OBSTETRICS

Cerebral autoregulation in different hypertensive disorders of pregnancy

Teelkien R. van Veen, MD; Ronney B. Panerai, PhD; Sina Haeri, MD; Jasbir Singh, MD; Jasvant A. Adusumalli, MD; Gerda G. Zeeman, MD, PhD; Michael A. Belfort, MD, PhD

OBJECTIVE: Cerebrovascular complications that are associated with hypertensive disorders of pregnancy (preeclampsia, chronic hypertension [CHTN], and gestational hypertension [GHTN]) are believed to be associated with impaired cerebral autoregulation, which is a physiologic process that maintains blood flow at an appropriate level despite changes in blood pressure. The nature of autoregulation dysfunction in these conditions is unclear. We therefore evaluated autoregulation in 30 patients with preeclampsia, 30 patients with CHTN, and 20 patients with GHTN and compared them with a control group of 30 normal pregnant women.

STUDY DESIGN: The autoregulatory index (ARI) was calculated with the use of simultaneously recorded cerebral blood flow velocity in the middle cerebral artery (transcranial Doppler ultrasound), blood pressure (noninvasive arterial volume clamping), and end-tidal carbon dioxide during a 7-minute period of rest. ARI values of 0 and 9 indicate absent and perfect autoregulation, respectively. We use analysis of variance with Bonferroni test vs a control group. Data are presented as mean ± standard deviation.

RESULTS: ARI was significantly reduced in preeclampsia (ARI, 5.5 ± 1.6; $P = .002$) and CHTN (ARI, 5.6 ± 1.7; $P = .004$), but not in GHTN (ARI, 6.7 ± 0.8; $P = 1.0$) when compared with control subjects (ARI, 6.7 ± 0.8). ARI was more decreased in patients with CHTN who subsequently experienced preeclampsia than in those who did not (ARI, 3.9 ± 1.9 vs 6.1 ± 1.2; $P = .001$). This was not true for women with GHTN or control subjects who later experienced preeclampsia.

CONCLUSION: Pregnant women with CHTN or preeclampsia (even after exclusion of superimposed preeclampsia) have impaired autoregulation when compared with women with GHTN or normal pregnancy. Whether the decreased ARI in patients with CHTN who later experience preeclampsia is due to preexistent differences or early affected cerebral circulation remains to be determined.

Key words: cerebral autoregulation, hypertension, preeclampsia, pregnancy, transcranial Doppler

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Hypertension is one of the most common medical complications of pregnancy, accounting for 16-38% of all maternal deaths.[1,2] Although multiple maternal organs can be affected, cerebrovascular involvement is one of the more serious because it can lead to death or long-term morbidity because of cerebrovascular hemorrhage or edema.[1,2] The cerebral manifestations in these patients are similar to those that are seen in the posterior reversible encephalopathy syndrome,[3,4] which is hypothesized to be related to impaired autoregulation and which leads to either over- or underperfusion of the brain.[3,5,6]

Hypertensive disorders of pregnancy range in a spectrum from chronic hypertension (CHTN) to gestational hypertension (GHTN), preeclampsia, and super-imposed preeclampsia (SiPE) in the setting of CHTN. Women with CHTN have an increased risk of the development of SiPE. The incidence has been reported to be from 12-29%,[7-9] although women with severe CHTN in the first trimester have been reported to go on to SiPE in up to 52% of cases.[10] The risk for cerebrovascular complications during pregnancy is increased with all hypertensive disorders[11-13] but is most pronounced with severe preeclampsia and SiPE.[12,13] These complications are believed to be caused by impaired cerebral autoregulation, which is related to endothelial dysfunction.[14]

Cerebral autoregulation is the ability of the cerebral vasculature to maintain adequate cerebral perfusion despite changes in blood pressure. The cerebral autoregulation can be assessed by the use of a combination of transcranial Doppler (TCD) imaging and continuous noninvasive blood pressure measurement.[15]

From the Department of Obstetrics and Gynecology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands (Drs van Veen and Zeeman); Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston (Drs van Veen, Haeri, and Belfort), and St. David's Women's Center of Texas, North Austin Maternal-Fetal Medicine, Austin (Drs Haeri, Singh, and Adusumalli), TX; and Department of Cardiovascular Sciences, University of Leicester, Leicester, England, UK (Dr Panerai).

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Corresponding author: Teelkien van Veen, MD. teelkien@gmail.com

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The functionality of the autoregulation can be expressed as the autoregulatory index (ARI), with 0 being absent and 9 perfect cerebral autoregulation.[16] This ARI has been shown to be lower in preeclampsia when compared with normotensive control subjects.[5] The ARI was independent of blood pressure and clinical symptoms, which may explain the reason that cerebral complications such as eclampsia and cerebrovascular hemorrhage can occur without sudden and/or excessive elevation in blood pressure.[5] The ARI of the other hypertensive disorders in pregnancy is not known. Based on the increased risks of cerebrovascular complications that are seen in pregnancies that are complicated by CHTN and preeclampsia, but not in GHTN, we hypothesize that the autoregulation is impaired in CHTN (as has been shown for preeclampsia), but not in GHTN.

