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Original article

Pre-eclampsia and nasal CPAP: Part 2. Hypertension during pregnancy, chronic snoring, and early nasal CPAP intervention

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Abstract

Objectives: To evaluate the potential benefit of nasal continuous positive airway pressure (CPAP) administration in pregnant women recognized to have hypertension early in pregnancy.
Methods: This is a randomized study comparing the addition of nasal CPAP treatment to standard prenatal care to standard prenatal care alone in hypertensive women treated with alpha-methyl dopa during early pregnancy. Pregnant women with hypertension were recruited by their obstetricians and completed baseline sleep questionnaires and visual analogue scales on snoring and sleepiness. Subjects were then randomized to receive either CPAP with standard prenatal care (treatment group) or standard prenatal care alone (control group) with routine obstetric follow-up. Nocturnal polysomnography was performed in all patients randomized to the treatment group for initial CPAP titration. Periodic assessment of blood pressure control and CPAP compliance was performed by the same specialist at each scheduled follow-up visit.
Results: In the control group ($n = 9$), a progressive rise in blood pressure with a corresponding increase in alpha-methyl dopa doses was observed, beginning at the sixth month of pregnancy. There was also an increase in the number of non-scheduled post-natal visits during the first postpartum month. Pre-eclampsia occurred in one subject; the remaining eight patients had normal pregnancies and infant deliveries. In the treatment group ($n = 7$), blood pressure was noted to decrease significantly as compared to the control group with associated decreases in doses of antihypertensive medications at six months of gestation. All treated patients experienced uncomplicated pregnancies and delivered infants with higher APGAR scores at one minute post-delivery compared to those of controls.
Conclusion: In pregnant women with hypertension and chronic snoring, nasal CPAP use during the first eight weeks of pregnancy combined with standard prenatal care is associated with better blood pressure control and improved pregnancy outcomes.

Keywords: Pregnancy; Hypertension; Pre-eclampsia; Nasal CPAP; Prevention; Snoring

1. Introduction

Hypertension complicates 12–22% of all pregnancies and occurs as a spectrum of related disorders, including chronic (pre-existing) hypertension, gestational hypertension, and pre-eclampsia. Chronic hypertension is a known risk factor for pre-eclampsia and has been associated with significant maternal–fetal morbidity and mortality. It has been shown that pregnancies complicated by pre-eclampsia are characterized by an increase in systolic blood pressure (BP) by 95% and in diastolic

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BP by 13% between mid-gestation and delivery. Additionally, systolic (but not diastolic) BP may be slightly elevated during the first half of pregnancy in women who develop pre-eclampsia compared to those with gestational hypertension [1]. The circadian pattern of BP may also be a valuable disease predictor as significant changes in the circadian rhythm-adjusted mean of both systolic and diastolic BP and elevation in the 24-h mean pulse pressure have been reported in women who develop pre-eclampsia [2,3]. Ultimately, these BP abnormalities may have significant clinical consequences as data from the Nationwide In Patient Sample (1993–2002) showed that women with pre-existing hypertension, gestational hypertension, and chronic hypertension with superimposed pre-eclampsia had an increased risk of intracerebral hemorrhage in pregnancy, with respective odds ratios of 2.61 (95% CI: 1.34–5.07), 2.41 (95% CI: 1.62–3.59), and 9.23 (95% CI: 8.32–12.98) [4].

It has been also shown in a retrospective, cross-sectional, consecutive case series of 502 women with singleton pregnancy that snoring was reported in 23% of the women during the last week of pregnancy. Hypertension developed in 14% of the snorers versus 6% of the non-snorers, and pre-eclampsia occurred in 10% of the snorers and only 4% of the non-snorers [5]. Investigations of nasal continuous positive airway pressure (CPAP) administration in women with pre-eclampsia admitted to the antenatal ward have shown a significant decrease in BP and improvement in cardiac output with use of CPAP compared to no therapy [6,7]. Furthermore, a preliminary study in women with known risk factors for pre-eclampsia and concurrent snoring or airflow limitation on polysomnography assessed the effect of nasal CPAP treatment in early pregnancy. Although this intervention did not prevent pre-eclampsia in all subjects, in those with pre-existing hypertension we observed that a small group of women normalized BP without change in antihypertensive medications, tolerated CPAP without difficulty, and had normal pregnancy outcomes. Based on these preliminary results, this randomized, controlled study was designed to investigate the effect of nasal CPAP on pregnant women with pre-existing hypertension controlled by antihypertensive medication and chronic snoring. Major outcomes of interest included BP patterns during pregnancy and newborn outcomes.

2. Materials and methods

2.1. Subjects

This study was performed in an obstetrics department responsible for providing perinatal care to high-risk women primarily from the lower and middle class in Sao Paulo, Brazil. Due to these socioeconomic factors and limited access to prenatal care in this population, a high rate of pregnancy-related complications (i.e., pre-eclampsia) has been observed. Women presenting to this obstetric clinic during the first weeks of pregnancy with pre-existing hypertension treated with medications and chronic snoring were considered for the study. Hypertension was defined as BP $\geqslant$140/90 mm Hg (measured after 15 min of rest confirmed by two subsequent readings at five-minute intervals) or use of antihypertensive medications for at least three months. Informed consent was obtained from all participants by their primary obstetricians. No exclusion criteria were specified.

A randomization table based on an anticipated total of 20 consecutive subjects was used to assign patients to control or treatment groups at the time of first consultation. Only 16 patients were eligible for study participation at the conclusion of the specified enrollment period which resulted in a slight difference in the number of patients assigned to each group. As such, seven women were randomized to receive standard prenatal care with CPAP (treatment group) versus nine patients who would receive standard care alone (control group). Fifteen of the subjects had known hypertension prior to pregnancy, and one patient developed hypertension with pregnancy onset. Following treatment with alpha-methyl dopa for one week, mean systolic BP was 123.6 mm Hg, and mean diastolic pressure was 80.9 mm Hg. None of the subjects were obese (mean body mass index 24.2 ± 1.8 kg/m^2, median 23.8 kg/m^2) or had any history of associated metabolic disorders (Table 1).

2.2. Study protocol

The study was approved by the Internal Review Boards of each investigator. After the women who provided informed consent were contacted by the research team, they underwent complete sleep evaluations, including specific questions regarding regular snoring during sleep. Subjects with pre-existing hypertension treated with medications and evidence of chronic snoring were randomized as above to nasal CPAP or no treatment. Both groups continued to receive standard prenatal care with regularly scheduled follow-up visits for medication adjustments and routine obstetric monitoring by the treating obstetrician.

Women in the treatment arm underwent a split-night sleep study for baseline assessment of sleep-related breathing and nasal CPAP titration. Four-channel electroencephalography (EEG), right/left eye electrooculography (EOG), submental and bilateral leg electromyography (EMG), modified V2-lead electrocardiography (ECG), nasal flow by nasal cannula-pressure transducer, mouth thermistor, thoracic and abdominal piezzo-electric bands, finger oximetry, neck microphone, and position sensor were all systematically monitored