EXAMINING
the Evidence

HRT and fracture incidence; periodontal disease and preterm birth

THE QUESTION: Does hormone replacement therapy reduce the incidence of fractures in postmenopausal women with coronary disease?

PAST STUDIE Observational findings have shown lower fracture rates in postmenopausal women who take hormone replacement therapy (HRT) compared with women who do not. It is estimated that taking HRT for 5 years or more will decrease the probability of vertebral fractures by 50% to 80%, and hip and wrist fractures by 25%.

THIS STUDY: About 2,763 postmenopausal women with coronary disease and an intact uterus were enrolled into the Heart Estrogen/progestin Replacement Study (HERS) and monitored every 4 months for about 4 years. The average age of the participants was 66.7 ± 6.7 years, and fewer than 15% had osteoporosis based on bone density. Women were excluded if their coronary event occurred within 6 months prior to the study, serum triglycerides were greater than or equal to 300 mg/dL, or if they had used hormones in the past 3 months. Women who had undergone a hysterectomy or had a history of deep vein thrombosis, pulmonary embolism, breast or endometrial cancer, uncontrolled hypertension, or diabetes could not participate.

Each woman was randomly assigned to take 1 tablet of either a placebo or a combination of 0.625 mg of conjugated equine estrogens and 2.5 mg of medroxyprogesterone acetate. During 10,554 person years of follow-up, 286 women experienced a fracture (138 in the treatment group and 148 in the placebo group). These included 58 wrist fractures (relative risk [RR] 1.01; 95% confidence interval [CI] 0.6 to 1.7), 27 hip fractures (RR 1.09; CI, 0.5 to 2.3), 32 spine fractures (RR 0.69; CI, 0.3 to 1.4), and 192 other fractures (RR 0.91; CI, 0.7 to 1.2). There was no difference in average height loss between the groups.

The researchers concluded that there was no evidence of a reduction in the incidence of fractures or rate of height loss in postmenopausal women without osteoporosis. More studies are needed to clarify the effect HRT has on fracture risk among women with and without osteoporosis.

FIND THIS STUDY: April 2001 issue of the *American Journal of Medicine*; abstract online at www.medicinedirect.com.

WHO MAY BE AFFECTED BY THESE FINDINGS? Postmenopausal women with and without osteoporosis.

EXPERT COMMENTARY: This study's findings support similar data suggesting that no drug therapy—including HRT—has proven effective for fracture prevention in postmenopausal women without osteoporosis. However, the appreciable relationship between changes in lumbar spine bone density and the magnitude of vertebral fracture risk suggest that HRT will have a largely positive effect on vertebral fracture incidence in women with osteoporosis.[1] For each standard deviation decline in bone mineral density (BMD) at the lumbar spine, there is a 2.3-fold increase in the risk of vertebral fracture.[2]

Since evidence for nonvertebral fracture reduction is much more difficult to ascertain, large clinical trials are necessary. Meanwhile, there is an appreciable trend suggesting that HRT reduces nonvertebral fracture risk by 35% to 50% when initiated before age 60.[3] Epidemiological studies suggest a 50% reduction in hip fracture with HRT.[4] However, confidence intervals from meta-analyses imply that HRT may have little effect. Furthermore,

none of the evidence to date considers the risks associated with HRT use.

Observational studies suggest that HRT's benefits include a reduction in cardiac events, including myocardial infarction and death. However, it has been found to have a negligible effect on the reversal of established cardiovascular disease.

THE BOTTOM LINE: HRT attenuates the rapid decline in BMD in the estrogen-depleted woman. For this reason, it is an important therapy to consider for the postmenopausal patient. More randomized, controlled trials on HRT and its role in preventing fractures in postmenopausal women with and without osteoporosis, along with long-term effects on other target areas are needed so that physicians and patients can adequately weigh their options.

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THE QUESTION: Does periodontal disease cause preterm birth?

PAST STUDIES: Research has suggested that chronic periodontal infection may be associated with preterm birth.

THIS STUDY: A total of 1,313 pregnant women were recruited from the Perinatal Research Center at the University of Alabama in Birmingham. Gravidas had a complete medical and periodontal workup between 21 and 24 weeks' gestation. After determining gestational age at delivery, the researchers calculated the relationship between periodontal disease and preterm birth, adjusting for smoking, parity, race, and maternal age.

Based on these findings, the authors concluded that preexisting periodontal disease in the second trimester of pregnancy increases the risk of preterm birth. In fact, a patient's risk increases 4.5-fold for delivery before 37 weeks' gestation to 7-fold for delivery prior to 32 weeks, depending on the severity of the disease.

FIND THIS STUDY: July 2001 issue of *The Journal of the American Dental Association*; abstract online at www.ada.org/prof/pubs/jada/index.asp.

WHO MAY BE AFFECTED BY THESE FINDINGS? Gravidas with periodontal infections and/or disease.

EXPERT COMMENTARY: Many dental practitioners would opine that dental caries and significant periodontal disease in early adulthood are markers of poverty. Interestingly, many studies on preterm birth have drawn similar conclusions, especially with regard to bacterial vaginosis (BV). Not only does BV seem to be associated with a higher rate of preterm birth, but studies also suggest that the infection may be more prevalent in lower socioeconomic groups. Therefore, it is important to examine socioeconomic status when determining the association between periodontal disease and preterm birth.

In this study, the researchers raised a number of important issues. Unfortunately, socioeconomic status was not among them. Interestingly, 82% of the study population was African American. In the United States, African Americans have a higher incidence of preterm delivery (PTD) than either the Caucasian or Hispanic populations. Therefore, the value of determining whether preterm birth is attributable to periodontal disease is suspect, unless it is used as a proxy for representing African Americans in a lower socioeconomic group. Perhaps it would be best to determine whether periodontal disease has the same association with prematurity across all US populations in order to determine whether the correlation is magnified in the lower socioeconomic groups.

Until we can eliminate poverty, obstetricians will have to continue to deal with the problems of low birth weight and prematurity.

What then can we conclude from the data? The relationship between periodontal disease and preterm birth is undeniable. Even more compelling is the notion of increasing prematurity with regard to the severity of periodontal disease. However, the authors firmly stated that it is still unknown whether treating periodontal disease will reduce the risk of preterm delivery, a finding that is reminiscent of studies of bacterial vaginosis and preterm birth. The only conclusion we can draw from this study is that periodontal disease should be avoided. Further, I would submit that

poor dental hygiene in young women is a marker for poverty, and therein lies the greatest risk factor for PTD. Until we can eliminate poverty, obstetricians will have to continue to deal with the problems of low birth weight and prematurity.

There is one other potential confounder worth mentioning: the contribution of other bacteria to the etiology of prematurity. Hill suggested that both oral and genital microflora may contribute to preterm birth.[1] If this observation is correct, it would seem that any intervention trial would need to take into account colonization in both the oral and genital sites.

THE BOTTOM LINE: Like many issues in medicine, prevention ultimately works better than treatment. Therefore, preventing periodontal disease or, at least, identifying and treating it at its earliest stages is the best approach. All Ob/Gyns should discuss dental hygiene with their patients to better assess preventive and treatment measures.

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