Consequently, the aim of this study was to evaluate cerebral autoregulation in hypertensive disorders of pregnancy (SiPE, preeclampsia, CHTN, and GHTN) and to compare this with a control group of normal pregnant women. Furthermore, we measured the more traditional parameters of cerebral blood flow velocity (CBFV), critical closing pressure (CrCP), and resistance-area-product to gain additional insight in the pathophysiologic condition.

Materials and Methods

We conducted a prospective cohort study in nonlaboring pregnant women who were recruited at 20-41 weeks' gestation. The Institutional Review Boards at Baylor College of Medicine in Houston, TX, and North Austin Medical Center in Austin, TX, approved this study; informed consent was obtained from each participant before data collection.

Patients were recruited and tested at Texas Children's Pavilion for Women in Houston and North Austin Maternal-Fetal Medicine in Austin, TX, either at the time of admission to the hospital for treatment of a hypertensive disorder or at the time of routine prenatal care. Inclusion criteria were maternal age >18 years and absence of a history of cerebrovascular disease or epilepsy. Hypertensive diagnoses were based on American College of Obstetricians and Gynecologists guidelines.[17,18] Exclusion criteria consisted of smoking, drug use, and the initiation of antihypertensive therapy or treatment with magnesium sulfate <48 hours before the examination.

With the use of a standard data collection sheet, demographic characteristics and obstetrics data were abstracted from patient interviews and medical records. The following maternal characteristics were based on self-report: race/ethnicity, height, current and prepregnancy weight, smoking, alcohol, and illicit substance use. Gestational age was determined by menstrual dating. In cases of uncertain menstrual dates, ultrasound estimates of gestational age were used. Patients were followed until 6 weeks after delivery.

At time of TCD examination, brachial systolic and diastolic blood pressures were measured. With the patients in semi-Fowlers position, bilateral maternal TCD examinations of the middle cerebral artery were carried out with the use of 2-MHz pulsed, range-gated TCD probes (Spencer Technologies, Seattle, WA) that were held in place with the use of a head frame.

Blood pressure was measured continuously noninvasively with finger arterial volume clamping (Finometer Pro; Finapres Medical Systems, Amsterdam, the Netherlands) with the servo-adjust switched off and was afterwards calibrated with the brachial blood pressure. The blood pressure tracing also served to mark each cardiac cycle. End-tidal CO_2 was measured with a nasal cannula (Nellcor Oximax N-85; Covidien, Mansfield, MA), and linearly interpolated at the end of each expiratory phase.

Patients were measured only once for a period of 7 minutes. All data were recorded at 50 Hz, interpolated to 200 Hz, and visually inspected during analysis to remove large spikes. A median filter was used to remove small spikes and artifacts in the CBFV signal. All signals were then low-pass filtered with a Butterworth filter with a cutoff frequency of 20 Hz.[19] Mean blood pressure, bilateral CBFV, end-tidal CO_2, and heart rate were then calculated for each beat. The CrCP and resistance-area product (RAP) were obtained with the use of the first harmonic of blood pressure and CBFV of each cardiac cycle.[20] All signals were then resampled at 5 Hz.[19]

Cerebral autoregulation was determined from the CBFV responses to spontaneous fluctuations in mean arterial blood pressure, as described previously.[19] Segments of 512 samples and 50% superposition were transformed with the fast Fourier transform algorithm, with the use of the Welch method, to obtain the transfer function parameters coherence, gain, and phase in the low frequency range (<0.1 Hz). The inverse fast Fourier transform was then performed to estimate the impulse and step responses. The CBFV step response to a sudden change in blood pressure was compared with 10 template curves proposed by Tiecks et al[16] and the best-fit curve that corresponded to the ARI. An ARI value of 9 represents the best observed cerebral autoregulation.[16]

Measurements were rejected if coherence did not reach 0.5 for any frequency <0.25 Hz. Reported baseline CBFV, blood pressure, RAP, and CrCP were the averages over the 7-minute baseline recording.

All data sets were checked for normalcy of distribution (Sigmastat 2004; Systat Software, Richmond, CA). Data are reported as mean and standard deviation or median with the corresponding range, as appropriate. Analyses were performed with analysis of variance with Bonferroni's post-hoc test, analysis of variance on ranks with Dunn's post hoc test (both comparisons vs the control group), and a second analysis that used multiple linear regression that included prepregnancy body mass index and gestational age at study that was performed to control for these potential confounders.

χ^2 without Yates correction was used for analysis between groups. The Student *t* test or Mann-Whitney Rank Sum test were used for subgroup analysis. Univariate regression analysis was used to