Treatment of localized periodontal disease in pregnancy does not reduce the occurrence of preterm birth: results from the Periodontal Infections and Prematurity Study (PIPS)

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Preterm birth is one of the most complicated and challenging research issues in perinatal medicine. Despite decades of scientific inquiry, the preterm birth rate has remained constant or increased annually in the United States. Nearly 12% of all deliveries occur at <37 weeks of gestation. Spontaneous preterm birth is a complex and heterogeneous public health problem with multiple risk factors. Some of these risk factors are social (such as maternal race/ethnicity and poverty), and some are individual (such as underweight, tobacco use, and maternal infection). Many of these risk factors occur in combination, which complicates preventive strategies.

Periodontal disease is an infectious stimulus that has been associated with preterm birth. Periodontal disease is a Gram-negative anaerobic infection of the mouth that occurs in 40% of pregnant women. Infection and subsequent inflammation of the gingival and local support attachments of the teeth can result in tissue, bone, and, ultimately, tooth loss. This destructive process involves both direct tissue damage from plaque bacterial products and indirect damage through bacterial stimulation of local and systemic inflammatory and immune responses. In a recent metaanalysis of the association between maternal periodontal disease and preterm birth, Vergnes and Sixou examined 17 studies and reported a pooled estimate odds ratio for preterm birth of 2.83 (95% confidence interval [CI], 1.95–4.10; P < .0001). Polyzozs et al conducted a meta-analysis of randomized clinical trials to determine whether periodontal treatment during pregnancy reduced preterm birth. After examination of 7 trials that included 2663 patients (1491 patients were assigned randomly to periodontal treatment and 1172 patients were assigned to no treatment), they found that periodontal treatment during pregnancy resulted in significantly lower preterm birth (odds ratio, 0.55; 95% CI, 0.35–0.86; P = .008).

Although these data support a relationship between maternal periodontal disease and preterm birth, several studies have failed to demonstrate such an association. In one of the largest studies to date, Moore et al examined the relationship between multiple periodontal parameters (including mean gingival probing depths, percent of tooth sites with probing depths ≥ 4 mm, percent of sites with bleeding on gingival probing, and percent of sites with loss of tooth attachment ≥ 2 or 3 mm) and found no difference between women with preterm birth and without preterm birth. Although these disparate findings may be explained by population differences among studies and differences in definitions of periodontal disease or other possible confounders, the controversy regarding the association between maternal periodontal disease and preterm birth continues.

Several investigators have embarked on periodontal treatment trials during pregnancy in an effort to resolve the controversy regarding the association between periodontal disease and preterm birth. Initial studies were promising, which suggested that treatment of periodontal disease during pregnancy reduced the risk for preterm birth and improved the oral health of the mother. In this issue of the Journal, Macones et al report the results of the Periodontal Infections and Prematurity Study (PIPS), which was a randomized clinical trial of treatment of localized periodontal disease in pregnancy to reduce the occurrence of preterm birth. They screened >3500 pregnant women and found that the prevalence of periodontal disease was 50%. Women with periodontal disease were then assigned randomly either to active treatment by scaling and root planing or to placebo (tooth polishing). There was no significant difference in preterm birth at <35 weeks of gestation between the 2 groups; active treatment did not reduce significantly the risk of spontaneous preterm birth at <35 weeks of gestation. However, a greater proportion of women who received active treatment of their periodontal disease had a medically indicated preterm delivery at <35 weeks of gestation, compared with placebo (3.3% vs 1.1%; relative risk, 3.01; 95% CI, 0.95–4.24).

Some of the findings of Macones et al are concordant with 2 other recently published studies. Michalowicz et al reported no reduction in preterm birth at <37 weeks of gestation among women who received antepartum periodontal treatment compared with women who received postpartum treatment. However, they noted a nonsignificant reduction in preterm birth at <32 weeks of gestation (2% vs 4%). In the largest intervention trial to date, Offenbacher et al also noted no significant reduction in preterm birth risk among women who received periodontal treatment during, rather than after, pregnancy. Both of these studies were able to demonstrate significant im-

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improvement in maternal oral health as a result of periodontal treatment during pregnancy and found no increase in perinatal complications.

What is different and notable in the PIPS trial compared with previously published data is a higher rate of indicated preterm birth among women with active periodontal treatment compared with placebo. None of the other treatment trials have noted such an association, but this is certainly of concern if other investigators replicate it. Theoretically, the act of scaling and root planing could promote systemic dissemination of oral pathogens and/or their byproducts, and this dissemination could have deleterious effects that result in maternal or fetal disease that could require early delivery. Importantly, Macones et al acknowledge that this finding may be the result of a type I error.

One challenge with interpretation of the findings of the PIPS trial is the decision to stop enrollment before the achievement of their a priori sample size. Their final sample of 756 women fell significantly short of the planned enrollment of 1400 women; therefore, conclusions based on these data should be interpreted with caution. Although the authors make a cogent argument that it is unlikely that a type II error explains their negative findings, they base that argument on the increase in indicated preterm births among the treated group. Because their original assumptions did not include indicated preterm birth as a primary outcome and the original sample size calculation did not include trying to find differences in indicated preterm birth, post hoc power analyses that used these births need to be considered cautiously. The post hoc calculation performed by Macones et al suggests that the study was powered adequately to find a 60% reduction in preterm birth, although their original calculation was based on 50% reduction.

Despite this limitation, the PIPS trial yielded important information. Macones et al confirm findings of 2 recent US trials that also showed that periodontal treatment during pregnancy does not reduce preterm birth risk. Although other trials have not shown any deleterious effect of periodontal treatment during pregnancy, the findings from the PIPS trial suggest potential increased risk for indicated preterm birth. This finding needs further exploration. The PIPS trial also confirmed that periodontal treatment improves the oral health of pregnant women, and oral health for the sake of oral health cannot be disputed.

In conclusion, periodontal disease is a common infectious complication of pregnancy that is associated with preterm birth. Although promising, the current data do not support periodontal treatment during pregnancy to reduce the preterm birth risk. As obstetrician-gynecologists, we can educate our patients regarding the importance of oral health and important preventive measures to maintain oral health.

REFERENCES