e.g., endometrial carcinoma), abnormal genital bleeding of unknown etiology, known or suspected pregnancy, porphyria, hypersensitivity to any Vagifem<sup>®</sup> constituents, active thrombophlebitis or thromboembolic disorders, or a past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast malignancy).

Please see brief summary of Prescribing Information on adjacent page.



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