Chapter 3.

Maternal cerebral blood flow changes in pregnancy

ABSTRACT

Objective

To determine blood flow changes in the large cerebral arteries during normal pregnancy.

Study Design

Ten healthy pregnant volunteers underwent velocity-encoded phase contrast magnetic resonance imaging at 4 time intervals, 14-16, 28-32, and 36-38 weeks’ gestation, and at 6-8 weeks postpartum. Analysis consisted of serial paired Student t-tests, with \( p < 0.05 \) considered significant.

Results

Using postpartum values for comparison cerebral blood flow decreased by 14-16 weeks in the middle (\( p < 0.001 \)) cerebral artery, but was not significantly changed in the posterior cerebral artery. Significant decreases occurred in both the middle (\( p < 0.0001 \)) and posterior (\( p = 0.002 \)) cerebral arteries in late pregnancy.

Conclusion

An approximately 20 % reduction in large artery cerebral blood flow occurs during normal pregnancy, secondary to changes in velocity while the area of these vessels remains unchanged. These findings may represent generalized vasodilatation of downstream resistance arterioles, assuming constant blood flow at the tissue level.
INTRODUCTION

Normal pregnancy induces a multitude of rather profound physiologic hemodynamic alterations. Among these are substantive increase in total blood volume, cardiac output, and uterine blood flow. Technical challenges are encountered when assessing cerebral blood flow in the human. Accurate methods have been either invasive or they require radioactive substances. The non-invasive transcranial Doppler technique introduced by Aaslid is a method that is now widely used to assess the intracerebral circulation. It has been used extensively for neurosurgical patients for the early detection of cerebral vasospasm following subarachnoid hemorrhage. During the past decade, this technique has been increasingly used in obstetrics beginning with studies to estimate blood flow velocity in preeclampsia and eclampsia.

Other than early studies of cerebral blood flow by McCall, there are none that report use of invasive methods to assess cerebral blood flow. In the past decade, however, a number of researchers have reported pregnancy-induced changes from velocity measurements of the middle cerebral arteries utilizing transcranial Doppler. These have included both longitudinal as well as cross-sectional studies. In aggregate, these studies indicate that middle cerebral artery velocity decreases with advancing gestation and then returns to nonpregnant values in the puerperium. While these observations are compatible with physiological vasodilatation seen in other regional blood flow systems during pregnancy, the transcranial Doppler technique can be used only to estimate blood flow. Accurate assessment of absolute blood flow is dependent on vessel diameter, which cannot be determined with this method.

More recently, magnetic resonance imaging techniques have been developed that allow for accurate determination of absolute blood flow. Velocity-encoded phase contrast MRI has been used to measure flow in the intracranial, renal, and cardiopulmonary circulations. This method has excellent correlation with traditional invasive methods, such as cardiac catheterization and the Fick principle and thermodilution. Blood flow in cerebral vessels is accurate because the magnetic resonance technique offers higher spatial resolution for vessel localization and cross-sectional area measurement. In an earlier report, we documented the use of this technique to study cerebral blood flow in women with eclampsia and severe
The study now presented was designed to calculate maternal cerebral blood flow longitudinally in pregnancy and then postpartum in a group of healthy women.

MATERIALS AND METHODS

This prospective study was designed to evaluate cerebral blood flow longitudinally during pregnancy and at 6 weeks postpartum in healthy women. Volunteers were recruited from University of Texas Southwestern Medical School or Parkland Memorial Hospital and were either employees or relatives of employees. This study was approved by The University of Texas Southwestern Medical School Institutional Review Board and signed informed consent was obtained. None had a history of chronic hypertension or a history of cerebrovascular abnormalities. Their medications included only prenatal vitamins and iron, and none were smokers. They were scheduled for magnetic resonance imaging at four time intervals: 14-16, 28-32, and 36-38 weeks' gestation, and again at 6-8 weeks postpartum.

