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ABSTRACT

There is growing evidence that chronic periodontitis may be a risk factor for pre-term birth. The goal of this intervention study was to determine the effect of periodontal treatment on the pregnancy outcome in women with threatening pre-term birth and initial localized chronic periodontitis. Forty-one women with a singleton pregnancy were enrolled in the study. For this treatment group, oral hygiene instruction and periodontal therapy were provided in the third trimester, while those in the control group (42 persons) did not receive any periodontal treatment. In the treatment group, the mean weight of newborns was 3079.0 g, compared with the control group mean of 2602.4 g. The incidence of pre-term birth and low birthweight in the treatment group was significantly less than in the control group ($p = 0.015$). Periodontal treatment completed before the 35th week appeared to have a beneficial effect on birth weight and time of delivery.

KEY WORDS: newborn, pregnancy, periodontal therapy, periodontitis, pre-term birth.

Benefits of Periodontal Therapy When Preterm Birth Threatens

INTRODUCTION

The hypothesis that there is a possible connection between pre-term delivery and periodontal disease in pregnant women emerged in the early 1990s. However, there is still controversy as to whether there is a true correlation among periodontal infection, pre-term delivery, and restriction of fetal growth. Study designs have varied—some epidemiological (Offenbacher *et al.*, 1996; Farrell *et al.*, 2006), some microbiological (Madianos *et al.*, 2001; Urbán *et al.*, 2006), and others interventional (Jeffcoat *et al.*, 2003; Sadatmansouri *et al.*, 2006). A positive correlation between periodontitis and pre-term delivery (Dasanayake, 1998; Bosnjak *et al.*, 2006; Radnai *et al.*, 2006) was shown in a majority of these studies, although some epidemiological (Moore *et al.*, 2004; Skuldbøl *et al.*, 2006) and interventional (Mitchell-Lewis *et al.*, 2001; Michalowicz *et al.*, 2006) studies showed no significant relationship between maternal periodontitis and pre-term delivery. Hence, conclusive evidence appears to be lacking. An intervention study could provide further evidence of a possible causal effect of periodontitis on pre-term delivery. Thus, the aim of our investigation was to assess the potential beneficial effects of periodontal treatment during pregnancy on the birthweight and the time of delivery.

MATERIALS & METHODS

Study Population

The study population consisted of 83 systemically healthy Caucasian women who were hospitalized due to threatened pre-term delivery at the University of Szeged, Department of Obstetrics & Gynecology. The women were screened, and those with periodontal disease were randomized to either a periodontal treatment or a no-treatment protocol. After being informed of the aims and methods of the study, they agreed to participate. The study was approved by the Institutional Review Board for the protection of human study participants.

Women with any systemic medical problem, undergoing a multiple (twins, triplets, etc.) pregnancy, or with a history of previous pre-term birth or miscarriage were excluded. Mothers who smoked, consumed alcoholic drinks in a great amount, took drugs, or suffered malnutrition were also excluded, as were those who would require antibiotics for invasive procedures.

Sample Size

Before the study, a sample size calculation was performed which related birthweight assessment and time of gestation. Hence, assuming a 500 g birthweight difference at a 95% test power for a two-sample *t* test, $N = 39$ was the necessary minimum case number. To show a two-week difference in delivery time, at 2.5 SD and 95% power, the desired minimum sample size was $N = 42$.

Treatment and Control Group Enrollment

The study was carried out in 2005 and 2006. During the two study years, there were 4167 deliveries at the Department of Obstetrics & Gynecology in Szeged. Among

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those women who delivered during that time-span, 429 women were admitted to the hospital because of threatened pre-term birth, and were treated as in-patients. More than half did not meet inclusion criteria, or refused to participate (281 women). The periodontal status of 148 women was examined, and those who were periodontally healthy were identified. Initial localized chronic periodontitis was found in 89 women. For the allocation of the participants for periodontal treatment, we used a block randomization with blocks of two. We generated a random sequence of 1's and 2's, and the treatment was allocated accordingly to the 1st or 2nd person in the blocks, leaving the other for the control group. There were 43 women in the treatment and 46 in the control group. Finally, data pertaining to 83 women were analyzed (Fig.), since six women were not available for follow-up (two in the treatment, four in the control groups). The dentist who examined and treated the women was blind to the pregnancy outcome.