Magnetic resonance imaging studies (Figures I - IV) were done using a 1.5T magnet (Signa Horizon LX NVI, GE, Milwaukee, WI). Using magnetization transfer contrast enhancement, the women, while supine, underwent a rapid two-dimensional time-of-flight (2D TOF) magnetic-resonance angiogram sequence (TR=22, TE=4, flip angle =20°, NSA=1). The resulting magnetic resonance angiogram maximum intensity projection (MIP) was reconstructed from a data matrix of 64 slices (1.6 mm thickness, 18 cm FOV, 256 x 224 matrix). In order to ensure that the velocity images were obtained in a straight section of the artery under investigation, a scout image (TR=34, TE=17, flip angle = 20°, 20 cm FOV, 512 x 256 matrix) perpendicular to the vessel in the circle of Willis visualized in the MIP was recorded for each artery. A peripherally gated phase contrast sequence (TR=34, TE=7, flip angle=40°, 3 mm slice thickness, 20 cm FOV, 256 x 256 matrix) was applied lateral to the bifurcation of the internal carotid artery and perpendicular to the course of the artery as seen on the scout image to obtain velocity data. Velocity encoding was in the slice select direction with a set value of 120 cm/s. This range of encoded velocities has been found to be effective for measuring normal cerebral arterial flow velocities.\textsuperscript{12,16}
Cerebral blood flow [Flow (mL/min) = vessel area (cm²) x velocity (cm/min)] was determined at the bilateral proximal middle and posterior cerebral arteries. Flow measurements were analyzed using serial paired two-tailed Student t tests, which tested for flow differences between the 4 time intervals in each artery for each patient. Statistical significance was defined as p<0.05.

RESULTS

Of the 11 women recruited, one experienced significant claustrophobia and withdrew from the study. Another woman developed severe preeclampsia and her data were excluded from analysis. The other nine women, eight of Caucasian and one of African-American descent, remained normotensive and all delivered a term infant of 3477±547 grams. Five women were nulliparous; the mean age of the participants was 32.4±3.8 years. Shown in Table I are the means and standard errors for calculated flow at the four time intervals of the study. The p-values are shown in Table II. The values for the right and left middle cerebral arteries as well as for the right and left posterior cerebral arteries were averaged. Two women did not undergo the 36-38 weeks study due to missed appointments. Using postpartum values as the baseline non-pregnant blood flow, there was a significant decrease in flow in the middle cerebral arteries but not in the posterior cerebral arteries by the first examination at 14-16 weeks’ gestation.
Table I. Cerebral blood flow at four time intervals

<table>
<thead>
<tr>
<th>Artery*</th>
<th>14-16 weeks</th>
<th>28-32 weeks</th>
<th>36-38 weeks</th>
<th>Postpartum (6-8 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA</td>
<td>135.2 ± 5.5</td>
<td>132.5 ± 4.6</td>
<td>118.2 ± 4.6</td>
<td>147.9 ± 5.0</td>
</tr>
<tr>
<td>PCA</td>
<td>52.4 ± 2.9</td>
<td>51.2 ± 2.4</td>
<td>44.2 ± 2.4</td>
<td>55.8 ± 2.7</td>
</tr>
</tbody>
</table>

* MCA = middle cerebral artery; PCA = posterior cerebral artery

Values are expressed as the mean ± Standard Error

Table II. Comparison of pairwise means for both cerebral arteries

<table>
<thead>
<tr>
<th>Comparison of Pairwise Means for MCA</th>
<th>PCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-16 weeks – 28-32 weeks</td>
<td>0.53</td>
</tr>
<tr>
<td>14-16 weeks – 36-38 weeks</td>
<td>0.004</td>
</tr>
<tr>
<td>14-16 weeks – nonpregnant</td>
<td>0.29</td>
</tr>
<tr>
<td>28-32 weeks – 36-38 weeks</td>
<td>0.005</td>
</tr>
<tr>
<td>28-32 weeks – nonpregnant</td>
<td>0.20</td>
</tr>
<tr>
<td>36-38 weeks – nonpregnant</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Flow remained unchanged by 28-32 weeks but decreased significantly again in late pregnancy for both the middle (Figure A) and posterior (Figure B) cerebral arteries. The diameter of the middle and posterior cerebral arteries showed no significant changes in any of the analyses, with a range of 2.43 to 2.49 mm for the middle cerebral arteries and 1.75 to 1.83 mm for the posterior cerebral arteries.
Figure A Middle cerebral arterial blood flow and vessel diameter determined longitudinally during pregnancy and compared with nonpregnant postpartum values in 9 healthy women.