Collection of Demographic and Socioeconomic Data

A questionnaire was used to record demographic data, and actual and previous general medical and obstetric histories, including information regarding the socio-cultural status and educational levels of both the mother and the father. Educational levels were defined as follows: primary school (8 yrs), technical school (3 yrs post-primary school), grammar school (4 yrs after primary school), and higher education (university or college). The parents' occupations were categorized as manual worker, intellectuals/professionals, or 'other occupation,' e.g., taxi driver, housewife, office worker. Place of residence was defined as being either in a city or in a village.

Periodontal Status Measurements

Periodontal examinations were completed at the Department of Obstetrics & Gynecology, where a dental unit with an ultrasonic scaler was installed. This area was suitable for dental examinations and the undertaking of professional oral hygiene treatment and periodontal status measurements. Examinations and periodontal treatment were carried out by the same dental clinician.

To measure probing depth, the clinician used a disposable periodontal probe with a tip diameter of 0.5 mm. The depth was taken from the gingival margin to the most apical point of the sulcus/pocket, at 6 sites *per* tooth, i.e., mesiobuccal, midbuccal, distobuccal, mesiolingual, mid-lingual, and distolingual. Bleeding on probing was regarded as positive if it occurred within 15 sec after the probing depth was measured at any tooth site, and was recorded dichotomously.

Examinations were completed by the same team member, and the examiner, who was an experienced periodontologist, re-examined 20 women after a 30-minute time period had elapsed, to test reproducibility.

Definition of Preterm Delivery and Threatened Preterm Birth

Premature delivery (WHO, 1950) implies labor that occurs at fewer than 37 complete wks of gestation, and is generally accompanied by low birthweight, i.e., a birthweight < 2500 g.

Gestational age at delivery and periodontal treatment were calculated from the first day of the last menstrual period, or based on the results of ultrasonic examination, which was provided in the first trimester of pregnancy. Threatened pre-term birth, between the completed 24th and 37th wks, includes obstetric events during pregnancy, such as premature rupture of the membranes, or necessity of treatment for premature uterine activity and/or cervical dilation. Women with this condition received special obstetric treatment to maintain their pregnancy as long as possible. The therapy consisted of, first, bed rest, then tocolytic agents (intravenous MgSO_4 /Gynipral), and antibiotic administration for the prevention of genito-urinary infection (based on the antibiogram).

Participant flow

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Assessed for eligibility: N = 429
↓
Did not meet inclusion criteria: N = 267
Refused to participate: N = 14
↓
Did not have periodontitis: N = 59
↓
Had periodontitis: N = 89
↓
Randomized for treatment and control groups:
N = 83
↓
Treatment group: N = 43 - Lost to follow-up:
N = 2 → Treatment group: N = 41
Control group: N = 46 - Lost to follow-up:
N = 4 → Treatment group: N = 42
  
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Figure. Study Flow Diagram (randomization with 89 women)

Before the 35th wk of pregnancy, where pre-term birth is threatened, an intramuscular steroid was given to prevent infantile respiratory distress syndrome. As a result of such treatments, labor could possibly be delayed until after the 37th wk of gestation.

Initial Localized Chronic Periodontitis Criteria

A pregnant woman was regarded as having periodontitis if she had ≥ 4 mm probing depth, at least at one site, and bleeding on probing (BOP) for $\geq 50\%$ of teeth. Participants having no ≥ 4 mm pockets or BOP occurring at less than 50% of teeth were regarded as periodontally healthy.

Periodontal Treatment

The participants underwent periodontal examination within two days after being admitted as in-patients at the hospital due to a threatened pre-term delivery. The periodontal treatment was carried out in the third trimester, around the 32nd wk of pregnancy, and consisted of oral hygiene instruction, supra- and subgingival scaling carried out with hand instruments and/or an ultrasonic scaler, and finished by polishing of the teeth with a fluoride-containing polishing paste. For those who received no periodontal treatment during pregnancy, it was suggested post-delivery.

Statistical Analysis

Descriptive statistics were used to assess the demographic and socioeconomic data. For comparison of mean values, Student's *t* test was used, as well as Mann-Whitney tests where non-normality was determined. Normal distribution of samples was tested by the Kolmogorov-Smirnov test. Association of treatment with categorical data was analyzed by the chi-square test and Fisher's exact test, including the calculation of unadjusted odds ratios. The significance level was set at $p < 0.05$.

RESULTS

The effect of periodontal treatment on the birthweight of the newborn and the dates of delivery of 83 women (Table 1) was analyzed statistically in the present study. With respect to calibration of the periodontal examinations, the intra-class correlation coefficient was 0.94 or greater for the different periodontal scores and indices.

Table 1. Demographic Characteristics and Baseline Periodontal Status in Treatment and Control Groups

	Treatment* N = 41	Control N = 42	All N = 83 (100%)	p-value
Age (yrs)				<i>t</i> test
Mean	29.1 ± 6.4	28.9 ± 5.4	29.0 ± 5.8	0.888
Minimum	17.7	16.2	16.2	
Maximum	43.1	41.1	43.1	
Educational level of mothers				Chi ² -test
Primary school	7 (38.8%)	11 (61.2%)	18	
Technical school	10 (38.5%)	16 (61.5%)	26	
Grammar school	17 (56.6%)	13 (43.4%)	30	
Higher education	7 (77.8%)	2 (22.2%)	9	0.134
Occupation of mothers				Chi ² -test
Manual worker	19 (48.7%)	20 (51.3%)	39	
Intellectual	4 (44.4%)	5 (55.6%)	9	
Other	18 (51.4%)	17 (48.6%)	35	0.926
Educational level of fathers				Chi ² -test
Primary school	4 (28.6%)	10 (71.4%)	14	
Technical school	20 (52.6%)	18 (47.4%)	38	
Grammar school	15 (60.0%)	10 (40.0%)	25	
Higher education	2 (33.3%)	4 (66.7%)	6	0.212
Occupation of fathers				Chi ² -test
Manual worker	26 (50.9%)	25 (49.1%)	51	
Intellectual	8 (66.6%)	4 (33.4%)	12	
Other	7 (35.0%)	13 (65.0%)	20	0.120
Place of residence				Fisher test
Village	20 (47.6%)	22 (52.4%)	42	
City	21 (51.2%)	20 (48.8%)	41	0.827
Number of pregnancies				Chi ² -test
1	23 (54.8%)	19 (45.2%)	42	
2	11 (61.1%)	7 (38.9%)	18	
3	6 (42.9%)	8 (57.1%)	14	
4	1 (11.1%)	8 (88.9%)	9	0.072
Time of hospitalization (wks)	Mean ± SD	Mean ± SD	Mean ± SD	Mann-Whitney test
	31.63 ± 2.6	31.45 ± 2.8	31.54 ± 2.7	0.822
Periodontal status				
Probing depth (mm)	2.15 ± 0.23	2.11 ± 0.41	2.13 ± 0.33	0.316
Frequency BOP (%)	63.1 ± 10.7	70.8 ± 16.7	67.0 ± 14.5	0.051

* Treatment: periodontally treated group.

Control: group not periodontally treated.

Significance level was set at $p < 0.05$.

There was no statistically significant difference between the treatment and control groups relative to demographic and periodontal data.