Figure B Posterior cerebral arterial blood flow and vessel diameter determined longitudinally during pregnancy and compared with nonpregnant postpartum values in 9 healthy women.
DISCUSSION

Most invasive methods used to determine cerebral blood flow, or those in which radioisotopes are used, cannot be used in normal pregnancy. Transcranial Doppler ultrasound is inaccurate to measure cerebral blood flow because vessel diameter cannot be measured. In this study velocity-encoded phase-contrast MRI was used to ascertain blood flow longitudinally in normal pregnancy and again postpartum. This noninvasive technique is ideal for absolute blood flow determination because it allows precise vessel localization with cross-sectional area measurement, as well as velocity determination. Another advantage is the ability to determine blood flow in the posterior cerebral circulation not accessible by sonography.

Diameters of the middle and posterior cerebral arteries bilaterally remained unchanged throughout pregnancy and postpartum. Another seminal observation was that blood flow in the middle cerebral artery had decreased significantly by the end of the first trimester. Flow remained constant until 36-38 weeks at which time there was another significant fall at term. Taken together, this represents a 20% decrease in blood flow at term, caused by a decrease in velocity and not large cerebral artery vessel diameter. The posterior cerebral artery showed significant changes in flow only in women near term and not as early as the middle cerebral artery. We believe this is secondary to the quantitatively lesser flow in the posterior circulation in the normal state and not secondary to redistribution. If we had a larger series of patients, we predict there would be a significant early changes in the posterior cerebral artery as well.

To our knowledge our study is the first in which magnetic-resonance imaging techniques have been used to measure cerebral blood flow longitudinally during pregnancy. The nonpregnant cerebral blood flow values in our study correspond well with those values of the only study that has used this technique to measure cerebral blood flow in nonpregnant subjects. Our findings are in agreement with most studies in which middle cerebral arterial flow velocities were determined using transcranial Doppler. These investigators all documented decreased blood flow velocity as pregnancy advanced which suggests diminished flow assuming a constant vessel diameter.

One explanation for decreased cerebral blood flow in the large cerebral arteries during pregnancy is generalized vasodilation of the downstream resistance
vessels in the cerebral circulation in order to maintain a steady hemodynamic state. Burton and Burns have discussed the notion that around 40% of the resistance in the human circulation occurs at the level of distal arterioles. Because middle and posterior arterial blood flow significantly decreases near term, in spite of normally rising mean arterial pressure and unchanged vessel diameter in the large cerebral arteries, we assume that the downstream resistance arterioles become more dilated in order to maintain constant blood flow at the tissue level.

Belfort et al have corroborated this by showing that there is a progressive decrease in resistance index in the middle cerebral artery with advancing gestation as well as progressively decreased mean velocity. The reasons for these changes in cerebral blood flow in late pregnancy are unknown. Brackley et al describes decreased vessel wall tone using transcranial doppler of the middle cerebral arteries as pregnancy progresses. It is interesting to speculate that local autoregulatory changes in the cerebral circulation are due to altered vascular responsiveness or bioavailability of vasoactive mediators such as prostacyclin, nitric oxide and angiotensin II as well as a variety of other substances such as progesterone secondary to pregnancy.

The study provides physiological normative data of cerebral blood flow in two major regional arteries in both hemispheres during normal pregnancy. These data could be used to study abnormalities in cerebrovascular hemodynamics associated with preeclampsia and eclampsia. Using transcranial Doppler ultrasound, most investigators have reported that blood flow velocity increases as preeclampsia develops and worsens. Increased resistance at the arteriolar level is widely felt to be the etiology of the increased velocity in this setting, either secondary to loss of autoregulation and hyperperfusion, or vasospasm and hypoperfusion. This is important as we have recently reported that eclamptic convulsions, but not usually severe preeclampsia, are associated with hyperperfusion and this may imply loss of autoregulation. Our one patient who developed preeclampsia at 34 weeks did not demonstrate increased cerebral blood flow at 28 weeks, suggesting that such changes may occur later in pregnancy.

Using MR flow acquisition techniques, exquisite and accurate evaluation of the flow in large cerebral vessels is now possible in pregnancy. The potential of this technique to evaluate the underlying pathophysiology and to modify subsequent management of preeclampsia and eclampsia appears very promising.
REFERENCES