There were 41 women in the treatment group and 42 control individuals (not receiving periodontal treatment). The mean age was 29.0 yrs, and the age distribution was found to be normal, with no significant difference between the mean age of the treatment (29.1 yrs) and control (28.9 yrs) groups ($p = 0.888$). The youngest mother was 16.2 yrs old and the oldest 43.1 yrs old (Table 1). Participants had different educational levels and occupations and came from all social strata. With respect to socio-economic (education, occupation, residency) data, there was no significant difference between treatment and control groups. The number of pregnancies was also very similar in both treatment and in the control groups ($p = 0.072$), with most of the mothers having their first or second pregnancy during the study (Table 1).

Signs of threatened pre-term birth started around the 32nd gestational wk in both groups (Table 1). There was no significant difference concerning the times of hospitalization between treatment and control groups ($p = 0.822$).

The current periodontal status of the women was described by probing depth (mean 2.15 mm in the treatment group, 2.11 mm in control individuals) and frequency of bleeding on probing (63.1% in the treatment group, 70.8% in the control group), showing no significant difference between these parameters ($p = 0.316$ and $p = 0.051$, respectively) (Table 1).

The mean weight (Table 2) of newborns of treated women was 3079.0 g, while it was much less for control individuals, at 2602.4 g, the difference being highly significant ($p = 0.001$). The length of pregnancy (Table 2) also differed significantly between groups, at 37.5 wks in the treatment, and 36.1 wks in the control group ($p = 0.013$).

The incidence of deliveries at ≤ 37 weeks' gestation (Table 3) was 24.3% in the periodontally treated group, but significantly greater at 52.4% in control individuals ($p = 0.013$). Regarding low birthweight (< 2500 g), it was 14.6% for the treated, and 42.9% for control individuals ($p = 0.007$). Both pre-term birth and low birthweight occurred in only four women (9.8%) in the treatment group, and in 14 control individuals (33.3%) ($p = 0.015$).

The calculated odds ratios showed that periodontal therapy increased the chance of normal delivery, being 3.4 times more likely than in control individuals, while for infant birthweight of ≥ 2500 g, it was 4.3 times higher in the treatment group than in control

individuals (Table 3). Furthermore, normal gestation, coupled with a normal birthweight, was 4.6 times more likely in mothers who underwent periodontal treatment.

DISCUSSION

As far as the authors are aware, this was the first study to report the possible effects of periodontal therapy on the incidence of pre-term birth and low birthweight in a demographically homogeneous Caucasian European population. The study concentrated on the potential effects of periodontal treatment on the outcome of the pregnancy. Here, significant differences were found between treatment and control groups relative to each new-

born's birthweight and time of delivery. The mean weight of the newborns was significantly greater (on average, 476.6 g) for women who received periodontal treatment, and their gestation times were longer (on average, 1.4 wks), than those of the control individuals—both factors of great clinical importance in the developmental status of the newborn. Although the periodontal treatment was provided only in the third trimester, it is probable that this treatment played a part in the positive outcome of the pregnancy.

In this study, initial localized chronic periodontitis (Armitage, 1999) was determined by measurement of critical probing depth (Lindhe *et al.*, 1982) and frequency of bleeding on probing, since these periodontal status parameters reflect mainly on the current inflammatory burden. These criteria for initial localized chronic periodontitis were chosen because a probing depth of less than 4 mm can be regarded as within normal limits (Lindhe and Nyman, 2003). Bleeding on probing was the other criterion for chronic periodontitis, since many studies have shown it as a reliable inflammatory sign (Davenport *et al.*, 1982; Lang *et al.*, 1986). Additionally, it has been stated that these two parameters should also be taken into consideration as important factors in a woman's risk assessment for the recurrence of periodontitis (Lang and Tonetti, 2003).

Alveolar bone level was not assessed radiographically, because radiographic evaluation is not always reliable in the early stage of periodontitis. Additionally, the size of the surface area of the pocket (Slots, 2003), through which bacteria and their products can invade the periodontal tissues, has been found to be more important than bone levels *per se*, since these indicate the outcome of only previous inflammation.

The suggestion from the first interventional study (Mitchell-Lewis *et al.*, 2001) was that periodontal therapy is a possible means of reducing the incidence of pre-term birth. It has been found that pre-term birth at < 35 wks occurred in 0.8% women who received scaling and root planing during pregnancy, while it was 6.3% in their non-treated counterparts (Jeffcoat *et al.*, 2003). In another study, it was found that periodontal treatment significantly reduced the pre-term low-birthweight rate in a study population of women with pregnancy-associated gingivitis (Lopez *et al.*, 2005), while in a more recent publication, a positive effect of periodontal treatment during pregnancy was reported (Sadatmansouri *et al.*, 2006). However, in these studies,

Table 2. Mean Birthweight of Newborns, and the Times of Delivery in Treatment and Control Groups

	Treatment (N = 41) Mean \pm SD	Control (N = 42) Mean \pm SD	Total (N = 83) Mean \pm SD	Mann-Whitney Test* p-value
Weight (g)	3079.0 \pm 592.3	2602.4 \pm 668.3	2837.8 \pm 672.2	0.001
Minimum	1480.0	950.0	950.0	
Maximum	4300.0	3820.0	4300.0	
Time (wks)	37.5 \pm 1.7	36.1 \pm 2.8	36.7 \pm 2.4	0.013
Minimum	32	26	26	
Maximum	40	40	40	

* Mann-Whitney test showed significant difference between the treatment and control groups relative to birthweight and time of delivery. Significance level was set at $p < 0.05$.

Table 3. Incidence of Pre-term Delivery and Low Birthweight in Periodontally Treated and Control Groups (odds ratios of normal delivery related to periodontal treatment)

	Treatment N = 41 100%	Control N = 42 100%	Total N = 83 100%	Fisher's Exact Test p-value	Odds Ratio	CI 95% Lower–Upper Limits
Time of d.*				0.013	3.4	1.3-8.6
< 37 wks	10 (24.3%)	22 (52.4%)	32 (38.6%)			
\geq 37 wks	31 (75.6%)	20 (47.6%)	51 (61.4%)			
Birthweight				0.007	4.3	1.5-12.6
< 2500 g	6 (14.6%)	18 (42.9%)	24 (28.9%)			
\geq 2500 g	35 (85.4%)	24 (57.1%)	59 (71.1%)			
Pre-term low birthweight				0.015	4.6	1.3-15.5
Yes	4 (9.8%)	14 (33.3%)	18 (21.7%)			
No	37 (90.2%)	28 (66.7%)	65 (78.3%)			

* Time of d.: Time of delivery.

Pre-term low birthweight Yes: delivery at < 37 wks and birthweight < 2500 g.

Pre-term low birthweight No: delivery at \geq 37 wks or birthweight \geq 2500 g.

CI 95%: confidence interval.

Fisher's Exact test showed a significant difference between treatment and control groups relative to the incidence of pre-term delivery, low birthweight, and pre-term low birthweight. The odds ratios showed that the periodontal treatment had a positive effect on the outcome of pregnancy.

most or all of the women were African-American, Hispanic, or Indian and/or had low socio-economic status, characteristics which are significant risk factors for periodontal disease and pre-term low birthweight (Bobetsis *et al.*, 2006). In contrast, not all intervention studies showed a beneficial effect of oral health measures on pregnancy outcomes (Huojel *et al.*, 2006; Michalowicz *et al.*, 2006).

The above studies and the present investigation may not provide definitive scientific evidence of a causal effect of periodontitis on pre-term delivery; therefore, larger multi-center trials would be required to prove or disprove this hypothesis. These findings are the first to suggest that incorporating periodontal care as an integral component of antenatal obstetric management of threatened pre-term deliveries may result in improved pregnancy outcomes.

In conclusion, the results of the present study showed that women with threatened pre-term delivery and initial localized chronic periodontitis had a significantly lower chance of adverse

pregnancy outcome if they received periodontal therapy before the 35th gestational wk. Current results might also provide indirect evidence for the assumption that maternal periodontitis may cause pre-term birth.

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